

ABSTRACTS

71. Jahrestagung

Deutsche Gesellschaft für Neurochirurgie



21.-24. JUNI

2020

9. Joint Meeting mit der Japanischen Gesellschaft
für Neurochirurgie

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Grußwort/Greeting

Liebe Kolleginnen und Kollegen,

zur 71. Jahrestagung der Deutschen Gesellschaft für Neurochirurgie und dem 9. Joint Meeting mit der Japanischen Gesellschaft für Neurochirurgie vom 21. bis 24. Juni 2020 darf ich Sie im Namen des Vorstands der DGNC ganz herzlich einladen. Die letzte Tagung fand im Jahre 2000 durch meinen Vorgänger Prof. Hans Arnold in Lübeck statt und wir waren bereits weit in den Vorbereitungen fortgeschritten, Ihnen ebenfalls in Lübeck ein wissenschaftliches und Rahmenprogramm in gewohnter Weise zu präsentieren. Durch die COVID-19 Pandemie und den Erlass unserer Landesregierung am 19.04.2020 mit Versammlungsverbot, Einreise- und Beherbergungsverbot war dann aber klar, dass die Jahrestagung nicht im ursprünglich geplanten Format durchgeführt werden konnte. Nach intensiven Beratungen im Vorstand haben wir uns entschieden, den Versuch eines digitalen Kongresses gemeinsam mit unserer Kongressorganisation zu wagen. Ein Wagnis deshalb, weil zum damaligen Zeitpunkt noch keinerlei Erfahrung mit dem Abhalten einer solch großen Veranstaltung mit wissenschaftlichen und administrativen Sitzungen, Wahlen und Industrieausstellung vorlag und die DGNC somit eine Vorreiterrolle einnahm. Bis dahin und auch danach wurden die meisten Kongresse und Meetings in vergleichbarer Größe abgesagt oder in das Folgejahr verschoben.

Wir sind jedoch überzeugt, dass wir die technischen Herausforderungen bewältigen werden und Ihnen ein neues spannendes Veranstaltungsformat mit Live-Vorträgen, Diskussionen und „Chat-Räumen“ bieten können. Möglicherweise wird sich dieses Format auch nach der Krise bei vielen Veranstaltungen durchsetzen.

Unabdingbar für den Erfolg unserer Veranstaltung war die Bereitschaft unserer japanischen Kollegen uns auf unserem „digitalen Weg“ zu begleiten und auch die anderen nationalen und internationalen Referenten haben sofort zugesagt, sodass wir keinerlei Abstriche an unserem wissenschaftlichen Programm machen müssen. Auch unsere Partner der Industrie waren bereit, diese Veranstaltung in geänderter Form zu begleiten. Auch wenn wir Chirurgen das haptische Moment bei der Beurteilung von Mikroskopen und Instrumenten uvm. besonders lieben, werden wir versuchen, den Rundgang durch die Industrieausstellung virtuell so lebensecht wie möglich zu gestalten.

Letztlich wird dieser Kongress nur durch Ihre Bereitschaft zur Teilnahme gelingen. Für diese Bereitschaft, sich auf ein neues Kongresserleben einzulassen, danken wir Ihnen ganz herzlich!

Bewusst haben wir in diesem Jahr wieder konkrete Hauptthemen gewählt. Von neuroonkologischer Seite werden wir uns der interdisziplinären Behandlung spinaler und zerebraler Metastasen widmen. Dennoch wird die Therapie hirneigener Hirntumore einen breiten Raum einnehmen, wie uns Ihre angemeldeten Beiträge gezeigt haben. Mit Rücksicht auf die demographische Entwicklung unserer Bevölkerung und der Zunahme von Patienten jenseits der 80 mit degenerativen und traumatischen Wirbelsäulenerkrankungen in unseren Kliniken wollen wir die Indikationen zu operativen Maßnahmen kritisch prüfen, wohl wissend, dass immobilisierende konservative Therapien oftmals keine Alternative für diese Menschen bedeuten. Weitere Schwerpunkte sind die funktionelle Neurochirurgie – insbesondere die Schmerztherapie – sowie die Intensivmedizin. Zuletzt wollen wir uns mit den Chancen und Herausforderungen der Digitalen Medizin befassen, aber auch kritische ethische Aspekte dieser Entwicklung beleuchten.

Wir werden zum 8. Mal ein Joint Meeting mit der Japanischen Neurochirurgischen Fachgesellschaft feiern und das erste digitale Joint Meeting in der Geschichte der DGNC. Dieses Joint Meeting soll vor allen Dingen in den Plenarsitzungen zum Ausdruck kommen. Wir werden hier versuchen, den Referenten aus unterschiedlichen Zeitzeonen möglichst gerecht zu werden.

Begonnen wird die Jahrestagung mit dem Educational Day in Zusammenarbeit mit der Neurochirurgischen Akademie (NCA). Wir freuen uns, dass wir in diesem Jahr 2 Ehrungen, nämlich die Fedor-Krause- und die Otfrid Foerster-Medaille, vergeben dürfen. Die Laudationes und Vorträge werden digital gehalten. Die Überreichung der Medaillen im feierlichen Rahmen wird zu einem gesonderten Termin geschehen.

Wir wünschen Ihnen und uns für die Jahrestagung 2020 einen intensiven wissenschaftlichen, Erfahrungs- und Gedankenaustausch in einer freundschaftlichen und kollegialen Atmosphäre von Bildschirm zu Bildschirm.

Wir freuen uns auf Ihre digitale Teilnahme und bleiben Sie gesund!

Prof. Dr. med. Volker Tronnier
Präsident der Deutschen Gesellschaft für Neurochirurgie e.V. (DGNC)

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Conventus Congressmanagement & Marketing GmbH
Franka Kümmel
Carl-Pulfrich-Straße 1
07745 Jena, Germany
Phone +49 3641 31 16-334
Fax +49 3641 31 16-243
dgnc-kongress@conventus.de
www.conventus.de

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Gliome klinisch I/*Gliomas clinical I*

V001

Die Entmystifizierung eines Mythos – Vorteile der Resektion von Gliomen im *Corpus callosum* *Demystifying a myth – benefits of glioma resection in the corpus callosum*

M. T. Forster¹, M. Behrens², I. Lortz¹, C. Senft¹, M. Voss³, M. Rauch⁴, V. Seifert⁵

¹Johann Wolfgang Goethe-Universität Frankfurt am Main, Klinik für Neurochirurgie, Frankfurt am Main, Germany

²Johann Wolfgang Goethe-Universität Frankfurt am Main, Klinik für Neurologie, Frankfurt am Main, Germany

³Johann Wolfgang Goethe-Universität Frankfurt am Main, Dr. Senckenbergisches Institut für Neuroonkologie, Frankfurt am Main, Germany

⁴Johann Wolfgang Goethe-Universität Frankfurt am Main, Institut für Neuroradiologie, Frankfurt am Main, Germany

⁵Johann Wolfgang Goethe-Universität Frankfurt am Main, Klinik für Neurochirurgie, Frankfurt am Main, Germany

Objective

The impact of surgical resection on patients' overall survival has been demonstrated for all types of glioma. However, due to anticipated postoperative neuropsychological sequelae, patients with gliomas infiltrating the corpus callosum rarely undergo tumor resection and mostly present in a poor neurological state. Thus, we aimed at investigating the benefit of glioma resection in the corpus callosum, hypothesizing neuropsychological deficits were mainly caused by tumor presence.

Methods

Between 01/2017 and 10/2019, all patients who underwent both, glioma resection in the corpus callosum and preoperative neuropsychological testing were identified. Neuropsychological function was equally assessed postoperatively as well as after 6 months applying a vast battery of neurocognitive tests (attention, executive functions, language, working and visual memory, bimanual manipulation, object recognition and affects).

Results

A total of 20 patients (11 female; mean age 46.8 ± 15.3 years) could be identified. Neuropsychological testing after surgery and after 6 months was possible in 13 and 10 patients, respectively, considering 2 patients not having reached the 6 months" follow-up period to date. Interestingly, neurocognitive function declined in many domains after surgery, with significant deterioration of executive functions. After six months, only word fluency was reduced compared to preoperatively, whereas visuo-construction showed a trend to improve.

Gross total and subtotal tumor resection could be achieved in 14 and 5 patients, respectively, in one patient resection had to remain partial. Diagnosis was glioblastoma in 15 patients, anaplastic oligodendroglioma in 2 patients and anaplastic astrocytoma and diffuse astrocytoma in one patient each. Median overall survival was 15.1 ± 6.1 months, with 8 patients having died from glioblastoma during a median follow-up period of 17 months.

Conclusion

There is no long-term decline in neuropsychological function following tumor resection in the corpus callosum. In patients with gliomas infiltrating the corpus callosum the benefit of tumor resection clearly outweighs morbidity.

Gliome klinisch I/*Gliomas clinical I*

V002

Funktionelles Outcome nach prä- versus intraoperativer Sprach-Kartierung zur Resektion von Gliomen und Evaluation einer Klassifikation für Sprach-Eloquenz – eine vergleichende Kohorten-Studie

Functional outcome after pre- versus intraoperative language mapping for glioma resection and evaluation of a classification for language eloquence – a comparative cohort study

S. Ille, A. Schröder, L. Albers, A. Kelm, D. Droese, B. Meyer, S. Krieg

Technische Universität München, München, Germany

Objective

A considerable number of gliomas require resection via direct electrical stimulation (DES) during awake craniotomy. Likewise, the feasibility of resecting language-eloquent gliomas purely based on navigated repetitive transcranial magnetic stimulation (nrTMS) has been shown. This study analyzes the outcomes after preoperative nrTMS-based and intraoperative DES-based glioma resection in a substantially large cohort. Likewise, due to the necessity of making location comparable, a classification for language eloquence for gliomas is introduced.

Methods

Between 3/2015 and 5/2019, we prospectively enrolled 100 consecutive cases that were resected based on preoperative nrTMS language mapping (nrTMS group) and 47 cases via intraoperative DES mapping during awake craniotomy (awake group) following a standardized clinical workflow. Outcome measures were determined preoperatively, at 5 days after surgery, and at 3 months after surgery. To make functional eloquence comparable, we developed a classification based on prior publications and our own clinical experience. Groups and classification scores were then correlated with clinical outcomes.

Results

The functional outcome did not differ between groups. However, gross total resection was achieved in more cases of the nrTMS group (87%, vs. 72% in the awake group, $p = 0.04$). Nonetheless, the awake group showed significantly higher scores of eloquence than the nrTMS group (median 7 points; interquartile range 6-8 vs. 5 points; 3-6.75; $p < 0.0001$).

Conclusion

Resecting language-eloquent gliomas purely based on nrTMS data is feasible in a high percentage of cases if the described clinical workflow is followed. Moreover, the proposed classification for language eloquence makes language-eloquent tumors comparable, as shown by its correlation with functional and radiological outcomes.

Gliome klinisch I/*Gliomas clinical I*

V003

Patienten mit inoperablen, biopsierten Glioblastomen – Wer profitiert von einer adjuvanten Bestrahlung und/oder Chemotherapie?

Prognosis of patients with inoperable glioblastoma undergoing biopsy – Who benefits from adjuvant radiation and/or chemotherapy?

V. Malinova, K. Döring, D. Mielke, V. Rohde, H. C. Bock

Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Patients with inoperable glioblastoma (GBM) have usually a worse prognosis compared to those with a gross total tumor resection (GTR). Tumor biopsy (TB) is performed in these patients in order to establish the histological diagnosis and to plan the adjuvant treatment, consisting of radio-chemotherapy (R-CH). Considering the duration of treatment and possible side effects, the identification of patients who will probably benefit from the treatment is essential in order to facilitate the best achievable quality of life in these patients. The aim of this study was to evaluate clinical, molecular and imaging criteria associated with a better outcome after R-CH in patients with biopsied GBMs.

Methods

Consecutive patients with inoperable GBM, who underwent TB and R-CH (Stupp protocol) at our hospital from 2008 to 2018 were retrospectively included in the study. All patients had histologically confirmed GBM and subsequently underwent follow-up until death. The overall survival (OS) was calculated from the date of diagnosis to the date of death. Clinical, radiological and molecular predictors of OS and PFS were evaluated. The data were analyzed using the programming language and software distribution Python 3.7 (Python Software Foundation, Wilmington, Delaware). Survival analysis was done using Kaplan–Meier curve and significance determined by the log-rank test. Significant factors affecting survival were then processed in multivariate analysis using Cox's regression test. P-value <0.05 was considered significant.

Results

A total of 108 patients were enrolled in the study. The mean age was 65.0 years (range 31-88), 56.5% (61/108) were male and 43.5% (47/108) female. The mean postoperative Karnofsky status was 68.6% (range 30-100). The mean OS was 8.5 months (range 1-88). The following predictors of OS could be identified: age ($p=0.0007$), Ki67 ($p<0.0001$), positive Olig2 ($p=0.04$) and adjuvant treatment according to the Stupp protocol ($p<0.0001$). Imaging findings considering tumor localization were not a significant predictor.

Conclusion

The results of this study confirmed a survival benefit of R-CH in patients with inoperable GBM, whereas a younger age at diagnosis and a lower proliferation index were associated with a significantly longer OS. Also, Olig2 positive tumors were associated with longer OS under R-CH. A possible explanation might be a higher oligodendroglial involvement, which results in a less aggressive tumor behavior.

Gliome klinisch I/*Gliomas clinical I*

V004

Behandlung sehr alter Glioblastompatienten – wen man behandeln sollte

Treatment of very elderly glioblastoma patients – whom to treat

P. Baumgarten¹, G. Prange¹, D. Dubinski¹, M. T. Forster¹, P. N. Harter², M. Wagner³, J. Steinbach⁴, V. Seifert¹, C. Senft¹

¹Universitätsklinikum Frankfurt am Main, Klinik und Poliklinik für Neurochirurgie, Frankfurt am Main, Germany

²Johann Wolfgang Goethe-Universität Frankfurt am Main, Edinger Institut, Neuropathologie, Frankfurt am Main, Germany

³Universitätsklinikum Frankfurt am Main, Neuroradiologie, Frankfurt am Main, Germany

⁴Universitätsklinikum Frankfurt am Main, Neuroonkologie, Frankfurt am Main, Germany

Objective

The prognosis of patients ≥ 75 years of age suffering from glioblastoma is poor. Novel therapies are usually reserved for patients ≤ 65 years. In an aging population, the challenge remains how to treat very elderly patients ≥ 75 years.

Methods

Between 2010 and 2018, a total of 977 glioblastoma patients were treated at our institution. Of these, 144 patients were ≥ 75 years at diagnosis. Primary procedure was surgery or biopsy followed by adjuvant treatment, if possible. We retrospectively investigated progression free- (PFS) and overall survival (OS) and looked at potential prognostic factors influencing survival, including Karnofsky performance score (KPS), surgical therapy, adjuvant therapy as well as MGMT promotor methylation status.

Results

In very elderly patients, median age was 79 years (range: 75-110). Biopsy only was performed in 108 patients, resection was performed in 36 patients. Median OS for the entire cohort was 5.9 months. Survival of patients without adjuvant treatment was worse than for those receiving either radiotherapy and/or chemotherapy (1.2 vs. 8.4 months, $p < 0.001$). Multivariate analysis showed that KPS at presentation (≥ 70 vs. ≤ 60), surgery vs. biopsy, and MGMT status (methylated vs. non-methylated) were significantly associated with OS (6.3 vs. 3.9, $p = 0.002$; 12.6 vs. 4.9, $p = 0.003$; and 10.5 vs. 5.0 months, $p = 0.009$, respectively).

Conclusion

For glioblastoma patients ≥ 75 years of age, the natural course of the disease without treatment devastating.

Very elderly patients benefit from multimodal treatment including microsurgical tumor removal. Treatment options and outcomes should be thoughtfully discussed with patients before treatment decisions are made.

Gliome klinisch I/*Gliomas clinical I*

V005

Proliferation und Migration in Gliomen *Revisiting the go or grow hypothesis in glioma*

M. Ratliff¹, K. Kariman², E. Maier¹, T. M. Ratliff¹, E. Jung², N. Etminan¹, W. Wick², F. Winkler²

¹Universitätsklinikum Mannheim, Neurochirurgische Klinik, Mannheim, Germany

²Deutsches Konsortium für Translationale Krebsforschung (DKTK), Klinische Kooperationseinheit Neuroonkologie, Heidelberg, Germany

Objective

Glioblastomas continue to be a therapeutic challenge due to their aggressive growth, which is both rapid and diffusely infiltrative. It has been postulated in the past that tumor cells cannot invade ("go") and divide ("grow") at the same moment of time, disconnecting both pathological hallmarks of the disease.

Methods

To investigate the interrelation of glioblastoma cell invasion and proliferation patterns, we established a novel intravital microscopy methodology which allows to track invasion and proliferation in glioma microregions at the same time: by long-term following individual patient-derived glioblastoma cells expressing fluorescent markers which depict both the cytoplasm and the mitotic history of individual tumor cells in different disease stages and tumor regions.

Results

We found that, in contrast to the prevailing hypothesis, the most invasive tumor cells were also the most proliferative when followed over weeks. In established tumor regions, those glioblastoma cells that were particularly well connected to other tumor cells in the tumor microtube-connected tumor network were slow-cycling over weeks, supporting their potential stem-like identity.

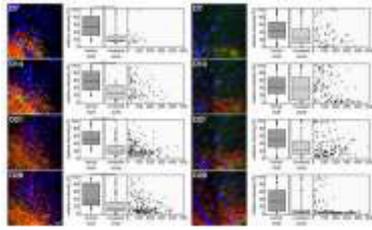
Figure 1:

In vivo MPLSM maximum intensity projections (MIPs) of S24 and P3XX GBMSCs growing in the mouse brain over 28 days progressively infiltrating into the normal brain; Over time they increasingly produce long intratumoral protrusions. GFP expression is quantified for each cell, its loss is a readout for cellular division (H2B-Gfp-Tet-off). GFP intensity inversely correlates with the distance a cell has migrated away from the tumor bulk. ($n=3$ mice per cell line, *in vivo* MPLSM. Error bars show s.d., scale bar 50 μm)

Conclusion

In summary, this data challenges the current "go-or-grow" hypothesis in glioma progression, and provides valuable insights into the interrelation of central traits of malignancy in glioma.

Fig 1



Gliome klinisch I / *Gliomas clinical I*

V006

Asymmetrische tumorbedingte Veränderungen in der netzwerkbasierten funktionellen Ruhekonnektivität bei Gliompatienten

Asymmetric tumour-related alterations in network-based resting-state functional connectivity in glioma patients

K. Jütten¹, V. Mainz², D. Delev¹, M. Wiesmann³, F. Binkofski⁴, H. R. Clusmann¹, C. H. Na¹

¹Universitätsklinikum RWTH Aachen , Klinik für Neurochirurgie, Aachen, Germany

²Universitätsklinikum RWTH Aachen , Institut für Medizinische Psychologie und Medizinische Soziologie, Aachen, Germany

³Universitätsklinikum RWTH Aachen , Klinik für Diagnostische und Interventionelle Neuroradiologie, Aachen, Germany

⁴Universitätsklinikum RWTH Aachen , Klinik für Neurologie, Aachen, Germany

Objective

Resting-state functional MRI (rs-fMRI) allows mapping temporally coherent brain networks and intra- and inter-network alterations have been described in different diseases. With regard to gliomas, findings are inconclusive: while both tumor-related increases and decreases in resting-state functional connectivity (RSFC) have been reported, recent studies suggest asymmetries in hemispheric vulnerability of networks. We investigated hemispheric RSFC differences in the Default-Mode and Fronto-Parietal Network (DMN, FPN) between left- and right-hemispheric (LH, RH) gliomas, addressing the role of asymmetry in the effect the tumor might have on network dynamics.

Methods

27 glioma patients (mean age: 49±17 years, 15 males, 16 LH gliomas, 26 right-handed) and 27 healthy controls (mean age: 46±13 years, 16 males, 26 right-handed) were preoperatively enrolled in the study and underwent anatomical and rs-fMRI as well as neuropsychological assessment. Independent Component Analyses and subsequent permutation tests were performed separately for controls and patients with LH and RH gliomas, respectively, to identify the DMN and FPN. Hemispheric DMN- and FPN-RSFC were computed, compared across groups and correlated with cognitive performance.

Results

Patient groups did not differ with regard to tumor grade or localization. RH gliomas showed higher DMN-RSFC than controls, both within the ipsi- and contra-tumoral hemisphere ($F=5.70$, $p=.010$; $F=15.60$, $p<.001$), and higher contra-tumoral DMN-RSFC than LH gliomas ($p=.001$). Differences between ipsi- and contra-tumoral DMN-RSFC varied between patient groups ($F=5.54$, $p=.027$), with higher contra- than ipsi-tumoral RSFC in RH gliomas and the opposite pattern being found in LH gliomas. With regard to the FPN, contra-tumoral RSFC was higher in both patient groups as compared to controls ($F=14.01$, $p<.001$). Overall, higher contra-tumoral DMN- and FPN-RSFC was associated with worse cognitive performance.

Conclusion

Hemispheric RSFC in glioma patients varied depending on tumor hemisphere and investigated network. While FPN-RSFC was increased in the contralesional hemisphere, DMN-RSFC was increased in the dominant left hemisphere, irrespective of tumor side, but with most prominent alterations being found for DMN-RSFC in RH gliomas. Increases in RSFC may vary in need and efficiency depending on the affected hemisphere. Larger samples are needed to better understand the effect of different tumor characteristics on network dynamics.

Bildgebung an der Wirbelsäule/*Spine imaging*

V007

Ein videobasiertes Exoskop als Alternative zum Operationsmikroskop in der spinalen Mikrochirurgie *A 3-dimensional exoscopic video-telescope as an alternative to the operating microscope in spinal microsurgery*

S. Siller, C. Zoellner, M. Fuetsch, R. Trabold, J. Tonn, S. Zausinger

Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik, München, Germany

Objective

Since the 1970s, the operating microscope (OM) is standard for visualization and illumination of the surgical field in spinal microsurgery. However, due to its limitations (e.g. size, high costs and limited movability of binocular lenses with uncomfortable surgeons' posture), there are efforts to replace the OM by exoscopic video-telescopes. We evaluated the feasibility of a new 3D exoscope (3D-E) as an alternative to the OM in spine surgeries.

Methods

Patients with single-level degenerative pathologies undergoing lumbar or cervical spinal surgery were enrolled from 01-09/2019 in a prospective cohort study for use of a 3D-E. Age-, sex-, and procedure-matched patients with use of the OM served as control group. Operative baseline and postop. outcome parameters were assessed. Periprocedural handling, visualization and illumination by the exoscope, as well as surgeons' comfort level of posture were scored via a questionnaire.

Results

40 patients undergoing lumbar posterior decompression (LPD) and 20 patients undergoing anterior cervical discectomy and fusion (ACDF) with a 3D exoscope were studied with an equal number of controls using OM. Compared to controls, there were no significant differences for mean operation time (LPD: 112 vs. 108min.; $p=0.58$ / ACDF: 131 vs. 119 min.; $p=0.26$) and blood loss ($p=0.95$). The same was true for postop. improvement of symptoms (neck disability index: $p=0.43$ / Oswestry disability index: $p=0.76$) and median length of hospital stay (LPD: 6 vs. 6 days; $p=0.60$ / ACDF: 5 vs. 6 days; $p=0.23$). There were no intraoperative complications during 3D exoscope procedures. According to the attending surgeon, the intraoperative handling of instruments was rated to be comparable to the OM, while comfort level of the intraoperative posture (esp. during "undercutting" procedures) was assessed to be superior. Esp. in case of ACDF procedures and long approaches, depth perception, image quality, and illumination were rated to be inferior compared to the OM. By contrast, for non-surgical staff participating in 3D exoscope procedures, the visualization of intraoperative process flow and surgical situs was rated to be superior compared to the OM, esp. for ACDF procedures.

Conclusion

A 3D exoscope seems to be a safe alternative for common spinal decompressive procedures with the unique advantage of excellent comfort for the surgical team, but the drawback of still slightly minor visualization/illumination quality compared to the OM.

Bildgebung an der Wirbelsäule/*Spine imaging*

V008

Intraoperative CT (iCT), cone-beam CT (CBCT) und robotische cone-beam CT (rCBCT) Bildgebung zur navigierten spinalen Instrumentierung

Intraoperative CT (iCT), cone-beam CT (CBCT) and robotic cone-beam CT (rCBCT) imaging for spinal navigation

P. Kendlbacher¹, L. Wolter¹, M. Czabanka¹, S. H. Bayerl¹, G. Bohner¹, J. Woitzik^{1,2}, P. Vajkoczy¹, N. Hecht¹

¹Charité – Universitätsmedizin Berlin, Berlin, Germany

²Carl von Ossietzky Universität Oldenburg, Oldenburg, Germany

Objective

Sophisticated intraoperative imaging technologies such as intraoperative CT (iCT), cone-beam CT (CBCT) or robotic CBCT (rCBCT) remain expensive and their benefits and limitations in combination with spinal navigation have not yet been characterized in a comparative fashion. Therefore, the purpose of this study was to assess workflow, handling, accuracy and image quality of iCT-, CBCT- and rCBCT-based spinal navigation.

Methods

Between 2014 and 2018, 2.536 pedicle screws were implanted in 445 patients with iCT- (1219), CBCT- (638) or rCBCT- (679) based spinal navigation and automatic patient/image co-registration. After attachment of the navigation tracking device to a spinous process or the iliac crest, an iCT / CBCT / rCBCT registration scan was performed to allow navigated, guide-wire assisted pedicle screw implantation. Screw positioning was assessed intraoperatively by a second iCT / CBCT / rCBCT scan and immediate repositioning was performed, if needed. Clinical, demographic and radiographic patient data was analysed by two independent observers.

Results

The indications for surgery were degenerative disease (64%), trauma (15%), tumour (11%), and infectious disease (10%). The median length of instrumentation was 3 (1-16) segments for iCT, 1 (1-16) for CBCT and 2 (1-10) for rCBCT (* $p < 0.0001$ for CBCT vs. iCT and rCBCT). All imaging modalities permitted direct intraoperative assessment of each implanted screw with image quality benefits of iCT in obese patients and in the cervico-thoracic region. Overall, screw accuracy was higher in iCT- (95.4%) and CBCT- (97.5%) than in rCBCT- (92.6%; * $p < 0.05$ vs. iCT and CBCT) based spinal navigation. Apart from image quality, the main benefit of iCT was the large gantry and scan area, which facilitated pelvic instrumentation and instrumentation > 5 segments. In contrast, the main benefit of CBCT and rCBCT was the independent usability by a qualified surgeon with a user interface in rCBCT technology that allows completely independent operation, which remains particularly useful when radiological assistance or specialized OR personnel is not readily available.

Conclusion

iCT, CBCT and rCBCT provide high pedicle screw accuracy and excellent image quality for reliable intraoperative screw assessment with the option of immediate revision, if needed. Overall, the individual preference remains determined by workflow, handling, patient characteristics and technical differences.

Bildgebung an der Wirbelsäule/*Spine imaging*

V009

Intraoperative CT-assistierte spinale Navigation bei dorsaler zervikaler Instrumentierung – ein Bericht über Genauigkeit im Vergleich zur konventionellen Instrumentierung in Bezug auf verschiedene Pathologien
Intraoperative CT-assisted spinal navigation in posterior cervical instrumentation – a report on accuracy compared to conventional instrumentation regarding different pathologies

U. Bertram¹, H. R. Clusmann¹, M. F. Geiger¹, A. Riabikin², C. A. Mueller¹, C. Blume¹

¹Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neurochirurgie, Aachen, Germany

²Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neuroradiologie, Aachen, Germany

Objective

While the use of intraoperative fluoroscopic, isocentric 3D C–arm imaging is still the most common clinical practice, a growing number of medical centers have introduced intraoperative CT (iCT) navigated posterior instrumentation as a new clinical standard. Due to the close proximity of vital anatomical structures, instrumentations of the cervical spine pose an especially delicate task. Navigated approaches might therefore prove to be beneficial regarding accurate screw placement. In this study we report on accuracy of conventional versus iCT-navigated posterior cervical spine instrumentation with focus on pedicle vs. lateral mass screws.

Methods

We analysed a consecutive series of cervical posterior instrumentation using iCT AIRO© as well as conventional instrumentation of the cervical spine. Patients with screw placement in C1/2, subaxial and combinations were included. The underlying pathologies were also taken into account. Each screw was individually assessed by an independent observer making use of a modified Gertzbein & Robbins classification.

Results

In total, 39 patients were treated using iCT (224 screws; 144 pedicle, 80 lat. mass screws), while 40 patients underwent conventional instrumentation (252 screws; 24 pedicle, 228 lat. mass screws). We achieved an initial accuracy of 94.2% (n=211 screws) with iCT- and 84,9% (n=214 screws) in the conventional (C) group (p=0.005). Additionally, significant differences were found regarding the accuracy of screw placement in cases of degenerative disorders (iCT vs. C; 93.7% vs. 82.8%; p=0.01). Other pathologies (trauma, pathological fractures, infectious) showed no significant differences in accuracy. Comparisons between accuracy of pedicle or lateral mass screw placement were found not significant (neither within, nor between iCT- and C-group).

Conclusion

The accuracy of iCT navigated instrumentation in the cervical spine was significantly higher than conventional screw-placement, reducing the risk of harming vital anatomical structures. Although no differences were found between lateral mass and pedicle screw accuracy, the overall tendency towards the use of pedicle screws with iCT navigation is evident, possibly increasing the mechanical properties of the implanted fixateur. AIRO © iCT appears to be especially strong in elective surgery cases of degenerative spinal disorders.

Bildgebung an der Wirbelsäule/*Spine imaging*

V010

Posteriore Fixation komplexer atlantoaxialer Frakturen mit Schrauben-, Schrauben-Stab- und Occiputplattensystemen mittels C-Bogen-Fluoroskopie in über 80-jährigen Patienten

Posterior fixation of complex atlantoaxial fractures with screws, screw/rod and occiput plate systems using C-arm fluoroscopy in octo- and nonagenarian patients

P. Oni, O. Müller, R. Schultheiß

Klinikum Dortmund, Neurochirurgie, Dortmund, Germany

Objective

Complex atlantoaxial fractures are associated with high mortality rates in elderly patients. Surgical management of these fractures in octo- and nonagenarian patients remains debatable. We report on our experience with posterior fusion of these cases.

Methods

The subjects were 19 females and 11 males who had undergone posterior fusion for atlantoaxial fractures using c-arm fluoroscopy between January 2008 and September 2019 in our clinic. The mean age at surgery was 85 ± 3.3 years (27 cases 80-89 yrs., 3 cases 90-91 yrs.) and mean follow-up was 11.4 months. All patients had pre- and postoperative CT scan. All 30 cases had C2 fractures consisting of 19 Type II and 8 Type III odontoid fractures, 2 C2 burst fracture and 1 C2 superior articular facet fracture with atlantoaxial rotatory subluxation. 10 (30%) cases had additional C1 fracture and in 24 (80%) cases C1/2 facet dislocation was present. Falls from a standing height accounted for 83% of injuries. The following parameters were assessed: fracture repositioning, bone union, length of hospital stay, complications, mortality rate and neurological status by Frankel scale

Results

Posterior C1/2 fusion was performed in 19 cases (15 C1/2 fusion by Harms, 2 C1/2 transarticular screws by Magerl and 2 C1/2 transarticular screw with C1 lateral mass screw). 7 cases were treated with occipitocervical fusion; 4 cases had extension of C1 fusion to subaxial spine. The mean operative time and hospital stays were 105 mins and 10.4 days (mean ICU Stay 1.7 days). There was no in hospital mortality. The 30-day and 3-month mortality were 0% and 10% respectively. Fracture reposition was obtained in all cases. But for the 3 patients lost during follow-up bone union was 100%. There were no adverse events such as spinal cord or vertebral artery injury, uncontrolled bleeding or cerebrospinal fluid leakage. There were 3 cases of severe delirium, 6 urinary tract- and 3 lung infections. No wound infection occurred. Postoperatively, Frankel scale was unchanged in 28 patients. There was a one point increase in 1 patient and a one point decrease in another.

Conclusion

Posterior fusion with screws, screw/rod and occiput plate systems using c-arm fluoroscopy are reliable and effective in surgical management of atlantoaxial fractures in octo- and nonagenarian patients

Fig 1



62 yrs. (a) pre- and (b,c) 3 months post-surgery

Fig 2



85 yrs. (a) Pre-surgery and (b,c) 1 yr post-surgery

Bildgebung an der Wirbelsäule/*Spine imaging*

V011

**Ist die altmodische röntgengestützte periradikuläre Infiltrationstherapie immer noch wettbewerbsfähig?
*Is old-school fluorescence-guided periradicular infiltration therapy of the lumbar spine still competitive?***

B. Sommer¹, M. Hazaymeh¹, C. Riedel², V. Rohde¹, I. Fiss¹

¹Universitätsmedizin Göttingen, Neurochirurgische Klinik, Göttingen, Germany

²Universitätsmedizin Göttingen, Abteilung für Neuroradiologie, Göttingen, Germany

Objective

Periradicular infiltration therapy (PRT) is a standard diagnostic and therapeutic procedure which has been used in an outpatient setting over decades. With grown availability of low-dose computed tomography (CT) imaging, PRTs have been predominantly performed by radiologists. The study aims to analyse intervention time, radiation exposure and efficiency of conventional PRT using fluoroscopy versus CT-guided injection.

Methods

Between July and November 2019, of 48 patients who underwent infiltration treatment, 15 patients (6 female, 9 male; age (median, 1 SD) 61.5±16.7 yrs) received CT-guided (Sensation 128, Siemens, Erlangen, Germany) as well as fluoroscopy-guided (Ziehm Vision RFD 3D, Ziehm Imaging, Nürnberg, Germany) PRT of lumbar and sacral nerve roots. Both interventions were performed using contrast agent (Solutrast) and local anesthetics. Pain reduction was recorded by changes in numerical rating scale (NRS). Duration of pain reduction, time of intervention, effective radiation dose and procedure-related complications were recorded.

Results

Preoperative diagnosis was radiculopathy due to neuroforaminal/recessal stenosis or disc herniation. Radicular numbness or paresthesia after injection of local anesthetic agent was seen in 12/15 patients in CT-PRT and 9/15 patients in fluoroscopy-guided PRT. Pain levels were reduced from NRS 8±1.6 to 4±2.7 lasting 18±22 days after CT-guided compared to 6.5±1.1 to 4.5±2.7 (p=0.031) lasting 26±20.9 days (n.s.) after fluoroscopy-guided treatment. Time of intervention was shorter using CT (5±2.3 min vs. 7±2.5 min, n.s.), however, fluoroscopy needed lower effective doses (2.82±0.55 mSv vs. 0.96±0.54 mSv, p<0.01). No complications occurred.

Conclusion

Even though treatment accuracy and pain reduction seems to be lower in fluoroscopy-guided PRT as compared to CT-guided injection, lower effective radiation dose as well as longer time span of pain relief and ubiquitous availability still justifies the use of this technique.

Bildgebung an der Wirbelsäule/*Spine imaging*

V012

Vorhersagemöglichkeit der Degeneration der humanen Halswirbelsäule mittels Metabolom Analyse mit 1H-NMR-Spektroskopie

Metabolomic profiling with 1H NMR spectroscopy to predict disc degeneration in the human cervical spine

K. Koch¹, M. Arrighi², R. Hartmann³, D. Willbold³, D. Hänggi², A. Petridis², S. Muhammad², E. Fritsche¹,
R. Bostelmann²

¹Leibniz-Institut für umweltmedizinische Forschung (IUF) , Leibniz Research Institute for Environmental Medicine, Düsseldorf, Germany

²Universitätsklinikum Düsseldorf, Neurochirurgische Klinik, Düsseldorf, Germany

³Forschungszentrum Jülich, Institute of Complex Systems (ICS), Jülich, Germany

Objective

Recently, imaging techniques providing metabolic representations of the tissue, such as magnetic resonance spectroscopy (MRS), are used to characterize disc degeneration. Only few studies focus on cervical intervertebral disc (IVD) degeneration. The purpose of this study is to identify promising biomarkers, detectable non-invasively by MRS in the patient, to provide novel *in vivo* imaging opportunities of discogenic pain in the human cervical spine.

Methods

Thirty biopsies of cervical pathological ID (Ranging-age: 20 -74 years) were dissected into annulus fibrosus (AF) and nucleus pulposus (NP). Water-soluble metabolites were extracted with the dual-phase method using methanol:chloroform:water (1:1:1). By 1H NMR spectroscopy the complete water-soluble metabolome was analysed on a HR 700 MHz spectrometer. Differences in metabolic composition of AP and NP were calculated and related to the degree of disc degeneration (I-V Miyazaki grading system, MGS). Significances were calculated with ANOVA analyses and Bonferroni's multiple comparison tests.

Results

We detected changes in a variety of well-studied metabolites including lactate (Lac), choline (Cho), creatine (Cre), chondroitin (Chond), glutamine (Gln), glutamate (Glu), Tyrosine (Tyr), Glycine (Gly), and Succinate (Suc). We observed significantly ($p < 0.0001$) increased concentrations of Chond and significantly ($p < 0.005$) decreased concentrations of Cre, Gln, and Cho in NP compared to AF tissue. Strikingly, the difference in relative Chond between NP and AF was highest in Grade 3 and significantly (p -value < 0.05) decreased with increasing MGS (4 and 5). Moreover, we calculated several metabolic ratios and compared to MGS. Furthermore, we could detect a linear trend between the MGS and the extent of the observed differences in metabolite ratios ($p < 0.05$).

Conclusion

By means of assessing metabolic biomarkers with non-invasive 1H MRS spectroscopy, early stages of IVD degeneration could be detected. Especially the identified metabolic ratios such as Lac/Cre, Chon/Cre, Glu/Cre, or Cho/Cre, have potential for prediction of severity of the disc degeneration.

TumortheraPIefelder/*Tumour Treating Fields*

V013

Einfluss der TTFields-Dosis auf das Tumorprogressionsmuster in der EF-14 Studie *Influence of TTFields dose on tumour progression pattern in the EF-14 trial*

M. Glas¹, Z. Bomzon², M. T. Ballo³

¹Universitätsklinikum Essen, Abteilung für Klinische Neuroonkologie, Abteilung für Neurologie, Essen, Germany

²Novocure GmbH, Haifa, Israel

³University of Tennessee Health Science Centre, West Cancer Center, Memphis, TN, United States

Objective

In the phase III EF-14 trial on newly diagnosed glioblastoma, adding Tumor Treating Fields (TTFields) to temozolomide chemotherapy resulted in significantly improved Progression Free Survival (PFS) and Overall Survival (OS). TTFields are applied through 2 pairs of transducer arrays and an individual array layout is generated based on previous imaging. As TTFields negatively affect cell division, it was hypothesized that the distribution of TTFields dose in the brain may correlate with patterns of failure in patients.

Methods

MRI scans of 249 EF-14 treatment arm patients were used to calculate the TTFields dose and evaluate disease progression. Virtual transducer arrays were placed on realistic computational head models for each patient and the intensity distribution of TTFields was calculated by means of a Finite Element Method. The TTFields dose (in mW/cm^3) was calculated by multiplying the TTFields intensity squared, tissue conductivity and average patient compliance during the initial 6 months of TTFields treatment. Regions of interest for the analysis were any residual gross tumor and an expansion margin of up to 20 mm around the residual tumor and resection cavity. For the analysis at baseline, the TTFields dose was calculated for areas containing normal brain or areas with residual tumor. Calculated doses were then correlated to subsequent recurrence.

Results

The analysis revealed that the average TTFields dose was significantly higher in regions of enhancing tumor that regressed to normal compared to normal brain that showed progression to enhancing tumor (N=194, $0.83 mW/cm^3$ vs $0.71 mW/cm^3$, $p < 0.001$). Even with different expansion margins used for calculation, the results showed that TTFields doses were lower in normal brain regions that progressed to enhancing tumor (normal to tumor) compared to normal brain that remained normal (normal to normal) at the time of progression.

Conclusion

Our analysis demonstrated that a higher TTFields dose correlated with local response, confirming the effectiveness of TTFields. Therefore, it will be crucial to further improve the patient-individual planning of the TTFields dose and optimize transducer array placement. Efforts to achieve this, similar to radiotherapy planning, are ongoing. In summary, our results underline the relevance of TTFields dose at the tumor bed as well as the clinical activity of TTFields in GBM.

TumortheraPIefelder/*Tumour Treating Fields*

V014

Untersuchung der *in vitro* TTFIELDS-Response und assoziiertes Genexpression in 45 humanen Zelllinien ***Investigation of *in vitro* response to TTFIELDS and related gene expression in 45 human cell lines***

A. Kinzel¹, G. Lavy-Shahaf², M. Giladi², R. Schneiderman², K. Gotlib², E. Zeevi², Y. Porat², M. Munster², U. Weinberg², E. Kirson², Y. Palti²

¹Novocure GmbH, Root D4, Switzerland

²Novocure GmbH, Haifa, Israel

Objective

Previous investigations showed Tumour Treating Fields (TTFIELDS) to have an inhibitory effect of variable extent in different cancer cell lines. In order to predict TTFIELDS response better in the future, we conducted various analyses of specific properties of cancer cell lines and their individual response pattern.

Methods

After determining their specific optimal frequency, 45 cancer cell lines of diverse human cancer types were treated for 72 h with TTFIELDS with equal nominal intensity of 1.7 V/cm. Cytotoxicity and clonogenic potential was assessed, respectively, and further analysis was conducted with the help of Cancer Cell Line Encyclopedia (CCLE) database. This included functional exploration of mutated or differentially expressed genes related to TTFIELDS response, and contrasting assessment of TTFIELDS sensitivity based on pharmacological profiling (CCLE).

Results

Cytotoxicity and clonogenicity presented very variably between cell lines with up to 86 % reduction in cell count and up to 88 % reduction in colony number, respectively, both with an average of around 50 %. Mutation and gene expression analyses showed pathways relevant in oxidative stress, migration, hypoxia, and DNA damage repair response to be differentially upregulated. We further found cells with a greater TTFIELDS response to be more sensitive to lapatinib, PHA-665752, and PLX-4720.

Conclusion

Our large-scale investigation of TTFIELDS response in various cancer cell lines demonstrated this therapy's broad effectiveness and established every cell line's optimal treatment frequency. We found first evidence for synergistic effects of TTFIELDS with therapeutic agents that need further investigation in pharmacological profiling studies, in addition to the discovered response-related mutations.

TumortheraPIefelder/*Tumour Treating Fields*

V015

Öffnung der Blut-Hirn-Schranke durch TTFIELDS – eine potentielle Methode zum Drug-delivery in das ZNS *TTFIELDS disruption of the blood brain barrier – a potential CNS drug delivery approach*

E. Salvador¹, A. F. Keßler¹, J. Hörmann¹, M. Burek², C. T. Brami³, T. V. Sela³, M. Giladi³, R. I. Ernestus¹, M. Löhr¹, C. Förster², C. Hagemann¹

¹Universitätsklinikum Würzburg, Neurochirurgische Klinik und Poliklinik, Tumorbiologisches Labor, Würzburg, Germany

²Universitätsklinikum Würzburg, Klinik und Poliklinik für Anästhesiologie, Würzburg, Germany

³Novocure GmbH, Haifa, Israel

Objective

Despite the availability of potent drugs, modern medicine is still faced with the problem of effectively delivering them into the central nervous system (CNS) due to the tight regulation of the blood brain barrier (BBB). Of late, tumour treating fields (TTFIELDS) have emerged as an effective treatment modality for glioblastoma. Moreover, TTFIELDS combined with chemotherapy significantly improve overall survival in patients. The influence of TTFIELDS on the BBB, however, has so far not yet been investigated. Our recent findings demonstrate that TTFIELDS administration has the potential to open up the BBB in vitro with an optimal frequency of 100 kHz. Consequently, in this study, we aimed to validate our data in vivo.

Methods

Rats were subjected to 100 kHz TTFIELDS or heat treatment for 72 h and subsequently i.v. injected with Evan's Blue (EB). Afterwards, rats were sacrificed, EB was extracted from the brain and quantified. Likewise, in separate experiments, rats were injected with TRITC-dextran (TD), and brain slices were photographed to localise the staining. In addition, cryosections of rat brains were prepared after TTFIELDS administration. Sections were stained for intercellular junction proteins claudin-5, occludin and PECAM-1 as well as immunoglobulin G (IgG) to assess vessel structure. Finally, serial dynamic contrast-enhanced (DCE) MRI with gadolinium (Gd) contrast agent was performed pre- and post TTFIELDS application.

Results

Accumulation of both EB and TD in the brain increased with TTFIELDS administration. Also, brain cryosections demonstrated delocalisation of claudin-5 and occludin but not PECAM-1 and build-up of IgG in the brain parenchyma. Validating these observations, DCE-MRI displayed significantly increased Gd in the brain post TTFIELDS application. These effects, however, reverted back to normal 96 h after end of treatment as no difference in contrast enhancement between controls and TTFIELDS-treated rats was found.

Conclusion

TTFIELDS of 100 kHz alter BBB integrity and permeability leading to opening of the latter. This suggests the possibility of using TTFIELDS for drug delivery to the CNS. Moreover, subsequent BBB recovery post-treatment demonstrate transient effects, thus potentiating a novel clinical approach of using TTFIELDS to open the BBB for enhanced and more effective drug delivery strategy targeting CNS disorders.

TumortheraPIefelder/*Tumour Treating Fields*

V016

TTFields in WHO Grad III Gliomen – Post-Marketing Surveillance-Analyse spricht für gute Verträglichkeit *TTFields in WHO grade III glioma – post-marketing surveillance analysis suggests favourable tolerance*

A. F. Keßler¹, R. Ritz²

¹Universitätsklinikum Würzburg, Abteilung für Neurochirurgie, Würzburg, Germany

²Schwarzwald-Baar Klinikum, Klinik für Neurochirurgie, Villingen-Schwenningen, Germany

Objective

Even with meaningful advancements in the molecular classification as well as growing data for specific therapy regimens, grade III glioma treatment is yet indistinct. Usually, this entity is treated similar to grade IV glioma: with resection and radio/chemotherapy. Tumour treating fields (TTFields) therapy is approved to treat newly diagnosed and recurrent glioblastoma and is also used by some physicians to treat patients with a grade III glioma. Further evaluation of the use of TTFields in grade III glioma is currently the subject of different clinical trials. This present study analysed safety data from post-marketing surveillance of TTFields treated grade III glioma patients in Germany to assess tolerance.

Methods

Available post-marketing surveillance data of patients treated with TTFields were revised. Reported adverse events (AEs) of grade III glioma patients (anaplastic astrocytoma and anaplastic oligodendroglioma) were investigated according to the MedDRA body system with system organ classes (SOCs) and preferred terms. Data cut-off was November 15, 2019.

Results

At data cut-off, a total number of 120 patients (32 % female, 68 % male) with grade III glioma were treated in Germany and were therefore included in the present analysis. Of those, 66 % reported one or more AEs. The most common reported AE was skin reactions with an incidence of 34 %. AEs related to the nervous system were reported by 30 %, comprising headache in 8 % and seizure in 12 %. 28 % of the patients reported general disorders, most of them (14 %) general physical health deterioration.

Conclusion

Our analysis of data on TTFields treated patients with grade III glioma from post-marketing surveillance in Germany revealed no serious adverse events related to TTFields and thus no reportable events in this subgroup. The incidence of skin reaction, the most common AE related to TTFields reported in the phase III trials for newly diagnosed (EF-14) and recurrent glioblastoma (EF-11) were seen similarly in this surveillance analysis of grade III glioma patients. Currently active clinical trials in this patient subgroup will contribute further to our understanding of safety and efficacy of TTFields therapy in grade III glioma.

Tumortherapiefelder/*Tumour Treating Fields*

V017

Aurora Kinase Inhibition und Bestrahlung verstärken den Effekt von Tumor-Therapiefeldern in der Therapie von Glioblastom-Rezidiven

Aurora kinase inhibition and radiation therapy enhance the efficacy of tumour treating fields in recurrent glioblastoma treatment

T. Thalmaier, D. Lachmann, S. Roos, P. Bartmann, W. Jugel, A. Hagstotz, A. Temme, S. Michen, [D. Krex](#)

Universitätsklinikum Carl Gustav Carus Dresden, Klinik für Neurochirurgie, Dresden, Germany

Objective

Tumor Treating Fields (TTFields) have been shown to be effective in prolonging progression-free and overall survival, thereby increasing the rate of two- and five-year survivors of patients with primary glioblastoma. However, the two-year survival rate is still below 50 %, and the TTFields effect in recurrent glioblastoma seems to be weaker than in primary therapy. A promising approach to enhance the efficiency of TTFields is the combination with drugs, which extend metaphase-anaphase transition and telophase.

Methods

In the present study we tested the efficacy of the combined treatment of TTFields (1.6 V/cm RMS, 200 kHz) and the Aurora A kinase inhibitor MLN8237 as well as the Aurora B kinase inhibitor AZD 1152 in the established glioma cell line U87-MG and three primary recurrent glioblastoma cell lines. In addition, we tested the additional effect of radiation of the cells before treatment with TTFields and MLN8237 and AZD 1152, respectively.

Results

We found that the combination of TTFields, MLN8237 and AZD 1152, respectively, (75 nmol/l each) and radiation (4 Gy – 8 Gy; 0,5 Gy/min) led to a significant reduction in the number of cells as compared to each treatment alone (Mann-Whitney-U-test, $p < 0.01$). Furthermore, we showed an increased DNA content in PI stained glioblastoma cells suggesting polyploidy and disturbed cell replication. Both light microscope and confocal laser scanning microscope imaging showed morphological changes such as multinuclear cells, increased cell size as well as cytoskeletal modifications due to the combination treatment with TTFields, MLN8237 or AZD 1152 and radiation compared to each treatment alone.

Conclusion

The results presented here demonstrate that the combination of TTFields and Aurora kinase inhibition can be an effective treatment for recurrent glioblastoma. The cytotoxic effect can be augmented by radiation pretreatment. These results resemble those, which we found in primary glioblastoma cell lines indicating that the combination therapy of TTFields and Aurora kinase inhibition is effective in first-line treatment as well as for recurrent glioblastoma.

TumortheraPIefelder/*Tumour Treating Fields*

V018

Analyse einer Plattform zum Erfahrungsaustausch von Patienten mit TTFIELDS-Therapie zur Verbesserung der Lebensqualität von Patienten mit hochgradigen Gliom

Analysis of a platform for exchange of patients' expertise in TTFIELDS practice to improve quality-of-life in high-grade glioma patients

A. F. Keßler¹, J. Weiland¹, V. Dufner¹, N. Lilla¹, T. Linsenmann¹, T. Westermaier¹, C. Hagemann¹, R. I. Ernestus¹, M. Löhr¹, E. Jentschke²

¹Universitätsklinikum Würzburg, Abteilung für Neurochirurgie, Würzburg, Germany

²Universitätsklinikum Würzburg, Abteilung für Neurochirurgie und Umfassendes Krebszentrum, Würzburg, Germany

Objective

Glioblastoma (GBM) Patients and their Relatives (PaR) face tremendous distress and psychological burdens due to limited survival and neurological/neuropsychological deficits. Tumor Treating Fields (TTFIELDS, alternating electric fields at 200 kHz) are a recently established therapy for treatment of newly diagnosed and recurrent GBM. TTFIELDS allows PaR to actively contribute to therapy, but does require concerted attention. Our clinical experience shows an urgent need for personal exchange in communicating with GBM patients. Establishing patient-driven support groups is limited by the rapid clinical progression of GBM. Here, the needs of PaR to implement a platform for personal interaction with focus on TTFIELDS treatment were systematically evaluated and the benefits experienced by PaR were analyzed.

Methods

For this analysis 26 PaR were assessed, including 11 females. Questionnaires to evaluate PaR's needs regarding meeting other PaR included: preferences for time, frequency, and maximal travel distance, type and frequency of the desired professional support. Quality-of-life and emotional function were determined two weeks before and after implementing this program by the questionnaires PHQ-2 (level of depression) and GAD-2 (level of anxiety). Additionally, perception of everyday life restriction and social exposure were analyzed by a 5-digit-scale.

Results

95% of the assessed PaR expressed general interest in meeting other patients, relatives, their physician and psychologist, respectively. Therefore, a meeting outside of the hospital was established, accompanied and supported by the treating physician and psychologist. Interestingly, anxiety and depression scores were relatively low at baseline. Additionally, PaR showed a tendency towards even lower scores two weeks after the meeting. Above that, perception regarding social exposure (patients: 2.5 vs 1.7; relatives: 2.3 vs 1.9; scale 1-5) and everyday life (patients: 2.5 vs 2.3; relatives: 2.9 vs 2.3; scale 1-5) was further improved.

Conclusion

This analysis strongly suggests that a communication platform for GBM patients reduces anxiety and depression of PaR and improves the perception of social exposure and everyday life by meeting the assessed PaR's needs. Data from an additional meeting will be included in the analysis and presented at the annual meeting of the DGNC.

Highlights DGNC 2019–2020

Sektion Wirbelsäule

BO-01

Spinale Hämangioblastome – Erfahrungen mit der minimalinvasiven Resektion bei 20 Patienten *Spinal haemangioblastoma – experience with minimally invasive resection in 20 patients*

J.-H. Klingler¹, C. Steiert¹, S. Gläsker², M. T. Krüger¹

¹Universitätsklinikum Freiburg, Klinik für Neurochirurgie, Freiburg, Germany

²Universitair Ziekenhuis Brussel, Brüssel, Belgium

Objective

Hämangioblastome sind gutartige, stark vaskularisierte Tumoren, die sporadisch oder im Rahmen der von Hippel-Lindau (VHL) Krankheit auftreten können. Traditionell werden spinale Hämangioblastome über einen offenen Zugang chirurgisch entfernt. In den letzten Jahren werden jedoch zunehmend minimal-invasive Techniken mit tubulären Retraktoren in der Wirbelsäulenchirurgie verwendet. Dies führt zu einem geringeren Gewebetrauma, stellt aber auch besondere Anforderungen an den Chirurgen dar, insbesondere bei stark vaskularisierten Tumoren wie Hämangioblastomen. Diese Studie untersucht die Sicherheit und Wirksamkeit der minimal-invasiven Resektion ausgewählter spinaler Hämangioblastome.

Methods

In dieser monozentrischen, retrospektiven Studie wurden von 2010 bis 2018 20 Patienten an insgesamt 21 spinalen Hämangioblastomen über einen minimal-invasiven tubulären Zugang operiert. Das primäre Outcome der Untersuchung war der neurologische Zustand anhand des modifizierten McCormick-Scores postoperativ versus präoperativ. Sekundäres Outcome waren das Ausmaß der Tumorsektion im postoperativen MRT sowie postoperative Komplikationen.

Results

Neunzehn Patienten wiesen postoperativ einen stabilen oder verbesserten McCormick-Score (95%) auf (follow-up: $4,3 \pm 2,6$ Monate). Einer der 20 Patienten (5%) zeigte im Langzeit-Follow-up zunehmende neurologische Symptome mit einem verschlechterten McCormick-Score. Siebzehn von 20 Patienten wiesen Hämangioblastome im Rahmen der VHL Erkrankung auf, drei Patienten hatten sporadische spinale Hämangioblastome. Das postoperative MRT zeigte in allen Fällen eine vollständige Resektion der Hämangioblastome. Perioperative oder postoperative Komplikationen traten nicht auf.

Diskussion

Die minimal-invasive Resektion ausgewählter spinaler Hämangioblastome ist eine sichere Methode, die eine vollständige Tumorsektion mit guten klinischen Ergebnissen ermöglicht.

Highlights DGNC 2019–2020

Sektion Neuroonkologie

BO-02

Die Dicke des Temporal Muskels als Outcome-Prädiktor bei Patienten mit primärem Glioblastom *Temporal muscle thickness as outcome predictor for patients with primary glioblastoma*

J. Steinmann¹, F. Staub-Bartelt¹, B. Turowski², H.-J. Steiger¹, D. Hänggi¹, M. Rapp¹, M. Sabel¹, M. Kamp¹

¹Heinrich-Heine Universität, Klinik für Neurochirurgie, Düsseldorf, Germany

²Heinrich-Heine Universität, Klinik für Radiologie, Düsseldorf, Germany

Background:

Patients with glioblastoma still have a very limited overall survival and reliable predictors for outcome are rare. Low skeletal muscle mass (sarcopenia) is known to be a poor prognostic factor for cancer patients. It is measured by CT lumbar skeletal muscle cross-sectional area (CSA). Recently a high correlation between CSA of lumbar skeletal muscle and temporal muscle thickness (TMT) was found. The aim of this study was to analyze a potential relation between temporal muscle thickness and outcome for patients with primary glioblastoma.

Methods:

A retrospective analysis was performed for patients with primary glioblastoma and complete surgical resection assessed by an early postoperative MRI < 72h. Temporal muscle thickness was measured in preoperative 1.5 T-MRI scan in axial T1 sequences on both sides. Mean TMT was calculated and linear regression was performed.

Results:

Analysis of the relation between TMT and outcome parameters under consideration of known predictors was performed in 49 patients with a mean age of 59 years (range 30 -83y). 16/49 (32%) patients were female and 33/49 (68%) male. Mean preoperative KPS was 90%. 21/47 (44%) patients had methylated MGMT promoter. Mean PFS was 13.1 months and mean OAS was 17 months. Mean TMT was 6.5mm (range 3.4 – 10.5mm). Linear regression showed, that TMT is an independent significant predictor of PFS ($p < 0.01$) and OAS ($p < 0.01$). An increase in every millimeter of TMT has an average survival benefit of 2.6 months.

Conclusion:

In the present cohort temporal muscle thickness (TMT) as a surrogate for the nutritional state of patients with primary glioblastoma is a significant predictor of outcome.

Highlights DGNC 2019–2020

Sektion Intrakranieller Druck, Hirndurchblutung und Hydrozephalus

BO-03

Perihaematomal thrombin expression is initiated in the early phase after intracerebral haemorrhage and correlates with worse neurological outcome in patients with ICH

H. Krenzlin¹, B. Alessandri², J. Masomi-Bromwasser¹, C. Frenz¹, T. Kerz¹, O. Kemspki², F. Ringel¹, N. Keric¹

¹Neurochirurgische Klinik und Poliklinik, Universitätsmedizin Mainz

²Institut für Neurochirurgische Pathophysiologie, Universitätsmedizin Mainz Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Spontaneous intracerebral hemorrhage (ICH) is a leading cause of disability and mortality. Thrombin induces brain edema and neuronal death. However, whether the perihematoma thrombin is generated by a local cerebral thrombin system or washed in from circulation, is still unknown. In our study, we utilize a unique mouse model (1) as well as cerebrospinal fluid (CSF) samples of patients with ICH (2).

Methods

(1) Prothrombin expression was analyzed using quantitative RT-PCR 4h and 24h after ICH in our mouse model. Further, perihematoma thrombin concentration 24h after ictus was measured using immunohistology. The neurological outcome was assessed using the Rotarod performance test. (2) Blood and CSF samples were obtained from 12 patients with ICH (7 male, 5 females; mean age 65±2 years) and 2 controls (both male) on days 1 and 3. Factor IIa was analyzed using enzyme-linked immunosorbent assay. Clot volumes were determined based on computed tomography and neurological outcome was determined 6 weeks after ICH onset using the modified Rankin Scale.

Results

(1) Animals receiving blood injections showed a 4.24±0.5 (P < 0.05) fold increase in thrombin concentrations 24h after ICH. Prothrombin transcription was increased 4h after ICH and decreased over the course of 24h (4.7±1.6 fold; P < 0.05). Elevated thrombin concentrations correlate with detrimental neurological outcome (sham: 72±8.85sec, blood: 3.5±.95). (2) CSF thrombin concentrations are likewise elevated after ICH (P < 0.05) compared to controls. The thrombin concentration does not correlate with the initial clot size (r² = 0.21, p = 0.15) or the presence of intraventricular hemorrhage. However, increasing thrombin concentration in CSF correlates with a detrimental neurological outcome 6 weeks after onset of ICH (r² = 0.5, p < .05).

Conclusion

Our study strengthens the importance of thrombin as contributor to secondary injury after ICH and as potential target for future pharmacotherapy.

Highlights DGNC 2019–2020

Sektion Schmerz

BO-04

Mikrovaskuläre Dekompression nach Jannetta bei Patienten über 70 Jahre – Effektivität und Sicherheit

T. Greve, J. C. Tonn, J.-H. Mehrkens

Klinik und Poliklinik für Neurochirurgie, Klinikum der Universität München – Campus Großhadern, München

Objective

Patienten mit Trigeminusneuralgie (TN) stehen abhängig von der zugrunde liegenden Pathophysiologie verschiedene Behandlungsoptionen zur Verfügung. Die mikrovaskuläre Dekompression nach Jannetta (MVD) ist eine effektive chirurgische Behandlungsmethode bei idiopathischer TN. Aufgrund allgemein erhöhter perioperativer Morbidität und Mortalität von Patienten im Senium werden hier oft andere Therapiekonzepte angeboten. Die Effektivität und Sicherheit der MVD bei Patienten über 70 Jahre verdient jedoch angesichts der steigenden Lebenserwartung und der sinkenden Altersmorbidity einer genaueren Untersuchung.

Methods

Zwischen 01/2012 und 06/2018 wurden 310 Patienten mit TN behandelt (463 Prozeduren). Hiervon wurden 105 Patienten eingeschlossen, die an idiopathischer TN litten, mittels MVD behandelt wurden und mindestens 18 Monate Follow-Up aufwiesen. 78 Patienten (74.3%) waren jünger als 70 Jahre (37w, 55,6 ± 11,1 Jahre, P70minus) und 27 (25.7%) waren 70 Jahre oder älter (14w, 74,0 ± 2,2 Jahre, P70plus). Das mediane Follow-Up lag bei 42,5 Monaten [18,6 – 93,1 Monate].

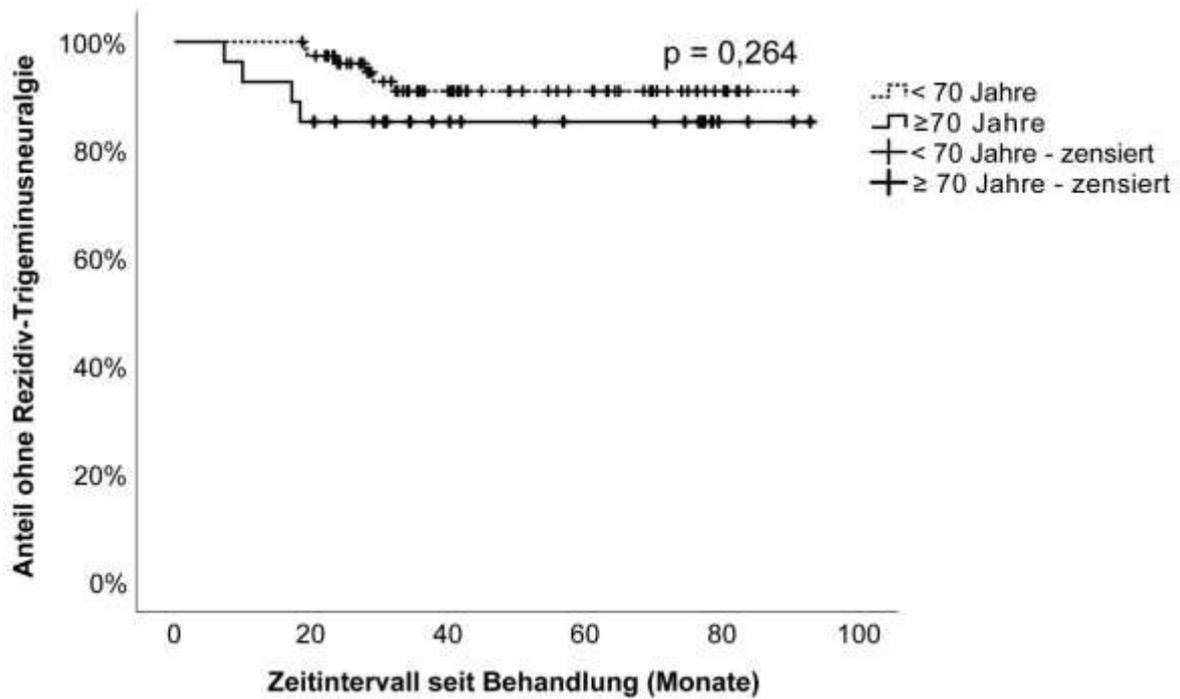
Results

In der Follow-Up Periode kam es bei P70minus zu 6 (7,7%) Rezidiven und bei P70plus zu 4 (14,8%) Rezidiven der TN ($p = 0,276$). Bei P70minus waren nach 1 Jahr 100% schmerzfrei, nach 2 Jahren 96% schmerzfrei und nach 3 Jahren 91% schmerzfrei. Bei P70plus waren nach 1 Jahr 93% schmerzfrei und nach 2 sowie 3 Jahren 85% schmerzfrei. Eine Kaplan-Meier-Analyse zeigte keinen signifikanten Unterschied im schmerzfreien Intervall (P70minus 84,4 vs. P70plus 80,9 Monate, $p = 0,264$, Abb. 1). Die Krankenhausverweildauer wies keinen signifikanten Unterschied auf (P70minus 8,9 ± 2,5 Tage vs. P70plus 9,8 ± 2,0 Tage, $p = 0,070$). Bei P70minus traten als Komplikation 1 (1,3%) Status epilepticus, 2 (2,6%) leichte Hörminderungen sowie 5 (6,4%) passagere Hypästhesien des N. trigeminus auf. Bei P70plus traten 1 (3,7%) passagere Trochlearisparese, 2 (7,4%) passagere Stimmlippenparesen, 2 (7,4%) passagere Hypästhesien des N. trigeminus, 1 (3,7%) Sinusvenenthrombose und 1 (3,7%) passagere leichtgradige Fazialisparese als Folge einer strategisch lokalisierten pontinen Ischämie auf. Schwere internistische Komplikationen und periprozedurale Todesfälle traten in keiner Gruppe auf. Die Gesamtkomplikationsrate ist somit in der P70plus Gruppe gering erhöht ($p = 0,017$). Im Gegensatz hierzu ist die Rate permanenter neurologischer Defizite in beiden Gruppen null.

Conclusion

Die MVD ist laut der hier präsentierten Daten bei Patienten über 70 Jahre eine effiziente und sichere Behandlungsoption. Limitationen sind die geringere Anzahl an über 70-Jährigen Patienten in dieser Studie sowie der aufgrund von Vorerkrankungen resultierende Selektions-Bias bei über 70-Jährigen.

Abbildung 1 Kaplan-Meier Analyse des schmerzfreien Intervalls nach MVD.



Highlights DGNC 2019–2020

Sektion Vaskuläre Neurochirurgie

BO-05

Kollagen-Abbauprodukte als serologische Marker für strukturelle Instabilität von intrakraniellen Aneurysmen *Collagen breakdown products as biomarkers for structural instability in intracranial aneurysms*

K. Hackenberg¹; P. Richter¹; J. Böhme²; A. Abdulazim¹, M. Neumaier³; E. Neumaier-Probst², M. Alzghoul², C. Groden², N. Etminan¹

¹Neurochirurgische Klinik, Universitätsmedizin Mannheim, Universität Heidelberg, Theodor-Kutzer-Ufer 1-3, Mannheim

²Neuroradiologie, Universitätsklinikum Mannheim, Universität Heidelberg, Theodor-Kutzer-Ufer 1-3, Mannheim

³Institut für Klinische Chemie, Universitätsklinikum Mannheim, Universität Heidelberg, Theodor-Kutzer-Ufer 1-3, Mannheim

The estimation of the individual rupture risk of intracranial aneurysms (IA) remains challenging. Structural integrity of IA is predominantly determined by collagen type I, the main molecular constituent in IA. A hallmark of IA pathogenesis is ongoing collagen remodelling in the IA wall and synthesis of immature/structural deficient collagen. To date, in vivo biomarkers for molecular instability in IA are lacking. We endeavoured to detect breakdown products of collagen derived from human IA in serum as potential surrogates for IA instability.

Two blood samples from intra-aneurysmal (intra-IA) and the femoral artery were obtained during catheter angiography from patients undergoing endovascular repair of their IA. Additionally, venous blood samples were obtained from IA patients as well as control subjects (no known presence of IA). Detection of collagen breakdown products cross-linked C-telopeptide of collagen type I (CTx) was performed by serum immunoassay. Recently grown or ruptured IA were defined as unstable. Correlation, logistic regression and receiver operating characteristic (ROC) analyses were performed.

Between 10/2018 and 11/2019 27 IA patients (15 female, 12 male) with 57.3±12.2 years were included. There were 8 unruptured, 19 ruptured and 5 stable, 22 unstable IA. 18 control subjects (7 female, 11 male) with 45.4±16.6 years were included. Intra-IA CTx levels were higher in ruptured compared to unruptured IA (0.63±0.28ng/ml vs. 0.35±0.24ng/ml, p=0.02) and higher in unstable compared to stable IA (0.62±0.28ng/ml vs. 0.27±0.10ng/ml, p=0.01). Intra-IA CTx levels predicted IA rupture in univariate analysis (likelihood ratio (LR) 6.6, p=0.01; OR 275.4, 95% CI 1.1-72395.9) and after including age, smoking, hypertension in multivariate analysis (LR 5.6, p=0.02; OR 223.0, 95% CI 0.8-63843.5). ROC analysis demonstrated a good test accuracy (AUC 0.72, 95% CI 0.45-0.98) for intra-IA CTx levels with a threshold ≥ 0.464 ng/ml for IA rupture. Venous CTx levels were higher in IA patients compared to controls (0.33±0.18ng/ml vs. 0.20±0.08ng/ml, p=0.004). There was a strong correlation between intra-IA and venous CTx levels (r=0.53, p=0.004).

Our pilot study indicates that arterial and even venous CTx levels could serve as a novel indicator for increased instability in patients for assessment of their IA.

Zerebrovaskuläre Erkrankungen I/*Cerebrovascular diseases I*

V019

Bestimmung der kumulativen Strahlenexposition in der akuten Phase nach einer Subarachnoidalblutung *Assessment of the cumulative radiation exposure in the acute phase after aneurysmal subarachnoid haemorrhage*

K. Döring, D. Mielke, V. Rohde, V. Malinova

Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

Objective

The acute phase after aneurysmal subarachnoid hemorrhage (aSAH) is associated with a high risk for the formation of early and delayed ischemic and other complications. This leads to a relevant use of diagnostic tools including computer tomography (CT) and fluoroscopy-based imaging, associated with a significant radiation exposure (RE). Since aSAH occurs often in younger patients compared to ischemic stroke, the assessment of RE is a relevant issue in this patient population. The aim of this study was to calculate the average cumulative RE in the acute phase after aSAH and to evaluate its impact on long-term outcome.

Methods

We performed a retrospective analysis of patients with aSAH treated between 2008 and 2018. The radiation dose of every single examination such as CT, CT-angiography (CTA), CT-perfusion (CTP), diagnostic digital subtraction angiography (DSA) and endovascular intervention as a rescue treatment for refractory vasospasm or aneurysm occlusion was calculated. The long-term outcome was assessed according to the modified Rankin scale (mRS) at least 3 months after the ictus, whereat a mRS \leq 3 was considered as good clinical outcome. The correlation between RE and the aSAH grade, ischemic complications and long-term outcome was evaluated.

Results

A total of 375 patients were included. The mean age was 55.2 \pm 14,3, 65.3% were female. A high grade aSAH (Hunt&Hess I-III) had 64.9% of the patients. The calculated radiation doses per examination were as followed: CT 2 mSv, CTA 3 mSv, CTP 5 mSv, DSA 22 mSv, Coiling 33,5 mSv, dilatation 19 mSv. The average cumulative RE per patient was 76.5 mSv. A higher aSAH-grade was associated with a higher RE (mean 59.3 mSv vs 32.1 mSv, linear regression, p=0.00002). Patients with a better outcome (mRS 0-3 or GOS 4-5) also received significantly lower radiation doses in the acute phase after aSAH (Welch t-test, p=0.00008). Furthermore, dilated patients (Welch t-test, p=0.01), clipped patients (Welch t-test, p=0.02), patients with DCI (Welch t-test, p=0.0008) or with delayed infarction (Welch t-test, p=0.00008) had a significantly higher RE.

Conclusion

This study confirms a significant imaging-related RE in patients with a complication-rich aSAH-course. A meticulous decision-making process and an elaboration of imaging-protocol with lower RE for the deployment of CT and fluoroscopy-based imaging is indicated in the acute phase of aSAH in order to reduce the RE in this patient population.

Zerebrovaskuläre Erkrankungen I/*Cerebrovascular diseases I*

VO20

Primäre dekompressive Kraniektomie bei Patienten mit raumforderndem sylvischem Hämatom aufgrund einer aneurysmatischen Subarachnoidalblutung

Primary decompressive craniectomy in patients with space-occupying sylvian haematoma due to aneurysmal subarachnoid haemorrhage

F. Wenz¹, K. Hackenberg¹, A. Ziebart¹, D. Hänggi², N. Etminan¹, A. Abdulazim¹

¹Universitätsklinikum Mannheim, Klinik für Neurochirurgie, Mannheim, Germany

²Universitätsklinikum Düsseldorf, Klinik für Neurochirurgie, Düsseldorf, Germany

Objective

Decompressive craniectomy (DC) is commonly performed for the management of increased intracranial pressure, especially in patients after malignant cerebral infarction or traumatic brain injury. In patients with aneurysmal subarachnoid haemorrhage (SAH) and space-occupying sylvian haematomas early DC may be considered during surgical treatment of ruptured intracranial aneurysm with the intention to improve local perfusion and thereby limit secondary brain injury. We investigated the efficacy of primary DC with respect to functional outcome as well as the occurrence of delayed cerebral ischemia (DCI) and angiographic vasospasm.

Methods

Between 2010 and 2019, 501 consecutive SAH patients were admitted to our hospital. We identified 44 patients with SAH and space-occupying sylvian haematomas with at least 20ml of clot volume and/or 5mm of resulting midline-shift. 26 patients received primary DC with clipping and haematoma evacuation (cohort I), while 18 patients received clipping and haematoma evacuation only (cohort II). The two groups were compared with respect to functional outcome at 3 months using dichotomized extended Glasgow Outcome Scale (eGOS 1-5: unfavourable and eGOS 6-8: favourable). Additionally, we evaluated the rate of clinical DCI, angiographic vasospasms, DCI-related infarctions and secondary DC.

Results

Despite generally comparable baseline characteristics, cohort I tended to have larger clot volumes and higher rates of midline shifts (Table 1). There was no statistically significant effect of primary DC on good functional outcome at 3 months (23.1% vs. 16.7%; OR: 1.50 [0.32-6.99]). Furthermore, the incidence of clinical DCI (aOR: 0.85 [0.21-3.45]) as well as angiographic vasospasm (aOR: 0.79 [0.22-2.88]) did not differ significantly in cohort I. However, the rate of DCI-related infarctions in cohort I was significantly lower (15.4% vs 47.1%; OR: 0.20 [0.05-0.85]), which was even more evident after adjustment for patient age, WFNS grade, midline shift and clot volume (OR:0.09 [0.01-0.64]). Notably 33.3% of patients of cohort II received secondary DC due to increasing brain swelling or infarction, of which 80% were performed within 96 hours after aneurysm treatment.

Conclusion

Our data highlight that primary DC in patients with SAH and space-occupying haematoma may be associated with a reduced rate of DCI-associated infarctions. However, large patient samples are required to investigate the effect of early DC in this specific subset of SAH patients on functional outcome.

Fig 1

Table 1

Patient characteristics			
	Cohort I (n=26) Primary DC	Cohort II (n= 18) No primary DC	p value
Age (mean)	58.31 ± 9.40y	56.00 ± 9.87y	
Sex (M:F)	3 (11.5%) : 23 (88.5%)	2 (11.1%) : 16 (88.9%)	
WFNS grade			0.64
II	1 (3.8%)	-	
III	6 (23.1%)	6 (33.3%)	
IV	7 (26.9%)	6 (33.3%)	
V	12 (46.2%)	6 (33.3%)	
Clot volume	52.27 ± 24.77ml	45.39 ± 18.21ml	0.29
Midline shift	7.35 ± 4.43mm	5.78 ± 2.07mm	0.12

Fig 2

Table 2

Effect of initial decompressive hemicraniectomy on primary and secondary outcomes. OR = odds ratio, aOR = adjusted odds ratio; * Adjustment for age, WFNS grade, midline shift and clot volume

Outcomes	OR (95% CI)	p-value	aOR (95% CI) *	p-value
eGOS 6-8 at 3 months	1.50 (0.32-6.99)	0.61	n.a.	0.11
Clinical DCI	0.65 (0.19-2.23)	0.50	0.85 (0.21-3.45)	0.82
Angiographic vasospasms	0.70 (0.20-2.42)	0.58	0.79 (0.22-2.88)	0.73
DCI-related infarction	0.20 (0.05-0.85)	0.03	0.09 (0.01-0.64)	0.02

Zerebrovaskuläre Erkrankungen I/*Cerebrovascular diseases I*

V021

Der Einfluss der ABO Blutgruppe auf Subarachnoidalblutungen *The effects of ABO blood type on subarachnoid haemorrhage*

M. Strey, J. Küchler, C. Ditz, V. M. Tronnier, K. Krajewski

Universitätsklinikum Schleswig-Holstein, Neurochirurgie, Lübeck, Germany

Objective

The O blood type has been shown to be significantly associated with mortality in patients with severe trauma injury in major series. Pathophysiologically, vWF levels in type O patients are known to be reduced. Few studies exist on the effects of blood type on subarachnoid hemorrhage (SAH), especially after correcting for anticoagulant use. The aim of this study was to examine the effects of blood type after correcting for anticoagulant use on Hunt and Hess grade, vasospasm, shunting, mortality and unfavorable outcome according to the modified rankin scale (mRS).

Methods

A retrospective analysis of all consecutive SAH patients treated at our single university center from 2007-2017 was performed. Data were acquired from the electronic patient chart and discharge summaries. Questionnaires were sent to all patients regarding anticoagulant use. For further analysis, the following variables were dichotomized: Hunt and Hess grade (I-II: "low", III-V: "high") as well as mRS (0-2: "favorable", 3-6: "unfavorable"). Logistic regression was performed with SPSS. Analyses were carried out for aneurysmal and non-aneurysmal cohorts separately. P values < 0.05 were considered significant. Results are presented as odds ratio with 95% confidence intervals.

Results

A total of 397 patients (median age: 55y) were included. 315 patients had angiographic confirmation of aneurysm, 82 were non-aneurysmal. For aneurysmal SAH, risk factors for vasospasm were decreasing age (OR 0.98, CI: 95.7-99.7, p=0.023) and high H&H grade (OR 1.8, CI: 1.1-3.0, p=0.022) but not blood type O or anticoagulant use. Unfavorable outcome at 6 months was also not associated with blood type or anticoagulants. Among high-grade H&H patients, only blood type O was associated with a lower OR for death (OR 0.383, CI:0.185-0.792, P=0.010). Excluding patients with a history of anticoagulant use did not change any findings.

For the naSAH group, high H&H grade was highly associated with poor outcome at 3 months (OR 73.9, CI: 4.3-1254.7, p=0.003). No risk factors were identified for outcome at 6 months, death (n=5 patients), vasospasm, vasospastic infarction or shunt. Excluding anticoagulant use had no effect.

Conclusion

Blood type O may lower the risk of death for high-grade aSAH patients. We found a history of anticoagulant use has no effects on H&H grade, vasospasm, or outcome incl. death. Few predictive factors exist for naSAH patients with respect to outcome.

Zerebrovaskuläre Erkrankungen I/*Cerebrovascular diseases I*

V022

Intensivmedizin in aneurysmatischer Subarachnoidalblutung in Deutschland – fehlende Leitlinien fördern Heterogenität

Intensive care management of aneurysmal subarachnoid haemorrhage in Germany – lack of guidelines fosters treatment heterogeneity

S. Hernández-Durán¹, C. Salfelder¹, J. Schaper¹, O. Mörer¹, V. Rohde², D. Mielke², C. Von der Brölie²

¹Universitätsmedizin Göttingen, Klinik für Anästhesiologie und Intensivmedizin, Göttingen, Germany

²Universitätsmedizin Göttingen, Klinik für Neurochirurgie, Göttingen, Germany

Objective

Current evidence-based guidelines for the management of aneurysmal subarachnoid hemorrhage (SAH) focus primarily on the timing, modality and technique of aneurysm occlusion, and the prevention and treatment of delayed cerebral ischemia. Significant aspects of management in the intensive care unit (ICU) during the later course of SAH are completely unaddressed, such as ventilation and sedation (VST). SAH patients present unique challenges not accounted for in general VST recommendations and guidelines, which is why we attempted to elucidate VST practices in SAH patients in Germany.

Methods

We conducted a nation-wide survey on VST practices in SAH in Germany. Secondly, we assessed the existence of and compliance with current guidelines regarding VST practices. The questionnaire was designed in interdisciplinary fashion and distributed online via the kwiksurvey® platform (Bristol, UK).

Results

A total of 50 responses were received, accounting for a response rate of 49%. Twenty-one were university hospitals (UH), 23 high-volume centers (HVC), 6 low-volume centers (LVC). Half of the participating centers do not take into consideration WFNS at presentation to indicate ventilation. While 42% of centers rely on the Horowitz index to indicate ventilation, 62% of them have a cutoff-value of <200, and 38% of <100. Most UH and HVC use propofol for induction of sedation (95%); LVC employ benzodiazepines (100%). Sedation enhancement is done with ketamine in UH (75%) and HVC (60%), whereas LVC use clonidine (100%). These results show great heterogeneity in clinical practice, especially between UH/HVC and LVC. When analyzing existing ICU guidelines, including AWMF, AHA and Neurocritical Care Society, there is a paucity of SAH-tailored recommendations, possibly contributing to the variability reflected in our survey.

Conclusion

Our study clearly demonstrates that attitudes and practices pertaining to VST in SAH are enormously heterogeneous, reflecting the lack of good quality evidence and differing interpretations thereof. While the overall outcome of SAH depends on a multitude of factors, the establishment of evidence-based protocols for the management of these patients in the ICU can potentially solve one part of the puzzle and lead to improved outcomes.

Zerebrovaskuläre Erkrankungen I/*Cerebrovascular diseases I*

V024

Hirnstamm-Kavernome – intensivmedizinische Aspekte und Relevanz für den Krankenhausaufenthalt *Brainstem cavernous malformation (CCM) – intensive care therapy and relevance for hospitalisation*

A. Herten, D. V. Saban, S. Rauscher, R. Jabbarli, K. H. Wrede, U. Sure, P. Dammann

Universitätsklinikum Essen, Klinik für Neurochirurgie, Essen, Germany

Objective

To estimate different aspects of postoperative intensive care therapy and complicated course in patients with a brainstem cavernous malformation. To examine duration of hospitalization, possible complications and relevance of location of brainstem cavernous malformation (CCM).

Methods

87 cases of brainstem CCM, who have been treated surgically between 2008 and 2018, were observed for postoperative course and complications: Duration of hospitalization/ intensive care therapy, need of reintubation/ tracheostomy, occur of pneumonia, possibility of discharge home or transfer to a rehabilitation clinic. Descriptive analysis was accordingly performed. Impact of CCM location was examined with logistic regression analysis.

Results

Average duration of hospitalization was 18,2 days (2- 64) in total, 3,93 days (0-36) in the intensive care unit and 1,49 days (0-32) in the intermediate care unit. 7 patients suffered from respiratory failure and required reintubation postoperatively, 5 received a tracheostomy, 6 suffered from pneumonia (4 with tracheostomy). 41 patients were discharged home, while 41 were send to another clinic/ rehabilitation clinic directly. CCM were located in one (or multiple) parts of the brainstem, 55 in the pons, 27 in the mesencephalon, 14 in the medulla oblongata and 7 in the thalamus. A CCM located in the pons or medulla oblongata provoked a more complicated postoperative course with longer hospitalization and worse functional outcome (mRS). These locations also significantly correlated with impaired functional outcome (mRS >1) (medulla $p=0,04$, pons $p=0,004$). Need for reintubation and tracheostomy was almost exclusively found in cases with CCM located in the pons or medulla oblongata. However, statistical significance was only seen for medulla oblongata location ($p=0,048$).

Conclusion

Patients with brainstem cavernoma and surgical therapy typically need a special postoperative care. ICU course and complications depend on the specific location in brainstem.

Kopf- und Gesichtsschmerz/*Headache and facial pain*

V025

Die präoperative Symptomdauer ist der einflussreichste Risikofaktor für das Behandlungsversagen nach mikrovasculärer Dekompression bei Trigeminusneuralgie – eine europäische multizentrische Studie mit 1101 Patienten

Preoperative symptom duration is the most influential risk factor for treatment failure following microvascular decompression for trigeminal neuralgia – a European multi-centre study with 1101 patients

E. Shiban¹, A. P. Fritsche², B. Schatlo³, S. Hernández-Durán³, V. Rohde³, C. F. Freyschlag⁴, C. Thomé⁴, P. da Cunha⁵, M. Barbosa⁵, S. Maurer⁶, A. Jödicke⁶, M. Gandia-Gonzalez⁷, A. Demetriades⁸, A. Natalwala⁸, L. Barthel⁹, U. Sure⁹, V. Vanaclocha¹⁰, G. Blasco¹¹, L. Mastronardi¹², F. Ringel¹³, N. Keric¹³, M. Ottenhausen¹³, P. González-López¹⁴, R. Lau Rodriguez¹⁵, P. Vajkoczy¹⁶, D. Seggewiß¹⁶, F. Ruiz Juretschke¹⁷, R. Garcia Leal¹⁷, L. Ley¹⁸, S. Rocha Romero¹⁹, W. Stummer²⁰, C. Ewelt²⁰, M. Bolcha²¹, M. Sameš²¹, A. Naboichenko²², A. Moiraghi²³, P. Bijlenga²³, P. Alvarez Bonillo²⁴, M. Garcia Bach²⁴, B. Meyer²⁵, J. Lehmberg²

¹Universitätsklinikum Augsburg, Klinik für Neurochirurgie, Augsburg, Germany

²München Klinik Bogenhausen, Neurochirurgie, München, Germany

³Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

⁴Medizinische Universität Innsbruck, Klinik für Neurochirurgie, Innsbruck, Austria

⁵University of Coimbra, Neurosurgery, Coimbra, Portugal

⁶Vivantes Klinikum Neukölln, Neurochirurgie, Berlin, Germany

⁷University Hospital La Paz, Neurosurgery, Madrid, Spain

⁸University of Edinburgh, Department of Neurosurgery, Edinburgh, United Kingdom

⁹Universitätsklinikum Essen, Klinik für Neurochirurgie, Essen, Germany

¹⁰University of Valencia, Department of Neurosurgery, Valencia, Spain

¹¹La Princesa University Hospital, Department of Neurosurgery, Madrid, Spain

¹²San Filippo Neri Hospital, Department of Neurosurgery, Rom, Italy

¹³Universitätsmedizin Mainz, Neurochirurgie, Mainz, Germany

¹⁴General Hospital University of Alicante, Department of Neurosurgery, Alicante, Spain

¹⁵Bellvitge University Hospital Barcelona, Department of Neurosurgery, Barcelona, Spain

¹⁶Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

¹⁷General Hospital University Gregorio Marañón, Department of Neurosurgery, Madrid, Spain

¹⁸Ramon y Cajal University Hospital, Department of Neurosurgery, Madrid, Spain

¹⁹Hospital Virgen del Rocío, Department of Neurosurgery, Sevilla, Spain

²⁰Universitätsklinikum Münster, Neurochirurgie, Münster, Germany

²¹Jan-Evangelista-Purkyně-University, Neurosurgery, Ústí nad Labem, Czech Republic

²²National Academy of Medical Sciences of Ukraine, Medical Clinic IV Endocrinology, Kiev, Ukraine

²³Genfer Universitätsspital, Neurochirurgie, Genf, Switzerland

²⁴Mútua Terrassa University Hospital, Department of Neurosurgery, Barcelona, Spain

²⁵Technische Universität München, Klinik für Neurochirurgie, München, Germany

Objective

The gold standard for the treatment of classic trigeminal neuralgia (TN) is carbamazepine. However, the efficacy of carbamazepine is compromised by its adverse effects. Furthermore, after long-term follow-up only 22% of participants still find carbamazepine effective. Aim of this study is to assess the clinical outcome following the surgical treatment of TN and find potential factors for treatment failure.

Methods

A multicenter retrospective data analysis was performed. Primary outcome was the rate of pain free patients at last follow up. The following factors were analyzed as possible risk factors for treatment failure: 1)

Duration of symptoms 2) surgical experience 3) Technique: Neurovascular interposition or neurovascular transposition 4) Number of affected nerve branches 5) Presence or absence of neurovascular conflict on MRI 6) Indication for surgery: medical treatment failure (persisting pain) or intolerable adverse effects of the medication. At final follow up a telephone interview for patients satisfaction was conducted.

Results

1101 patients from 23 European institutions were analysed. Follow up data was obtained from 1012 (91.9%). 450 patients were male (41%) mean age was 61 years. Mean duration of symptoms until surgery was 70.6 months (5.8 years). From 989 patients with available imaging data 700 (71%) had a visible conflict on the MRI. 68.2% of patients were pain free at last follow up. Facial hypoesthesia was the most common complication and was seen in 18.4% of patients. There were no mortalities. Regression analysis revealed that only preoperative duration of symptoms correlated with treatment failure ($p=0.0012$). Telephone interview was conducted with 830 (75%) patients. Of Those 693 (84%) were satisfied with surgery and 554 (67%) would have preferred earlier surgery.

Conclusion

Microvascular decompression for trigeminal neuralgia is a safe and effective treatment method and should probably be done early on. A randomized controlled study comparing MVD to best medical management is warranted.

Kopf- und Gesichtsschmerz/*Headache and facial pain*

V026

Wertvolle Prädiktoren für das Ergebnis der mikrovaskulären Dekompression bei Hemifazialem Spasmus *Valuable predictors to the outcome of microvascular decompression of haemifacial spasm*

E. EL Refaee^{1,2}, S. Fleck¹, J. Baldauf¹, M. Matthes¹, H. W. S. Schroeder¹

¹Universitätsmedizin Greifswald, Neurochirurgie, Greifswald, Germany

²Cairo University, Department of Neurosurgery, Kairo, Egypt

Objective

Microvascular decompression represents the best definitive treatment of hemifacial spasm. The outcome of surgery is variable with percentage of recurrent spasms and other unfavorable manifestations like hearing dimution and facial paresis.

Methods

In this study, we performed a retrospective analysis of the prospectively collected database to detect the valuable predictors of the unfavorable recurrent or residual spasms directly after surgery and along the long-term postoperative follow up

Results

We studied data of 413 surgical procedures performed to 387 patients. Among these 21 needed a redo operation, and 2 patients needed 3 surgeries. The follow-up interval reached 18 months in 268 patients. Several factors were analysed to detect which of them would be of value in predicting unfavorable outcome as : age, sex, offending vessels, grooving, site of grooving, and lateral spreads. Grooving, site of grooving and offending vessel(s) were the main factors that can predict unfavorable outcome with P value of 0.0111 ,0.0104, 0.0106 directly after surgery in the forementioned factors respectively. For the long-term follow-up, P value reached 0.0344 in site of grooving and 0.0004 in the offending vessel respectively. The worst outcome was with vertebral artery and/or posterior inferior cerebellar arteries as offending vessels.

Conclusion

Grooving at the compression site of the facial nerve, along with the compression with vertebral artery and/or PICA represent valuable predictors for the risk of worse outcome. The data for these predictors could be best obtained from the intraoperative endoscopic visualization of the neurovascular conflict at the compression site.

Kopf- und Gesichtsschmerz/*Headache and facial pain*

V027

Verbesserte Abschätzung des klinischen Ergebnisses nach mikrovaskulärer Dekompression durch hochauflösende MRT-Kombinationen für die Unterscheidung zwischen arteriellen und venösen neurovaskulären Konflikten bei der Trigeminusneuralgie

Enhanced estimation of the clinical outcome after microvascular decompression by superb reliability of MRI for the distinction of arterial and venous conflicts in trigeminal neuralgia

L. Tanrikulu^{1,2}, S. Müller^{1,2}, E. Khadhraoui^{1,2}, M. Psychogios^{1,2}, V. Rohde^{1,2}

¹Universitätsmedizin Göttingen, Göttingen, Germany

²Universitätsmedizin Göttingen, Göttingen, Germany

Objective

Balanced Steady State Free Precession(b-SSFP) sequences, such as CISS or FIESTA, and the newly developed Fast-Spin-Echo(FSE)-Sequences, for example SPACE and VISTA, enable an optimized visualization of causative neurovascular compression (NVC) in patients with trigeminal neuralgia (TN). Microsurgically-found arterial conflicts are mostly associated with a favorable outcome of MVD compared to venous conflicts. An additional Time-of-Flight(ToF) angiography facilitates the differentiation between causative arteries and veins. The goal of this study is to analyze the reliability and impact of the combination of high-resoluted MRI techniques on the prediction of vessel type and the estimation of clinical postoperative outcome of microvascular decompression (MVD).

Methods

48 patients (m/f: 32/16) underwent MVD of the trigeminal nerve. We analyzed the visualization of cranial nerves (SPACE/VISTA or CISS/Fiesta-C). An additional time of flight angiography was available in 38 cases. The patients were categorized into four subgroups: 1) NVC negative, 2) venous NVC, 3) arterial NVC, 4) combined arterial and venous NVC. The preoperative MRI findings were compared to the intraoperative morphological findings. Outcome was quantified by the Barrow Neurological Institute pain score.

Results

25 pure arterial NVC, 9 venous NVC and 5 combined NVC were seen by MRI. In 9 cases NVC was absent. The neurovascular findings from the MRI correlated in 91.7% of the patients with the intraoperative findings. The examined cases matched in 80% without MRI-TOF, the consistency was enhanced to 94.7% with MRI-TOF. Cronbach"s Alpha was 0.89 overall, 0.90 with MRI-TOF and 0.77 without.

Conclusion

The visualization of CN V using sequences such as b-SSFP or FSE in combination with 3D-ToF angiography enables an optimized delineation of arterial and venous neurovascular conflicts and may allow a more reliable differentiation between veins and arteries, resulting in a better prediction of clinical outcome compared to T2 imaging data alone.

Kopf- und Gesichtsschmerz/*Headache and facial pain*

V028

Perkutane Thermokoagulation für die Behandlung von Trigeminusneuralgie im Schlaf-Wach-Verfahren unter Anleitung des Neuromonitorings

Radiofrequency thermocoagulation for trigeminal neuralgia in a sleep-awake procedure under neuromonitoring guidance

T. Abboud, A. Nazarenius, V. Rohde, D. Mielke

Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Radiofrequency thermocoagulation (RT) for the treatment of trigeminal neuralgia (TN) is a well-established technique. This procedure is usually performed in awake patients to localize the involved trigeminal branches. It is often a painful experience for the patient, which diminishes the reliability of the patient's response. Therefore, we applied a sleep-awake technique with placement of the RT cannula under intraoperative monitoring, which might be a good alternative. We present our case series to investigate the feasibility and outcome of this technique.

Methods

We reviewed five cases of patients suffering from pharmaco-resistant TN, who previously underwent a microsurgical decompression of the trigeminal nerve at least once. For RT, the patient underwent a short general anesthesia using a laryngeal tube in the supine position. Pairs of EMG-needles were implanted subdermally near the supraorbital, infraorbital, and mental foramina. Insertion of the radiofrequency cannula was done using typical anatomical landmarks under x-ray guidance. The trigeminal nerve roots were stimulated through the foramen ovale with the tip of the radiofrequency cannula at 0.5 V, and antidromic sensory evoked responses were recorded from the 3 divisions of the trigeminal nerve as well as the mandibular muscle in the face. Repositioning of the cannula was performed until the desired nerve divisions could be stimulated. Afterwards, anesthesia was stopped, the laryngeal tube was removed and the stimulation was repeated (0.05-0.15V) to obtain a verbal response from the patient. Lesioning was performed with radiofrequency for 90 seconds at an intensity of 75°C.

Results

Antidromic sensory evoked potentials of all trigeminal nerve branches could be obtained in all five patients and repositioning of the cannula under stimulation enabled localizing of the desired branches (V2 and V3 in 3 patients and V2 in 2 patients). After awaking, patients confirmed the effect of stimulation at the face. Radiofrequency lesioning resulted in an immediate pain relief in all patients. Temporary hypalgesia in the territory of the lesioned branches occurred in all patients, but recovered during hospital stay.

Conclusion

In TN, RT of trigeminal nerve under neuromonitoring guidance in a sleep-awake modus is feasible and could be an alternative for uncooperative, anxious or even all patients. Antidromic sensory evoked potentials allowed an accurate localization of the involved branches of the trigeminal nerve.

Kopf- und Gesichtsschmerz/*Headache and facial pain*

V029

Radiochirurgie zur Behandlung der Trigeminusneuralgie *Radiosurgery for the treatment of trigeminal neuralgia*

G. Lütjens, A. T. Van Eck, O. Bundschuh, G. Horstmann

Gamma Knife Zentrum Krefeld, Hannover, Germany

Objective

Medically refractory trigeminal neuralgia can be treated by microvascular decompression of the trigeminal nerve, by ablative percutaneous treatments such as thermocoagulation, glycerol/ alcohol injection and balloon compression of the Gasserian ganglion or, far less invasive, by radiosurgery that has been proven to elegantly and highly effectively treat this pain condition. We here report about the results at our institution.

Methods

We evaluated our outcomes retrospectively in our patients with medically refractory trigeminal neuralgia treated with radiosurgery. One 4mm shot was placed along the trigeminal nerve (either retrogasserian, mid-cisternal or at the root entry zone) as the chosen target. Pain scores and side effects were documented regularly.

Results

232 patients treated between the years 1999-2019 were included into this study. 15 patients received repeated gamma knife radiosurgery. The average age was 65 years. 58 patients had prior therapies other than medication. Mean follow up was 406 days. Multiple sclerosis as a comorbidity was present in 38 patients.

Pain condition last in average 10 years till radiosurgery was performed. The average maximum dose was 89 Gy. The 10 Gy volume of the brain stem in average was 0,12ccm. Radiosurgery was successful in 78% as defined by the Barrow neurological institute pain score (BNI) I-III and failed in 22% of the patients. Hypesthesia was seen in 12%. Pain quality changed to ongoing pain in 4 patients. No life threatening events occurred.

Conclusion

Radiosurgery is proven to be an effective and safe treatment option for trigeminal neuralgia and long-term results are available. In our patients side effects were rare and less present than generally cited in the literature and its risk profile is lower compared to any other treatment. Given the fact of absent invasiveness radiosurgery should be considered in the first place in patients with (high risk) comorbidities, elderly patients and patients with prior surgically treatments and refractory/ relapse pain condition.

Kopf- und Gesichtsschmerz/*Headache and facial pain*

V030

Die Bedeutung des chirurgischen Zuganges für den akuten Postkraniotomiekopfschmerz – eine prospektive konsekutive Fallserie

The impact of surgical approach on acute postcraniotomy headache – a prospective consecutive case series

T. Huckhage¹, M. Westphal¹, R. Klinger²

¹Universitätsklinikum Hamburg-Eppendorf, Klinik und Poliklinik für Neurochirurgie, Hamburg, Germany

²Universitätsklinikum Hamburg-Eppendorf, Klinik und Poliklinik für Anästhesiologie, Hamburg, Germany

Objective

The latest version of the International Classification of Headache Disorders delineates diagnostic criteria for acute headache attributed to craniotomy, but data on possible predisposing factors are scarce. This study aims to evaluate the impact of the surgical approach on the severity of acute postcraniotomy headache.

Methods

64 consecutive adults (mean age 54.2±15.2 years; 26 male) undergoing cranial neurosurgery for various reasons without preoperative acute or chronic headache were included. After regaining consciousness, all patients were surveyed about their average daily headache on a numeric pain rating scale (NRS 0-10; 0=no headache; 10=maximum headache) as well as analgesic consumption from day 1 to 3 after surgery. Three distinct patient cohorts were built with respect to the surgical approach (temporal/nuchal muscle saving (n=20) and muscle transecting craniotomies (n=36) as well as burr hole procedures (n=8)) and group comparisons performed using the Kruskal-Wallis test (level of significance p<0.05). Results are presented as mean values ± standard deviation.

Results

There were no significant group differences with regard to age, gender or general health condition (American Society of Anesthesiologists Physical Status). Craniotomy patients with muscle transection suffered from significantly higher postoperative NRS scores compared to their counterparts without procedure-related muscle injury (3.4±2.3 versus 2.3±1.9) as well as patients undergoing burr hole surgery (1.2±1.4; p=0.02). Moreover, the consumption of non-opioid analgesics was almost doubled following muscle transecting surgery as compared to muscle preserving procedures (p=0.03). Only one patient received opioids during the postoperative period.

Conclusion

Iatrogenic muscle damage may be an important predisposing factor for the development of acute postcraniotomy headache. Therefore, if a transmuscular approach is unavoidable, the neurosurgeon should be aware of the need for adequately-adjusted, postoperative analgesia in these cases.

Chirurgie peripherer Nerven/*Peripheral nerve surgery*

V031

Angereicherte humane Endothelzellen isoliert aus peripheren Nerven – ein potentielles Werkzeug in der Forschung sowie in der Entwicklung von zellularisierten künstlichen Nerventransplantaten
Enriched human endothelial cells isolated from peripheral nerves – a potential tool for research and the further development of artificial nerve grafts

P. Dömer¹, C. Heinen², B. Kewitz¹, J. Woitzik², U. Janssen-Bienhold^{1,3}, T. Kretschmer⁴

¹Carl von Ossietzky Universität Oldenburg, Abteilung für Neurowissenschaften, Oldenburg, Germany

²Evangelisches Krankenhaus Oldenburg, Abteilung für Neurochirurgie, Oldenburg, Germany

³Carl von Ossietzky Universität Oldenburg, Forschungszentrum für Neurosensorik, Oldenburg, Germany

⁴Klinikum Klagenfurt am Wörthersee, Abteilung für Neurochirurgie, Klagenfurt, Austria

Objective

Over the last years, endothelial cells (ECs) have come into scientific focus in peripheral nerve research, as they were shown to be a major constituent of the blood-nerve-barrier (BNB) and provide axonal guidance in peripheral nerve regeneration. However, mainly animal models and commercially available primary human umbilical-vein endothelial cells (HUVECS) were used in research, since previous protocols for the isolation of human nerve derived ECs were labour-intensive and required substantial experience in density centrifugation. Additionally, studies have shown different physiological properties and protein expression profiles for human nerve ECs compared to commercially available HUVECS and animal derived ECs. Thus, we established an easy-to-follow, time-efficient and inexpensive EC isolation protocol for human sural nerves, facilitating immunomagnetic cell sorting by means of CD31 coated Dynabeads.

Methods

For the EC isolation, sural nerve tissue derived from autologous nerve transplantations was enzymatically digested to gain a single cell solution. In a second step, a highly specific anti-CD31 antibody, which selectively binds to ECs, was conjugated to streptavidin coated superparamagnetic Dynabeads (\varnothing 1 μ m, Invitrogen, Carlsbad, CA, USA). Following incubation of the nerve cell solution with the CD31-Dynabeads, bead-bound ECs were retained magnetically, while the supernatant containing the other cell-types was discarded.

Results

The ECs reached a purity of > 95% and were seeded in gelatin coated cell culture plastic, where they started to proliferate within 24 hours. When ECs reached confluency, splitting of cells was performed using trypsin-EDTA, which resulted in a removal of Dynabeads from the ECs probably due to CD31 epitope cleavage by trypsin. The ECs could be subcultured for up to 6 passages until the proliferation rate declined.

Conclusion

This easy-to-follow isolation protocol simplifies the access to human primary nerve-derived ECs in basic research and allows the use of these ECs in clinically relevant applications. One area of application would be the experimental *in-vitro*vascularization of artificial peripheral nerve grafts with autologous patient derived ECs, extracted for instance from neuroma biopsies. Another application could be the introduction of patient derived ECs into the suture site to improve the axonal crossing of the injury-site, since ECs were shown to mediate axonal guidance.

Meningeome experimentell/*Meningiomas experimental*

V032

Einfluss von Decitabin auf hTERT Promotor Methylierung, TERT Aktivität und Expression sowie Proliferation in Meningeom-Zelllinien

Efficacy of decitabine in malignant meningioma cells is related to promoter demethylation of distinct tumour suppressor and oncogenes but independent of TERT

L. Stögbauer¹, W. Stummer¹, B. Brokinkel¹, N. Warneke¹, V. Senner¹, O. Grauer², W. Paulus^{2,3}, C. Thomas³, E. C. Bunk¹

¹Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

²Universitätsklinikum Münster, Neurologie, Münster, Germany

³Universitätsklinikum Münster, Neuropathologie, Münster, Germany

Objective

Alternative systemical treatment options for meningiomas are still lacking. As one key feature in oncogenesis, Human Telomerase Reverse Transcriptase (hTERT) promoter methylation with subsequent TERT expression and Telomerase activity is present in the majority of high-grade meningiomas. The aim of this study is to investigate the impact of the chemotherapeutical demethylating agent Decitabine (5-aza-2"-deoxycytidine) on both survival and DNA methylation in meningioma cell lines.

Methods

hTERT promoter methylation, Telomerase activity, TERT expression, cell viability and proliferation were analysed prior and after incubation with Decitabine in two benign (HBL-52 and Ben-Men 1) and one malignant (IOMM-Lee) meningioma cell line. Global effects of Decitabine on DNA methylation were additionally explored by 850K methylation analyses.

Results

High levels of TERT expression, Telomerase activity and hTERT promoter methylation were found in IOMM-Lee and Ben-Men 1 but not in HBL-52 cells. Decitabine induced a dose-depending significant decrease of proliferation and viability after incubation with doses from 1-10µM in IOMM-Lee but not in HBL-52 or Ben-Men 1 cells. However, effects in IOMM-Lee were not related to TERT expression, Telomerase activity or hTERT promoter methylation. Genome-wide methylation analyses revealed distinct demethylation of 14 DNA regions after drug exposition in the Decitabine-sensitive IOMM-Lee but not in the resistant HBL-52 cells. Differentially methylated regions covered promoter regions of 11 genes, including several oncogenes and tumor suppressor genes not described in meningiomas yet.

Conclusion

Decitabine significantly decreases proliferation and viability in high-grade but not in benign meningioma cell lines. However, effects of Decitabine are TERT-independent but related to DNA methylation changes of promoters of distinct tumor suppressor and oncogenes.

Meningeome experimentell/Meningiomas experimental

V033

Expressionsunterschiede von Somatostatinrezeptoren 1-5 in Meningeomen

Expression difference of somatostatin receptors 1-5 in meningiomas

F. Behling¹, C. K. Fodi¹, I. Gepfner-Tuma^{1,2}, K. Machetanz¹, M. Skardelly¹, M. Renovanz¹, K. Kaltenbacher², C. La Fougere^{3,4}, J. Honegger⁵, G. Tabatabai^{1,2}, M. Tatagiba¹, J. Schittenhelm³

¹Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

²Universitätsklinikum Tübingen, Klinik für Neurologie, Tübingen, Germany

³Universitätsklinikum Tübingen, Institut für Neuropathologie, Tübingen, Germany

⁴Universitätsklinikum Tübingen, Nuklearmedizin und Klinische Molekulare Bildgebung, Tübingen, Germany

⁵Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

Objective

Beyond microsurgical resection and radiation therapy there are no established treatment alternatives for meningioma patients. In selected cases peptide radio receptor therapy (PRRT) can be implemented. In this study we analyzed the expression of somatostatin receptors 1, 2A, 3, 4 and 5 in meningiomas. Subgroup analysis has the potential to enable further refinement of this innovative treatment option.

Methods

Overall 786 meningiomas were operated in the authors' institution between 01/2013 and 03/2017 of which 562 tumor samples were processed into tissue microarrays and stained for SSTR1, 2A, 3, 4 and 5 immunohistochemically. Microscopic evaluation was done with a semiquantitative score regarding percentual quantification and staining intensity and results were correlated with clinical data.

Results

The analyzed cohort consisted of 399 female and 163 male patients (f/m-ratio 2.4) with a mean age of 59.0 years (range 8.3 – 90.0 years). WHO grade I was diagnosed in 479 cases while 76 tumors were grade II and 7 grade III. Brain invasion was observed in 40 cases. There was a significant lower rate of SSTR3 and SSTR4 expression in meningiomas of male patients ($p=0.0317$ and 0.0216 , respectively) but no significant correlation between patient age and SSTR expression. Significant expression differences were observed for SSTR3 and SSTR4 between WHO grades I through III with less expression in higher grades ($p=0.0005$ and $p=0.023$, respectively). Similar results were observed for brain invasion with lower expression rates in meningiomas featuring invasive growth into central nervous system tissue ($p=0.0275$ and 0.0073 , respectively). Expression of SSTR1 and 5 was highest in spinal meningiomas ($p=0.0107$ and $p<.0001$, respectively) while skull base meningiomas showed the highest expression for SSTR2A and 3 ($p=0.0374$ and $p<.0001$, respectively). No significant differences were observed for tumor location and SSTR4 expression.

Conclusion

Expression of SSTR3 and 4 is higher in WHO grade I tumors and female patients. Spinal meningiomas show higher expression levels of SSTR1 and 5 while SSTR2A and 3 are increased in skull base meningiomas. Currently used PRRT substances target SSTR2A. Marked differences of SSTR expressions between subgroups have the potential to select PRRT substances, depending on subtype expression for potentially more treatment efficacy.

Meningeome experimentell/*Meningiomas experimental*

V034

Hochdurchsatz-Screening von FDA-zugelassenen antineoplastischen Medikamenten zur Behandlung von aggressiven Meningeomen

High-throughput drug screening of FDA-approved antineoplastic drugs for the treatment of aggressive meningiomas

G. Jungwirth, T. Yu, F. Liu, R. Warta, C. Herold-Mende, A. W. Unterberg

Ruprecht-Karls-Universität Heidelberg, Abteilung für Experimentelle Neurochirurgie, Heidelberg, Germany

Objective

Treatment of aggressive meningiomas is still challenging for a couple of reasons, including (1) high rate of recurrence of higher-grade meningiomas, (2) impossible total resection and (3) a lack of effective chemotherapies. To address this urgent need for more successful treatments of aggressive meningiomas, we tested 147 FDA-approved antineoplastic drugs on two different meningioma cell lines Ben-Men-1 (WHO^I) and NCH93 (WHO^{III}).

Methods

Cell proliferation was assessed by crystal violet assay or manual counting. The wound healing assay was performed with IC₅₀ values of each drug. Pictures were taken at 0 and 12h after treatment. For colony formation assay, the cells were treated for 48h with IC₅₀ values and thereafter, drugs were washed off and the cells were seeded into a 10 cm dish. After an incubation period of 10d, colonies were then stained with crystal violet and manually counted. For flow cytometry, cells were treated with 10xIC₅₀ and stained with PI and annexin V after 24 and 48h, respectively.

Results

The impact of FDA-approved drugs on tumor cell proliferation was assessed in a high-throughput 386-well format and revealed Bortezomib (BTZ), Carfilzomib (CFZ), Omacetaxine (HHT), Paclitaxel (PTX) and Ponatinib (POT) as the top 5 most effective drugs. Dose-curve analysis revealed IC₅₀ values of these drugs in Ben-Men-1 and NCH93 cell lines in the nM and lower μM range as follows: BTZ 16.2 and 5.7 nM, CFZ 4.8 and 2.6 nM, HHT 5.0 and 8.9 nM, PTX 2.6 and 1.9 μM, and POT 278 and 206 nM, respectively. Drug concentrations of IC₅₀ and 10xIC₅₀ values lead to an average inhibition of proliferation of both cell lines by up to 90% after 48h (P<.001). Furthermore, migration was reduced with all tested drugs by up to 60% after 12h (P<.05). Additionally, BTZ, CFZ and PTX significantly impaired the formation of colonies in both cell lines (P<.001). The impact of the drugs on cell cycle and apoptosis was analyzed by flow cytometry. Especially BTZ, CFZ and PTX resulted in a G₂/M arrest of treated cells (P<.001) and subsequently, all drugs induced apoptosis after 48h, whereof BTZ led to the most pronounced effect by up to 80% apoptotic cells (P<.001).

Conclusion

In conclusion, we identified five potent drugs for the treatment of aggressive meningiomas by applying a high-throughput drug screening of 147 FDA-approved antineoplastic drugs. Functional testing revealed profound effects of all tested drugs on proliferation, migration, cell cycle, colony formation and on the induction of apoptosis.

Meningeome experimentell/*Meningiomas experimental*

V035

Parasagittale Tumorlokalisation als starker Prädiktor für hTERT Promoter-Mutationen in höhergradigen Meningeomen

Parasagittal tumour location strongly predicts hTERT promoter mutations in high-grade meningiomas

S. Peetz-Dienhart¹, D. C. Spille², P. B. Sporns³, A. Adeli³, E. C. Bunk², A. Wagner¹, W. Paulus¹, W. Stummer², K. Heß¹, B. Brokinkel²

¹Universitätsklinikum Münster, Institut für Neuropathologie, Münster, Germany

²Universitätsklinikum Münster, Klinik und Poliklinik für Neurochirurgie, Münster, Germany

³Universitätsklinikum Münster, Institut für Klinische Radiologie, Münster, Germany

Objective

Mutations of the human Telomerase Reverse Transcriptase (hTERT) promoter and loss of histone H3K27M trimethylation (Me3) have been shown to predict recurrence in meningiomas. While unselected screening is critical regarding their low frequency and the considerable financial expense, risk factors for these alterations are sparsely known.

Methods

Correlations of hTERT promoter mutations and loss of H3K27Me3 with radiological variables (including tumour and edema volumes, contrast heterogeneity and intensity of the tumour on T2-weighted imaging, contrast-enhancement of the capsule, intratumoural calcifications, integrity of the arachnoid layer, tumour shape and location) were analyzed in samples from 96 surgeries for high-grade meningiomas in 72 patients in uni- and multivariate analyses.

Results

hTERT promoter mutations were found in 16 (17%) and loss of H3K27Me3 in three samples (3%). None of the tumours harbored both alterations. Recurrence occurred in 33 of 72 patients (46%). hTERT promoter mutations (HR: 2.81, 95%CI 1.20-6.59; p=.018) were correlated with progression. One of the three individuals with loss of H3K27Me3 developed recurrence. Promoter mutations were found in 47% of parasagittal meningiomas (N=9 of 19) but only in 11% (N=5 of 46), 7% (N=2 of 27) and 0% of tumours arising from the convexity, the skull base and other locations, respectively (p=.001). While parasagittal tumour location was confirmed as an independent predictor in multivariate analyses (OR: 8.20, 95%CI 2.21-30.39; p=.002), no correlations between hTERT promoter mutations and any of the other variables were found. Loss of H3K27Me3 was observed in two convexity and one parasagittal meningioma. Hence, 53% of the samples from parasagittal/ falcine meningiomas carried one of the two analyzed alterations.

Conclusion

Prediction of prognostic molecular alterations in high-grade meningiomas utilizing variables available in the routine preoperative setup is difficult. Determination in parasagittal meningiomas will reveal promoter mutations in almost 50% and can improve estimation of prognosis in these often incompletely resected tumours. However, determination of hTERT promoter mutations in H3K27Me deficient samples might not improve estimation of prognosis.

Meningeome experimentell/*Meningiomas experimental*

V036

Schätzung der Gesamt-DNA-Methylierung in Gewebe- und peripheren Blutproben als Malignitätsmarker bei intrakraniellen Meningeomen

Total DNA methylation estimation in tissue and peripheral blood samples as tumour malignancy marker in intracranial meningiomas

A. M. Barciszewska

Karol Marcinkowski University of Medical Sciences, Neurosurgery and Neurotraumatology, Posen, Poland

Objective

Meningiomas are the most common primary intracranial tumors in adults. They are initially detected with neuroimaging techniques, but definite histological diagnosis requires surgical procedure to collect tumor tissue. Gross total resection is an optimal and final treatment for majority of patients, followed by radiotherapy in malignant or refractory cases. However, there are lots of uncertainties about i.a. need for intervention in incidental cases, estimation of growth kinetics, risk of malignant transformation or response to radiotherapy. It has already been shown that epigenetics plays a crucial role in cancer biology, development and progression. Therefore, we decided to look on meningioma through changes of the most studied epigenetic mark, 5-methylcytosine in DNA.

Methods

We performed the analysis of the total amount of 5-methylcytosine in DNA isolated from intracranial meningioma tissues and peripheral blood samples of the same patients, using thin layer chromatography separation and identification of radioactively labelled nucleotides.

Results

The analyzed cohort consisted of 100 individuals diagnosed with brain meningioma, aged from 27 to 80 years. The most abundant histological variant of meningioma in analyzed cohort was meningothelial, followed by fibrous, angiomatous, transitional, mixed, atypical, anaplastic, and psammomatous types. We found that the 5-methylcytosine level in DNA from intracranial meningiomas changes depending on the malignancy grade. The m5C level in intracranial meningioma DNA negatively correlates with tumor grade. The less malignant tumors show higher m5C contents than more malignant, and the difference is statistically significant. The amount of 5-methylcytosine in tumor tissue and peripheral blood is almost identical. The calculated r correlation coefficient for the whole group of patients with tissue-blood pair was 0.72

Conclusion

The total DNA methylation of intracranial meningiomas can serve as a tool for their characteristics and malignancy estimation. Moreover, while the level of methylation values (R) for tissue and peripheral blood samples from patients with intracranial meningiomas are almost at the same level, that also enables to use peripheral blood as a sample for detecting the tumor or monitoring of the disease.

Meningeome experimentell/*Meningiomas experimental*

V037

Die genomische Signatur in Meningeomen definiert eine Subgruppe von Tumoren mit einem niedrigen Rezidivrisiko

Mutational signature in meningiomas defines tumour sub-classes with distinct risk-of-progression

I. Prilop¹, T. Penson², S. Tummala², F. Barker², P. Brastianos³, D. Cahill², T. Juratli^{1,2}

¹Universitätsklinikum Carl Gustav Carus Dresden, Neurochirurgie, Dresden, Germany

²Massachusetts General Hospital, Department of Neurosurgery, Boston, MA, United States

³Massachusetts General Hospital, Division of Neuro-Oncology, Department of Neurology, Boston, MA, United States

Objective

Meningiomas are the most prevalent primary brain tumor. While most have a benign natural history, a subset has aggressive regrowth, resulting in high morbidity and mortality. Prior genomic characterization of meningiomas discovered mutations in *TRAF7* (and the frequently co-mutated *AKT1* and *KLF4* genes) in lower-grade lesions, compared to the well-established *NF2* alterations in these tumors. Here, we sought to assess the mutational signature of a cohort of progressive/high-grade meningiomas, with an aim to identify biomarkers associated with risk-of-progression.

Methods

We performed whole-exome sequencing (WES) in a cohort of 34 progressive/high-grade meningiomas samples from 24 patients, containing 10 matched samples. In addition, targeted sequencing was carried out in matched samples of an extended cohort, inclusive of the WES cohort, totaling 64 progressive meningiomas (n= 36 patients) to determine *TRAF7*, *KLF4*, *AKT1* and *TERT* promoter (*TERTp*) hotspot mutations.

Results

We detected frequent genomic alterations that are known to be associated with an unfavorable prognosis in meningiomas: *NF2* mutations (n=11, 45.8%), *TERTp* hotspot mutations (n=4, 17%) and *DMD* deletions (n=5, 21%). In contrast, none of the samples harbored a *TRAF7*, *KLF4* or *AKT1* mutation. Compared to pooled data from prior large-scale sequence surveys of meningiomas, which reveals a *TRAF7* mutation rate of 23% (183 of 798 cases), the absence of *TRAF7* mutation in our progressive/higher-grade cohort was highly significant (p=0.0002). Thus, we confirm that *TRAF7* mutations identify a subclass of meningioma with a lower risk of progressive recurrence. In our cohort, *TRAF7* mutations were mutually exclusive with *NF2*, *TERTp* and *DMD* alterations.

Conclusion

TRAF7 mutant meningiomas have a favorable natural history and therefore may require less intensive adjuvant treatment after initial surgical resection. This finding has important implications for clinical trials, as *TRAF7* mutant meningioma patients are not likely to experience progressive disease during follow-up observation.

Meningeome experimentell/*Meningiomas experimental*

V038

Der Einfluss von Advanced Glycation Endproducts auf Meningeomzellen *The effect of advanced glycation endproducts on meningioma cells*

M. Scheer, C. Straus, P. Selke, R. Horstkorte

Universitätsklinikum Halle-Wittenberg, Neurochirurgie, Halle/Saale, Germany

Objective

Meningiomas are the most common tumor in the brain. Like most other tumors, also meningioma prefer anaerobic glycolysis for energy production (Warburg effect). This results in an increased formation of the metabolite methylglyoxal (MGO), which is known to react with aminogroups of proteins thereby forming advanced glycation endproducts (AGEs). In this study, we investigated the influence of AGEs on growth and adhesion. We used two meningioma cell lines, representing the WHO grade I (BEN-MEN-1) or the WHO grade III (IOMM-Lee). We cultured both cell line in the absence or presence of MGO.

Methods

Fig.1: Meningioma cell lines (BEN-MEN-1 [A,C] and IOMM-Lee [B,D]) were incubated for 24 h with different concentrations of MGO in low serum containing medium (1 % FCS). The images in Fig. 1 A and B were taken with brightfield microscopy. Scale bar correspond to 100 μ m. Proteins were isolated and glycation were detected by western blot using a monoclonal CML (Carboxymethyl-Lysin)-26 antibody. Representative blots from at least 3 independent experiments are shown (Fig 1 C and D).

Fig.2: The adhesion of both meningioma cell lines was measured by Real Time Cell Analyzer (RTCA). The E-Plates were coated with 10 μ g/ml of fibronectin (FN; A) or collagen IV (CollIV; B) for 1 h. The matrix was treated for 24 h with 0.3 mM MGO. After washing with 1x PBS, plates were blocked with 0.5 % BSA for 1 h. Then, cells were seeded in a concentration of 50000 cells/ml in a total volume of 100 μ l of low serum medium (1% FCS) and treated with 0.3 mM MGO. Data in Fig.2 A and B represents average mean \pm SD of 4 independent experiments.

Results

Treatment of cells with MGO has no effect on cell viability in low concentrations in both cell lines. However, at higher concentrations, MGO is cytotoxic in both cell lines. Furthermore, the Western blot analysis reveals a concentration-dependent formation of AGEs, which could be detected with the antibody CML-26. In the analysis of adhesion, differences were found on the different media, depending on the cell line. A change of adhesion by glycation with a low concentration of MGO could not be observed.

Conclusion

These first results indicate that MGO has an influence on the growth, but there is no effect of 0.3 mM MGO on the adhesion of both meningioma cell lines. The WHO Grade I cells have a stronger adhesion to the matrix compared with the WHO Grade III cells. Additionally, the cells have a different adhesion to fibronectin compared with collagen IV.

Fig 1

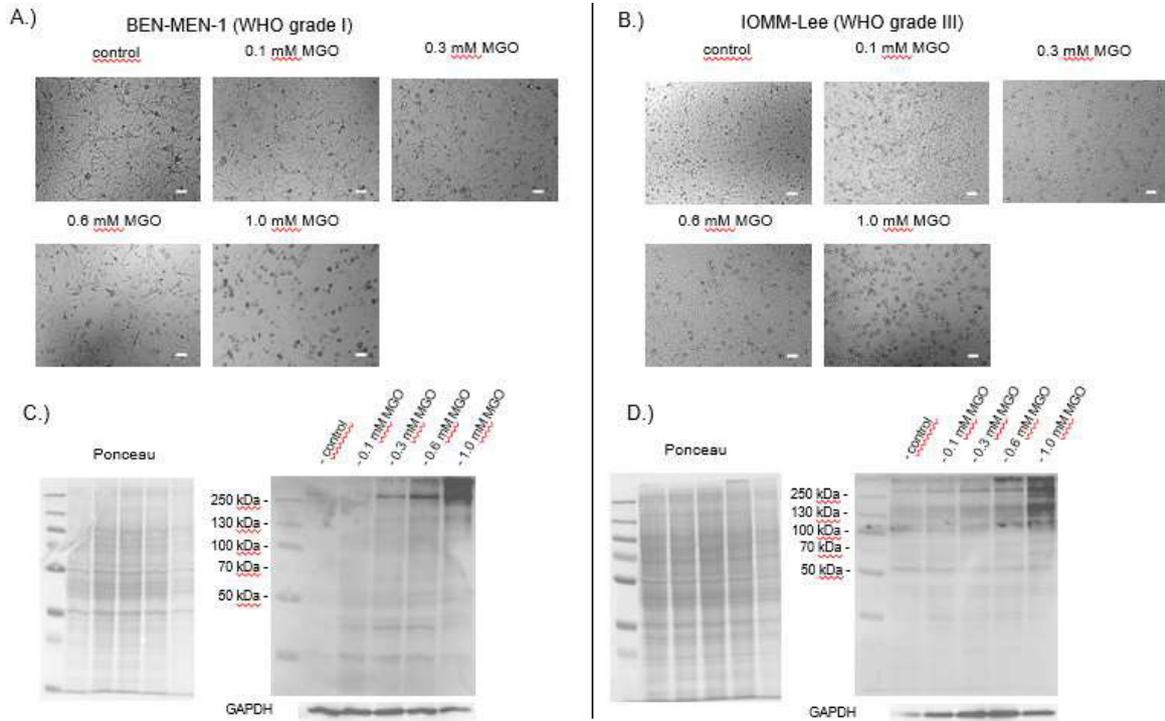
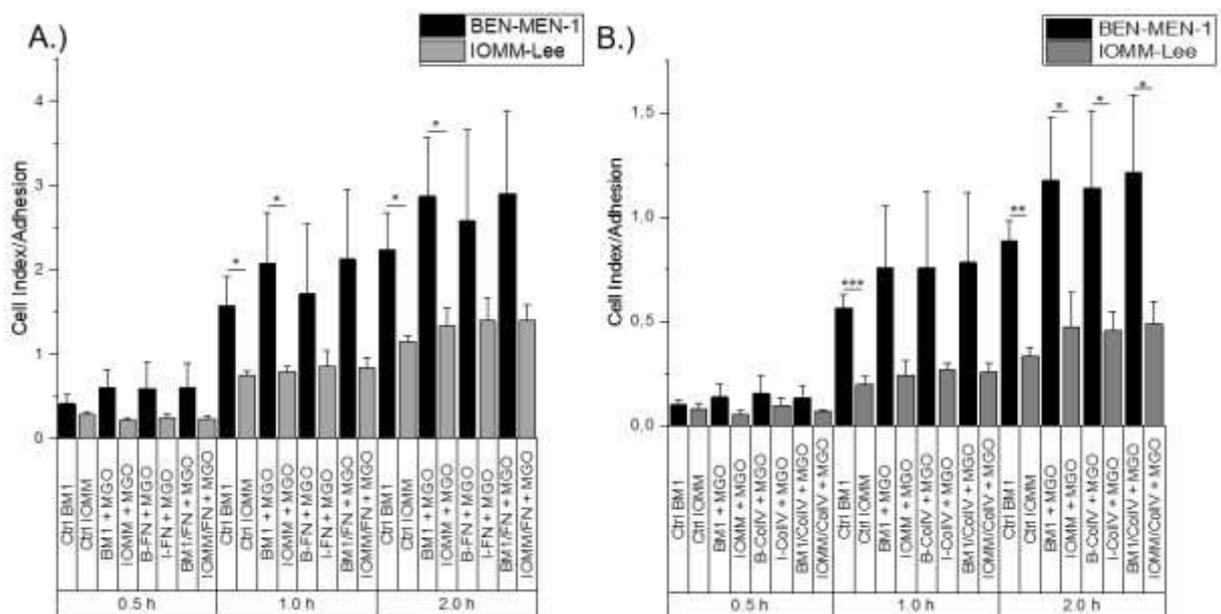


Fig 2



Meningeome experimentell/*Meningiomas experimental*

V039

Die prognostische Wertigkeit der H3K27 Trimethylierung in Meningeomen *The prognostic role of H3K27 trimethylation in meningioma*

F. Behling¹, C. K. Fodi¹, I. Gepfner-Tuma^{1,2}, K. Machetanz¹, K. Kaltenbacher², M. Renovanz¹, M. Skardelly¹, M. Tatagiba¹, G. Tabatabai^{1,2}, J. Schittenhelm³

¹Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

²Universitätsklinikum Tübingen, Klinik für Neurologie, Tübingen, Germany

³Universitätsklinikum Tübingen, Institut für Neuropathologie, Tübingen, Germany

Objective

The prognostic role of the histone methylation H3K27 in meningioma has been described recently and is currently examined in several cancer types. The methylation can be detected immunohistochemically and is potentially integrable into daily neuropathology practice to provide prognostic information after meningioma resection. The objective of this study was to assess the prognostic value of H3K27 histone methylation in a large cohort of meningiomas to provide more evidence and support for its clinical application.

Methods

In a retrospective analysis tumor specimen of 429 patients with meningiomas who underwent surgery from April 2011 to December 2015 in our department were assessed for H3K27me3 immunohistochemically. Further clinical data (WHO classification, brain invasion, Simpson grade, age, gender, progression free survival) were derived from medical records. Univariate analysis was done with Fisher's exact and Log-Rank test and multivariate analysis via linear regression.

Results

A total of 429 meningiomas were analyzed with a female to male ratio of 3.2, mean age at diagnosis of 59 years (range 15.84 – 89.95) and mean follow-up at 31 months (range 1.76 – 95.72). Univariate analysis showed a significant negative prognostic impact of male gender ($p=0.0236$), WHO grade II/III ($p=0.0057$), Simpson grade >2 ($p<0.0001$) and H3K27me3 loss ($p=0.0007$). In the multivariate analysis only Simpson grade and H3K27me3 status remained independent prognostic factors for meningioma recurrence ($p = 0.0001$ and 0.0084 , respectively). H3K27 trimethylation loss was more common in male patients in this cohort explaining the loss of prognostic impact of gender after inclusion of the histone methylation status in the multivariate analysis.

Conclusion

Loss of the trimethylation of H3K27 is an independent prognostic factor together with Simpson grade in our cohort and in line with prior studies. The growing evidence suggests the integration of H3K7me3 immunohistochemistry into neuropathology practice for meningiomas.

Meningeome experimentell/*Meningiomas experimental*

V040

In vivo Messung der elektrischen Leitfähigkeit von intrakraniellm Gewebe und von Hirntumoren
In vivo measurement of electrical resistivity of intracranial tissues and brain tumours

T. Abboud, A. Nazareus, D. Mielke, V. Rohde

Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Reported brain tissue resistivity to date is usually obtained from sample investigation in vitro. There is also a lack of information regarding conductivity of brain tumors. This is a pilot study to investigate the feasibility of a new technique to perform an in-vivo measurement of electrical resistivity of intracranial tissue and brain tumors.

Methods

Patients who were admitted at our institute between November 2017 and August 2019 for operative treatment of brain tumor were screened for the study. Intraoperative measurement of tissue resistivity was performed using a bipolar probe with a defined distance between the two poles applying an alternating current of 0.7 μ A with a frequency of 140 Hz. The measurement was conducted on the dura, cortex and the exposed solid tumor tissue subsequently as well as white matter when possible. Impedance values were expressed in ohm (Ω). Resistivity values expressed in Ω .m were extrapolated through calibration of the measurement device and calculation of the geometrical factor of the measurement probe. Resistivity values were compared between different intracranial tissues and brain tumors.

Results

Eighty-one patients were included in the study. Median of resistivity values of the dura was 15.9 Ω .m (5.51-34.6), brain cortex 10.01 Ω .m (3.78-23.17), white matter 12.75 Ω .m (11.2-15.14), peritumoral edema 8.39 Ω .m (6.7-10.08) and tumor 5.01 Ω .m (1.64-10.64). Values of dura were the highest followed by white matter, cortex, peritumoral edema and tumor, $p < 0.001$. Mean of resistivity values of WHO grade II tumors was 6.75 ± 2.12 Ω .m, WHO grade III tumors 6.76 ± 1.42 Ω .m, WHO grade IV tumors 4.44 ± 1.41 Ω .m and metastases 4.99 ± 1.57 Ω .m. The measurement made at different three points within the tumors showed significant differences, $p < 0.05$. Resistivity values of metastases were similar to those of glioblastoma, $p = 0.199$. Values of glioblastoma were higher than those of anaplastic and low grade glioma, $p < 0.001$, while the difference between anaplastic and low grade gliomas was not significant, $P = 0.993$.

Conclusion

The new technique enables in-vivo measurement of electrical resistivity of brain tissue and brain tumors with reproducible results and without damaging brain tissue. First results showed significant differences in tissue resistivity between brain tumors and white matter as well as between different subtypes of brain tumors. Further studies will be necessary to investigate the clinical application of the new technique.

Degenerative Wirbelsäulenerkrankungen/*Degenerative spine diseases*

V041

Der sagittale Profiltyp beeinflusst das klinische Resultat von Patienten mit lumbaler Spinalkanalstenose, die eine mikrochirurgische Dekompression erhalten haben – ein Verlauf über 5 Jahre

The sagittal spinal profile type influences the clinical outcome in patients with lumbar spinal stenosis after microsurgical decompression – a prospective five-year follow-up

S. H. Bayerl, M. Dinkelbach, F. Pöhlmann, T. Finger¹, V. Prinz, P. Vajkoczy

Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

Objective

30-40% of patients with symptomatic lumbar spinal stenosis do not benefit from microsurgical decompression. A possible cause might be the anatomical precondition and the spinal alignment of these patients. Recently we presented in a prospective five-year follow-up that the preoperative sagittal balance is not the critical factor concerning patients' outcome. However, we already know that the Sagittal Profile Type defined by Roussouly influences the 1-year outcome scores after microsurgery. Now we were able to analyse the influence of the sagittal profile type (SPT) on surgical results in a long-term prospective manner.

Methods

Prospective collected five-year follow-up data of 72 patients with lumbar spinal stenosis, who received decompressive surgery, were analysed. Patients were divided into 4 groups according to their SPT. Outcome scores (Numeric Pain Rating Scales for leg and back pain, walking distance, Oswestry Disability Index, Roland and Morris Disability Questionnaire, Odom's criteria and the SF-36 score) were collected and changes of radiographic parameters were analysed using full spine lateral radiographs.

Results

All patients showed a significant benefit of leg pain and claudication pain after microsurgical decompression. However, Patients with SPT1 did not significantly benefit from surgical decompression concerning back pain scores and back pain associated disability. Their results were significantly worse compared to the groups with other SPTs (DNRSback SPT1= -1,4; DNRSback SPT2= -3,0; DNRSback SPT3= -3,4; DNRSback SPT4= -4,3; DODI SPT1= -14; DODI SPT2= -24; DODI SPT3= -27; DODI SPT4= -29). The success rate (Odom's criteria) of the SPT1 group was less than 50% compared to 70-80% in all other groups.

Conclusion

The SPT1 with a small pelvic incidence combined with a short lordosis and long kyphosis results in a high load on dorsal lumbar structures. After microsurgical decompression addressing these structures back pain release is not satisfying. Patients are increasingly restricted in their everyday lives over the long-term. After his results we should reconsider whether there might be alternative treatment options for patients with spinal stenosis and SPT1.

Degenerative Wirbelsäulenerkrankungen/*Degenerative spine diseases*

V042

Akutoperation bei symptomatischem lumbalen Bandscheibenvorfall mit Parese – Notwendig oder übertrieben?

Emergency surgery in symptomatic lumbar disc herniation with acute motor deficits – Overkill therapy or appropriate treatment?

O. Petr, N. Kögl, K. Brawanski, C. Preuß Hernández, M. Dostal, C. Thomé

Medizinische Universität Innsbruck, Abteilung für Neurochirurgie, Innsbruck, Austria

Objective

Patients with lumbar disc herniation (LDH) undergo disc surgery in case of persisting pain or neurologic deficits. Recently published literature suggests early surgical nerve decompression in case of moderate or severe motor deficits. In cauda equina syndrome urgent surgery within 48 hours has been advocated.

The aim of this high-volume single-centre analysis was to assess the role of early surgical intervention in patients with acute LDH associated paresis in order to achieve favourable long-term outcome.

Methods

Three hundred and thirty patients who underwent microscopic disc surgery between 01/2013 and 12/2015 were included. All patients presented with a motor deficit (MRC 0-4) at the time of admission. Patient demographics, neurologic deficits, duration of motor deficit, treatment characteristics, and short-term outcome measurements were collected retrospectively. Long-term follow-up was performed prospectively to assess the motor recovery over time. Patients were subdivided into groups according to the severity of the paresis (MRC $\leq 2/5$ vs. MRC 3/5 vs. MRC 4/5). Groups were retrospectively analysed regarding the duration and degree of the neurologic deficits.

Results

Patients with moderate and/or severe paresis (MRC $\leq 3/5$) benefit from very early surgical intervention within 48 hours as they showed significantly higher complete recovery rates at long-term (5years-) follow-up (94.8% vs. 37.3%; $p < 0.001$). The recovery rate in patients with LDH associated mild motor deficits (MRC 4/5) also decreased significantly (97% vs. 72.2%) if surgery was delayed (>7 days) ($p = 0.005$). Overall, 95.2% of all patients treated within a 48hour period showed full-strength (MRC 5/5) during manual testing at last follow-up compared to only 26.5% if treated after 7 days ($p < 0.001$).

Conclusion

Immediate surgery should be offered to patients with severe and moderate motor impairment to increase the likelihood of long-term neurological recovery. Early surgical intervention shows better long-term outcome also in patients with mild paresis and must be considered in particular cases.

Degenerative Wirbelsäulenerkrankungen/*Degenerative spine diseases*

V043

Die endoskopische Dekompression bei unilateraler monosegmentaler *Rezessus lateralis* Stenose – Ist die Dekompression und partielle Diskektomie der alleiniger Dekompression überlegen? – ein Bericht einer konsekutiven Serie von 66 Patienten

Endoscopic surgery of monosegmental unilateral lumbar recess stenosis – Is decompression and partial discectomy advantageous over decompression alone? – a report of 66 consecutive patients

B. Burkhardt, J. Oertel

Universität des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

Objective

Lumbar lateral recess stenosis (LRS) typically results in radiculopathy. Yet, it remains uncertain if there is a difference in clinical outcome for decompression alone (DA) and decompression with partial discectomy (DPD) in endoscopic procedures.

Methods

Sixty-six consecutive patients who underwent endoscopic decompression for LRS were identified from a prospectively collected database. Preoperative MRI and endoscopic video were analysed with special focus on the technique of nerve root decompression. DPD was performed once DA and dissection of adhesive epidural tissue was not sufficient to completely mobilize the dura and the exiting nerve root. Clinical outcome was assessed via a personal examination, a standardized questionnaire including the Oswestry Disability Index (ODI), and the modified MacNab criteria to assess clinical success.

Results

DA was performed in 19 (28.8%) patients and DPD in 47 patients (71.2%). The mean follow-up was 44.0 months (range: 3-82 months) at which 60 patients attended (90.1%). Fifty-six patients reported to be free of leg pain (93.3%), full muscle strength was found in 52 patients (86.7%), and in fifty patients no sensory disturbance was noted (83.3%). The mean ODI was 16% (range: 0%-60%). Clinical success was noted in 52 patients (86.6%). Clinical success rate was significantly higher in patients treated with DPD compared to DA ($p=0.04$). The reoperation rate at the index segment was 10.0%. There were no differences between DA and DPD with respect to ODI and the rate of reoperation ($p=0.686$, $p=0.897$).

Conclusion

Endoscopic DA and DPD of LRS offers a high rate of clinical success and relief of radicular pain. DPD had a significantly higher success rate compared to DA. Repeated procedure at the index segment was performed in 10.0%. There was no significant difference for the rate of reoperation and ODI for both techniques.

Degenerative Wirbelsäulenerkrankungen/*Degenerative spine diseases*

V044

Identifikation von Mitarbeitern, welche eine Wirbelsäulenerkrankung entwickeln können – Untersuchung von >20.000 Mitarbeitern

Identifying healthy individuals at risk for chronic spinal disorders-prevalence of spinal disorders among >20,000 employees

S. O. Eicker¹, T. Krätzig¹, H. Heigel², M. Mohme¹, M. Dreimann³, K. C. Mende¹

¹Universitätsklinikum Hamburg-Eppendorf, Neurochirurgie, Hamburg, Germany

²Heigel GmbH, Hanstedt, Germany

³Universitätsklinikum Hamburg-Eppendorf, Unfallchirurgie, Hamburg, Germany

Objective

Back pain is a frequent and often multifactorial conditioned cause of health-related absence of employees. However, little information is available on prevalence of spinal disorders among these persons of different branches.

Methods

Data of >20.000 employed persons were assessed with whole-body examinations and questionnaires by experienced spine surgeons during company-based back screenings conducted in 15 different branches from retail trade to large industry with different physical and mental stress.

Results

In total 27492 employed persons were assessed. 41.5% female (N=11306). Most worked in a sitting position 74.8% (N=20557) compared to 7.8% in a mostly standing position (N=2138). 17.4% in varying positions (N=4797). Light carrying loads <10kg were reported for 19.5% (N=5373) and in 9.6% regular loads of >20kg (N=2628), 70.9% were not working in a physical manner (N=19491). 77.1% were working at a computer workstation (N=21199). 8.3% (N=2285) worked double shifts, 3.2% (N=885) triple shifts and 15.8% (N=4337) worked "other" shift systems; 74.4% did not work in a shift system (N=20459). Lower back pain was reported "permanently" in 4.3% (N=1185), "frequently" in 25.8% (N=7103), "rarely" in 35.6% (N=9729) and never in 17.4% (N=4783), data was missing for 16.8% N=4629. Neck pain was reported "permanently" in 3.3% (N=894), "frequently" in 20.0% (N=5485), "rarely" in 20.6% (N=5674) and never in 30.6% (N=8421), data was missing in 25.5% (N=7018). People working at a computer workstation were asymptomatic for neck pain in 39.9% compared to those with different work models in 48.2% (p<0.001). Comparable results were seen for work in a sitting position 39.2% versus 47.0% (p<0.001). 40.4% of workers without physical moderate or heavy workload were asymptomatic for neck pain compared to 43.0% of those with physical moderate or heavy workload (p<0.001). If the physician diagnosed a stress disorder there was no elevation in the prevalence of back or neck pain, neither if a depressive condition was diagnosed. Spearman Correlation between BMI and prevalence of back and neck pain did not show strong correlations (Rho < 0.1; p<0.001).

Conclusion

Back pain is a frequently detected condition in employees of different branches. Work in a sitting position / at a computer presented lower rates of asymptomatic workers for neck and back pain. Psychological stress or depression were not correlated with back or neck pain, neither was the BMI.

Degenerative Wirbelsäulenerkrankungen/*Degenerative spine diseases*

V045

Instrumentierung der lumbosakralen Wirbelsäule mittels Sakral-Alar-Ilium-Technik reduziert Schraubenlockerung bei Verbesserung von glutealem Schmerz

Instrumentation of the lumbosacral spine by the sacral-alar-iliac technique can reduce screw loosening whilst improving gluteal pain

N. Sollmann¹, S. Ille², B. Meyer², S. Krieg²

¹Klinikum rechts der Isar München, Abteilung für Diagnostische und Interventionelle Neuroradiologie, München, Germany

²Technische Universität München, Neurochirurgische Klinik und Poliklinik, München, Germany

Objective

Instrumentation of the lumbosacral spine continues to be a challenging area in spine surgery, which is particularly due to complex local anatomy, unique biochemical force distributions, and comparatively poor sacral bone quality. Concepts for construct improvement are therefore welcomed. This study aims to investigate differences in outcome between patients treated with S2-alar-iliac (S2AI), S2-alar (S2A), and iliac (I) instrumentation as the most caudal level.

Methods

Sixty patients underwent stabilization by one of the three techniques between 01/2012 and 06/2017 (S2AI: 18 patients, 50% females, 72.1 ± 7.4 years; S2A: 20 patients, 35% females, 69.8 ± 8.6 years; I: 22 patients, 41% females, 69.5 ± 9.0 years). Outcome (screw loosening and gluteal pain due to sacroiliac joint [SIJ] pain) was compared between the three groups considering preoperative, 3-months follow-up (FU), and maximum FU examinations. Bone mineral density (BMD) was opportunistically assessed in preoperative imaging by computed tomography (CT).

Results

All patients completed 3-months FU, maximum FU time was 2.3 ± 0.9 (S2AI), 3.0 ± 1.7 (S2A), and 2.4 ± 1.6 (I) years ($p = 0.38$). A median of 5 segments (S2AI, S2A) and 3 segments (I) were operated on ($p = 0.26$), extending to S2 or the os ilium, respectively. BMD did not significantly differ between the groups ($p = 0.66$), cages were more frequently implanted in patients of the S2A group ($p = 0.04$). Screw loosening of sacral or iliac screws was more common in patients of the S2A and I when compared to the S2AI group (S2AI: 16.7%, S2A: 55.0%, I: 27.3% of patients; $p = 0.03$). Furthermore, SIJ pain was more often improved in the S2AI group for 3-months FU, but also for maximum FU (S2AI: 61.1%, S2A: 25.0%, I: 22.7% of patients showing improvement; $p = 0.020$).

Conclusion

Instrumentation by S2AI might be considered superior to S2A and I stabilizations by showing lower incidences of screw loosening of the most caudal level and enhanced alleviation of SIJ pain. Future studies enrolling larger series are necessary to confirm these initial results.

Degenerative Wirbelsäulenerkrankungen/*Degenerative spine diseases*

V046

Strahlenbelastung von Chirurg und Patient bei der Kyphoplastie – dosimetrische Ergebnisse nach 40 Kyphoplastien

Radiation exposure of surgeon and patient in kyphoplasty – dosemetric results in 40 kyphoplasties

J. H. Klingler, C. Scholz, F. Volz, R. Roelz, U. Hubbe, Y. Naseri

Universitätsklinikum Freiburg, Freiburg, Germany

Objective

Dosimetric data on intraoperative radiation exposure to surgeon and patient during cement augmentation is scarce. Often only fluoroscopy times with values up to 27.7 min (vertebroplasty) are reported. Radiation-protective working methods are becoming more and more important as the annual dose limits become increasingly strict. The aim of the study is the dosimetric assessment of radiation exposure during kyphoplasty using a radiation-protective surgical technique

Methods

The prospective study examines the intraoperative radiation exposure of surgeon and patient during kyphoplasty in thoracolumbar vertebral body fractures. Using film, eye lens and ring dosimeters, the radiation exposure of surgeon and patient is measured at different locations. The applied radiation-protective surgical technique according to the ALARA (as low as reasonably achievable) principle includes the use of radiation protection equipment and beam collimation as well as keeping distance to the radiation source and avoiding continuous fluoroscopy. Dose values are reported under consideration of lower detection limits of dosimeters.

Results

35 patients (BMI 25.9 ± 5.2 kg/m²) underwent kyphoplasty in 40 thoracolumbar vertebral bodies (19 A1 fractures, 16 A2 fractures and 5 A3 fractures). T12 (n=8) was most frequently affected, followed by L4 (n=7) and L1 (n=6). Table 1 shows the dosimetric results of the radiation exposure of surgeon and patient.

The fluoroscopy time per kyphoplasty was 42.7 ± 17.8 sec with 32 ± 13 intraoperative single radiographs and a dose area product of 105 ± 101 cGy/cm². The duration of the operation was 35.1 ± 9.8 min (single-level procedures only). On average, 2.6 ± 0.8 ml of bone cement per vertebral body were placed on each side. Low-grade prevertebral cement leakage with no clinical relevance was observed in four patients. All patients reported reduced back pain at the first postoperative day (VAS 2.4 ± 1.6 versus 6.7 ± 1.5 preoperatively; $P < 0.0001$, Wilcoxon matched-pairs signed rank test).

Conclusion

The radiation exposure of surgeon and patient in kyphoplasty can be significantly reduced compared to previous data by using a radiation-protective surgical technique. Applying this technique, the current annual limits for occupational radiation exposure are not exceeded. Nevertheless, all radiation protection measures should be applied in an optimized manner, since there is no threshold dose below which ionizing radiation poses no risk.

Fig 1

Location	Patient			Surgeon				
	Thyroid	Chest	Gonad	Eye lenses	Thyroid	Chest		Finger
Lead protection	no	no	no	no	no	no	yes	no
Radiation exposure [mSv]	0.082 ± 0.096	0.290 ± 0.388	0.161 ± 0.225	0.031 ± 0.004	0.051 ± 0.042	0.046 ± 0.012	< 0.044	0.036 ± 0.035

Table 1 showing mean radiation exposures (\pm standard deviation) of patient and surgeon at various locations in consideration of lower detection limits of doseimeters (0.030 mSv for eye lens and finger doseimeters and 0.044 mSv for film doseimeters, respectively).

Degenerative Wirbelsäulenerkrankungen/*Degenerative spine diseases*

V047

Operative Therapie rezidivierender lumbaler Spinalstenosen – eine retrospektive Ergebnisanalyse, Komplikationen und Risikofaktoren

Surgical treatment of recurrent lumbar spinal stenosis – a retrospective analysis of results, complications and risk factors

T. Kratzsch, O. L. Bieschke, P. Vajkoczy, S. H. Bayerl

Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

Objective

Microsurgical decompression (MD) of lumbar spinal stenosis (LSS) is a high frequent spinal surgery. However, a certain amount of recurrences occur. We analysed therapy options as well as characteristics in spine imaging of patients with recurrent LSS.

Methods

In this retrospective monocentric study, we analysed 899 patients after MD of LSS within a 5-year period. Recurrent disease of the index segment was defined as recurrent narrowing of the central spinal canal, lateral recess or neural foramen, or new segmental instability, with new symptoms of claudication or sciatica. Ethical approval was obtained.

Results

78 patients with recurrent LSS were identified (24% female, 76% male, average age 68 ± 10 years). A microsurgical decompression was performed in patients with new central spinal canal or recess stenosis without signs of instability (52 patients, 67%), and a spinal fusion was performed after occurrence of instability in dynamic X-ray radiographs, progressive spondylolisthesis, or neuroforaminal stenosis (26 patients, 33%). Average time between the first decompression and the operation on the recurrent disease was 3.7 ± 5.7 and 1.7 ± 1.1 years. In the instrumentation group, the rate of initial static spondylolisthesis was higher (23%) compared to the decompression only group (6%). In the instrumentation group, 19% were preoperatively diagnosed with new instability in functional radiographs and 58% had lateral recess or foraminal stenosis, compared to 0% instability in dynamic X-ray radiographs and 60% central spinal canal stenosis in the decompression group. In the stabilisation group, facet joints were always involved in the recurrent disease, compared to 60% in the decompression group. The percentage of initial Pfirrmann grade 4 - disc degeneration was 68% in the instrumentation group, compared to 51% in the decompression group. In the decompression group, 9 patients (17%) had to undergo a consecutive fixation operation (after 0.8 ± 1.0 years), due to new instability, progressive spondylolisthesis or foraminal stenosis.

Conclusion

Surgery of recurrent disease of lumbar spinal canal stenosis consisted either of MD or additional fusion. We characterized typical imaging characteristics in both treatment groups. The rate of spinal fusion after MD of the recurrent disease was high within 1 year after Redo-MD. Therefore surgeons should be very critical with their indication to perform a Redo-MD without instrumentation.

Degenerative Wirbelsäulenerkrankungen/*Degenerative spine diseases*

V048

Operative Therapie der degenerativen thorakalen Spinalkanalstenose – postoperativer Langzeitverlauf und Lebensqualität nach dorsaler Dekompression über einen uni- oder bilateralen Zugang

Surgery of degenerative thoracic spinal stenosis – postoperative long-term outcome with quality-of-life after posterior decompression via a unilateral or bilateral approach

S. Siller, L.Pannenbaecker, J. Tonn, S. Zausinger

Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik, München, Germany

Objective

The incidence of degenerative thoracic spinal stenosis (TSS) as underlying pathology for clinical myelopathy is not precisely known, but low compared to cervical spinal stenosis, and larger case series are only available for the Asian region. We present one of the largest European series of TSS patients to evaluate incidence and clinical outcome after posterior decompression via an unilateral or bilateral approach.

Methods

28 patients who underwent surgical treatment for TSS between 2013 and 2018 in a university neurosurgical clinic were included. We investigated the patients' characteristics, imaging and surgical parameters as well as outcomes and quality-of-life (QOL) after long-term follow-up.

Results

From altogether 645 patients with decompressive surgery due to degenerative spondylotic myelopathy, 28 patients suffered from thoracic spinal stenosis, accounting within 6 years for 4.3% of patients in this population. Mean age was 68.2 years, with a predominance of the female sex (m:f=1:1.3). The most frequent symptoms were spinal ataxia (61%) and sensory changes (46%) with a mean duration of 7.6months. There were 29 levels of stenosis (one patient with 2-level stenosis), mostly resulting from a combined osseous and ligamentous hypertrophy and disc prolapse predominantly located below Th9 (72%); the median Naganawa grade was 3 (i.e. severe cord impingement/deformity). 19 patients with a lateralized compression of the spinal cord underwent bilateral decompression via an unilateral approach (fenestration/hemilaminectomy with "undercutting" procedure) and 9 patients with circular pathology underwent bilateral-approached decompression via laminectomy. No patient required additive stabilization. There were no significant differences of patients' characteristics, intraoperative blood loss, operation time and length of in-patient stay between both surgical groups. Independent on the mode of surgical decompression, the spinal canal was significantly ($p<0.001$) widened (median Naganawa grade: 0, i.e. no stenosis) and back pain ($p=0.04$), myelopathic symptoms (mJOA-Score: $p=0.01$) and QOL (Oswestry-Disability-Index: $p=0.03$; SF-36-MCS: $p=0.01$) were significantly improved at long-term follow-up (mean: 35.1months).

Conclusion

Non-tumorous clinical myelopathy is caused in about 4% of the patients by spondylotic compression of the spinal cord at predominantly the lower thoracic spine and can be effectively treated by surgical decompression via both a unilateral or bilateral approach.

Degenerative Wirbelsäulenerkrankungen/*Degenerative spine diseases*

V049

Lebensqualität nach mikrochirurgischer Dekompression bei Patienten mit lumbaler Spinalkanalstenose – eine Langzeitstudie

Quality of life after microsurgical decompression in lumbar spinal canal stenosis – a long-term follow-up study

B. H. V. Nguyen, M. Bruder, G. Marquardt, V. Seifert, B. Behmanesh, M. Setzer

Universitätsklinikum Frankfurt am Main, Klinik für Neurochirurgie, Frankfurt am Main, Germany

Objective

The aim of this prospective study was to evaluate the long-term quality of life of patients after microsurgical decompression for lumbar spinal stenosis (LSS).

Methods

272 patients with LSS presenting with neurogenic claudication, back and leg pain and neurological symptoms underwent microsurgical decompression. Demographic and clinical characteristics were evaluated. Long-term quality of life was assessed using the 36-Item Short Form Health Survey (SF-36) scales and summary scores with a follow-up of 3-8 years.

Results

Patients with higher BMI, longer operative time and longer hospitalization had significantly worse physical health component summary scores (PCS) whereas women showed significantly worse mental health component summary scores than men. Those preoperatively showing a spondylolisthesis °I had a reoperation rate of 2.4%, compared to 1.3% in those without . Furthermore, women had higher rates of spondylolisthesis and lower mental health summary scores than men.

Conclusion

Female gender is significantly associated with the presence of spondylolisthesis and worse mental health summary scores, whereas higher BMI is significantly associated with worse physical health in long-term quality of life. Overall patients of this study achieved good and satisfactory PCS, comparable to mean PCS scores of similar populations.

Zerebrale Vasospasmen/*Cerebral vasospasms*

V050

Komplikationsrate von Rescue Therapiestrategien bei verzögerter zerebraler Ischämie nach aneurysmatischer Subarachnoidalblutung

Complication rates of rescue therapies for delayed cerebral ischemia after aneurysmal subarachnoid haemorrhage

M. Neyazi¹, A. Abdulazim¹, K. Hackenberg¹, E. Neumaier-Probst², C. Groden², D. Hänggi¹, N. Etminan¹

¹Universitätsklinikum Mannheim, Klinik für Neurochirurgie, Mannheim, Germany

²Universitätsklinikum Mannheim, Abteilung für Neuroradiologie, Mannheim, Germany

Objective

The appropriate management of delayed cerebral ischemia (DCI) after aneurysmal subarachnoid haemorrhage (SAH) remains controversial, especially in view of increasing data on extracranial complications of DCI treatment. We recently described the efficacy of a standardized protocol for detection and treatment of DCI. However, the risk benefit ratio of such standardized protocols, especially with respect to extracranial complications remains uncertain. Here, we investigated specific complications of rescue therapy for DCI after SAH.

Methods

A prospective cohort (I) of 158 consecutive SAH patients admitted to our department between January 2016 and July 2018 was managed according to a standardized, escalating treatment protocol comprising serial perfusion-CT imaging, induced hypertension and intra-arterial vasodilator therapy in high-grade SAH patients with refractory DCI. This group was compared to a historical cohort II (144 patients, from January 2012 to August 2014) where continuous intra-arterial nimodipine catheters were facilitated in patients with any angiographic vasospasm. The two cohorts were compared with respect to treatment-associated extracranial complication rates, including pulmonary and cardiac dysfunction, gastrointestinal ischemia, renal failure as well as thromboembolic complications. Further, the rates of DCI-treatment associated complications were evaluated.

Results

Despite generally comparable baseline characteristics, cohort I had a higher proportion of Fisher grade III/IV SAH, compared to cohort II (79.7% vs. 59.4%; $p < 0.01$) and thereby a higher risk for DCI. The overall incidence of clinical DCI in cohort I was significantly higher compared to cohort II (44.3% vs. 31.5%; $p < 0.05$) whereas the incidence of angiographic vasospasm was comparable (42.4% vs. 48.3%). In cohort I, 98.4% of patients with confirmed DCI received induced hypertension, 46.8% intraarterial nimodipine bolus application, and 11.1% a continuous nimodipine catheter compared to 6.7%, 4.4%, and 84.4% in cohort II. The overall treatment associated complication rates between the two cohorts was comparable (32.8% vs. 52.1%, $p = 0.076$). However, DCI-treatment associated complication rates were significantly lower in cohort I (4.1% vs. 60.7%, $p < 0.01$).

Conclusion

Our data highlight that the DCI-treatment associated complication rates may be significantly reduced with the use of standardized protocols for escalating rescue therapy, whereas the incidence of extracranial complications seems comparable.

Fig 1

General treatment-associated complications		
	Cohort I (n=39)	Cohort II (n=49)
Pneumonia	10 (25.6%)	19 (21.6%)
Cardiac dysfunction	5 (12.8%)	1 (2.0%)
GI-Ischemia	5 (12.8%)	13 (26.5%)
Renal failure	1 (2.6%)	-
DVT	1 (2.6%)	-
Pulmonary embolism	1(2.6%)	-
Systemic Infection	11(28.2%)	9 (18.4%)
Meningitis	5(12.8%)	8 (16.3%)

Fig 2

DCI treatment-associated complications

	Cohort I (n=5)	Cohort II (n=17)
Cardiac dysfunction	2 (40%)	-
GI-Ischemia	4 (80%)	8 (47.1%)
Vessel dissection	-	1 (5.9%)
Cerebral thrombembolism	2 (40%)	5 (29.4%)
Catheter-associated complications	1 (20%)	4 (23.5%)

Zerebrale Vasospasmen/*Cerebral vasospasms*

V051

Einfluss der Behandlungsmodalität intrakranieller Aneurysmen auf das Risiko von verzögerter zerebraler Ischämie nach aneurysmatischer Subarachnoidalblutung

Effect of intracranial aneurysm repair treatment modality on the risk of delayed cerebral ischemia after aneurysmal subarachnoid haemorrhage

A. Abdulazim¹, K. Hackenberg¹, R. L. Macdonald^{2,3}, D. Hänggi¹, N. Etminan¹

¹Universitätsklinikum Mannheim, Klinik für Neurochirurgie, Mannheim, Germany

²University of Toronto, Division of Neurosurgery, Toronto, Canada

³University of California San Francisco, Department of Neurosurgery, Fresno, CA, United States

Objective

In the management of patients with aneurysmal subarachnoid haemorrhage, surgical intracranial aneurysm (IA) repair has been previously reported as a detrimental determinant for the risk of delayed cerebral ischemia (DCI). To further elucidate this, we compared data of a prospective-randomized Phase III trial (NEWTON-II) with our institutional aSAH cohort with respect to the incidence of DCI and functional Outcome in relation to treatment modality for IA.

Methods

The NEWTON-II study cohort included 285 aSAH patients with WFNS grades II-IV. This cohort was compared to an aSAH cohort including 81 aSAH patients with WFNS grades II-IV that were treated at our institution between January 2016 and July 2018. Exploratory statistics and logistic regression analyses were performed to investigate whether IA modality is associated with the risk of DCI after aSAH.

Results

The two cohorts were comparable with respect to age, sex, and WFNS grade distribution though the proportion of Fisher grade III/IV SAH was higher in the NEWTON-II study cohort (94.0% vs. 86.4%, $p=0.02$) (**table 1**). However, the proportion of clipping procedures for IA repair was significantly higher in our institutional aSAH cohort (59.3% vs. 35.4%, OR: 2.65 [1.60-4.39]) and consecutively higher rates of clinical DCI (49.4% vs. 26.7%, OR: 2.68 [1.61-4.62]). However, after adjustment for treatment modality, there was no association of aneurysm repair modality and the risk of DCI as the odds ratio did not differ decisively (aOR: 2.74 [1.63-4.62]). Treatment modality was also not a determinant for DCI risk according to individual WFNS groups in the logistic regression model. Comparing only patients who received clipping in both cohorts still showed a significantly higher odds for DCI in our institutional cohort (50% vs. 31.2% OR: 3.21 [1.72-5.98]). The DCI associated infarction rate was comparable, however functional outcome at 3 months was significantly better in our institutional cohort (OR: 2.89 [1.65-5.09]) (**table 2**).

Conclusion

Our data refutes the previous notion that surgical IA repair is an additional risk factor for DCI and indicate that factors other WFNS grade, Fisher or IA repair modality determine the risk of DCI and the proportion of overall functional outcome.

Fig 1

Patient characteristics			
	UMM (n=81)	NEWTON II (n= 285)	p value
Age (mean)	56.58 ± 11.78y	56.11 ± 10.77y	
Sex (M:F)	22 (27.2%) : 59 (72.8%)	86 (30.2%) : 199 (69.8%)	
WFNS grade			0.73
II	42 (51.9%)	145 (50.1%)	
III	11 (13.6%)	31 (10.9%)	
IV	28 (34.6%)	109 (38.2%)	
Fisher Score			0.02
I-II	11 (13.6%)	17 (6%)	
III - IV	70 (86.4%)	268 (94,0%)	
Treatment modality			<0.01
Clipping	48 (59.3%)	101 (35.4%)	
Coiling	33 (40.7%)	184 (64.6%)	

Fig 2

Outcome			
	UMM (n=81)	NEWTON II (n=285)	p value
Functional Outcome at 3 Months			<0.01
1-5	30 (37.5%)	151 (54.9%)	
6-8	50 (62.5%)	124 (45.1%)	
Clinical DCI			<0.01
Yes	40 (49.4%)	76 (26.7%)	
No	41 (50.6%)	209 (73.3%)	
DCI associated infarction			0.28
Yes	15 (18.5%)	38 (13.3%)	
No	66 (81.5%)	247 (86.7%)	

Zerebrale Vasospasmen/*Cerebral vasospasms*

V052

Verzicht auf induzierte Hypertonie nach SAB reduziert unerwünschte kardiovaskuläre Ereignisse
Withholding induced hypertension after subarachnoid haemorrhage reduces cardiovascular adverse events

M. Bissolo

Universitätsklinikum Freiburg, Neurochirurgie, Freiburg, Germany

Objective

Induced hypertension (iHTN) is the mainstay of therapy for cerebral vasospasm (CVS) after subarachnoid hemorrhage (aSAH). Safety and efficacy of this treatment have been challenged by results from a recent randomized clinical trial (HIMALAIA).

Implementing cisternal blood clearance using stereotactic catheter ventriculostomy (STX-VCS) into clinical practice was associated with a decline of cerebral vasospasm and – consequentially – the use of iHTN. Here, we assess the effects of withholding iHTN in a consecutive and unselected aSAH cohort.

Methods

441 consecutive aSAH patients admitted to our center in a 7-year period (04/2012 – 04/2019) were included in this study. STX-VCS was available in the second half (3.5 year period) and 57 of 215 patients (27%) considered at high risk for delayed cerebral ischemia (DCI) were offered STX-VCS on the basis of individual treatment decisions. Cisternal lavage was administered via STX-VCS using Urokinase or Nimodipine.

Adverse events (AEs) during intensive care therapy were recorded and graded according to the CTCAE terminology by a blinded physician who was not involved in the treatment of the patients. Cerebral vasospasm was recorded by transcranial doppler ultrasonography (TCD). The total daily dose of infusion fluids and norepinephrine were documented

Results

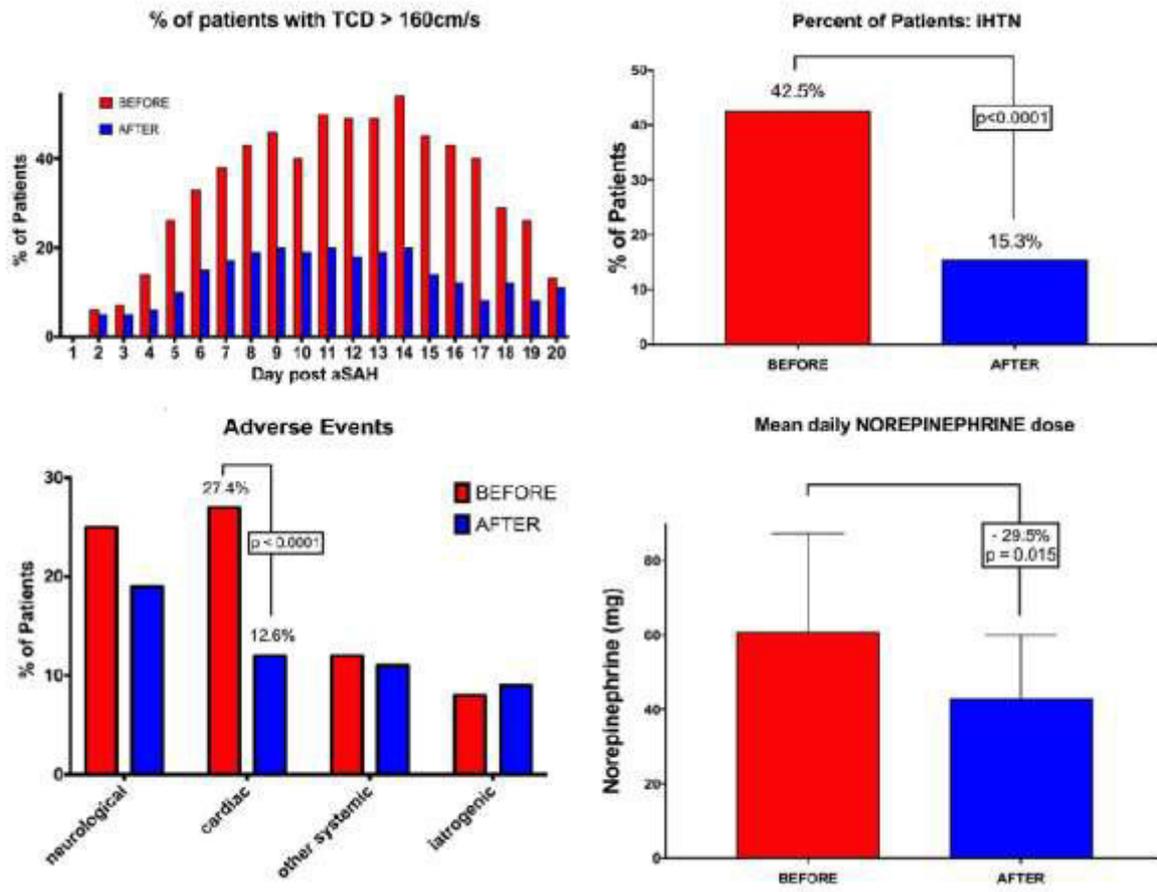
The mean prevalence of CVS (mean flow velocity > 160cm/s) during the first 21 days after aSAH was 34% BEFORE and 14% AFTER implementation of STX-VCS ($p < 0.0001$). Consequentially, iHTN was applied in 96 of 226 (42.5%) patients BEFORE vs. 33 of 215 (15.3%) patients AFTER ($p < 0.0001$). The mean daily volume of fluids applied in the BEFORE cohort was 6063ml vs 4813ml in the AFTER cohort ($p < 0.0001$). The mean daily dose of norepinephrine was 60.8 mg vs. 42.8 mg ($p = 0.015$), respectively.

Cardiovascular Adverse events occurred in 27.4% of patients BEFORE and 12.6% of patients AFTER ($p < 0.0001$). Further adverse events occurred at comparable frequencies in both cohorts.

Conclusion

Implementing STX-VCS was associated with a 50% reduction of CVS. Withholding iHTN as CVS therapy was associated with a sharp decline of cardiovascular adverse events.

Fig 1



Zerebrale Vasospasmen/*Cerebral vasospasms*

V053

Einfluss der endovaskulären Therapie auf das Langzeit-Outcome von Patienten mit aneurysmatischer Subarachnoidalblutung und refraktären Vasospasmus

The impact of endovascular rescue therapies for refractory vasospasm on long-term functional outcome in patients with aneurysmal subarachnoid haemorrhage

D. Mielke, K. Döring, V. Rohde, V. Malinova

Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Cerebral vasospasm (CV) represents one of multiple contributors to delayed cerebral ischemia (DCI) in patients with aneurysmal subarachnoid hemorrhage (aSAH). Especially, the management of CV refractory to medical treatment is a challenging task during the acute treatment of aSAH-patients. Endovascular rescue therapies (ERT) such as medical/mechanical dilation is performed in these patients with a decision-making on an individual base. The effective impact of these treatment options on the functional outcome of aSAH-patients is insufficiently evaluated. The aim of this study was to assess the impact of ERT on long-term functional outcome in aSAH-patients with refractory CV.

Methods

We performed a retrospective analysis of aSAH patients treated between 2008 and 2018. CV was considered refractory if it persisted despite of oral Nimodipine application and induced hypertension. The decision to perform ETR was made on an individual base according to the "tissue at risk" detection in computer tomography perfusion (CTP) and CV in computed tomography angiography (CTA) or digital subtraction angiography (DSA). The functional outcome was assessed according to the modified Rankin scale (mRS) at least 3 months after the ictus, whereas a mRS \leq 3 was considered a good outcome.

Results

A total of 375 patients were included. 321 patients (85.9%) were treated without ERT (group 1) and 54 patients (14.1%) with ERT (group 2). A good aSAH-grade (Hunt&Hess I-III) was found in 60.4% in group 1 compared to 67.1% in group 2. Delayed infarction occurred in 21% in group 1 compared to 40.7% in group 2 (Welch t-test, p=0.0073). A good clinical outcome had 47.6% in group 1 vs 63.63% in group 2 (Welch t-test, p=0.002). The radiation exposure (RE) in patients with ERT was significantly higher compared to the patient group without ERT (Welch t-test, p=0.014).

Conclusion

Although, the rate of delayed infarction was significantly higher in the patient group with ETR, ETR resulted in a significantly better functional outcome compared to the patient group without ETR. Since ERT is associated with RE and other procedure-related complications selection criteria are essential in aSAH patients. A CTP-based identification of "tissue at risk" seems to be a reliable tool for patient selection.

Zerebrale Vasospasmen/*Cerebral vasospasms*

V054

Procalcitonin als Biomarker für DCI nach aneurysmatische Subarachnoidalblutung

Procalcitonin as a biomarker for delayed cerebral ischemia in aneurysmal subarachnoid haemorrhage

M. Veldeman¹, D. Lepore², A. Höllig¹, H. R. Clusmann¹, G. A. Schubert¹, W. Albanna¹

¹Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neurochirurgie, Aachen, Germany

²University Hospital of Liège, Lüttich, Belgium

Objective

Aneurysmal subarachnoid hemorrhage (aSAH) initiates a deleterious cascade activating multiple inflammatory agents contributing to the development of delayed cerebral ischemia (DCI). Procalcitonin (PCT) has gained its credentials in sepsis diagnosis and treatment monitoring. The course of this inflammation marker during DCI and its potential as a biomarker for DCI, however, remains unclear. The goal of this analysis is to characterize the time course of PCT around the occurrence of DCI and to assess its potential as a predictive or confirmative biomarker.

Methods

A prospective series of 169 patients after aSAH were routinely monitored for PCT level as part of an observational trial. Only patients with daily measurements were eventually included (n=132), culminating in a total of 1.848 data points. The time course of levels before and after the development of DCI are plotted after exclusion of patients with SIRS or sepsis. Patients were further dichotomized according to the presence or absence of DCI (DCI, noDCI) and with and without DCI related infarction (DCIinf, noDCIinf).

Results

Baseline levels of PCT were not predictive for eventual DCI development. However, once DCI developed, it induced a spike in PCT levels around day 2 after the first DCI event. In cases without progression into cerebral infarction, PCT values normalized, but peaking again around day 10. In patients developing DCI related infarction, PCT levels steadily increased after the first DCI event reaching a plateau phase around day 14.

Conclusion

PCT is not able to predict DCI but significantly increases with DCI occurrence and secondary deterioration. The value of PCT in treatment monitoring beyond natural disease progression is still unclear. Frequent complications of ICU treatment such as SIRS or sepsis preclude a routine utilization of PCT.

Zerebrale Vasospasmen/*Cerebral vasospasms*

V055

Die kontinuierliche intraarterielle Nimodipin Infusion als Behandlungsoption der verzögerten zerebralen Ischämie nach aneurysmatischer Subarachnoidalblutung

Continuous intraarterial nimodipine infusion as a treatment of delayed cerebral ischemia after aneurysmal subarachnoid haemorrhage

A. Kramer¹, M. Selbach², T. Kerz¹, M. A. Brockmann², C. Brockmann², F. Ringel¹

¹Universitätsmedizin Mainz, Neurochirurgie, Mainz, Germany

²Universitätsmedizin Mainz, Neuroradiologie, Mainz, Germany

Objective

Delayed cerebral ischemia (DCI) is a frequently occurring complication in patients with aneurysmal subarachnoid hemorrhage (aSAH), that may lead to disabling neurological deficits or death despite maximal intensive care therapy. Multiple factors may contribute to DCI with vasospasm of large intracranial vessels being the most widely recognized. Continuous intraarterial nimodipine infusion (CIAN) represents a promising therapeutic option in severe cases of DCI, which are refractory to standard therapy. We report our experience with CIAN in 17 of such cases.

Methods

CIAN was initiated and ended based on an individual interdisciplinary evaluation of the clinical and diagnostic course of the patient using transcranial Doppler, CT angiography (CTA), CT perfusion (CTP) and digital subtraction angiography (DSA). One or two microcatheters were placed into the internal carotid or vertebral artery according to the site and severity of vasospasm. Nimodipine (NDP) was administered continuously in a rate of 0.5 - 2 mg/h. During CIAN, intensive care including ICP/ CPP-measuring was conducted. The therapeutic effect was measured by evaluating the Glasgow Outcome Scale (GOS) at discharge and within 1 year after aSAH and by occurrence of infarctions in subsequent CT/MRI-scans.

Results

In the period of May 2016 to January 2018, 17 patients received CIAN. The median treatment onset of CIAN was 9 (3-13) days; the median duration was 5 (1-13) days. Favorable outcome (GOS 4 or 5) was achieved in 9 patients (53%) at discharge and in 13 patients within 1 year (76%). Follow-up imaging showed minor cerebral infarction in 5 and major infarction in 3 patients. One patient developed a localized cerebral edema as a possible side effect. One patient died due to malignant posthemorrhagic edema. Normalization of CTP-parameters within 2 days was observed in 9/17 patients. The remaining 6 patients showed clinical response and thus did not receive short-term CTP imaging.

Conclusion

CIAN is a feasible, safe and effective therapeutic option for patients with severe therapy-refractory delayed cerebral ischemia. Our results concerning the outcome within one year are in line with previously published retrospective studies. The study is limited by its retrospective character, the lack of a control group and the small number of patients. A prospective randomized clinical trial is needed to confirm the positive retrospective results of this study and previously published studies.

Zerebrale Vasospasmen/*Cerebral vasospasms*

V056

Das Muster angiographischer Vasospasmen und deren Einfluss auf den weiteren klinischen Verlauf von Patienten mit spontaner Subarachnoidalblutung und zerebralen Vasospasmen
Angiographic pattern of cerebral vasospasm and its impact on the clinical course of patients with spontaneous subarachnoid haemorrhage and cerebral vasospasm

C. Ditz¹, J. Leppert¹, A. Neumann², H. Schacht², J. Gliemroth¹, V. M. Tronnier¹, J. Küchler¹

¹Universitätsklinikum Schleswig-Holstein, Neurochirurgie, Lübeck, Germany

²Universitätsklinikum Schleswig-Holstein, Neuroradiologie, Lübeck, Germany

Objective

Cerebral vasospasm (CVS) is a common complication of spontaneous subarachnoid hemorrhage (sSAH) and associated with delayed cerebral ischemia (DCI) and unfavourable outcome. Only poor data exist about the detailed angiographic pattern of CVS and its impact on the further clinical course. This study aimed to analyze detailed characteristics of angiographic CVS, identifying patients with a potential higher risk for an unfavorable clinical course.

Methods

A retrospective single-center study of sSAH patients admitted in a 6-year period. Patients with clinical suspicion of CVS who underwent cerebral angiography for confirmation of CVS were included. Clinical and demographic data as well as outcome parameters were collected. Angiographic characteristics (e.g. distribution and severity of CVS, intra-arterial treatment) were analyzed.

Results

85 patients with a median age of 52 years were assessed. A total of 311 arterial territories in 85 angiographies demonstrated angiographic CVS. ACA was the most common site of angiographic CVS (42.1 %), followed by MCA (26.7 %). In 29 angiographies (34%) severe CVS was found in more than 3 vessels and a bilateral pattern has been found in 53 cases (62%). Older age (3.24 [1.30-8.07], $p = 0.012$) and the onset of neurological deficits prior to DSA were identified as significant risk factors for CVS-related infarction (OR 22.67, $p = 0.015$). Poor functional outcome was associated with older age (OR 3.24, $p = 0.023$) and poor WFNS grade (OR 3.64, $p = 0.015$). Multivariate analysis of the angiographic characteristics did not reveal any risk factors for poor functional outcome. Concerning the occurrence of CVS-related infarction, we identified the distal localization of CVS as a significant risk factor (OR 2.89, $p=0.026$).

Conclusion

Angiographic CVS after sSAH shows a specific distribution pattern in favor of ACA and ACM with a majority of 2-3 affected vessels, often bilaterally. Patients exhibiting distal CVS localization seem to be at higher risk for the occurrence of CVS-related infarction and should be observed very closely. However, the majority of angiographic characteristics did not allow conclusions about the functional outcome nor the occurrence of CVS-related infarction in sSAH patients with CVS.

Zerebrale Vasospasmen/*Cerebral vasospasms*

V057

Intraarterielles Nimodipin versus induzierte Hypertension bei verzögerter Ischämie nach aneurysmatischer Subarachnoidalblutung – Untersuchung eines modifizierten Behandlungsprotokolls
Intraarterial nimodipine versus induced hypertension in refractory DCI after aneurysmal subarachnoid haemorrhage – investigation of a modified treatment protocol

M. Weiss¹, W. Albanna¹, C. Conzen¹, K. Seyfried¹, M. Wiesmann², H. Schulze-Steinen³, H. R. Clusmann¹, G. A. Schubert¹

¹Rheinisch-Westfälische Technische Hochschule Aachen, Abteilung für Neurochirurgie, Aachen, Germany

²Rheinisch-Westfälische Technische Hochschule Aachen, Institut für Diagnostische und Interventionelle Neuroradiologie, Aachen, Germany

³Rheinisch-Westfälische Technische Hochschule Aachen, Abteilung für operative Intensivmedizin und perioperative Pflege, Aachen, Germany

Objective

Rescue treatment for delayed cerebral ischemia (DCI) after subarachnoid hemorrhage may include induced hypertension (iHTN) >180mmHg (first-line) and the addition of continuous intraarterial nimodipine (IAN) in refractory cases (second-line). The combination of iHTN and IAN may lead to a critical exacerbation of vasopressor demand with considerable complications. In case of unsustainable doses, iHTN is often prioritized over IAN. However, evidence in this regard is largely lacking. For this purpose, we investigated the effects of a classical and modified treatment protocol.

Methods

Until 07/2018, iHTN at our institution was maintained at >180mmHg with initiation of IAN if patients showed refractory hypoperfusion. Escalated noradrenaline demand or display of complications typically triggered a secondary reduction or termination of IAN (group I). After 07/2018, we preemptively lowered pressure target to >140mmHg with initiation of IAN (group II), adequacy of treatment effect ensured by CT perfusion. We assessed noradrenaline dose for 24hours after treatment escalation and compared the need for retreatment, the rate of DCI related infarction and clinical outcome.

Results

In the n=25 and n=8 patients treated according to the original or modified protocol, respectively, mean IAN dose was comparable (I: 18.5±7.5 vs II: 17.7±9.6µg/kg/min, ns), while duration of IAN was longer in the cohort with modified protocol (I: 7.3±4.6 vs II: 12.7±6.6days, p<0.05), but MAP was lower (I: 113.9±8.4 vs II: 94.9±12.0mmHg, p<0.001). Vasopressor support was lower with the modified protocol, though the difference in noradrenaline requirements was initially not significant (I: 0.60±0.48 vs II: 0.16±0.24µg/kg/min, p=0.08). There were no differences in need for retreatment (I: 48.1% vs II: 37.5%, ns), DCI related infarction (I: 24.2% vs II: 12.5%, ns) or clinical outcome (GOS 4-5 I: 35.5% vs II: 37.5%, ns).

Conclusion

Assuming the potential of iHTN to be maxed out at time of secondary deterioration, continuous IAN may serve as a last-resort measure to bridge hypoperfusion in the DCI phase. However, combination of iHTN and IAN may carry a considerable risk profile, and microcirculatory organ perfusion may become severely impaired. With close monitoring, preemptive lowering of pressure target in favor of IAN may then be a safe option to alleviate total noradrenaline load without critically jeopardizing brain supply.

Zerebrale Vasospasmen/*Cerebral vasospasms*

V058

Eine initiale Entzündungsreaktion bei Patienten mit niedriggradiger aneurysmatischer Subarachnoidalblutung ist ein unabhängiger Prädiktor für ein schlechtes neurologisches Outcome

Inflammatory response at admission is an independent predictor of unfavourable outcome in good-grade aneurysmal subarachnoid haemorrhage patients

A. Hadjiathanasiou¹, C. Coch², R. Fimmers³, I. Ilic¹, T. Y. Kern¹, S. Brandecker¹, İ Güresir¹, H. Vatter¹, P. Schuss¹, E. Güresir¹

¹Universitätsklinikum Bonn, Abteilung für Neurochirurgie, Bonn, Germany

²Universitätsklinikum Bonn, Institut für Klinische Chemie und Klinische Pharmakologie, Bonn, Germany

³Universitätsklinikum Bonn, Institut für Medizinische Biometrie, Informatik und Epidemiologie, Bonn, Germany

Objective

Patients with good-grade aneurysmal subarachnoid hemorrhage (SAH) are considered to have a favorable neurological outcome. However, a small but significant number of such patients might only achieve unfavorable outcome. Therefore, the purpose of the present study was to determine if routine biochemical markers of acute phase response are associated with unfavorable outcome in patients with good-grade aneurysmal SAH.

Methods

231 patients with aneurysmal SAH and a World Federation of Neurosurgical Societies (WFNS) grade I and II were included in the present study. C-reactive protein (CRP) and procalcitonin (PCT) were measured within 24h of admission as part of routine laboratory workup. Outcome was assessed according to the modified Rankin Scale (mRS) after 6 months and stratified into favorable (mRS 0-2) vs. unfavorable (mRS 3-6).

Results

The multivariate regression analysis revealed "elevated baseline CRP" (p=0.02, OR 2.6, 95% CI 1.2-5.5), "elevated baseline PCT" (p=0.004, OR 29.5, 95% CI 3.0-287.9), "presence of CVS" (p=0.01, OR 3.0, 95% CI 1.3-6.9), "age > 65 years" (p=0.009, OR 2.9, 95% CI 1.3-6.5), and "development of DCI" (p=0.001, OR 5.9, 95% CI 2.0-17.7) as a model for the prediction of unfavorable outcome in patients with good-grade SAH.

Conclusion

Several independent factors, easy to measure, at the time of admission were found to be associated with unfavorable outcome in patients with good-grade aneurysmal SAH in the present study. An initial inflammatory response might be one explanation for poor outcome in good-grade patients. These findings might help to identify a subgroup of good grade SAH patients who are at greater risk for unfavorable outcome early during treatment course.

Epilepsiechirurgie/*Epilepsy surgery*

V059

Visualisierung struktureller Konnektivität iktaler epileptischer Aktivität durch globale Fiber-Traktographie – Eine Zukunftsperspektive im Rahmen der prächirurgischen Diagnostik?

Visualising structural connectivity of ictal epileptic activity by quantitative global fibre tractography – A future perspective in presurgical diagnostics?

J. M. Nakagawa¹, M. Reisert², E. T. Hammen³, E. Kellner², I. Mader⁴, P. C. Reinacher⁵

¹Universitätsklinikum Freiburg, Klinik für Neurochirurgie, Freiburg, Germany

²Universitätsklinikum Freiburg, Klinik für Radiologie, Medizinphysik, Freiburg, Germany

³Universitätsklinikum Freiburg, Epilepsiezentrum, Freiburg, Germany

⁴Universitätsklinikum Freiburg, Klinik für Neuroradiologie, Freiburg, Germany

⁵Universitätsklinikum Freiburg, Klinik für Neurochirurgie, Abteilung Stereotaktische und Funktionelle Neurochirurgie, Freiburg, Germany

Objective

Structural changes are a major cause of pharmaco-resistant focal epilepsy. Surgical therapeutic options are based on the identification of the epileptogenic focus and its structural connectivity. The intention of our study was to analyze structural epileptic connectivity and to approach a diagnostic tool based on quantitative global fiber tractography.

Methods

Fifteen patients with focal epilepsy undergoing invasive epileptological assessment were included in the study.

Pre-operative high-angular diffusion weighted images were acquired with 61 directions on a 3T MRI scanner and whole brain global fiber tracking was performed. A connectivity matrix of the epileptogenic focus and propagation pattern was developed based on functional stereo-EEG data. Therefore, multiple temporal and extratemporal depth electrodes were placed (mean n=10/patient) in frame-based stereotactic surgery and the position confirmed by post-operative MRI. The exact electrode contact positions (total n=128) detecting the epileptogenic focus and the target points of early propagation were identified on the stereotactic treatment plan and were transferred into a MCP-based coordinate system. MRI T1w3D sequences were superimposed on color encoded DTI images, postprocessed for global fiber tracking and transferred into a common space using an inhouse software. Epileptic fiber tracts (n=318) were extracted and structural connectivity was analyzed along the functional propagation pathways and compared to those without functional connectivity. Based on graph and streamline representations a visualization tool was developed in a web-based visualization and study processing platform (www.nora-imaging.org).

Results

The exact localization of ictal epileptogenicity and delineation of fiber tracts by global fiber tracking provides evidence of increased structural connectivity (49.6%) along pathways of epileptic propagation compared to those without functional connectivity (41.1%; p=0.01) enabling the development of a web-based visualization tool.

Conclusion

The analysis of functional and structural connectivity based on a high spatial accuracy and global tractography method reveals an increase of structural connectivity along pathways of early epileptic propagation that can be visualized based on inferred network dynamics. In future, this approach may be advanced to a non-invasive



diagnostic tool for presurgical evaluation, development of the surgical strategy and assessment of therapeutic prospects.

Epilepsiechirurgie/*Epilepsy surgery*

V060

Protokoll zum Mapping des supplementär-motorischen Areals mittels repetitiver transkranieller Magnetstimulation

Protocol for mapping of the supplementary motor area using repetitive navigated transcranial magnetic stimulation

M. Engelhardt^{1,2}, J. Karhu^{3,4}, T. Picht^{1,5}

¹Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

²Charité – Universitätsmedizin Berlin, Einstein Centre for Neurosciences, Berlin, Germany

³University of Eastern Finland, Department of Physiology, Kuopio, Finland

⁴Nexstim, Helsinki, Finland

⁵Humboldt-Universität zu Berlin, Cluster of Excellence Matters of Activity, Berlin, Germany

Objective

The supplementary motor area (SMA) has been suggested to mediate movement planning, execution and coordination. Navigated transcranial magnetic stimulation (nTMS) offers the possibility to induce transient lesions of the SMA to study the specific role on this region in performance of motor tasks. Further, it enables a detailed mapping of functionally relevant areas within the SMA, potentially aiding preoperative diagnostics in patients. The aim of this study was the development of a repetitive nTMS protocol for non-invasive functional mapping of the SMA.

Methods

The SMA was mapped in the dominant hemisphere of five healthy subjects (28 ± 8.7 years, 2 females) using repetitive nTMS at 20 Hz (120% RMT), while subjects performed a finger tapping task. The location of induced errors was marked in each subject's individual MRI. Additionally, a SMA hotspot was defined as the point consistently eliciting the largest disruptions of task performance upon stimulation. To exclude effects due to indirect stimulation of M1, effects of SMA stimulation were directly compared to effects of M1 stimulation in four different tasks (finger tapping, writing, line tracing, pointing at small circles with a pencil). M1 was therefore targeted with the intensity of the residual electric field reaching the motor hotspot during SMA stimulation.

Results

Mapping of the SMA was possible in 4 of 5 subjects. Stimulation of the SMA compared to M1 led to a reduction of finger taps (34.8 ± 7.6 vs. 41.8 ± 3.8 taps), reduced number of circles targeted (15.9 ± 3.6 vs. 17.3 ± 3) as well as increased number of circles missed (3.5 ± 2.3 vs. 1.3 ± 1.1) and less accurate line tracing and writing. Further, effects of SMA disruption increased with stimulation time, while effects were immediately present when stimulating M1.

Conclusion

Mapping of the SMA using repetitive nTMS is feasible in the majority of the subjects. While errors induced in the SMA are not entirely independent of M1 due to the proximity of both regions, disruption of the SMA seems to induce functionally distinct errors. Thus, error maps of the SMA assessed with nTMS can give valuable insights into the functional organization of this region, potentially guiding preoperative diagnostics in patients with brain lesions.

Epilepsiechirurgie/*Epilepsy surgery*

V061

Graphentheoretische Netzwerkveränderungen in prächirurgischen Epilepsiepatienten sind unabhängig von der zugrundeliegenden Pathologie

Graph theoretical network changes in presurgical epilepsy patients are independent of the underlying pathology

T. Leonidas¹, S. Rona¹, M. Fudali¹, T. Wuttke¹, H. Lerche², J. Honegger¹, G. Naros¹

¹Eberhard Karls Universität Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

²Eberhard Karls Universität Tübingen, Abteilung Neurologie mit Schwerpunkt für Epileptologie, Tübingen, Germany

Objective

Several aspects of abnormal reorganization have been elucidated using a graph theory approach in describing the cortical network in presurgical epilepsy patients. While most studies concentrate on temporal lobe epilepsy, less is known about epilepsies caused by other pathologies, such as tumor, dysplasia, cavernoma, etc. The present study uses the principles of graph theory to support the hypothesis that the epileptogenic hemisphere shows similar graph theoretical network changes independent of the underlying pathology.

Methods

This retrospective study enrolled 25 patients (31.7 ± 25.6 years) with epilepsy deriving from various pathologies. These were divided in two groups: patients with tumour-induced epilepsy ($n=15$) and patients with epilepsy due to other type of pathology ($n=10$). Individual 3D MR images were coregistered to a brain atlas covering 88 region-of-interest (ROI). Finally, DTI connectivity between these ROIs and graph theory parameter (i.e. density and betweenness centrality) were calculated.

Results

The epileptogenic hemisphere shows higher density (0.33 ± 0.06 and 0.29 ± 0.06 , $p < 0.05$) but lower betweenness centrality (0.057 ± 0.008 and 0.060 ± 0.006 , $p < 0.05$) in comparison to the non-epileptogenic hemisphere. There was no group effect of the underlying pathology.

Conclusion

Our preliminary results show chronic epileptic attacks causing graph theoretical network changes within the epileptogenic hemisphere. These changes are independent of the underlying pathology.

Epilepsiechirurgie/*Epilepsy surgery*

V062

Hippocampale Moosfasersprossung in die CA2 Region bei Temporallappenepilepsie *Hippocampal mossy fibre sprouting into CA2 in temporal lobe epilepsy*

B. Puhahn-Schmeiser, U. Häussler, J. Zentner, S. Dooskamp, M. Prinz, J. Beck, C. Haas, T. Freiman

Universitätsklinikum Freiburg, Neurochirurgie, Freiburg, Germany

Objective

Hippocampal sclerosis (HS) in Temporal Lobe Epilepsy (TLE) is characterized by selective neuronal death in the hippocampal subregions of the cornu ammonis (CA) CA1, CA3 and CA4. Granule cells (GC) and CA2 neurons are less affected. It is assumed that GC axons, the mossy fibers (MF), loose targets in CA3 and CA4 and sprout to the surviving GC layer (GCL), the so-called MF sprouting (MFS). We examined in TLE whether MF sprout only to the GCL or also to CA2 and whether MFS is associated with the death of the CA3 and CA4 target neurons.

Methods

In total, 319 hippocampal specimens of patients with TLE were analyzed. Immunohistochemical stainings for neuronal nuclei (NeuN) were used to determine neuronal loss and for synaptorin (SPO) to localize MF terminals. Cell death was analyzed according to two HS classifications, the Wyler grade and the International League against Epilepsy (ILAE) types. Clinical patient records were compared

Results

The hippocampal subregions CA1 and CA2 are normal, absent of SPO-positive background. In HS Wyler III and IV as well as ILAE 1, 2, 3, CA2 and to a lesser extent CA1 was significantly correlated with SPO-positive axon terminals and granule cell dispersion (GCD). In addition, SPO-positive axon terminals were associated with cell death in CA3 and CA4 in the classical severe HS ILAE type 1, whereas this was not the case in atypical HS ILAE type 2.

Conclusion

These SPO-positive axon terminals were interpreted as atypical MFS into CA1 and CA2 in patients with TLE. The sprouting process also seems to appear without cell death of target neurons in CA3 and CA4 and seems to be directed to the surviving cell populations of GCL and CA2 even if it was also observed to a lesser extent in CA1, where cell death was most severe

Epilepsiechirurgie/*Epilepsy surgery*

V063

Die histologische Diagnose beeinflusst maßgeblich das Anfallsoutcome bei erwachsenen Epilepsiepatienten *The histopathological diagnosis determines the chance for favourable seizure outcome in adult epilepsy patients*

T. Sauvigny¹, K. Katharina¹, F. L. Ricklefs¹, M. Lanz², J. Matschke³, M. Westphal¹, T. Martens⁴, L. Dührsen¹

¹Universitätsklinikum Hamburg-Eppendorf, Klinik und Poliklinik für Neurochirurgie, Hamburg, Germany

²Evangelisches Krankenhaus Alsterdorf, Klinik für Neurologie und Epileptologie, Hamburg, Germany

³Universitätsklinikum Hamburg-Eppendorf, Institut für Neuropathologie, Hamburg, Germany

⁴Asklepios Klinik Sankt Georg, Klinik für Neurochirurgie, Hamburg, Germany

Objective

In addition to hippocampal sclerosis (HS), long-term epilepsy associated tumors (LEATs) and focal cortical dysplasias (FCDs) are the most common histological diagnoses in adult patients with drug-resistant epilepsy who require surgery. However, there are few studies comparing detailed epileptological characteristics and seizure outcome in these groups, which would be valuable for individualized therapy planning.

Methods

We evaluated the clinical and histopathological data of patients, who underwent surgery in our epilepsy center between 2009 and 2018. We stratified the patients according to the histological diagnosis in 7 groups (HS, FCD, cavernous malformation, glioneuronal tumors, diffuse gliomas, gliosis, FCD type III according to Blümcke 2011) and analyzed patient characteristics in the respective group. Statistical analyses were performed by a univariate analysis using Kruskal-Wallis test or ANOVA tests depending on the scale of the measurements and homogeneity of variances, to examine correlations between the parameters using IBM SPSS Statistics 25 (IBM Corporation, Armonk, NY, USA). A multivariate regression analysis was calculated for the entire cohort to assess parameters associated with favorable seizure outcome, which was defined as Engel I.

Results

In this period 426 patients (45.4% female) underwent epilepsy surgery of which 322 patients had the first resection and were selected for further analysis. The mean duration of epilepsy was 17.8 years, the mean age at surgery 39.4 years. Age at seizure onset differed significantly between the histological groups showing the earliest onset in the FCD group (8.7 years, $p < 0.001$). The proportion of patients with bilateral tonic-clonic seizures was highest in the hippocampal sclerosis group (87.5%, $p = 0.011$). The seizure outcome varied considerably, being best in the glioneuronal tumor group (with Engel Ia as median) and the FCD type III group ($p = 0.008$). The mean follow-up interval was 31.3 months. A additional regression analysis revealed the diagnosis of a glioneuronal tumor as independent predictor for a favorable seizure outcome ($p = 0.021$).

Conclusion

Glioneuronal tumors as important representatives of LEATs showed the best seizure outcome. Our study provides a detailed overview of histological findings in an adult surgical epilepsy patient cohort and underlines the role of accurate histological examination for prognostic assessment after epilepsy surgery.

Epilepsiechirurgie/*Epilepsy surgery*

JM–JNS01

Die Operation für epileptische Krämpfe

The surgery for epileptic spasms

H. Uda¹, T. Uda¹, N. Kunihiro², I. Kuki³, T. Inoue³, Y. Nakanishi², R. Umaba¹, S. Koh¹, N. Yamamoto³, S. Nagase³, M. Nukui³, S. Okazaki³, H. Kawawaki³, S. Sakuma⁴, T. Seto⁴, K. Ohata¹

¹Osaka City University, Neurosurgery, Osaka, Japan

²Osaka City General Hospital, Pediatric Neurosurgery, Osaka, Japan

³Osaka City General Hospital, Pediatric Neurology, Osaka, Japan

⁴Osaka City University, Pediatrics, Osaka, Japan

Objective

The cause of epileptic spasm(ES) has been considered to be related with widespread epileptic networks including cerebral hemisphere and thalamus. In the case with medically intractable epilepsy, surgery could be a therapeutic option, however even with the surgical treatment, there are some cases without achieving seizure relief. This study aimed to examine the seizure outcomes of surgery for ES in our institutions.

Methods

151 patients(209 surgeries) with medically intractable epilepsy underwent epileptic surgery between May 2015 to April 2019 in our institutions. Among them, we excluded cases with epileptic syndrome presenting various seizure type including ES, and cases with ES only in the past. Thirty-seven patients(48 surgeries) were presented with ES as the most disabling seizure type and were retrospectively reviewed. They were composed of 20 males and 17 females and their age was 5.7 years old in average, ranging from 4 months to 16 years. Initial surgeries were corpus callosotomy (CC) in 31 cases, hemispherotomy in 2 cases, frontal lobectomy or disconnection in 3 cases, subtotal hemispherotomy in one case. Eight cases underwent additional resection or disconnection of the epileptic focus to cure after CC. Three cases underwent vagus nerve stimulation therapy (VNS) after intracranial surgeries. Among them, 29 patients were followed up over one year after the last surgery and were evaluated their seizure outcomes. Nineteen patients underwent only CC and were evaluated with Oguni's classification (Group 1). Over 50 % improvement (A,B and C in Oguni's classification) was defined as favorable prognosis in the present study. Ten patients underwent some kind of focus resection or disconnection and were evaluated with ILAE classification (Group 2).

Results

The outcomes in Group 1 showed that 4 patients were Class A, 1 patient was Class B, 6 patients were Class C, and 8 patients were Class D and none of the patients were Class E. Fifty eight percent of patients in Group 1 demonstrated favorable prognosis. The outcomes in Group 2 showed 7 patients were Class 1 and 3 patients were Class 5. Seventy percent of patients in Group 2 achieved complete seizure free after surgery. Three patients underwent VNS were Class 5.

Conclusion

Even when the medical treatment is insufficient, surgical treatment including CC and/or focus resection /disconnection can cure ES. Surgery might be an acceptable option for medically intractable ES.

Epilepsiechirurgie/*Epilepsy surgery*

V064

Stereotaktische Radiofrequenzablation zur Diskonnektion epileptogener hypothalamischer Hamartome *Stereotactic radiofrequency thermocoagulation for disconnection of epileptogenic hypothalamic hamartomas*

P. C. Reinacher^{1,2}, V. Coenen¹, M. J. Shah³, C. Steiert³, D. M. Altenmüller⁴, R. Roelz³, A. Schulze-Bonhage⁴, J. Jacobs-Le Van^{4,5}

¹Universitätsklinikum Freiburg, Stereotaktische und Funktionelle Neurochirurgie, Freiburg, Germany

²Fraunhofer-Institut für Lasertechnik ILT, Klinische Diagnostik und mikrochirurgische Systeme, Aachen, Germany

³Universitätsklinikum Freiburg, Klinik für Neurochirurgie, Freiburg, Germany

⁴Universitätsklinikum Freiburg, Epilepsiezentrum, Abteilung Prächirurgische Epilepsiediagnostik, Freiburg, Germany

⁵Universitätsklinikum Freiburg, Klinik für Neuropädiatrie und Muskelerkrankungen, Freiburg, Germany

Objective

To evaluate safety and efficacy of disconnection of epileptogenic hypothalamic hamartomas with stereotactic radiofrequency thermocoagulation (SRT).

Methods

Between 07/2015 and 11/2019 we treated 19 consecutive patients (6 female, 13 male, age 1-55 years, median 7 years) with epileptogenic hypothalamic hamartomas (13 Delalande II, 3 Delalande III, 3 Delalande IV) with SRT. All patients underwent (at least 72h) video-EEG prior to treatment. A neuropsychologist evaluated pre- and postoperative intellectual and behavioral condition. 8 patients had previously undergone other treatments with no lasting improvement (3 open surgery, 5 stereotactic brachytherapy). 16 Patients had gelastic seizures (GS), 18 patients had non-gelastic seizures (nGS).

We carried out 1 procedure in 14, 2 procedures in 4 and 3 procedures in 1 case. Between 1 to 5 trajectories (median 3) with a total of 1 to 17 (median 6) coagulation targets were used per procedure (75°C, 60 seconds per target). Intraoperative stereotactic fluoroscopy was used to confirm the electrode position for each trajectory.

Results

At follow-up (0-38 months, median 12 months) freedom from GS was achieved in 94% (15/16) and freedom from nGS in 83% (15/18). All patients but two showed recovery or considerable improvement of their epilepsy (Engel Class 1: 74%, Engel Class 2: 11%, Engel Class 3: 5%, Engel Class 4: 11%).

1 patient had a bleeding in the hamartoma with a mild isolated deficit in verbal long-term memory (but he remained free of seizures), one patient had a weight gain of 10 kg, one patient a horner-syndrome and three a transient emotional facial paresis. Postoperative neuropsychological performance was unchanged or improved in 17/19 patients.

Conclusion

This minimally invasive approach appears to be a safe and effective alternative to surgery or radiation in patients with hypothalamic hamartomas.

Abb 1. Seizure outcome.

Abb 2. Stereotactic planning of 3 trajectories and 4 spherical lesions (left), Intraoperative stereotactic digital fluoroscopy showing correct placement of the thermocoagulation probe in the planned target (right)

Fig 1

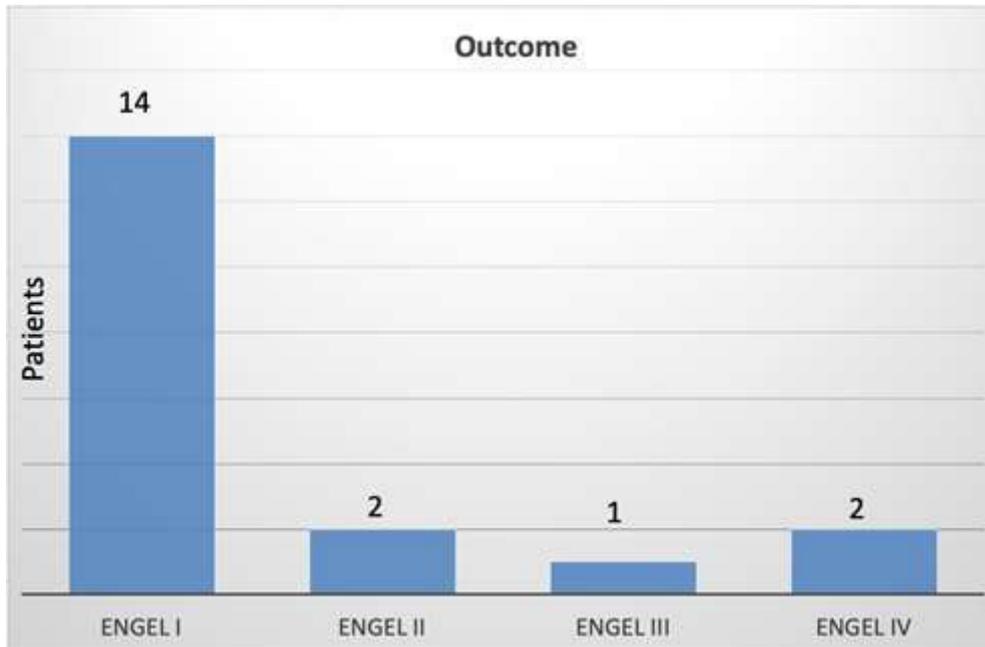
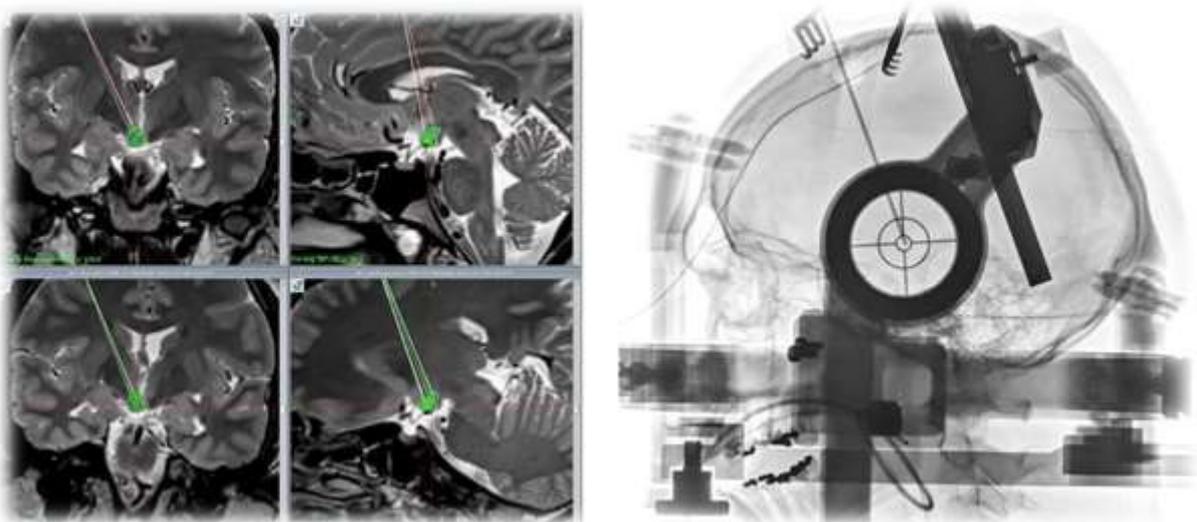


Fig 2



Epilepsiechirurgie/*Epilepsy surgery*

V065

Erweiterte Resektion des piriformen Cortex ist entscheidend für die post-operative Anfallsfreiheit nach einer selektiven Amygdalohippocampektomie

Extended resection of piriform cortex predicts post-operative seizure freedom following selective amygdalo-hippocampectomy

V. Borger¹, M. Schneider¹, A. L. Potthoff¹, V. C. Keil², M. Hamed¹, G. Aydin¹, I. Ilic¹, L. Solymosi², C. E. Elger³, E. Güresir¹, R. Fimmers⁴, P. Schuss¹, R. Surges³, H. Vatter¹

¹Universitätsklinikum Bonn, Klinik und Poliklinik für Neurochirurgie, Bonn, Germany

²Universitätsklinikum Bonn, Neuroradiologie, Bonn, Germany

³Universitätsklinikum Bonn, Klinik für Epileptologie, Bonn, Germany

⁴Universitätsklinikum Bonn, Institut für Medizinische Biometrie, Informatik und Epidemiologie, Bonn, Germany

Objective

Transylvian selective amygdalo-hippocampectomy (tsSAHE) represents a valid surgical procedure for drug-resistant mesial temporal lobe epilepsy (mTLE). However, although postoperative seizure freedom can be achieved in about 70% of tsSAHE, there is a considerable amount of patients with persisting postoperative seizures. This might partly be reasoned in differing extents of resection of various tsSAHE target volumes. In the present study we therefore analyzed the resected proportions of hippocampus, amygdala as well as piriform cortex in regard of postoperative seizure outcome.

Methods

Between 2012 and 2017, 82 of 103 patients with mTLE who underwent tsSAHE at our center were included in the analysis. Patients were stratified according to favorable (International League against Epilepsy (ILAE) class 1) and unfavorable (ILAE class 2-6) seizure outcome and resected proportions of hippocampus, amygdala and piriform cortex as target structures of tsSAHE were volumetrically assessed.

Results

Patients with favorable seizure outcome revealed a significantly larger proportion of resected piriform cortex volumes compared to patients with unfavorable seizure outcome (mean resected proportion was 45% versus (vs.) 12%, $p=0.0001$). Resected proportions of hippocampus and amygdala did not significantly differ for these groups [hippocampus: 80% vs. 82% ($p=0.58$); amygdala: 99% vs. 98% ($p=0.7$)]. Resection of at least 27% of preoperative piriform cortex volumes was associated with a 78-fold increase in the probability of becoming seizure-free (95% CI, $p=0.001$).

Conclusion

These results strongly suggest piriform cortex to constitute a key target volume in respect of acquiring postoperative seizure freedom following tsSAHE.

Epilepsiechirurgie/*Epilepsy surgery*

V066

Anfallsfreiheit nach wiederholter Epilepsieoperation bei anhaltender oder wiederkehrender Anfallsaktivität *Seizure free outcome after repeated epilepsy surgery for persistent or recurrent seizures*

M. Kunz¹, A. Peraud², I. Borggraefe³, J. Tonn¹, F. W. Kreth¹, S. Noachtar³, C. Vollmar³

¹ Ludwig-Maximilians-Universität München, Klinik und Poliklinik für Neurochirurgie, München, Germany

² Universität Ulm, Neurochirurgie, Ulm, Germany

³ Ludwig-Maximilians-Universität München, Neurologie, München, Germany

Objective

Seizure-free outcome in patients undergoing resective surgery for pharmacoresistant focal epilepsy can be achieved in around 80%. Here we report on a series of patients with persistent or relapsing seizures after initial epilepsy surgery, undergoing repeated presurgical evaluation with video-EEG-monitoring for tailored reoperation.

Methods

From 2015 to 2019, a cohort of 23 consecutive patients with pharmacoresistant focal epilepsy were reevaluated after unsuccessful initial epilepsy surgery. 19 Patients were examined with scalp EEG, 16 had invasive EEG recording using stereotactically implanted depth electrodes. All patients had repeated MRI scans, 10 had ictal SPECT and 8 had FDG-EPT scans for reevaluation. Image processing was used for coregistration and combined 3D visualization of all imaging modalities to localize the epileptogenic zone (EZ) and eloquent areas in the context of the patients' individual brain surface anatomy. Individual 3D maps of the EZ were used to guide subsequent tailored focus resection. The outcome (f/u >6months, n=21) was rated according to the Engel and the ILAE classification.

Results

Median age was 31 yrs [0.8-74]. After initial epilepsy surgery, 10 patients showed reduced but persistent seizure activity; 13 patients were initially seizure free but developed relapsing seizure activity within a median of 3,5 yrs [3months – 25 yrs]. Time between initial and second resection was in median 70 months [6-340] with a median follow-up of 14 months [6-44] thereafter. The EZ was adjacent to the initially resected EZ in 16 patients and distant in 7. Surgical procedures included unilobar resections (n=13), multilobar resections (n=5), hemispherectomy/disconnection (n=4) and callosotomy (n=1). Seizure-free outcome (Engel class I A-C, ILAE class 1-2) was achieved in 81% of the study cohort. Outcome was similar for patients with lesional or non-lesional (n=11, 82% vs n=10, 80%), temporal or extratemporal (n=7, 86% vs n=14, 79%), right- or left-hemispheric epilepsy (n=8 87% vs n=13, 77%) and with an EZ adjacent or distant from eloquent cortex (n=12, 75% vs n=9, 88%).

Conclusion

Repeated surgery after unsuccessful initial epilepsy surgery can achieve seizure free outcome comparable to the rate obtained with initial focus resection. Reoperations should therefore be considered in all patients with persistent or relapsing pharmacoresistant seizures.

Bildgebung/Imaging

V067

Frühe Veränderungen in der MRT Bildgebung und Untersuchung des Blutflusses und des Blutvolumens nach Protonentherapie des Glioblastoms

Early magnetic resonance imaging changes and the evaluation of local blood flow and blood volume following proton therapy of glioblastoma – single-centre experience

M. Stein¹, A. Jensen², M. Kolodziej¹, E. Uhl¹, T. Struffert³

¹Justus-Liebig-Universität Gießen, Klinik für Neurochirurgie, Gießen, Germany

²Justus-Liebig-Universität Gießen, Klinik für Strahlentherapie, Gießen, Germany

³Justus-Liebig-Universität Gießen, Klinik für Neuroradiologie, Gießen, Germany

Objective

Pseudoprogression (PP) is an important clinical problem after radiation therapy of glioblastoma (GBM). From neuroradiological perspective, PP is defined as a new or enlarging contrast enhancement, in the absence of tumor growth. This condition subsides or stabilizes without a change in the therapy. Clinical definitions for PP are not standardized. This explains the variability in the published rates of PP with 10 to 31% after photon therapy in the first-line therapy of GBM. There is concern for higher rates of PP after proton therapy. The purpose of this study was to evaluate early magnetic resonance imaging (MRI) changes, PP, and local blood circulation after proton therapy for GBM.

Methods

Serial MRI scans of 26 patients with GBM were reviewed. Progressive disease (PD) was defined by the RANO criteria for radiographic response assessment in GBM. Cerebral blood flow (CBF) and cerebral blood volume (CBV) in the tumor area were analyzed by perfusion MRI with dynamic susceptibility contrast (DSC) technique. All patients were treated with initial tumor resection followed by combined chemo- and radiation therapy. Radiation therapy were performed in all cases with 50.0 Gy photons followed by a proton boost with 10 Gy equivalent (Gy(RBE)).

Results

MRI scans at 4 weeks after the end of radiation therapy and at 3 months were available in all patients.

Perfusion MRI for the evaluation of CBF and CBV was performed in 18 patients (69.2%). Increase in contrast enhancement and progress in T2 FLAIR hyperintensity at 4 weeks and at 3 months after the end of radiation therapy were observed in 65% (N=17/26) and 34.6% (N=9/26), respectively. A PD at 4 weeks by RANO criteria was observed in 53.8% (N=14/26) of the cases. PP was observed in 57.1% of the cases with a PD at 4 weeks (N=8/14). The cumulative incidence of PP was 30.8% (N=8/26) at 3 months. DSC imaging at 4 weeks showed an absence of increased CBF and CBV at the former tumor area in 87.5% (N=7/8) of the patients with PP compared to only 16.7% (N=1/6) of the patients with PD ($P=0.008$). A sensitivity of 87.5% and a specificity of 83.3% for the prediction of PP by DSC imaging were calculated.

Conclusion

Early changes in MRI after proton boost therapy are common. By the RANO criteria PP rates are in the range of patients after photon therapy. MRI with DSC is very sensitive in the prediction of PP and could be helpful for early detection of PP after proton therapy.

Bildgebung/Imaging

V068

Intraoperative Visualisierung funktioneller Hirnareale – eine Vergleichsstudie zur thermischen und optischen Bildgebung

Intraoperative visualisation of functional brain areas – a comparative study of thermal and optical imaging

J. Müller¹, M. Oelschlägel¹, U. Morgenstern², G. Steiner¹, E. Koch¹, S. B. Sobottka³, G. Schackert³, M. Kirsch^{3,4}

¹Technische Universität Dresden, Klinik für Anästhesiologie und Intensivtherapie, Klinisches Sensoring und Monitoring, Dresden, Germany

²Technische Universität Dresden, Fakultät für Elektrotechnik und Informationstechnik, Institut für Biomedizinische Technik, Dresden, Germany

³Technische Universität Dresden, Klinik und Poliklinik für Neurochirurgie, Dresden, Germany

⁴Asklepios Kliniken Schildautal Seesen, Abteilung für Neurochirurgie, Seesen, Germany

Objective

Intraoperative imaging techniques should support the surgeon in his decision-making process of effective tumour treatment while preserving functional brain tissue. Previous studies proved that both Intraoperative Optical Imaging (IOI) and Intraoperative Thermal Imaging (ITI) can visualise functional brain areas by monitoring changes in cerebral metabolism in a contactless, non-invasive, and marker-free manner. This work provides a direct comparison of both imaging techniques to investigate their potential.

Methods

Measurements were performed on 10 patients with cortical lesions that underwent craniotomy for tumour resection near the somatosensory cortex. In all cases, median nerve stimulation was performed for 9 minutes with alternating 30 s rest and 30 s stimulation periods. During stimulation, IOI and ITI were acquired simultaneously. By calculation of the spectral power density for stimulation frequency, two-dimensional maps were created visualising areas of neuronal activity following stimulation. The localisation of the somatosensory cortex was validated with electrophysiological measurement (phase reversal).

Results

In 9 out of 10 cases, both IOI and ITI were able to identify and differentiate the postcentral region corresponding to the electrophysiological measurements. In one case, the stimulated area was not trepanned and appropriately IOI and ITI displayed no activity. Three measurements showed only a low ITI activity in accordance with also a low activity in IOI, whereas the electrophysiology still delivered plausible results. Detailed analysis revealed variations in the position and size of the detected activity regions on the somatosensory cortex. Different measuring principles with specific signal properties, imaging and preprocessing methods lead to slightly different regions between IOI and ITI. Furthermore, while it is known that IOI displays blood volume changes, the physiological effects resulting in the observed thermal signal of ITI due to neural activation will require further investigations.

Conclusion

Both intraoperative imaging techniques reveal a high sensitivity to the detection of functional areas within the central region. IOI can easily be integrated into a clinical routine due to its standard hardware setup whereas the application of ITI is illumination independent and also suitable for further perfusion analysis. When selecting an appropriate imaging method respective advantages should be considered individually.

Bildgebung/Imaging

V069

Präoperative funktionelle MR-Bildgebung – Gewebshypoxie, Perfusionsrestriktion und Störungen der Gefäßarchitektur sind assoziiert mit neurovaskulärer Entkopplung in der Nähe von Gehirnläsionen
Preoperative functional MR imaging – tissue hypoxia, perfusion restriction and distortions in vascular architecture are associated with neurovascular uncoupling in the vicinity of brain lesions

S. Brandner¹, M. Buchfelder¹, I. Eyüpoglu¹, A. Dörfler², A. Stadlbauer¹

¹Universitätsklinikum Erlangen, Neurochirurgische Klinik, Erlangen, Germany

²Universitätsklinikum Erlangen, Neuroradiologische Abteilung, Erlangen, Germany

Objective

Functional MR imaging (fMRI) is commonly used for the preoperative localization of eloquent cortical areas. Lesion-induced attenuation of neurovascular coupling (NVC) in the lesion border zone, however, can lead to false-negative fMRI results. The purpose of this study was to investigate physiological factors influencing the NVC.

Methods

Twenty patients suffering from brain lesions were preoperatively examined using a multimodal approach including fMRI and magnetoencephalography (MEG) during language or sensorimotor tasks (depending on lesion location) as well as a novel physiologic MRI method for combined determination of oxygen metabolism (cerebral metabolic rate of oxygen, CMRO₂; and mitochondrial oxygen tension, mitoPO₂), perfusion (cerebral blood volume, CBV; and microvascular CBV, μ CBV), and vascular architecture (microvessel density, MVD; and vessel size index, VSI).

Results

Congruence of brain activity patterns between fMRI and MEG were found in 13 patients (Fig.1, upper panel). In 7 patients, however, we observed missing fMRI activity in perilesional brain regions that demonstrated activity in MEG, which was interpreted as lesion-induced attenuation of NVC (Fig.1, lower panel). In these brain regions with attenuated NVC, physiologic MRI revealed significantly reduced mitoPO₂ ($P < 0.001$), i.e. significant brain tissue hypoxia, as well as significantly decreased macro- and microvascular perfusion (CBV: $P < 0.001$; μ CBV: $P \leq 0.02$) and vascular architecture (MVD: $P < 0.05$; VSI: $P < 0.03$) compared to brain regions with intact NVC (Fig.2). CMRO₂ was increased but did not reach significance compared to brain regions with intact NVC.

Conclusion

We demonstrated that perilesional hypoxia and reductions in vascular perfusion and architecture are associated with lesion-induced attenuation of NVC, making fMRI unreliable for resection planning. Our physiologic MRI approach is a clinically applicable method for preoperative risk assessment for the presence of false-negative fMRI results and may prevent serve postoperative functional deficits.

Fig 1

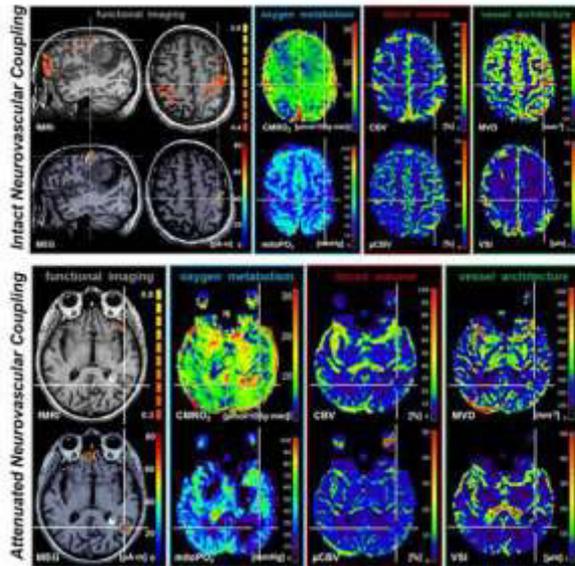


Fig. 1: Preoperative functional imaging (fMRI and MEG) and physiological MRI (oxygen metabolism, perfusion, and vascular architecture) in a patient with an anaplastic astrocytoma (WHO grade III) and intact NVC (upper panel) and a patient with a cavernoma and attenuated NVC (lower panel).

Fig 2

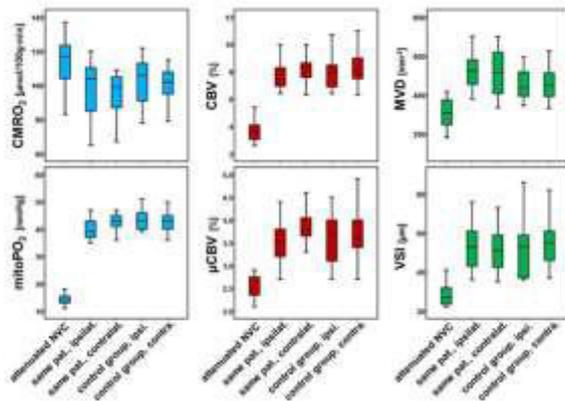


Fig. 2: Overview of imaging biomarkers for oxygen metabolism (CMRO₂ and mitoPO₂), perfusion (CBV and μCBV), and vascular architecture (MVD and VSI) in brain regions with attenuated NVC, with intact NVC on ipsilateral side to the attenuated NVC within the same patient, and with intact NVC on ipsilateral side to the attenuated NVC within the same patient, as well as in control patients without any indication for attenuation of NVC on ipsi- and contralateral side to the lesion, respectively.

Bildgebung/Imaging

V070

Funktionelle Kartierung kortikaler Sprachareale mittels Doppelpuls- und hochfrequenter repetitiver TMS *Functional mapping of cortical language areas using paired-pulse and higher-frequent repetitive TMS*

C. Nettekoven¹, J. Pieczewski¹, D. Klütsch¹, K. Jonas², R. H. Goldbrunner¹, C. Weiß Lucas¹

¹Universitätsklinikum Köln, Klinik für Allgemeine Neurochirurgie, Köln, Germany

²Universität zu Köln, Department Heilpädagogik und Rehabilitation, Köln, Germany

Objective

During the last years, a lot of effort has been made to investigate the cortical distribution of language-relevant areas on the individual level. For language mapping with repetitive transcranial magnetic stimulation (rTMS) a stimulation frequency of 5-10 Hz is most commonly used. Nevertheless, this rTMS protocol still has some limitations like small number of evoked language errors. We, therefore, designed new TMS protocols using paired-pulse (pp) TMS as well as higher-frequent rTMS aiming at improved language mapping, i.e. evoking a higher number of language errors.

Methods

20 healthy, right-handed subjects (w=11, 23 ± 3 years) were investigated using three different rTMS protocols : (i) 5 Hz rTMS, (ii) introductory pp followed by 32 Hz rTMS (pp + 32 Hz) and (iii) bursts of paired-pulses with a repetition rate of 32 Hz (32 Hz-pp). TMS protocols were applied in a pseudo-randomized order during a picture naming task (picture-to-trigger interval: 0 ms) over the inferior frontal gyrus, primary motor cortex, supramarginal gyrus, angular gyrus, superior and middle temporal gyrus (as defined by fMRI).

Results

Overall, lowest error rates were found for the standard protocol of 5 Hz (15 ± 9 %, p<0.05, FDR-corrected). There was no significant difference between the standard and the 32 Hz-pp protocol (19 ± 11 %, p>0.1, FDR-corrected), whereas a significant higher number of errors could be evoked using the pp + 32 Hz protocol (27 ± 13 %).

Conclusion

We found promising results in terms of increased error rates especially when using combined pp- and rTMS for mapping of cortical language areas. In our series, the pp + 32 Hz protocol was clearly superior to the standard technique and should be further evaluated. Clinical studies are planned to demonstrate the validity of this improved language mapping protocol in patients. Moreover, train duration and picture-to-trigger interval may be optimized with regard to the location-dependent dynamics of cortical language processing.

Bildgebung/Imaging

V071

Digitaler Knochenabtrag – voxel-basierte, kalte Ultrakurzpulslaser-Knochenablation bei neurochirurgischen Operationen

Digital bone removal – voxel-based, cold ultra-short pulsed laser bone ablation for neurosurgical applications

P. C. Reinacher^{1,2}, L. Bochvarov², C. Tulea², R. Roelz³, A. Lenenbach²

¹Universitätsklinikum Freiburg, Abteilung Stereotaktische und Funktionelle Neurochirurgie, Freiburg, Germany

²Fraunhofer-Institut für Lasertechnik ILT, Klinische Diagnostik und mikrochirurgische Systeme, Aachen, Germany

³Universitätsklinikum Freiburg, Klinik für Neurochirurgie, Freiburg, Germany

Objective

Surgical bone removal relies on mechanical instruments with inherent limitations (drills, rongeurs). Currently available laser systems generate heat to remove tissue. Advances in laser ultra-short pulsed technology enable a plasma induced cold ablation process without vibration and acoustic sound. We investigated picosecond laser radiation to remove bone in combination with optical coherence tomography (OCT) to continuously monitor the ablation process for precise voxel based bone cutting.

Methods

A picosecond laser with a maximum average power of 200 W and 200 kHz repetition rate was used to perform a plasma induced ablation process. During the ablation the laser beam is focused by a f-theta lens with a focal length of 160 mm. A galvanometer scanner is moving the laser focus along the kerf in the bone. The process energy is applied in short laser pulses of discrete amount $E_p \leq 1$ mJ and a pulse duration of $\tau \leq 20$ ps, whereas a single laser pulse causes a defined ablation volume (voxel) of micrometer dimensions. The whole kerf of the laser cutting process can be fragmented into a 3D-grid of voxels. The bone tissue is ablated in a digital manner addressing voxel by voxel with the scanned laser focus. The cutting process is monitored with a high speed 80 kHz OCT system. This delivers a 3D-real time map of the kerf and the residual bone thickness. Laser cutting experiments were performed on bovine bones.

Results

We developed a handpiece with integrated compact galvanometer scanner, focusing optics, OCT sensor and rinsing system to remove ablated tissue and blood out of the process volume. In total 138 laser cutting experiments resulted in a bone removal rate with infrared laser light ($\lambda = 1030$ nm) of $dV/dt = 2.5$ mm³/s for a laser power of $P = 130$ W. Histologically there was no carbonization at the borders of resection.

Conclusion

The availability of ultra-short pulsed lasers opens new possibilities of ablation procedures in neurosurgery such as precise bone removal without heat, vibration and acoustic sound. A handpiece with integrated compact galvo scanner and OCT sensor allows for a voxel based cutting of a predefined 3D geometry with a real time cutting control by an OCT sensor. Applications include bone removal in spine surgery, awake surgery (Deep Brain Stimulation, tumor resection) and skull base surgery.

Fig1. Laser ablation process (left) and OCT monitoring of residual bone thickness (right)

Fig2. Handpiece with integrated galvanometer scanner, focusing optics and OCT sensor

Fig 1

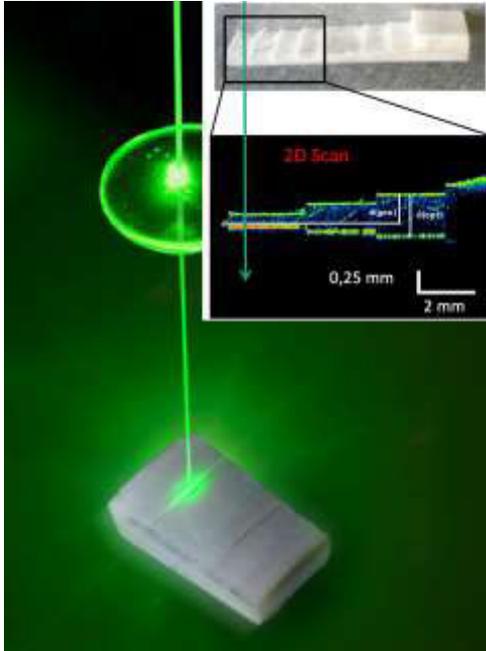


Fig 2



Bildgebung/Imaging

V072

Vergleichende Analyse von anatomiebasierten, nTMS-basierten und kombinierten Strategien der DTI-Darstellungen des Sprachnetzwerkes

Evaluating distinct approaches to language pathway tractography – anatomy-based versus nTMS-based versus nTMS-enhanced DTI-FT

L. Silva^{1,2}, M. Tuncer¹, P. Vajkoczy¹, T. Picht¹, T. Rosenstock^{1,3}

¹Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

²Charité – Universitätsmedizin Berlin, Klinik für Anästhesiologie und Intensivmedizin, Berlin, Germany

³Berliner Institut für Gesundheitsforschung, Berlin, Germany

Objective

Preoperative visualization of subcortical language pathways by means of DTI-FT is evolving as an important tool for surgical planning and decision-making in patients with language-eloquent brain tumors. Navigated nTMS cortical language mapping is an additional non-invasive method to further extend the basis for treatment choices. Efforts to incorporate nTMS data into DTI-FT are promising, but lack of standardized protocols make it hard to assess clinical usefulness. This work was conceived to evaluate the clinical usefulness of three distinct approaches to language pathway tractography.

Methods

30 patients with left-hemispheric perisylvian lesions received preoperative nTMS language mapping and DTI. Language Tractography was conducted as follows.

1a: Tractography of five major language-relevant fascicles was carried out based on verified anatomical landmarks.

1b: Tracts with minimum tumor-distances greater than 20mm were hidden in order to reduce the representations complexity.

2a: All language-positive spots identified in nTMS were defined as a single ROI for DTI-FT.

2b: Streamlines located in the anatomical pathways of the five major language-relevant fascicles were isolated in order to reduce the representations complexity.

3: Tractograms resulting from *Method 1b* as well as individual language-positive spots identified by nTMS located below the projected craniotomy were defined as ROIs.

The results of each approach were rated by neurosurgeons from different hospitals in respect to usefulness for surgical planning and risk assessment, overall information content and perceived accuracy of tracts. Additionally, objective measures such as success to visualize specific tracts and tract volume comparisons were studied.

Results

Results reveal high usefulness ratings for anatomy-based approaches, as well as for the combined nTMS-enhanced approach. Post-processed representations had a more balanced perceived information content than unprocessed tractographies. The order of overall preferred methods was 1b>3>1a>2b>2a.

Conclusion

Results suggest that DTI-FT can be enhanced by nTMS data in a clinically meaningful way. Yet, relying solely on functional data for DTI-FT seeding cannot be recommended, as usefulness ratings were higher for all alternative approaches. Future work should explore the effect of different approaches on clinical outcome in order to guide the process of establishing meaningful standards.

Bildgebung/Imaging

V073

Fokales Kontrastmittelenhancement intrakranieller Aneurysmen im MR vessel wall imaging ist kolokalisiert mit vermindertem Fluss und histologischen Zeichen der Inflammation

Focal enhancement in intracranial aneurysms in MR vessel wall imaging is colocalised with low-flow conditions and associated with histologic signs of inflammation

C. Flüh¹, N. Larsen², S. Saalfeld^{3,4}, S. Voß^{3,5}, D. Trick⁶, M. Synowitz¹, O. Jansen², P. Berg^{5,4}

¹Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Kiel, Germany

²Universitätsklinikum Schleswig-Holstein, Klinik für Radiologie und Neuroradiologie, Kiel, Germany

³Otto-von-Guericke-Universität Magdeburg, Institut für Simulation und Graphik, Magdeburg, Germany

⁴Otto-von-Guericke-Universität Magdeburg, Forschungscampus STIMULATE, Magdeburg, Germany

⁵Otto-von-Guericke-Universität Magdeburg, Laboratorium für Strömungsmechanik und Technische Strömungen, Magdeburg, Germany

⁶Universitätsklinikum Schleswig-Holstein, Institut für Pathologie, Kiel, Germany

Objective

Circumferential enhancement has been proposed as a possible imaging marker of a higher risk of rupture in intracranial aneurysms. Hemodynamic studies have identified low flow conditions as possibly associated with focal enhancement and rupture sites. Focal enhancement is frequently encountered in unruptured aneurysms on MR vessel wall imaging, but its implication for risk stratification and patient management remains unclear. This study was conducted to investigate the association of focal wall enhancement in unruptured intracranial aneurysms with focal hemodynamic conditions and histologic markers of wall inflammation and degeneration.

Methods

Patients with an unruptured middle cerebral artery aneurysm who underwent 3T MR vessel wall imaging showing focal wall enhancement and DSA were retrospectively identified. Aneurysms were dichotomized either into group 1 (enhancement of <50% of the aneurysm surface) or group 2 (≥50% enhancement). Enhanced vessel wall regions were manually segmented and co-registered with an aneurysm surface mesh. Hemodynamic simulations derived from 3D rotational angiography data were carried out. Average wall shear stress (AWSS), low shear area (LSA), and maximum oscillatory shear index (maxOSI) were compared between enhanced regions and the entire aneurysm surface, and between group 1 and group 2. Histologic features were compared between group 1 and 2.

Results

Twenty-two aneurysms were analyzed. Lower AWSS, increased LSA and lower maxOSI were significantly associated with enhanced regions. AWSS was significantly lower in aneurysms showing focal enhancement of ≥50% of the aneurysm surface. Aneurysms with a greater extent of focal enhancement exhibited histologic signs of inflammatory and degenerative changes of the aneurysm wall, whereas these changes could not be detected in aneurysms with enhancement in <50% of the aneurysm surface.

Conclusion

Focal wall enhancement is associated with low flow conditions and inflammatory changes. Not only circumferential, but also focal wall enhancement in a larger extent could serve as a surrogate marker for aneurysm instability.

Bildgebung/Imaging

V074

Intraoperative optische Bildgebung – Möglichkeiten und Grenzen der Methode bei Wachoperationen *Intraoperative optical imaging – possibilities and limitations of the method during awake surgery*

M. Oelschlägel¹, T. Meyer², U. Morgenstern³, H. Wahl⁴, J. Gerber⁴, G. Reiss⁵, E. Koch¹, G. Steiner¹, M. Kirsch^{5,6}, G. Schackert⁵, S. B. Sobottka⁵

¹Technische Universität Dresden, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie, Klinisches Sensing und Monitoring, Dresden, Germany

²ABX-CRO advanced pharmaceutical services Forschungsgesellschaft mbH, Dresden, Germany

³Technische Universität Dresden, Institut für Biomedizinische Technik, Dresden, Germany

⁴Universitätsklinikum Carl Gustav Carus Dresden, Institut und Poliklinik für Diagnostische und Interventionelle Neuroradiologie, Dresden, Germany

⁵Universitätsklinikum Carl Gustav Carus Dresden, Klinik und Poliklinik für Neurochirurgie, Dresden, Germany

⁶Asklepios Kliniken Schildautal Seesen, Abteilung für Neurochirurgie, Seesen, Germany

Objective

Intraoperative Optical Imaging (IOI) is a marker free and non-invasive imaging technique that can be utilized for visualization of metabolic changes within the cerebral cortex. In the past, we used the technique for the identification of functional brain areas while the patients were under general anesthesia. In this work, we investigated the potential of the method for surgical decision-making during awake surgery.

Methods

Measurements in 10 patients that underwent surgical resection of lesions near or within cortical language or motor processing sites were performed. IOI was applied in three different scenarios: identification of motor areas using finger tapping tasks, identification of language areas using speech tasks (overt and silent speech), and a novel approach - the application of IOI as a visual feedback tool during direct electrical stimulation (DES) mapping of language. The functional maps (activity maps), calculated from the IOI data for the speech and motor tasks were qualitatively compared towards the preoperative acquired fMRI and the electrophysiological testing results during the surgical procedure. Additionally, the extent of activation during language mapping with DES was quantized.

Results

The results reveal that the intraoperative identification of motor sites is possible in good agreement to fMRI and the intraoperative electrophysiological measurements. The identification of language processing sites with IOI was also possible, but in the majority of cases, significant differences between fMRI, IOI, and DES were visible. During language mapping procedure with DES, we were able to visualize and calculate the spatial extent of activation for each single stimulation. A high inter-stimulation variability was observed (range of activated area: $A_{\min} = 44 \text{ mm}^2$ to $A_{\max} = 155 \text{ mm}^2$, no. of stimulations $n = 15$).

Conclusion

A promising new application of IOI is the combined use with DES during the standard language mapping procedure. Here, IOI is able to provide visual feedback about the extent of each single stimulated area. This might enable the surgeon to optimize the mapping process in the future. The application of the technique for motor site identification seems to be also promising and beneficial for the surgery. According to our findings,

the results of the speech tasks are too unspecific to be useful for intraoperative decision-making in respect to exact language localization. Here DES mapping will remain the method of choice.

Bildgebung/Imaging

V075

Eine Risikostratifizierung für sprach-eloquente Gliome basierend auf präoperativer Traktografie *Towards a tractography-based risk stratification for language eloquent gliomas*

M. Tuncer¹, L. F. Salvati², L. Silva^{1,3}, H. Schneider¹, I. Bährend^{1,4}, P. Vajkoczy¹, T. Rosenstock^{1,5}, T. Picht¹

¹Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

²University of Turin, Department of Neurosurgery, Turin, Italy

³Charité – Universitätsmedizin Berlin, Klinik für Anästhesiologie und Intensivmedizin, Berlin, Germany

⁴Vivantes Klinikum Neukölln, Klinik für Neurochirurgie, Berlin, Germany

⁵Berliner Institut für Gesundheitsforschung, Berlin, Germany

Objective

The resection of language eloquent brain tumors is a challenge, whereby the surgical planning still depends strongly on anatomical models and individual experiences. Since morbidity is typically caused by an impairment of *white matter* connectivity, we aim to establish language tractography as a valid tool for preoperative risk assessment and surgical planning in a routine neurosurgical work flow.

Methods

This prospective study includes a series of 50 surgical cases of patients with left perisylvian gliomas. Every patient received a preoperative DTI tractography of the 5 main language tracts (AF, ILF, IFOF, UF, FAT) and a detailed analysis of the spatial relations of the tumor and the respective tracts. The language status was assessed preoperatively, postoperatively and after 3 months by using the Aachener Aphasia Test (AAT). The postoperative MRI scan was fused with the preoperative MRI applying careful distortion correction to detect potential impairment of tracts and correlated with the functional outcome 3 months after surgery.

Results

In 27 % of patients a new permanent language deficit was detected. The minimal distance between AF and tumor ($p = 0,034$) and especially an overlap between the temporo-parietal part of the AF and tumor ($p = 0,007$) correlated with new permanent aphasia. In respect to the postoperative resection map analysis, injury of the temporo-parietal as well as the temporal part of the AF ($p = 0,009$; $p = 0,004$) and injury to the anterior ILF ($p = 0,01$) and the middle part of the IFOF ($p = 0,001$) significantly correlated with new language deficits. The important role of the temporo-parietal AF ($OR: 6,429$; $CI: 1,421 - 29$), anterior ILF ($OR: 4,971$; $CI: 1,171 - 21,101$) and middle IFOF ($OR: 8,679$; $CI: 2,053 - 36$) for preservation of language function was confirmed by univariate binary logistic regression ($p < 0,05$).

Conclusion

The spatio-functional correlation between tumor and the subcortical language network as revealed by DTI tractography correlates with the individual postoperative functional outcome. In line with earlier studies applying intraoperative mapping during awake surgery, the temporo-parietal AF, the anterior ILF and the middle IFOF were identified as especially vulnerable parts within the network. Based on these findings, standardized presurgical tractography of language tracts can be regarded as a promising technique for preoperative risk stratification in patients with language eloquent gliomas.

Spondylodiszitis/Spondylodiscitis

V076

Chirurgische Behandlung und Outcome in einer konsekutiven Serie von 237 Patienten mit Spondylodiszitis *Surgical treatment and outcome in a consecutive series of 237 patients with spondylodiscitis*

M. Pojskic¹, B. Saß¹, B. Völlger¹, V. Schmöckel¹, C. Nimsky², B. Carl²

¹Universitätsklinikum Gießen und Marburg, Klinik für Neurochirurgie, Marburg, Germany

²Philipps-Universität Marburg, Klinik für Neurochirurgie, Marburg, Germany

Objective

Spinal infections are a source of significant morbidity due to spinal instability, neurological deficits, and sepsis. The traditional conservative therapy has been replaced in clinical practice by surgery. The aim of this study was to evaluate surgically treated patients with spondylodiscitis, to identify factors, which determine the outcome and to develop recommendations for treatment and follow up.

Methods

We performed a retrospective review of all patients who underwent surgical treatment for spondylodiscitis between 2010 and 2018. Data were gathered through a review of patients' case notes, relevant imaging, and electronic records.

Results

We have identified 237 consecutive patients who underwent surgery for spondylodiscitis. The mean age of presentation was 71.4 years. Distribution of the spondylodiscitis was 45 in cervical, 73 in thoracic and 119 in the lumbar spine. 26 patients had an infection in more than one segment of the spine. An epidural abscess was found in 146 cases. 225 patients had pain and 176 patients had a neurological deficit. Decompression surgery without instrumentation was performed in 26 patients. In patients who underwent instrumentation, the ventral approach was used in 54 cases, dorsal in 134 cases and 360° fusion in 23 cases. The most common cause was infection with Staph. aureus. Endocarditis was the most common concomitant infection (10 patients). In 57 cases the microorganism could not be isolated in the intraoperative specimen. 26 patients died during the follow-up, out of them 21 during the primary hospital stay. Neurological status improved in 38 of 211 patients, in 160 it remained unchanged and in 13 it worsened. Antibiotic i.v. therapy was performed for 9.6±3.4 days and subsequent oral therapy for 47.4±0.9 days. Recurrence occurred in 18 patients who needed further surgery. Complete healing defined as normalization of infection parameters (leukocyte count and C-reactive protein) was achieved in 211 (89%) of cases. 156 patients had an excellent outcome (healed infection without neurological deficits), which was significant in comparison to patients with moderate and poor outcomes ($p < 0.05$).

Conclusion

Surgical treatment with spinal instrumentation in the cases of instability together with i.v. antibiotic use is the mainstay of the therapy of spondylodiscitis. Antibiotic therapy should be applied until normalization of the infection parameters.

Spondylodiszitis/Spondylodiscitis

V077

Untersuchung der Lebensqualität bei Patienten mit Spondylodiszitis *Long-term quality of life in patients with pyogenic spondylodiscitis*

T. Abboud, M. Krolikowska Flouri, A. Alaid, V. Rohde, B. Schatlo

Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Spondylodiscitis is a serious disease that usually affects a fragile patient population with multiple comorbidities and can lead to a severe limitation of quality of life. The aim of this study was to assess different domains of quality of life among patients who underwent surgical treatment for pyogenic spondylodiscitis.

Methods

Data of 218 patients, who were treated for spondylodiscitis at our institution between January 2008 and July 2017 were reviewed retrospectively. A survey was conducted using following questionnaires; Oswestry disability index (ODI), Short-form McGill pain questionnaire, work Ability Index short form and short form (36) health survey, which were sent to patients. We investigated the correlation between the assessed variables and clinical data including patient age, comorbidity score at admission, number of operated levels, corpectomy and length of hospital stay.

Results

At follow-up, 100 patients had died, 74 patients were lost to follow-up or refused to participate in the study. 44 patients responded to the survey and had a mean age of 73 years. The average percentage of permanent pain-related disability on ODI was $45,78 \pm 8,21\%$ with the highest rates seen in lifting (55.16%), standing (47.56%) and sex life (47.5%) and the lowest in sleeping (25%). On Short-form McGill pain questionnaire the average sensory pain index was calculated to be 20% (6.5/33), the average affective pain index was 21% (2.48/12) and overall patient pain appraisal (zero is pain free and 5 is agonizing pain) averaged to be 2.3. Most patients (72,09%) had a work ability index of "bad". Patients scored best in general mental health (60.13%) followed by social functioning (51.79%) and worst in role limitation due to physical health (13%). Affective pain index correlated with involvement of lumbar segment, $p=0.035$. Role limitations due to physical health correlated with corpectomy, $p=0.023$ and general health correlated with Charlson comorbidity score, $p=0.018$.

Conclusion

Patients with spondylodiscitis are prone to a long-term limitation in all domains of quality of life especially in physical health and work ability. Involvement of lumbar spine and corpectomy might be predictors of worse outcome.

Spondylodiszitis/Spondylodiscitis

V078

Der Stellenwert des Interleukin-6 als Surrogatparameter für sekundäre Wundinfektionen nach vorangegangenen Wirbelsäuleneingriffen Interleukin-6 as inflammatory marker of secondary surgical site infection following spinal surgery

M. Lenski, J. Tonn, S. Siller

Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgie, München, Germany

Objective

In order to elucidate whether serum inflammatory markers identify patients with local surgical site infection (SSI) as underlying disease for recurrent or new symptomatology following spine surgery, we evaluated the diagnostic potential of interleukin-6 (IL-6) as a marker of SSI in patients undergoing spinal re-operation. The diagnostic impact of IL-6 was compared to the standard serum inflammatory markers C-reactive Protein (CRP) and white blood cell count (WBCC).

Methods

98 consecutive patients with re-operation after spinal surgery of degenerative spinal canal stenosis entered the study. Baseline patients' characteristics as well as the above mentioned inflammatory markers were collected and arithmetical means with standard deviation, area under the curve (AUC), thresholds, sensitivity, specificity, positive (+) likelihood ratio (LR) and negative (-) LR with corresponding 95% confidence interval (95%CI) were calculated and correlated with presence or absence of SSI. The AUC describes the diagnostic potential of an inflammatory marker.

Results

9 Patients suffered from a SSI, whereas the remaining patients had a re-stenosis without any suspicion of SSI. The **most significant parameter for diagnosing a SSI was serum IL-6** (cut-off-value > 15.3 pg/ml, AUC = 0.954, SE = 85.7% (95%CI 0.487 – 0.974), SP = 97.3% (95 CI 0.861 – 0.995), +LR = 31.7 (95%CI 4.48 – 224.43), -LR = 0.15 (95%CI 0.02 – 0.90), **followed by CRP** (AUC = 0.916), **and WBCC** (AUC = 0.745).

Conclusion

In case of recurrent symptomatology pre-operative raised serum IL-6 levels are significantly associated with SSI. Hence, serum concentrations of IL-6 should be obtained in patients with recurrent symptoms; increased IL-6 levels higher than 15.3 pg/ml should direct the surgeon's attention to SSI.

Fig 1

Table 1. Inflammatory markers in surgical site infections after spinal surgery

	n	AUC	cutoff	Mean ± SD infection	Mean ± SD aseptic	SE	SP	+LR	-LR
IL-6 (pg/ml)	82	0.954	15.3	56.2 ± 39.1	7.8 ± 3.6	85.7% (0.487 – 0.974)	97.3% (0.861 – 0.995)	31.7 (4.48 – 224.43)	0.15 (0.02 – 0.90)
CRP (mg/dl)	86	0.916	0.8	10.0 ± 9.4	0.5 ± 0.7	88.9% (0.565 – 0.980)	84.5% (0.731 – 0.916)	5.7 (3.0 – 10.3)	0.13 (0.02 – 0.84)
WBCC (·10 ³ /µL)	89	0.745	9.7	11.7 ± 6.6	7.4 ± 2.1	66.7% (0.354 – 0.875)	86.2% (0.751 – 0.928)	4.8 (2.2 – 10.7)	0.39 (0.15 – 0.98)

Values in brackets are the corresponding 95% confidence intervals. AUC = Area under the curve, SE = sensitivity, SP= specificity, SD = standard deviation, -LR = positive likelihood ratio, +LR= negative likelihood ratio, IL-6 = interleukin-6, CRP= C-reactive Protein, WBCC= white blood cell count, n= number.

Spondylodiszitis/Spondylodiscitis

V079

Wird Osteoporose unterdiagnostiziert in Patienten mit Spondylodiszitis?
Do we underdiagnose osteoporosis in patients with pyogenic spondylodiscitis?

C. Bettag¹, T. Abboud¹, C. Von der Brelie¹, P. Melich², V. Rohde¹, B. Schatlo¹

¹Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

²Universitätsklinikum Köln, Neurochirurgie, Köln, Germany

Objective

Pyogenic spondylodiscitis (PS) affects a fragile patient population. Surgical treatment frequently entails instrumentation. Loosening of the implanted construct has been reported in patients with PS. As it usually occurs in the elderly, a poor bone quality might be one reason leading to subsequent construct loosening. We hypothesized that osteoporosis is underdiagnosed in patients undergoing surgery for PS.

Methods

We undertook an opportunistic estimation of bone density based on computed tomography (CT) scans of the thoracolumbar spine obtained prior to surgery. Based on a validated axial normative CT-scan we assessed the average Hounsfield units (HU) in vertebral bodies of L1 and L4 in patients with spondylodiscitis. We defined a conservative cut off value of ≤ 110 HU as a limit for a diagnosis of osteoporosis. Baseline and outcome variables including construct loosening were entered into a multivariate logistic model for statistical analysis.

Results

Out of 200 consecutive patients who underwent fusion surgery for PS, 64% were male (n=127). N=132 (66%) were older than 65 years. A total of 14 out of 200 patients (7%) had a known past medical history of osteoporosis. L1 and L4 measurements revealed a mean attenuation value of 120.6 ± 47.3 and 118.4 ± 54.6 , respectively. With the threshold of 110 HU, the correlation between the two measured levels was excellent (Pearson correlation coefficient of 0.820, p-value less than 0.001). Our attenuation analysis revealed values compatible with osteoporosis in 95 patients (49%). Binary logistic regression showed that age greater than 65 years was the most reliable predictor for osteoporosis (OR 3.09; CI95% 1.91-7.96; p-value less than 0.001). The need for subsequent revision surgery due to construct failure showed a trend towards an association with osteoporosis (OR 2.11; CI95% 0.95-4.68; p=0.067).

Conclusion

Relying on past medical history of osteoporosis is insufficient in the management of patients with pyogenic spondylodiscitis. Half of the patients presenting with spondylodiscitis also had severely reduced bone mass compatible with a diagnosis of osteoporosis. We advocate routine opportunistic CT evaluation to better guide the type of surgery and potentially reduce the risk of construct failure.

Spondylodiszitis/Spondylodiscitis

V080

Die routinemäßige histopathologische Untersuchung von Bandscheibengewebe nach operativer Versorgung lumbaler Bandscheibenvorfälle ist entbehrlich

Routine histopathological examination after nucleotomy of lumbar herniated discs is unnecessary

H. Abdelrahman^{1,2}, A. Shawky^{1,2}, E. Sadaat¹, D. Prsa¹, A. Ezzati¹

¹Helios-Klinikum Erfurt, Wirbelsäulenchirurgie, Erfurt, Germany

²Assiut University, Assiut, Egypt

Objective

Lumbar disc herniation (LDH) is one of the most common reasons for spine surgery. Management of sciatica that is caused by LDH varies considerably and there is considerable evidence that surgical intervention provides effective clinical relief for carefully selected patients.

Histopathological examination of the disc material is routine in many hospitals. However, the clinical benefit and therapeutic consequences are very limited. The cost-effectiveness of this routine exercise should be assessed.

Methods

Histopathological reports from 1150 patients were analysed for lumbar spine discectomy between January 2013 and December 2018. The presence of a purulent or specific infection or malignancy was assessed and whether any therapeutic consequences were made according to the histopathological findings.

Results

Over a 6-year period, 1150 patients (653 men, 497 women) were examined. The average age was 53.8 years (22-87). Suppurative inflammation, specific infections or malignancies were not found in any patient. Highly degenerative and slightly regressively altered disc tissue was the finding in > 95% of cases. No granulation tissue formation, no purulent or specific granulomatous inflammation, no malignancy in 100% of cases.

Conclusion

Routine histopathological examination of discectomy material in degenerative disc disease does not provide clinically relevant data or therapeutic consequences. A multicentre study is recommended and accordingly the current practice should be changed.

Gliome experimentell I/*Gliomas experimental I*

V082

Die kombinierte Behandlung mit ABT-263 und Vacquinol zeigt synergistische Aktivität gegen Glioblastomzellen *in vitro* und kann durch Hemmung von Autophagie verstärkt werden

Combined treatment with ABT-263 and vacquinol exhibits synergistic anti-glioblastoma activity in vitro which can be further enhanced by inhibition of autophagy

J. Antonymuthu¹, C. Golla¹, A. Dwucet¹, M. Pruss¹, M. Hlavac¹, R. E. Kast², C. R. Wirtz¹, M. E. Halatsch¹, M. D. Siegelin³, M. A. Westhoff¹, G. Karpel-Massler¹

¹Universitätsklinikum Ulm , Ulm, Germany

²IIAIGC Study Center, Burlington, VT, United States

³Columbia University, New York, NY, United States

Objective

Vacquinol represents an experimental anti-malaria drug which has been previously described to provide anti-glioma activity. The purpose of this study was to examine whether treatment with vacquinol would enhance the pro-apoptotic reprogramming of glioblastoma cells following selective Bcl-2/Bcl-xL inhibition by ABT-263.

Methods

Drug testing was performed on primary cultured ULM-GBM-PC38 and ULM-GBM-PC128 glioblastoma cells. MTT assays were used to provide a rigorous characterization of the drug-drug interaction of vacquinol and ABT-263 including isobologram analyses. Annexin-V/PI and TMRE staining followed by flow cytometric analyses were done to assess pro-apoptotic effects. Western blot analyses were performed to assess the expression of anti-apoptotic members of the Bcl-2 family of proteins and to determine the LC3 conversion.

Results

Combined treatment with vacquinol and ABT-263 resulted in synergistic anti-proliferative and pro-apoptotic effects in ULM-GBM-PC38 and ULM-GBM-PC128 cells. Mechanistically, the pro-apoptotic effect of the combination treatment was associated with a significant decrease of the mitochondrial outer membrane potential and a decreased expression of Bcl-2 and Bcl-xL in ULM-GBM-PC38 cells. Western blot analyses showed that the combination treatment led to increased LC3 conversion. Additional treatment with an inhibitor of autophagy (chloroquine) resulted in increased anti-proliferative and pro-apoptotic effects.

Conclusion

Our data suggest that combined treatment with vacquinol and ABT-263 has superior anti-glioblastoma activity compared to single agent treatments. However, this potential therapeutic approach is associated with the induction of protective autophagy in our setting and should be complemented by an inhibitor of autophagy. The promising results of this study warrant further investigation.

Gliome experimentell I/*Gliomas experimental I*

V084

Welche Patienten könnten von einer gegen monopolar spindle 1 kinase (MPS1/TTK) gerichteten Therapie profitieren?

Which patients might benefit from therapies targeting monopolar spindle 1 kinase (MPS1/TTK) in gliomas?

A. F. Keßler¹, J. Feldheim¹, D. Schmitt^{1,2}, J. Feldheim¹, C. M. Monoranu³, R. I. Ernestus¹, M. Löhr¹, C. Hagemann¹

¹Julius-Maximilians-Universität Würzburg, Klinik und Poliklinik für Neurochirurgie, Tumorbiologisches Labor, Würzburg, Germany

²Julius-Maximilians-Universität Würzburg, Nuklearmedizin, Würzburg, Germany

³Julius-Maximilians-Universität Würzburg, Institut für Pathologie, Abteilung für Neuropathologie, Würzburg, Germany

Objective

Recently, we demonstrated that the effects of vincristine chemotherapy or Tumour Treating Fields in experimental glioblastoma multiforme (GBM) were augmented and accelerated by inhibition of the protein kinase MPS1, a mitotic spindle checkpoint regulator. It is overexpressed in astrocytic tumours and therefore represents a potential therapeutic target. The purpose of this study was to provide information on MPS1 expression in clinical subgroups of GBM and other gliomas and to evaluate its impact on the patients' clinical course.

Methods

We analysed MPS1 mRNA expression by qPCR in a collection of GBM (n=57), gliomas WHO grade II/III with (n=25) or without (n=11) IDH mutation, adult pilocytic astrocytomas (n=4) and healthy brain specimens (n=7). Subsequently, we examined associations of MPS1 mRNA expression with the patients' clinical course.

Results

We confirm MPS1 overexpression in glial tumours (ANOVA, all p < 24 months, p=0.009, Hazard ratio=8.0, 95% CI: 1.7-38.4). However, if evaluated separately, it was associated with poorer survival in low-grade gliomas (LogRank: p=0.02, Cox regression: p=0.06, Hazard-Ratio: 8.0, 95% CI: 0.9-66.7), but not with the survival of GBM patients (LogRank: p>0.05). Although GBM patients with high MPS1 developed clinical symptoms at an earlier stage and therefore started treatment with a lower tumour volume (median tumour volume: 45ccm vs. 25ccm, p=0.043, unpaired two-tailed t-test), they did not benefit in terms of overall survival, most likely due to a more aggressive tumour growth. Interestingly, patients with high MPS1 expression more frequently were initially submitted to the hospital with epileptic seizures or focal neurological deficits.

Conclusion

MPS1 mRNA was overexpressed in gliomas, associated with patients' survival and increased tumor aggressiveness. Therefore, we hypothesize that patients with the worst outcome might benefit best from a treatment directed against MPS1.

Gliome experimentell I/*Gliomas experimental I*

V085

Stereotaktische interstitielle photodynamische Behandlung von Glioblastomrezidiven *Stereotactic interstitial photodynamic treatment of glioblastoma recurrences*

S. Lietke¹, M. Schmutzer¹, A. Rühm^{2,3}, C. Heckl^{2,3}, M. Aumiller^{2,3}, R. Sroka^{2,3}, F. W. Kreth¹

¹Klinikum der Ludwig-Maximilians-Universität München, Abteilung für Neurochirurgie, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, Medizinische Klinik IV Endokrinologie, München, Germany

³Klinikum der Ludwig-Maximilians-Universität München, Abteilung für Urologie, München, Germany

Objective

Stereotactic interstitial photodynamic therapy (iPDT) using 5-aminolevulinic acid (5-ALA) induced protoporphyrin IX (PPIX) as a selectively working photosensitizer has been shown to be a feasible treatment option for selected small sized unresectable glioblastoma recurrences. We here present for the first time outcome measurements and the risk profile of salvage iPDT of a large and consecutively treated study cohort. The study was approved by the institutional ethical board.

Methods

From our prospective data base we identified all patients undergoing iPDT of a glioblastoma recurrence after previously performed standard treatment. Patients had to have biopsy-proven glioblastoma recurrences with a maximum diameter of 3 cm not suitable for safe complete resection. Treatment decision in favor of iPDT was an interdisciplinary consensus. A modified 3-D treatment-planning software was used to calculate both the treatment volume and the exact position of the light diffusers within the lesion to ensure complete light irradiation. We estimated time-to-treatment-failure (which had to be proven by biopsy) and post-recurrence survival (PRS) and the risk profile of iPDT. Prognostic factors were obtained from logistic regression models.

Results

A total of 59 patients (median age: 48.5 yrs) were included. A median number of 4 laser fibers were stereotactically implanted. Median irradiation time was one hour. Median time-to-treatment-failure was 6.53 months and median PRS was 12.50 months. The 2- and 5-year PRS rates were 22.0 and 6.1%, respectively. 24 patients developed transient peri-operative complications. There was no permanent morbidity. Neither molecular, patient- nor treatment-related markers impacted treatment response.

Conclusion

Outcome after iPDT is heterogeneous and cannot currently be predicted. The procedure deserves further prospective evaluation particularly with respect to assumed favorable impact on adapted immunity in selected patients.

Gliome experimentell I/*Gliomas experimental I*

V086

Hochdurchsatz- Medikamentenscreen in IDHmut Gliom-Stammzellen identifiziert multiple FDA-zugelassene Chemotherapeutika

Large-scale drug screen in patient-derived IDHmut glioma stem cells identifies several FDA-approved antineoplastic agents

P. Dao Trong¹, G. Jungwirth¹, T. Yu¹, S. Pusch², C. Herold-Mende¹, R. Warta¹, A. W. Unterberg¹

¹Universitätsklinikum Heidelberg, Sektion Experimentelle Neurochirurgische Forschung, Heidelberg, Germany

²Universitätsklinikum Heidelberg, Neuropathologisches Institut, Heidelberg, Germany

Objective

The discovery of the Isocitrate Dehydrogenase (IDH) mutation in glioma has led to a paradigm shift on how we see glioma biology. While it is clear, that IDH mutated (IDHmut) and wildtype (IDHwt) tumors have to be viewed as separate entities, the underlying biological differences are still matter of extensive research. Difficulties in cultivating IDHmut glioma stem cells (GSC) have led to a paucity of preclinical models in IDHmut glioma making the discovery of new effective chemotherapeutic agents problematic. We therefore sought to perform a repurposing drug screen in six patient-derived IDHmut GSC lines to discover potential effective antineoplastic agents, already approved by the FDA.

Methods

Patient tumor tissue was obtained in our neurosurgical department to isolate and establish IDHmut GSC lines. (D)-2-hydroxyglutarate (2HG) levels were measured in the cell culture supernatant of IDH1mut GSCs using an enzymatic diaphorase/resazurin system. Intracranial xenotransplantation was performed in NOD/SCID mice for two IDHmut GSCs. The drug library consisted of 146 FDA-approved drugs. Cells were cultured as neurospheres and subjected to the test compounds for 72h in concentrations ranging from 0.1nM – 1µM. Cell viability was assessed with the CellTiterGlo assay (Promega) and apoptosis was analyzed by Annexin V FACS staining.

Results

Despite several passages NCH551b, NCH1681 showed a stable production of 2HG and a robust take rate in xenotransplanted NOD/SCID mice and were therefore considered suitable for the drug screen. Among the 147 FDA-approved drugs seven compounds with a half maximal inhibitory concentration (IC50) below 1µM were identified in two IDHmut GSC lines (NCH551b, NCH1681). The cytotoxic potential could be confirmed in additional four IDHmut GSC lines (NCH612, NCH620, NCH645, NCH3763). Annexin V FACS stainings showed that the rate of cells undergoing apoptosis was significantly elevated in cells treated with the candidate drugs.

Conclusion

In this study, we present a feasible preclinical model for a high-throughput drug screen in patient-derived IDHmut GSCs and identified seven FDA-approved antineoplastic agents with a high cytotoxic potential which warrant further investigations.

Gliome experimentell I/*Gliomas experimental I*

V087

TERT und seine Bindungsproteine – Überexpression von GABPA/B in malignen Gliomen *TERT and its binding protein – overexpression of GABPA/B in high-grade gliomas*

E. Papazacharias¹, S. Kuhl², R. H. Goldbrunner², M. Timmer²

¹Klinikum rechts der Isar München, Neurochirurgie, München, Germany

²Universitätsklinikum Köln, Klinik für Neurochirurgie, Köln, Germany

Objective

Enhanced expression of TERT in gliomas is a result of two hotspot mutations, C228T and C250T, at the promoter region. The GABP of the ETS family selectively binds at these positions respectively causing an activation of the promoter and overexpression of TERT. GABP is a multimeric protein consisting of GABPA and GABPB with its isoforms GABPB1, GABPB1-L, GABPB1-S, GABPB2. In this study, we investigated the expression of TERT and GABPA/B isoforms in the glioma grades.

Methods

Glioma tumor samples were stored in frozen liquid nitrogen at -80°C. We performed quantitative real time-PCR for TERT and GABPA/B isoforms in controls, grade II, III gliomas and primary, secondary glioblastomas with and without chemotherapy with use of SYBR green and SDHA as the housekeeping gene. The statistic was analyzed with Kruskal-Wallis, Mann-Whitney-U-test and correlation.

Results

TERT is mainly expressed in primary glioblastomas. All GA-binding proteins progress through the glioma grades and in secondary glioblastomas they have the highest expression levels (A: mean= 0.221, 95% CI= 0.09-0.35, B1: 0.66, 0.52-0.8, B1-L: 0.705, 0.48-0.92, B1-S: 0.836, 0.46-1.2). In secondary glioblastomas after chemotherapy, B1 (0.308 ± 0.198; p=0.001) and B1-L (0.464 ± 0.495; p=0.035) are lower expressed than without treatment. In high grades TERT, A, B1, B1-L, B1-S are statistically significantly overexpressed compared to low grades. Between primary and secondary glioblastomas with and without chemotherapy, TERT is overexpressed in the former (0.118, 0.05-0.17; p< 0.0001) while B1 is increased in the secondary glioblastomas of the same treatment status (0.484, 0.36-0.6; p= 0.043). In primary glioblastomas B1-S tends to positively correlate with TERT.

Conclusion

TERT is mostly expressed in primary glioblastomas. GABPA/B levels are rising with the malignancy of gliomas with the most expression in the secondary glioblastomas. Chemotherapy treatment decreases the expression of B1 and B1-L in secondary glioblastomas and in high grades TERT, A, B1, B1-L, B1-S are overexpressed. In primary glioblastomas B1-S has a trend to increase with TERT overexpression. The association between TERT and GABPA/B isoforms in gliomas could be an aim for a targeted therapy.

Bildgebung/Imaging

V088

¹⁸F- FET-PET Bildgebung im Spotlight der WHO 2016 Klassifikation

¹⁸F-FET-PET imaging results in the spotlight of the WHO 2016 classification system

K. Hakvoort^{1,2}, J. Ort^{1,2}, J. Kernbach^{1,2}, K. J. Langen^{3,4,5}, P. Lohmann^{3,5}, G. Neuloh¹, H. R. Clusmann¹, D. Delev^{1,2}

¹Rheinisch-Westfälische Technische Hochschule Aachen, Abteilung für Neurochirurgie, Aachen, Germany

²Rheinisch-Westfälische Technische Hochschule Aachen, Neurosurgical Artificial Intelligence Laboratory Aachen (NAILA), Department of Neurosurgery, Aachen, Germany

³Forschungszentrum Jülich, Institut für Neurowissenschaften und Medizin (INM-4), Jülich, Germany

⁴Rheinisch-Westfälische Technische Hochschule Aachen, Abteilung für Nuklearmedizin, Aachen, Germany

⁵Jülich Aachen Research Alliance (JARA) , Jülich, Germany

Objective

PET using ¹⁸F-Fluoroethyltyrosine (FET) represents an important imaging modality to assess tumor extent, treatment response and tumor progression of malignant glioma. In patients with suspected recurrent glioma, ¹⁸F-FET-PET additionally differentiates between malignant progression and pseudoprogression. The new WHO 2016 classification system highlights the pivotal role of molecular markers and their importance for oncological outcome. The aim of the study was to evaluate FET-PET imaging results with a particular focus on the revised WHO-classification.

Methods

We reviewed histopathological results as well as preoperative ¹⁸F-FET-PET imaging results in glioma patients (n=39) who underwent surgical resection between 2014 and 2018. ¹⁸F-FET-PET was performed in 26 patients before initial resection and in 13 additional cases before resection of suspected recurrent glioma.

Results

¹⁸F-FET-PET showed a biologically active tumor volume (FET-PET positive result) prior to initial resection in 21 patients (81%). There was a significant correlation between FET-PET positivity and WHO grade (p=0.002, 95% CI 0.23 to 0.77); there were 15 high grade gliomas (WHO grade IV), who were all FET-PET positive, and 11 lower-grade gliomas (WHO grade II and III) of whom 5 cases had positive FET-PET results. *IDH*-wildtype status was significantly associated with FET-PET positivity (p<0.001, 95% CI -0.82 to -0.35). All *IDH*-wildtype tumors (n=16) were FET-PET positive, while the *IDH*-mutated tumors were equally distributed between FET-PET positive (n=5) and FET-PET negative (n=5). 1p/19 co-deletion was found in 7 patients, with 4 of them (57%) showing FET-PET positive results. MGMT was methylated in 13/21 (62%) patients, with 9 of them (69%) showing FET-PET positive results.

In the patient group with suspected recurrent glioma that underwent re-resection after FET-PET, 12 (92%) showed biologically active tumor. All 5 FET-PET negatives (4 in the first resection and 1 in the re-resection group) were *IDH*-mutated; all 4/4 were MGMT-methylated and 4/5 showed a 1p/19q-codeletion.

Conclusion

IDH-wildtype gliomas are biologically active tumors with highly malignant characteristics, which can be well detected by ¹⁸F-FET-PET. This may play an important role during the "preoperative tumor staging" and help to individualize patient's oncological treatment.

Bildgebung/Imaging

V089

Multiparametrische Magnetresonanz-Bilder für nichtinvasives Meningiom-Grading

Accuracy of radiomics-based feature analysis on multiparametric magnetic resonance images for noninvasive meningioma grading

M. Timmer¹, K. R. Laukamp², G. Shakirin², B. Baeßler², F. Thiele², D. Zopfs², N. Hokamp², C. Kabbasch², M. Perkuhn², J. Borggrefe²

¹Universitätsklinikum Köln, Klinik für Neurochirurgie, Köln, Germany

²Universitätsklinikum Köln, Radiologie, Köln, Germany

Objective

Meningioma grading is relevant to therapy decisions in complete or partial resection, observation, and radiotherapy because higher grades are associated with tumor growth and recurrence. The differentiation of low and intermediate grades is particularly challenging. This study attempts to apply radiomics-based shape and texture analysis on routine multiparametric magnetic resonance imaging (MRI) from different scanners and institutions for grading.

Methods

We used MRI data (T1-weighted/T2-weighted, T1-weighted-contrast-enhanced [T1CE], fluid-attenuated inversion recovery [FLAIR], diffusion-weighted imaging [DWI], apparent diffusion coefficient [ADC]) of grade I (n = 46) and grade II (n = 25) nontreated meningiomas with histologic workup. Two experienced radiologists performed manual tumor segmentations on FLAIR, T1CE, and ADC images in consensus. The MRI data were preprocessed through T1CE and T1-subtraction, coregistration, resampling, and normalization. A PyRadiomics package was used to generate 990 shape/texture features. Stepwise dimension reduction and robust radiomics feature selection were performed. Biopsy results were used as standard of reference.

Results

Four statistically independent radiomics features were identified as showing the strongest predictive values for higher tumor grades: roundness-of-FLAIR-shape (area under curve [AUC], 0.80), cluster-shades-of-FLAIR/T1CE-gray-level (AUC, 0.80), DWI/ADC-gray-level-variability (AUC, 0.72), and FLAIR/T1CE-gray-level-energy (AUC, 0.76). In a multivariate logistic regression model, the combination of the features led to an AUC of 0.91 for the differentiation of grade I and grade II meningiomas.

Conclusion

Our results indicate that radiomics-based feature analysis applied on routine MRI is viable for meningioma grading, and a multivariate logistic regression model yielded strong classification performances. More advanced tumor stages are identifiable through certain shape parameters of the lesion, textural patterns in morphologic MRI sequences, and DWI/ADC variability.

Bildgebung/Imaging

V090

Klinische, bildmorphologische und molekulare prognostische Faktoren bei Patienten mit Glioblastomen im Bereich des *Corpus Callosum*

Clinical, imaging and molecular prognostic factors in patients with glioblastoma involving the corpus callosum

M. Hazaymeh, K. Döring, D. Mielke, H. C. Bock, V. Rohde, V. Malinova

Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

Objective

The management of patients with glioblastoma (GBM) involving the Corpus callosum (ccGBM) remains challenging and no standard treatment concerning the implementation of surgical and adjuvant therapeutic options has been established so far. The aim of this study was to evaluate clinical, imaging and molecular outcome predictors in patients with ccGBM. Additionally, the correlation of surgical and adjuvant treatment with survival was assessed.

Methods

A retrospective analysis of patients with GBM treated at our department from 2008 to 2018 were enrolled in the study. Overall survival (OS) was defined as the time from the date of presentation to the date of death.

Progression free survival (PFS) was calculated from the date of presentation to the date of first tumor progression on imaging. The extent of resection and the adjuvant treatment regime were documented. Imaging criteria as well as molecular markers (MGMT, IDH1, Ki67, p53) were further assessed. The data were analyzed using Python 3.7 (Python Software Foundation, Wilmington, Delaware). Survival analysis was done using Kaplan–Meier curve and significance determined by the log-rank test. Significant factors were further analyzed using multivariate analysis. A p-value < 0.05 was considered significant.

Results

A total of 78 patients with ccGBM were included. The mean age was 52.1 years (range 24-88), 57.7% (45/78) were male and 42.3% (33/78) were female. The mean pre-treatment Karnofsky Performance Status (KPS) was 74.0% (range 60-100). The extent of resection was as followed: biopsy in 53.3% (40/78), partial resection (PR) in 10.7% (8/78), and GTR in 36% (27/78). The mean PFS was 8.1 months (range 1-47) and the mean OS was 13.6 months (range 1-88). Significant predictors of OS were tumor volume (p=0.05), involvement of basal ganglia (p=0.05), the extent of resection (p=0.002) and the PFS (p=0.05).

Conclusion

Although the survival of patients with ccGBM is still poor, GTR leads to a survival benefit and should be considered as a treatment option, if achievable under consideration of other tumor characteristics, such as ependyma contact or involvement of the basal ganglia.

Bildgebung/Imaging

JM–JNS02

Diffusionsgewichtete Bildgebung zur Überwachung der Reaktion von malignen Gliomen auf die photodynamische Therapie

Diffusion-weighted imaging for monitoring the response of malignant gliomas to photodynamic therapy

Y. Fujita¹, T. Sasayama¹, K. Tanaka¹, K. Kyotani², H. Nagashima³, M. Kohta¹, H. Kimura¹, A. Fujita¹, E. Kohmura¹

¹Kobe University, Neurosurgery, Kobe, Japan

²Kobe University, Centre for Radiology and Radiation Oncology, Kobe, Japan

³Massachusetts General Hospital, Neurosurgery, Boston, MA, United States

Objective

Photodynamic therapy (PDT) is a novel treatment that provides effective local control, but little is known about PDT-induced changes on MR imaging. The aim of this study was to assess the utility of diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) in monitoring the response of malignant gliomas to PDT.

Methods

Time-dependent changes in DWI and ADC values after PDT were analyzed in a group that received PDT in comparison with a group that did not.

Results

Twenty-four patients were enrolled (PDT group, n=14; non-PDT group, n=10). In all patients who received PDT, linear high signals on DWI in the irradiated area were detected adjacent to the resection cavity and were 5–7 mm in depth from 1 day post-treatment and disappeared in about 30 days without any neurological deterioration. The non-PDT group did not show this change. The PDT group had significantly lower ADC values from 1 day post-treatment ($p < 0.001$) that increased steadily and disappeared by 30 days. There was no decline or time-dependent change in ADC values in the non-PDT group. Furthermore, only 3 patients in the PDT group exhibited local recurrence during a mean post-treatment follow-up of 17.4 months. All of the local recurrences in the PDT group arose from the non-irradiated area, which did not show a high signal on DWI.

Conclusion

The acute response of malignant gliomas to PDT was detected as linear high signals on DWI and as a decrease in ADC values. These findings were asymptomatic and transient. Although the PDT-induced acute response on MR imaging disappeared after approximately 30 days, it may be helpful for confirming the PDT-irradiated area and predicting the local recurrence site.

Bildgebung/Imaging

V091

Evaluation klinischer, bildmorphologischer und molekularer Prädiktoren für das Outcome von Patienten mit multifokalem Glioblastom

Evaluation of clinical, imaging and molecular predictors of outcome in patients with multilocular glioblastoma

K. Döring, D. Mielke, H. C. Bock, C. Wolfert, V. Rohde, V. Malinova

Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Glioblastoma (GBM) show variable presentation on magnetic resonance imaging (MRI), whereas in approximately 20% of the cases a multilocular spread is found (mGBM). The consideration of FLAIR (fluid-inversion-recovery)-sequence in the assessment of GBM facilitates a better evaluation of mGBM. A significantly worse survival of mGBM has been reported compared to patients with solitary GBM and the management of these patients remains challenging. The aim of this study was to evaluate clinical, imaging and molecular predictors of outcome in mGBM, that could be supportive in the treatment decision-making process in this patient population.

Methods

We performed a retrospective analysis of GBM-patients treated between 2008 and 2018. mGBM were defined as multiple tumor lesions in T1-enhanced and FLAIR-sequence of MRI. Overall survival (OS) was calculated from the date of diagnosis to the date of death. The extent of resection (EoR) and the adjuvant treatment regime were documented. Imaging criteria as well as molecular markers (MGMT, IDH1, p53, Ki67) were analyzed using Python 3.7 (Python Software Foundation). Survival analysis was done using Kaplan-Meier curve and significance was determined by the log-rank test. Significant factors affecting survival were then processed in multivariate analysis using Cox's regression test. A p-value <0.05 was considered significant.

Results

A total of 45 patients with mGBM were included. The mean age was 64.1 years (range 36-89), 64.4% (29/45) were male and 35.6% (16/45) were female. The achieved EoR was as followed: biopsy in 66.7% (30/45), and GTR in 33.3% (15/45). R-CH (Stupp) was performed in 86.7% (39/45). The mean OS was 13.87 months (range 1-104). Significant predictors of OS were age ($r=-0.43$, $p=0.003$) and Karnofsky Performance Status (KPS) before treatment ($r=0.3$, $p=0.05$). There was no significant correlation of imaging or molecular parameter with OS. We found no significant difference in OS between biopsied mGBM and mGBM with GTR.

Conclusion

The survival of patients with mGBM remains poor, whereas only younger age and a better clinical condition at presentation were associated with longer OS. The EoR had no positive influence on survival, which does not justify a surgical indication to resect multiple lesions in patients with mGBM. Therefore, GTR should not be considered as a treatment option in this patient population. An explanation for these findings might be a more advanced tumor expansion in mGBM-patients affecting the whole brain in contrast to solitary GBM.

Bildgebung/Imaging

V092

TSPO-Expression in humanen und murinen Glioblastomen als Grundlage für neue PET-imaging Strategien *TSPO-expression in human and murine glioblastoma as rationale for new PET-imaging strategies*

S. Kirchleitner¹, A. Holzgreve², J. Tonn¹, N. Albert², R. Glaß¹, R. E. Kälin¹

¹Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik und Poliklinik, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, Klinik und Poliklinik für Nuklearmedizin, München, Germany

Objective

Positron emission tomography (PET) with the amino acid analogue 18F-fluoro-ethyl-tyrosine (FET) has become extremely important for the diagnosis and therapy planning of glioma patients. New PET tracers against the translocator protein TSPO, which is overexpressed primarily by glioma cells and tumor-associated myeloid cells (TAM), are potentially of interest for diagnostics. The use of this new imaging target could visualize areas of increased inflammation. However, it is not yet fully understood if TSPO expression varies with inter-individual heterogeneity in GBM. We have investigated this in different preclinical models.

Methods

In a mouse model, primary human GBM cells and transgenic murine glioma cells (p53KOPDGFB, cdkn2aKOEGRvIII) with different GBM subtype-specific characteristics were implanted orthotopically. After i.v. application of TSPO ligand 18F-GE-180 (n=20), cryosections and autoradiographies were prepared; Subsequently, immunostaining of the tumors for TSPO, LAT1, AIF1 (Iba1), CD31 and PDGFRB was performed. In addition, human tumor samples were analyzed in situ (n=12) and silico (TCGA database, n=488) for the expression of TSPO and AIF1.

Results

In all models (biopsies, mouse models and database query), there was a marked increase in TSPO expression in the tumor compared to the tumor-free brain. In the autoradiographies we observed an increased accumulation of tracer in the tumor area. By immunostaining we detected TSPO not only in tumor cells, but also TAM, endothelial cells and pericytes. The expression of the amino acid transporter LAT1, however, was largely restricted to tumor cells. In the TCGA data analysis, TSPO and AIF1 showed significantly different expression levels depending on the genetic subclass of the highest expressing mesenchymal subtype. High TSPO and high AIF1 expression correlated with a significantly poorer clinical outcome of the patients.

Conclusion

TSPO is expressed both in glioma cells and in tumor parenchyma. A combination of TSPO- and FET-PET might be a promising way to visualize inter- and intratumor heterogeneity and to visualize tumor-associated myeloid cells. GBM of the mesenchymal subtype, which accumulates more TAM, has the highest TSPO expression. Our study shows that mouse models can provide an important contribution to the interpretation of GBM imaging data.

Subarachnoidalblutung klinisch/*Subarachnoid haemorrhage clinical*

V093

Krampfanfälle beim Blutungsereignis bei aneurysmatischen Subarachnoidalblutungen – Risikofaktoren und klinischer Einfluss

Seizures at the onset of aneurysmal subarachnoid haemorrhage – risk factors and clinical impact

M. Darkwah Oppong, D. Pierscianek, L. Droste, Y. Ahmadipour, K. H. Wrede, O. Gembruch, P. Dammann, U. Sure, R. Jabbarli

Universitätsklinikum Essen, Klinik für Neurochirurgie und Wirbelsäulen Chirurgie, Essen, Germany

Objective

Alongside with typical clinical symptoms like headache and impairment of consciousness, rupture of intracranial aneurysms might also cause seizures at the onset (SAO). There are conflicting reports on the causes and clinical value of SAO after aneurysmal subarachnoid hemorrhage (aSAH). This study aimed to analyze the incidence, predictors of and the impact of SAO in a large aSAH cohort.

Methods

All aSAH patients treated at a single center during the observational period between 01/2003 and 06/2016, were retrospectively reviewed. Patient charts and emergency protocols from first responders were screened for occurrence of SAO. Baseline demographic and clinical characteristics were also extracted from the digital patients' charts. Radiographic imaging was reviewed for the initial severity and occurrence of delayed complications. Patients with known epilepsy before aSAH were excluded before further analysis. Outcome parameters included in-hospital mortality and unfavorable outcome at six-month follow-up (mRS > 3). Univariate and multivariate analysis were performed.

Results

A total of 948 patients were included in the final analysis. aSAH patients with SAO (n=90, 9.5%) were younger (48 ± 13 vs. 55 ± 14 years; $p < 0.001$), had higher radiographic severity (Fisher Grades=3-4, $p = 0.007$, OR=3.76) and presented more commonly with intraventricular ($p < 0.001$, OR=2.43) as well as intraparenchymal hemorrhage ($p = 0.012$; OR=1.76). In multivariate analysis, SAO was associated ($p < 0.001$; aOR=2.53) with poor initial clinical condition (WFNS Grade 4-5) independently of age (>50 years, $p = 0.019$; aOR=1.42) and radiographic severity ($p < 0.001$; aOR=24.04). In the whole cohort, SAO was not associated with in-hospital mortality ($p = 0.514$) and functional outcome at six months ($p = 0.118$). At the same time, multivariate analysis within the WFNS Grade 4-5 patients showed independent association between the SAO and lower risk of in-hospital mortality ($p = 0.038$; aOR=0.43).

Conclusion

Younger individuals with severe aSAH, especially accompanied by blood distribution outside of the subarachnoid space, are at higher risk of SAO and, therefore, poorer initial clinical presentation. Due to inverse association between the mortality risk and SAO in WFNS Grade=4-5 aSAH patients, the occurrence of SAO in these patients might necessitate reconsidering their clinical grading and appropriate treatment decisions.

Subarachnoidalblutung klinisch/*Subarachnoid haemorrhage clinical*

V094

Eine beeinträchtigte Plättchenfunktion schützt vor verspäteter zerebraler Ischämie nach aneurysmatischer Subarachnoidalblutung – die Resultate der multizentrischen PlaFuSah Studie

Impaired platelet function may prevent delayed cerebral ischemia after aneurysmal subarachnoid haemorrhage – the multi-centre PlaFuSAH study

C. Von der Brölie¹, J. Custodis², A. Doukas², C. Ditz³, T. Sauvigny⁴, M. M. Mader⁴, T. Fortmann⁵, M. Holling⁵, J. Walter⁶, K. Zweckberger⁶, A. W. Unterberg⁶, D. Mielke¹, J. Regelsberger⁴, V. M. Tronnier³, M. Synowitz², W. Stummer⁵, V. Rohde¹, B. Schatlo¹

¹Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

²Universitätsklinikum Schleswig-Holstein, Neurochirurgie, Kiel, Germany

³Universitätsklinikum Schleswig-Holstein, Neurochirurgie, Lübeck, Germany

⁴Universitätsklinikum Hamburg-Eppendorf, Neurochirurgie, Hamburg, Germany

⁵Universitätsklinikum Münster, Neurochirurgie, Münster, Germany

⁶Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

Objective

Platelets are implicated in delayed cerebral ischemia (DCI) after aneurysmal subarachnoid haemorrhage (SAH) via microthrombosis, inflammation and vasoconstriction. However, it is unknown whether intact platelet function favours the occurrence of DCI. The aim of this study was to evaluate in-vitro platelet function and its association with DCI and neurological outcome after aneurysmal SAH.

Methods

In this prospective observational study, six German neurosurgical centers recruited patients with SAH. Peripheral venous blood was drawn upon admission and at multiple time points to assess platelet function using the platelet-function-analyser test (PFA). Prolonged PFA (Collagen/Epinephrin: >160 sec.; Collagen/ADP: >121 sec) indicates impaired platelet function. Based on PFA at admission, patients were divided into two groups: Normal versus prolonged PFA. Outcome variables included DCI, modified Rankin scale (mRS) at discharge and case fatality. Statistical analysis was performed using multivariate binary logistic regression.

Results

The study population consisted of 171 patients with a mean age of 56.6±12 years, 31.6% of which were male. High grade SAH (WFNS score≥3) was recorded in 45.6%. The overall rate of DCI was 39.2%. Admission PFA was prolonged in 49.1% of patients. In the patient cohort with normal PFA values, DCI occurred in 45 patients (49.5%), compared to 22 patients (27.5%) in the group with prolonged PFA. Patients with prolonged PFA had a lower rate of DCI compared to patients with normal PFA (OR = 0.49; 95% CI 0.25, 0.97; p-value=0.04). While poor outcome was less likely in the group with prolonged PFA (OR 0.41; 95% CI 0.17, 0.99, p-value=0.05), there was no association with case fatality (OR 0.31; 95% CI 0.07, 1.38; p-value=0.13).

Conclusion

Our multicenter study found a significant association between in-vitro platelet function and the rate of DCI. Normal platelet function predisposed to a two-fold higher risk of developing DCI. This observation also appeared to translate into favorable clinical outcome.

Subarachnoidalblutung klinisch/*Subarachnoid haemorrhage clinical*

V095

Clipping von zuvor gecoilten zerebralen Aneurysmen *Clipping of previously coiled cerebral aneurysms*

J. M. Lang¹, F. Götz², M. Nakamura³, J. K. Krauss¹

¹Medizinische Hochschule Hannover, Klinik für Neurochirurgie, Hannover, Germany

²Medizinische Hochschule Hannover, Institut für Diagnostische und Interventionelle Neuroradiologie, Hannover, Germany

³Kliniken der Stadt Köln, Klinik für Neurochirurgie, Köln, Germany

Objective

Recurrent, residual and regrowing cerebral aneurysms after coil embolization remain a challenging task. Depending on angiographic findings, treatment options include microsurgical clipping, re-coil embolization, flow diverter implantation or observation.

Methods

From 2006 to 2019, a total of 23 patients with residual, regrowing or recurrent previously coil embolized cerebral aneurysms were treated with microsurgical clipping. The mean age of the patients was 53 years (range 27-85 years) and the mean interval between coil embolization and microsurgical clipping was 105 weeks (range 0-547 weeks).

Results

20 patients (87%) initially had a subarachnoid hemorrhage from ruptured cerebral aneurysm. Three patients had an incidental aneurysm. Aneurysm location was anterior communicating artery in 9 patients (39%), middle cerebral artery in 5 patients (22%), posterior communicating artery in 4 patients (17%), and carotid internal artery in 3 patients. Fourteen patients showed regrowth of formerly coiled aneurysms, in five patients coil compaction was present, and four patients revealed a residual neck. Coil extrusion was observed intraoperatively in 9 patients (39%). Complete coil removal was performed in 6 patients, partial coil removal was necessary in 4 patients. In all 23 patients, a complete aneurysm occlusion was achieved successfully by microsurgical clipping. 22 patients (96%) showed no surgery-related complications, one patient had a hemiparesis postoperatively. One patient with subarachnoid hemorrhage developed severe cerebral vasospasm with consecutive fatal outcome.

Conclusion

Microsurgical clipping of previously coiled cerebral aneurysms with recurrent filling, residual neck or regrowth is a safe, effective and sustainable treatment option in selected patients when performed in experienced hands.

Subarachnoidalblutung klinisch/*Subarachnoid haemorrhage clinical*

V096

Automatisierte Beurteilung zerebraler Vasospasmen zur Standardisierung von CT-A Untersuchungen nach Subarachnoidalblutung

Automated grading of cerebral vasospasm to standardise computed tomography angiography examinations after subarachnoid haemorrhage

A. Neulen¹, S. Kunzelmann¹, M. Kosterhon¹, T. Pantel¹, M. Stein¹, M. Berres², F. Ringel¹, M. A. Brockmann³, C. Brockmann³, S. R. Kantelhardt¹

¹Universitätsmedizin Mainz, Neurochirurgische Klinik und Poliklinik, Mainz, Germany

²Universitätsmedizin Mainz, Institut für Medizinische Biometrie, Informatik und Epidemiologie, Mainz, Germany

³Universitätsmedizin Mainz, Klinik für Neuroradiologie, Mainz, Germany

Objective

Computed tomography perfusion imaging (PCT) and computed tomography angiography (CTA) are common diagnostic tools to evaluate the indication for endovascular vasospasm treatment in subarachnoid hemorrhage (SAH) patients with suspected delayed cerebral ischemia (DCI). However, objective parameters for CTA evaluation are lacking. In this study we applied a novel digital and automated CTA evaluation method for investigator-independent detection of vasospasms. We used the method to investigate (i.) the link between vasospasm and cerebral perfusion, and (ii.) the method's ability to predict subsequent endovascular vasospasm treatment in a cohort of SAH patients.

Methods

A retrospective chart review and analysis of imaging data of 40 consecutive SAH patients was performed. The cerebrovascular trees were reconstructed three-dimensionally from CTA data and the vessel volume per vessel length ratio (VLR, [$\mu\text{l}/\text{mm}$]) of the arteries of the circle of Willis and their peripheral branches were calculated. Thresholds for the VLR indicating severe vasospasm were determined for each vessel segment after ROC curve analysis based on comparison with digital subtraction angiographies (DSA).

Results

The threshold-based volumetric evaluation of CTA data allowed an automated, investigator-independent detection of severe vasospasms (e.g. VLR $< 5.0 \mu\text{l}/\text{mm}$ for the M1 segment). Presence of vasospasm on CTA based on low VLR exhibited a high sensitivity and negative predictive value, but a rather low specificity and positive predictive value to predict cerebral hypoperfusion on PCT (N=96, sensitivity 89%, specificity 41%, NPV 90%, PPV 39% if ≥ 1 vessel segment was affected). The combination of low VLR on CTA and cerebral hypoperfusion on PCT was superior to PCT or low VLR alone in predicting endovascular vasospasm treatment within 24 h after the exam (N=96, sensitivity 58%, specificity 92%, NPV 90%, PPV 65% if ≥ 3 vessel segments were affected).

Conclusion

Digital, volumetric analysis of the cerebrovascular tree allows an objective, investigator-independent detection and quantification of vasospasms. The method could be used as an additional tool in multimodal diagnostics to standardize selection of SAH patients with DCI for endovascular therapies.

Subarachnoidalblutung klinisch/*Subarachnoid haemorrhage clinical*

V097

Dekompressive Kraniektomien nach Subarachnoidalblutungen – ein systematisches Review und Meta-Analyse

Decompressive craniectomy after subarachnoid haemorrhage – a systematic review and meta-analysis

M. Darkwah Oppong, D. Pierscianek, T. F. Dinger, M. Chihi, K. H. Wrede, N. Özkan, L. Droste, U. Sure, R. Jabbarli

Universitätsklinikum Essen, Klinik für Neurochirurgie und Wirbelsäulen Chirurgie, Essen, Germany

Objective

Decompressive craniectomy (DC) is a standard neurosurgical procedure against intractable intracranial hypertension. Patients with severe aneurysmal subarachnoid hemorrhage (SAH) are prone to intracranial hypertension, necessitating DC in certain cases. However, the clinical utility of DC after SAH remains unclear. Hereby we present the first systematic review and meta-analysis summarizing the published studies on DC in SAH patients.

Methods

We systematically searched PubMed, Scopus, Web of Science and Cochrane Library for articles published before Jul 10, 2019 reporting on rates, indications, timing, complications and outcome of SAH patients undergoing DC. The quality of the included studies was analyzed according to the Newcastle-Ottawa Scale (NOS).

Results

Of 1085 identified unique records, 29 retrospective studies published between 1993 and 2018 were included to the final analysis. The data of 1.175 DC performed in the pooled cohort of 7.228 SAH patients was analyzed. In overall, the studies were characterized with low to moderate study quality, predominantly reporting on certain subgroups of DC patients with limited or no data regarding the non-DC cases. The mean DC rate was 12% (range 1.5% – 39.5%), whereat the majority of DC (57.7%) were performed secondarily. Younger age (54.5 vs 58.5 years), poor initial clinical condition (H&H/WFNS=4-5: 84.3% vs 19%), higher severity of SAH (o/mFS=3-4: 91.1% vs 25%), treatment modality (clipping) were associated with the indication to and the timing of DC. Functional outcome after primary DC was superior to secondary DC (mortality: 22.6% vs 47.9%, unfavorable outcome: 60.6% vs 81%).

Conclusion

Due to substantial heterogeneity and incompleteness of the reported data, the current evidence on DC after SAH remains very sparse. We recommend the initiation of a prospective multi-centric register for proper evaluation of the clinical value of DC in SAH patients.

Subarachnoidalblutung klinisch/*Subarachnoid haemorrhage clinical*

V098

Chirurgische Therapie des akuten ischämischen Schlaganfalls in der Ära der endovaskulären Interventionen *Surgical treatment of acute ischemic stroke in the era of endovascular interventions*

A. Minasyan¹, J. Thalwitzer², J. Schwarze³, R. Steinmeier¹

¹Klinikum Chemnitz gGmbH, Klinik für Neurochirurgie, Chemnitz, Germany

²Klinikum Chemnitz gGmbH, Institut für Radiologie und Neuroradiologie, Chemnitz, Germany

³Klinikum Chemnitz gGmbH, Klinik für Neurologie, Chemnitz, Germany

Objective

During the last years a number of randomized trials (MR CLEAN, SWIFT PRIME, REVASCAT, ESCAPE, DEFUSE 3, DAWN) have shown the efficacy and safety of the primary endovascular interventions (EI) in the management of acute ischemic stroke (AIS). On the other hand, the primary decompressive craniectomy (DC) has been shown to be beneficial (HAMLET, DECIMAL, DESTINY I & II) in the treatment of AIS as well. The goal of our study is to reveal the incidence and possible changes in indications of the DC with the growing number of EI in the treatment of AIS.

Methods

We have retrospectively investigated the medical records of total 5297 (969 in 2014, 1079 in 2015, 1190 in 2016, 1101 in 2017, 958 in 2018) patients with primary AIS treated in our neurovascular center during the period of 2014-2018. The EI included catheter aspiration only or in conjunction with mechanical thrombectomy with or without tandem stenting of ICA. DCs have been performed as minimum of 15cm in diameter with consequent patching of dura with autologous or allogenic material and installation of EVD or ICP sensor. We have analyzed the cases with primary DCs (both supra- and infratentorial) as well as DCs secondary to the EI. Statistical analysis was performed by SPSS 20.0.

Results

The number of primary EI was distributed as follows: 23(2,37%) in 2014, 40(3,71%) in 2015, 44(3,70%) in 2016, 75(6,81%) in 2017 and 109(11,38%) in 2018. The number of overall DCs (primary + secondary) was as follows: 10 (1,03%; 1,03% + 0%) in 2014, 13 (1,20 %; 1,02% + 0,19%) in 2015, 11 (0,92%+0,76% + 0,17%) in 2016, 11 (1,00%; 0,82% + 0,18%) in 2017 and 13 (1,36%, 1,04%+0,31%) in 2018. The data obtained have shown a significant increase in the number of EI in comparison to the DC (OR=3,22 (1,34-7,77; CI 95%, p=0.009), Fig.1). The number of DCs remained relatively unchanged, though the ratio of primary DCs was significantly decreased (from 100% in 2014 to 77% in 2018, OR=2,22; 0,17-3,22; CI 95%, p=0,045, Fig.2).

Conclusion

Though the number of primary DCs shows a tendency to decrease, the overall number of DCs remains unchanged due to the increasing number of failed EI. Despite the increasing number of EI the role of the DC remains stable in the management of AIS.

Fig 1

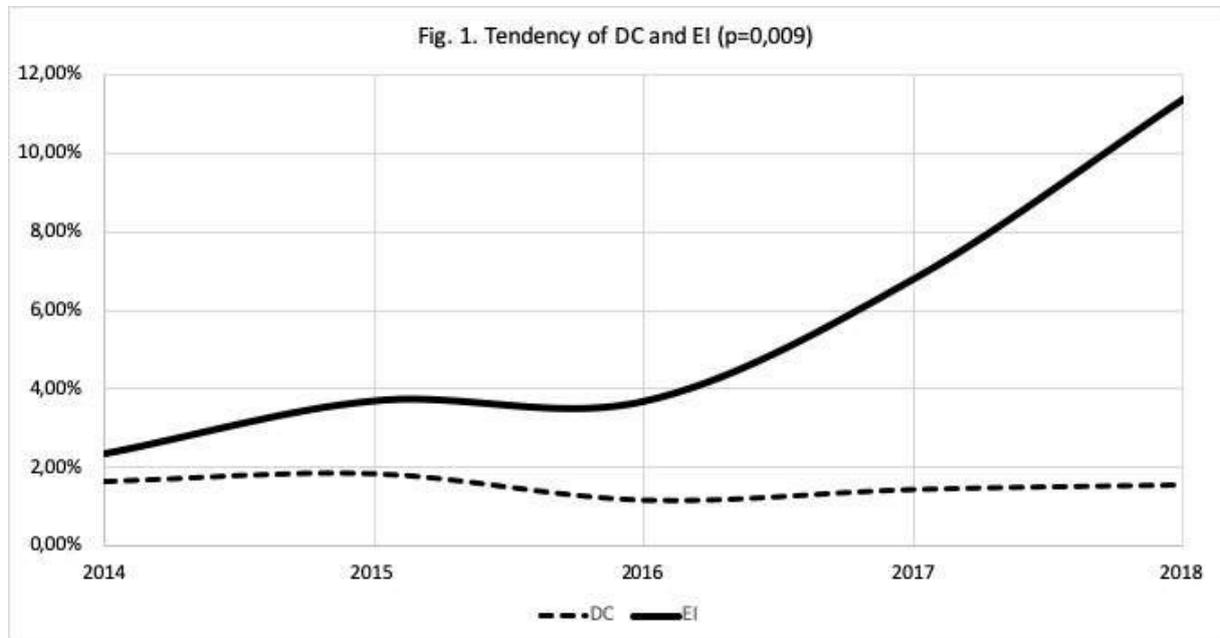
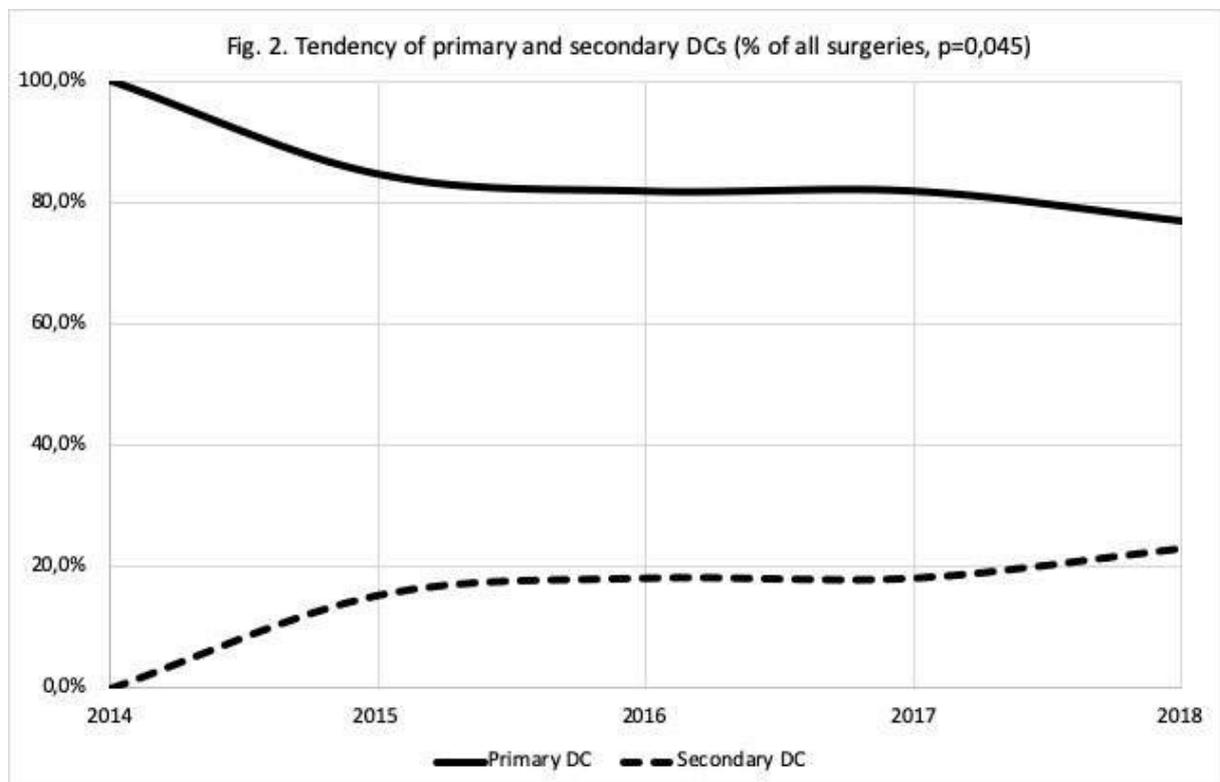


Fig 2



Spinale Neuromodulation/Spinal neuromodulation

V100

Untersuchungen des somatosensorischen Profiles mittels quantitativer sensorischer Testung (QST) während tonischer und BurstDRTM Stimulation zur Behandlung unilateraler chronischer neuropathischer Schmerzen
Analysis of the somatosensory profile using quantitative sensory testing (QST) during tonic and BurstDRTM stimulation for the treatment of unilateral chronic neuropathic pain

M. Morgalla, L. Domay, M. Tatagiba

Eberhard Karls Universität Tübingen, Neurochirurgische Klinik, Tübingen, Germany

Objective

Due to nerve damage, neuropathic pain often affects also other sensitive nerve fibre qualities. The aim of our study was to investigate the effects and possible differences of tonic and BurstDRTM stimulation (SCS) on the somatosensory profiles of patients with chronic neuropathic pain of one limb using quantitative sensory testing (QST).

Methods

We examined from 1/2017 until 12/2017 14 patients (9 female, 5 male; mean age 55,8 years, range 28-84 years) with previously implanted SCS systems for chronic neuropathic pain of one limb using QST (7 tests and 13 parameters for thermal, tactile, allodynia, pressure, vibration, and pain sensation). SCS was discontinued for 4 hours and the basic measurement was taken on the painful limb. Then in randomized fashion either tonic or BurstDRTM stimulation was performed for 30 minutes and the second measurement was performed. After another 30 min stimulation period using the remaining mode of stimulation, the third measurement was taken. The mean of each QST parameter was calculated for each stimulation method and compared. We also computed Z values using standard data and analyzed them for an approximation to zero, indicating a normalization tendency of the corresponding nerve fibre function.

Results

The QST raw data showed a statistically significant improved vibration sensation ($A\beta$) ($P=0,019$) and lower mechanical pain threshold ($A\delta$) ($P=0,031$) with BurstDRTM in comparison to tonic SCS. In the Z-value analysis, we found a significant improvement in vibration sensation and thus $A\beta$ fibre function under BurstDRTM compared to tonic SCS. As a trend under activated SCS, we found an improvement in the tactile detection threshold ($A\beta$). With regard to the Z values, BurstDRTM seemed to be superior regarding the normalization tendency of the $A\delta$ fibre function for the mechanical pain threshold and tonic SCS regarding the heat detection threshold (C) and cold pain threshold (C and $A\delta$). In the Z-profile of the examined patients, a normalization (Z-value within the 95% CI of the standard data) of individual parameters under active SCS was found.

Conclusion

Due to the small number of cases and the numerically small differences, the data we collected, does not permit any definite conclusions as to the influence of the different fibre functions by the various stimulation methods. However, we have been able to show that for some QST parameters and the fibre functions tested, normalization tendencies are recognizable.

Spinale Neuromodulation/*Spinal neuromodulation*

V101

Der Einfluss von BurstDRTM und tonischer Rückenmarkstimulation (SCS) bei chronischen neuropathischen Schmerzen auf den Blutglukose-Spiegel

Influence of BurstDRTM and tonic spinal cord stimulation (SCS) in chronic neuropathic pain on blood glucose levels

M. Morgalla¹, H. Fritschle¹, A. Vosseler², C. Benkendorff², A. Lamprinou², M. Tatagiba¹, A. Fritsche²

¹Eberhard Karls Universität Tübingen, Neurochirurgische Klinik, Tübingen, Germany

²Eberhard Karls Universität Tübingen, Medizinische Klinik IV Endokrinologie, Tübingen, Germany

Objective

Spinal cord stimulation (SCS) has been successfully used to treat chronic neuropathic pain. Little is known about the effect of this stimulation on other body functions. It is conceivable that SCS influences glucose metabolism by stimulating vegetative neurons (Kapural et al., 2004). Especially the spatial proximity between stimulation electrodes and sympathetic neurons suggests a possible influence. In this study, we tested the hypothesis that SCS improves glucose metabolism and, specifically, insulin sensitivity.

Methods

Ten subjects (4 men, mean age 48.8 years) were studied who had an SCS system implanted to treat chronic neuropathic leg or arm pain. All participants had no manifest diabetes mellitus. To record the glucose metabolism and insulin sensitivity, the gold standard of the euglycemic hyperinsulinemic clamp (EHC) was used with an insulin infusion of 1mU / kg body weight per minute. During the clamp, sham-stimulation, tonic stimulation and BurstDRTM stimulation were performed randomly in each case for 30 min (n = 4) or 45 min (n = 6). The glucose infusion rate during the last 30 minutes of the stimulation and the insulin sensitivity index (glucose infusion divided by insulin levels) were determined.

Results

During the EHCs blood glucose was kept constant at 90 mg / dl. The required glucose infusion rate showed a tendency to a higher glucose infusion rate during tonic stimulation compared to sham stimulation ($p = 0.047$). If the glucose infusion rates were adjusted to the insulin level during the respective stimulation (insulin sensitivity index), there is a better insulin sensitivity under tonic stimulation than under sham stimulation ($p = 0.037$). Burst stimulation alone does not lead to a significantly better insulin sensitivity compared to sham. However, the mean effect of burst and tonic showed an improved insulin sensitivity compared to sham.

Conclusion

The results of this pilot study show that BurstDRTM and tonic stimulation improved glucose and insulin sensitivity. Thus, it can be supposed that in patients treated with SCS the sensitivity is generally altered by the stimulation. Further investigations are needed to investigate the clinical relevance for the improvement of glucose metabolism in diabetic patients and the underlying mechanisms.

Literature

KAPURAL, L., HAYEK, S. M., STANTON-HICKS, M. & MEKHAIL, N. 2004. Decreased insulin requirements with spinal cord stimulation in a patient with diabetes. *Anesth Analg*, 98, 745-6

Spinale Neuromodulation/*Spinal neuromodulation*

V103

Prädiktoren für postoperative Komplikationen nach der selektiven dorsalen Rhizotomie – Gibt es Stolpersteine in der Patientenauswahl?

Predictors of postoperative complications following selective dorsal rhizotomy – Are there stumbling blocks in patient selection?

J. Wach, C. Yildiz, M. Schneider, S. Sarikaya-Seiwert, H. Vatter, H. Haberl

Universitätsklinikum Bonn, Neurochirurgie, Bonn, Germany

Objective

Selective dorsal rhizotomy (SDR) reduces spasticity in children with cerebral palsy (CP). Object of this study is to analyze potential preoperative predictors of surgical complications following SDR via a single-level laminectomy at the medullary conus.

Methods

140 SDRs performed via a single-level laminectomy in children (2-18 years old) were included in this retrospective study from 03/2016 - 07/2019. 69% of the children with CP were ambulatory (GMFCS II&III). Univariate -, binary logistic regression-, and receiver operating characteristic analyses were performed with regard to variables potentially associated with wound dehiscences, wound infections, CSF leaks and prolonged pain management via epidural catheters.

Results

Prolonged wound healing disorders were seen in 5 children (3.6%). Obesity (BMI-percentile \geq 95th) was statistically significant associated with delayed wound healing in the binary logistic regression analysis (OR:24.4; 95% CI:3-199;p=0.003).

2 (1.4%) superficial wound infections were observed. Obesity (p=0.004) and thrombocytopenia (<180.000 G/l; p=0.028) were associated with wound infections in the two-sided Fisher's exact test. AUC of BMI-percentile regarding SSI was 0.97 (95%CI:0.94-0.99, p=0.023). Sensitivity and specificity to observe a SSI were 100 % and 95.6 % if cut-off is set at \geq 93th BMI percentile.

CSF leaks were seen in 4 (2.9%) children. Pearson's (two-sided) chi-squared test analyzed that an age \leq 5 is associated with CSF leaks (p=0.029).

15 (10.7%) children required prolonged (4&5 days) pain treatment using epidural catheters. Non-ambulatory GMFCS levels (IV&V) were statistically significant associated with prolonged epidural pain treatment following SDR in binary logistic regression analysis (p=0.008; OR: 3.6; 95% CI:1.2-10.8).

Conclusion

SDR is a safe procedure among all GMFCS levels. Obesity is a predictor for prolonged wound healing and SSI. Prolonged pain management via epidural pain catheters is safe but has to be reminded in non-ambulatory children (GMFCS level IV&V).

Spinale Neuromodulation/*Spinal neuromodulation*

V104

Dorsal column mapping bei intramedullären Tumoren – ein prospektiver Vergleich zweier Methoden und neurologische Verlaufsbeobachtung

Dorsal column mapping in resection of intramedullary tumours – a prospective comparison of two methods and neurological follow-up

M. Ueberschaer, A. Szelényi, S. Zausinger, J. Tonn

Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgie, München, Germany

Objective

When performing surgery for intramedullary spinal cord tumours (imSCT) distortion of the regular anatomy makes visual identification of the dorsal columns (DC) and the midline for myelotomy challenging. For neurophysiological identification of the DC, dorsal column mapping (DCM) and spinal cord stimulation (SCS) are used. This study compares both methods in clinical use and describes their clinical impact.

Methods

In a single centre, prospective study patients with thoracic or cervical imSCT undergoing surgery from 04/2017 to 06/2019 were included. DMS was determined as follows: (1) visual identification and marking of the anatomical midline by the surgeon (2) recording of spinal SSEPs to follow tibial and/or median stimulation with an 8-channel DCM-electrode (AdTech Co., USA) and (3) SCS by bipolar concentric probe (Inomed Co., Germany) and recording of cortical SEP phase reversal at C3/C4. Time of measurement, handling, interpretation and reliability of both methods were analysed. Standardized neurological examinations were performed preoperatively and one week postoperatively.

Results

13 patients (8 f; median age 43 years (15-79)) with a median McCormick Score (McS) of 1 (0-3) were studied.

The DCM electrode detected the midline in 9/13 patients, with handling limitations in the remaining patients. SCS was applicable in all patients with reliable results in 9/13. If both recordings could be acquired (5/13), concordance was 100%. If standard SSEPs were poor, both methods were unstable. The SCS method was significantly less time-consuming (9min. Vs. 17min.; $p=0,001$).

The anatomical midline indicated by the surgeon diverged by a mean of 0.5 mm (± 0.8 mm) compared to the neurophysiologically identified midline. In 9/13 patients with distorted anatomy, DCM and SCS were helpful to confirm optimal region of myelotomy.

In the surgeon's perception implementation of the SCS probe was felt safer and easier compared to the DCM electrode. After myelotomy based on anatomical and neurophysiological findings, no losses of SSEPs occurred with worsening $>50\%$ in 3 patient. 3 patients deteriorated to a McS of >1 (med. 2 (1-3)).

Conclusion

DCM and SCS are helpful to identify the correct region for myelotomy in imSCT with a favourable clinical outcome in this cohort. Regarding reliability and interpretation of measurements both methods were comparable while the SCS method evolved to be superior to the DCM electrode concerning applicability and time expenditure.

Hydrozephalus/Hydrocephalus

V105

Zervikale Myelopathie durch shuntassoziierte Überdrainage – Fallserie *Overshunting associated myelopathy – case series*

A. K. Bruns¹, L. Stögbauer¹, S. D. Adib², M. Tatagiba², W. Stummer¹, M. Schwake¹

¹Universitätsklinikum Münster, Neurochirurgie, Münster, Germany

²Universitätsklinikum Tübingen, Neurochirurgie, Tübingen, Germany

Objective

Overshunting associated myelopathy (OSAM) is a rarely described condition, with only few reported cases. Many of them are misdiagnosed as cervical stenosis. This normally leads into worsening conditions. With this series we want to sensitize to this pathology, outline the clinical and radiological characteristics and propose treatment options.

Methods

Between 2014 and 2019 we treated four patients with overshunting associated myelopathy. We report their clinical findings, imaging and treatment.

Results

All four patients had a shunt dependent hydrocephalus and were admitted due to a progressive myelopathy. All underwent cervical MRI with contrast and cranial MRI or CT, two of them got a venous CTA. Imaging demonstrated enlarged epidural venous vessels and compression of the spinal cord. The ventral dura was thickened and irregular. Pat. 1 was initially misdiagnosed and treated with decompression of C1-C2. Later an adjustable shunt-valve was implanted followed by pressure adjustment. Pat. 2 underwent surgery for multilevel cervical stenosis and got an adjustable shunt-valve followed by pressure adjustment. Pat. 3 and 4 were treated with valve-adjustment.

Conclusion

Chronic over drainage may lead to an enlargement of the epidural venous plexus, according the Monroe-Kellie doctrine, causing cord compression and progressive myelopathy. Complex spinal surgery could be avoided in most cases by recognizing radiological patterns and valve-implantation/-adjustment. Wherefore a sensitization for this condition is important, as prevalence of OSAM may be underestimated and often misdiagnosed.

Hydrozephalus/Hydrocephalus

V107

Ein prospektiver Vergleich der Shuntventile proGAV 2.0 und CertasPlus in der Behandlung des idiopathischen Normaldruckhydrozephalus und des sekundär kommunizierenden Hydrozephalus

A prospective comparison of the shunt valves proGAV 2.0 and CertasPlus in the treatment of idiopathic normal pressure and secondary communicating hydrocephalus

I. Fiss, N. Eckert, B. Sommer, C. Bettag, C. Von der Brelie, V. Rohde

Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Implantation of a vp-shunt represents the current standard of care in hydrocephalus patients. Both combination valves implanted in this study contain a proprietary differential pressure valve, which is combined with a gravity-regulated anti-siphon device (ASD) in the proGAV (PG) valve and with a flow-controlled ASD in the CertasPlus (CP) valve. We sought to investigate whether the risk and performance profile differs in the two combination valves.

Methods

Assignment of patients to valve type was block randomized in this prospective observational study. The sample consisted of 79 adult patients with hydrocephalus who received a vp-shunt for the first time. The two largest diagnostic subgroups (66 patients in total) were analyzed, namely iNPH (44%, n=35) and secondary communicating hydrocephalus (39%, n=31). Analyzed frontal occipital horn ratio (FOHR) and Evans index were CT derived. FOHR, Evans index and Stein-Langfitt (SL) scores were assessed prior to valve implantation and at follow-up. Black grading scale was assessed at follow-up only.

Results

In this intermediate analysis, patients with iNPH compared to patients with secondary communicating hydrocephalus were significantly younger (75 ± 6 years vs. 58 ± 15 years, $p < 0.01$). In patients with secondary communicating hydrocephalus, FOHR and Evans index tended to improve due to valve-treatment ($p = 0.10$ and $p = 0.24$) while SL scores improved significantly ($p = 0.015$). No difference between valve types was found, neither on level ($p \geq 0.29$) nor on time-course ($p \geq 0.37$). In patients with iNPH, FOHR and Evans score changed significantly due to valve treatment ($p \leq 0.01$ and show a tendency for improvement of Stein-Langfitt ($p = 0.067$). Of note, in patients with iNPH, FOHR, Evans, and SL scores prior to valve-implantation had been significantly lower in CP compared to PG ($p = 0.0021$ multivariate joint test). Postoperative change in Evans ($p = 0.95$) and FOHR did not differ significantly ($p = 0.39$) and no differences were observed in median SL nor Black scale between valves ($p = 0.64$). There were 2 revisions in the PG group (1 wound dehiscence, 1 cranial catheter occlusion) and none in the CP group. No difference in number of valve adjustments between CP and PG ($p = 0.24$) was observed in both hydrocephalus subtypes.

Conclusion

VP-shunt insertion for treatment of hydrocephalus can be performed safely and effectively with both valve types. No difference in outcome was noted between both valve types.

Hydrozephalus/Hydrocephalus

V108

Vermeidbarkeit von Shunt-Revisionen

Shunt revision surgery – How many are avoidable?

S. Kaestner^{1,2}, U. Kehler³, M. Krause⁴, S. Antes⁵, W. Deinsberger^{1,2}

¹Klinikum Kassel, Neurochirurgie, Kassel, Germany

²University of Southampton, Kassel School of Medicine, Kassel, Germany

³Asklepios Klinik Altona, Neurochirurgie, Hamburg, Germany

⁴Universitätsklinikum Leipzig, Neurochirurgie, Leipzig, Germany

⁵Westpfalz-Klinikum, Neurochirurgie, Kaiserslautern, Germany

Objective

CSF shunt revision surgery accounts for a tremendous social and economic burden and lowering shunt revision rates is desirable. The amount of avoidable shunt revisions is unknown. Only a few studies analyzed the preventability of shunt revisions exclusively in pediatric cohorts. This study aimed to analyze the potential of avoidable shunt revisions in a mixed cohort of CSF-shunt patients.

Methods

A retrospective review of a prospectively maintained database identified all newly inserted shunt systems in a ten year period from 2007 to 2016 in a single center. Clinical data and all subsequent revision surgeries with a follow up of at least one year were documented. Every revision surgery was assigned to one of the following categories: preventable, partly preventable and unpreventable. The assignment was decided by a group of 5 experienced shunt surgeons throughout the country. The rate of avoidable revisions was calculated and correlated with clinical data.

Results

314 patients with a mean age of 49.9 years received 210 revision surgeries with a mean follow up of 4.2 years. 89 revisions were judged as unpreventable (42.4%). 67 revisions were partly preventable (31.9%), whereas 54 revisions (25.7%) were classified as preventable. Assuming a possible reduction of 50% in the "partly preventable" group the rate of avoidable revisions increases to 41.4%. The level of education and the years of surgical experience are linked to the rate of preventability, but even in very experienced hands 13.8% of their revisions are avoidable. Preventable and partly preventable revisions occur significantly earlier than unpreventable surgeries (mean 80, 130 and 547 days resp.) after index surgery

Conclusion

At least one fifth up to two fifth of all subsequent shunt revision surgeries are avoidable even in experienced hands. Avoidable revisions occur significantly earlier predominately within the first three months after surgery.

Hydrozephalus/Hydrocephalus

V109

Shuntoskop-gestützte versus freie Handtechnik bei Ventrikelkatheter-Anlage – Pilotstudie *Shuntoscope-guided versus free hand ventricular catheter placement – pilot study*

A. El Damaty, H. Bächli, A. W. Unterberg

Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

Objective

Despite the widespread use of external ventricular drainage, revision rates, and associated complications are reported between 10 and 40%. Current available image-guided techniques using stereotaxy, endoscopy, or ultrasound for catheter placements remain time-consuming techniques. We aimed to assess in a small cohort the usage of shuntoscope in ventricular catheter placement.

Methods

The study was prospectively started in July 2018. We divided the patients randomly into two groups where the catheter is either placed using free hand technique according to anatomical landmarks or with the aid of a shuntoscope. All patients were operated by the same neurosurgeon. We included only patients who received a ventricular puncture in a "virgin" ventricle which was never punctured before to avoid misleading previous tracts even if it was a shunt revision including placement of a new ventricular catheter in the other side. We reviewed the operative time, position of the catheter tip (three-point scales): 1) Grade I; optimal catheter tip position free-floating in CSF. 2) Grade II; catheter tip touching choroid plexus or ventricular lining wall. 3) Grade III; tip within parenchyma or failure to reach the intraventricular space, infection, need for revision surgery within 12 months after placement.

Results

We totally collected 30 patients. 16 patients were operated using shuntoscope and 14 patients using free hand technique. The mean operative time for complete shunt OP using shuntoscope group was 40 minutes vs 36 minutes in free hand group. We found in all cases of shuntoscope a Grade I catheter placement (100%), in comparison to 11 patients with Grade I (78.6%), 3 with Grade II (21.4%) in free hand group. 2 patients in shuntoscope group suffered from a shunt infection (12.5%) and needed revision surgery within 12 months. A single patient in the free hand group required surgery due to development of subdural hygroma as a sequel of overdrainage (7%).

Conclusion

We think that the use of shuntoscope could significantly improve the placement of ventricular catheter specially in difficult cases without significant prolongation of the operative time. A larger study recruiting more patients is needed to prove the validity of the primary results.

Hydrozephalus/Hydrocephalus

V110

Sekundäre Verschlechterung bei iNPH – Behandelbar oder nicht?

Secondary deterioration in idiopathic normal pressure hydrocephalus in the very long term – Treatable or not? – a retrospective analysis

S. Kaestner^{1,2}, R. Behrends^{1,2}, W. Deinsberger^{1,2}

¹Klinikum Kassel, Neurochirurgie, Kassel, Germany

²University of Southampton, Kassel School of Medicine, Kassel, Germany

Objective

Cerebrospinal fluid (CSF) shunting is a highly effective treatment in iNPH, but secondary deterioration can occur in the later course. The aim of this study was to evaluate the rate and causes of secondary deterioration.

Methods

A retrospective analysis of all patients with iNPH treated with CSF-shunt implantation since 1993 was performed. All patients with a secondary deterioration were offered a meticulous "shunt work up". Data related to the number and causes of deteriorations, the subsequent treatment, and the clinical outcome was extracted.

Results

A total of 169 patients with a mean follow-up of 69.2 months could be included. 119 patients (70.4%) experienced a total of 153 secondary deteriorations. In 9 cases delayed subdural haematoma caused the deterioration. In 27 events the cause for deterioration was a proven shunt dysfunction (22.1%). Invasive shunt testing was frequently necessary to confirm shunt failure. The majority of patients (19/27) experienced a good improvement after revision surgery. 86 deteriorations were due to non-surgical causes and the valve pressure was lowered in 79 patients, with only 16.5% showing good amelioration of symptoms.

Conclusion

The majority of shunted iNPH patients deteriorate in the long term. Shunt dysfunction is a valid cause of secondary deterioration. Since shunt revision surgery is highly effective, we recommend that patients with deterioration are screened for shunt dysfunction including invasive shunt testing.

Pädiatrische Neurochirurgie & neurovaskuläre Chirurgie/Paediatric neurosurgery & neurovascular surgery

P001

Einfluss des prädiagnostischen Intervalls bei Kindern mit Tumoren des zentralen Nervensystems *The influence of pre-diagnostic symptomatic interval (PSI) for neoplastic disorders of the central nervous system in children – a retrospective longitudinal study*

Y. Ahmadipour¹, L. Rauschenbach¹, O. Gembruch¹, D. Pierscianek¹, P. Dammann¹, K. H. Wrede¹, N. El Hindy², U. Sure¹, R. Jabbarli¹

¹Universitätsklinikum Essen, Klinik für Neurochirurgie und Wirbelsäulenchirurgie, Essen, Germany

²Sankt Christophorus-Krankenhaus Werne, Abteilung für Wirbelsäulen- und Periphere Nerven Chirurgie, Essen, Germany

Objective

Due to prevalence of non-specific clinical symptoms, timely diagnosis of neoplastic lesions of central nervous system (CNS) lesions might be challenging in pediatric population. Yet whether early diagnosis contributes to better life prognosis and functional outcome is not clear. We examined the time to diagnosis, the so called prediagnostic symptomatic interval (PSI) and its impact on prognosis and functional outcome in children with CNS tumors.

Methods

We retrospectively reviewed the records of 136 patients aged <18 years who were operated with a CNS tumor in our neurosurgical department between January 2010 and December 2015. Tumors entities were analyzed separately and in dichotomous manner according to the WHO classification (III-IV vs I-II). Presence and duration of clinical symptoms before and after surgery were analyzed. Univariate and multivariate analyses were performed.

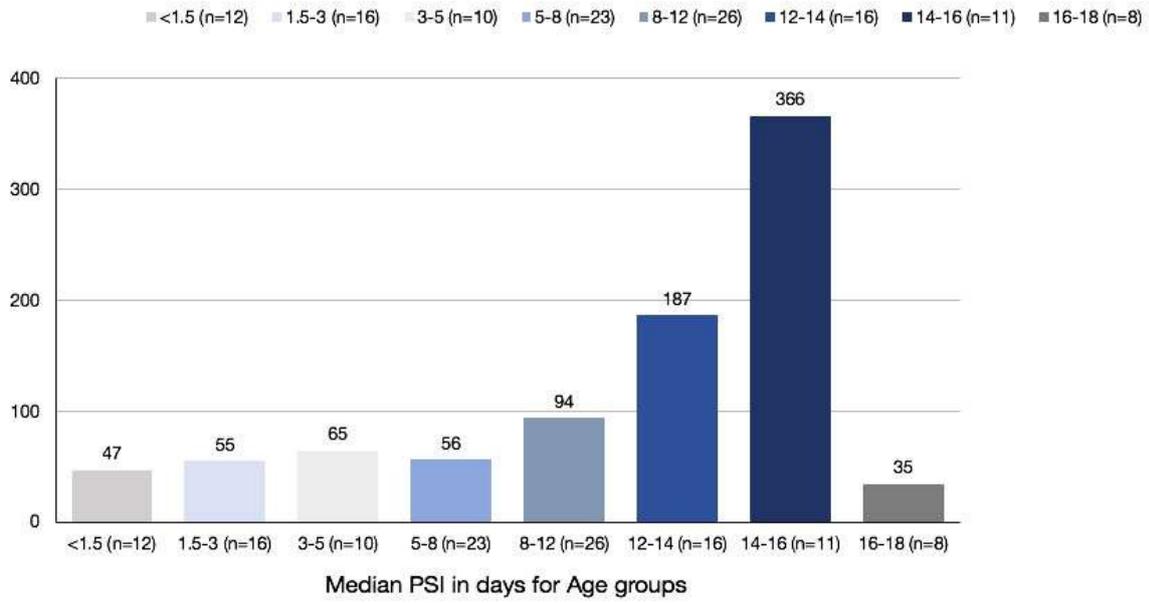
Results

The median age at diagnosis was 8.3 years (range 3 weeks–17.9 years). The male-to-female ratio was 1:1.2. Pilocytic Astrocytoma occurred as the most common diagnosis in 44 (32.4%) children followed by Anaplastic Ependymoma with 15 (11%). Median evaluated PSI was 74.5 days. Age group of 14 to 16 years revealed a significant higher ($p=0.01$) PSI. High-grade tumors were characterized with significantly shorter PSI (1.8 vs 3.6 months, $p<0.01$). Clinical symptoms like impaired vision ($p=0.02$) and vomiting ($p=0.042$) were associated with higher PSI whereas coordination disturbances ($p=0.02$) and increased head circumference ($p=0.04$) were related to shorter PSI. Overall survival ($p=0.75$) was not associated with the PSI.

Conclusion

PSI of children with CNS tumors might substantially vary, depending predominantly on the biological grading of the tumor. Moreover, presence of unspecific symptoms in adolescent might also lead to a higher PSI. Probably due to stronger impact of other confounders, timing of diagnosis was not associated with the patients' survival.

Fig 1



Pädiatrische Neurochirurgie & neurovaskuläre Chirurgie/Paediatric neurosurgery & neurovascular surgery

P002

Sekundäres Glioblastom als Lokalrezidiv nach Medulloblastom bei einem 17-Jährigen – Fallbericht über das Risiko von späten Komplikationen der Therapie
Secondary glioblastoma as a local recurrent after medulloblastoma in a 17-year old – case report on the therapeutic risk of late complications

F. S. Fritzsche¹, F. L. Ricklefs¹, G. Kammler¹, U. Schüller², M. Westphal¹

¹Universitätsklinikum Hamburg-Eppendorf, Neurochirurgie, Hamburg, Germany

²Universitätsklinikum Hamburg-Eppendorf, Neuropathologie, Hamburg, Germany

Objective

We report on a 17 year old boy who suffered local tumor reoccurrence 9 years after medulloblastoma (MB) diagnosis. Histopathological workup revealed a glioblastoma (GBM). Cases of secondary GBM after MB are reported rarely. The reasons for these infrequent cases are not consistently understood and probably very distinct. The occurrence of a late intracranial secondary malignancy still is associated with poor prognosis. The purpose of this description is to show the need for risk evaluation concerning adjuvant therapy in young individuals and to ask the question, which patients might be predestined to develop subsequential GBM.

Methods

This report describes the medical course of a single individual. Clinical records were completely available for analysis. Data was examined concerning clinical symptoms, MRI-studies, surgical procedures, histology and adjuvant therapy.

Results

The patient was 9 years of age at diagnosis of a MB (classical subtype, nuclear beta-catenin accumulation). The resection was subtotal, the clinical findings of 6th nerve palsy, ataxia, nystagmus were not completely resolved after surgery. An individual, alternating chemotherapy with VCR/CCNU/cisplatin, cyclophosphamide and carboplatin followed craniospinal radiation (helical tomotherapy 1,8 Gy, cs 18 Gy, boost fossa posterior 54 Gy, boost onto remaining tumor tissue 59,5 Gy). After 9 years of a disease-free survival the now 17 year old was admitted as an emergency with severe headache, nausea and an intracerebellar MRI lesion and occlusive hydrocephalus. Resection was gross total in the absence of spinal metastasis. Histology showed glioblastoma IDHwt, MGMT not methylated, no MSI and no relation to the original tumor. A combined radiotherapy and chemotherapy (VBL, valproate) is suggested by tumor board.

Conclusion

Secondary GBM in children and adolescents following a disease-free survival of 9 years after MB is considered rare. In those cases the role of molecular markers is significant. In the reported case neuropathological workup did not offer an individual targeted approach. Given the limited treatment options and the poor prognosis, extent of surgical resection is crucial. Such cases are to be collected in comprehensive registries including molecular analyses to gain insights into the pathways leading to possibly therapy associated secondary malignancy.

Pädiatrische Neurochirurgie & neurovaskuläre Chirurgie/Paediatric neurosurgery & neurovascular surgery

P003

Funktionelles Outcome nach Durchtrennung des Filum bei Kindern mit okkultem Tethered Cord Syndrom und Fatty Filum

Functional outcome after filum sectioning in occult tethered cord syndrome and fatty filum

S. Deininger¹, N. A. Terpolilli², M. Kunz², M. Schuler-Ortholi¹, A. Peraud^{1,2}

¹Universitätsklinikum Ulm, Neurochirurgie und Pädiatrische Neurochirurgie, Ulm, Germany

²Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgie, München, Germany

Objective

Minor variants of occult spinal dysraphism comprise the tight filum in occult tethered cord syndrome (OTCS) as well as the thickened or fatty filum (FF). The underlying abnormal tension of the spinal cord can lead to various clinical symptoms such as motor deficits, urological disturbances, and pain, despite relative discrete radiomorphological signs on MR images. The aim of the current study was to highlight clinical scenarios rectifying microsurgical detethering even in almost normal MR images, and to demonstrate postoperative outcome.

Methods

We retrospectively analysed clinical records of pediatric patients who underwent microsurgical filum sectioning for OTCS or FF at the Section of Pediatric Neurosurgery, University of Munich and Ulm between 01/2007 and 11/2019. All children underwent microsurgical detethering under intraoperative electrophysiological monitoring and had multidisciplinary follow-up.

Results

33 patients (17 male, 16 female) diagnosed for either OTCS (22 patients) or FF (11 patients) were included in the study. Mean age at surgery was 6.0 years (range 0.6–16.8 years). Presenting symptoms consisted in bladder (26, 78.8%) or bowel dysfunction (7, 21.2%; 3 caudal regression syndromes), motor deficits (21, 63.6%), foot deformities (15, 45.5%) and pain (8, 24.2%; leg, back, perineal). In addition to minimal signs of a tethered cord with tight or fatty filum, MR images showed syrinx in 9 and scoliosis in 4 patients. Postoperatively, bladder dysfunction improved in 16/26 (61.5%), bowel problems in 1/7 (14.3%), motor deficits in 14/21 (66.7%), pain in 4/8 (50%), and foot deformities in 1/14 (7.1%) patients. Apart from one superficial wound infection no complications occurred and none of the patients showed any worsening of their symptoms. Median follow-up was 2.3 years.

Conclusion

The results of the present study demonstrate a surprisingly high chance for improvement of bladder and motor deficits as well as pain in patients with either a tight or a fatty filum after sectioning of the filum. The complication rate is low. Thus, the indication for filum sectioning should always be considered in patients with typical symptoms even when MR images show only minimal or no clear signs for tethered cord.

Pädiatrische Neurochirurgie & neurovaskuläre Chirurgie/*Paediatric neurosurgery & neurovascular surgery*

P004

Partikelembolisation der *A. meningea media* zur Behandlung chronisch subduraler Hämatome – erste Erfahrungen

Middle meningeal artery embolisation as a treatment for chronic subdural haematoma – first single-centre experience

N. Grübel¹, B. Schmitz², M. Braun², C. R. Wirtz³, A. Pala¹

¹Bezirkskrankenhaus Günzburg, Neurochirurgie, Günzburg, Germany

²Bezirkskrankenhaus Günzburg, Neuroradiologie, Günzburg, Germany

³Bezirkskrankenhaus Günzburg, Neurochirurgie, Günzburg, Germany

Objective

Chronic subdural hematoma (cSDH) is a common disease which is increasing in frequency each year due to aging population and the use of anticoagulation and antiplatelet medication. High recurrence rates after operative treatment, cardiovascular and other comorbidities are common in this patient cohort, so that alternative treatment methods might improve outcome in selected cases. We used middle meningeal artery (MMA) embolization for patients with newly diagnosed cSDH who had critical cardiovascular risk factors and were in urgent need for antiplatelet medication as well as for patients with therapy refractory recurrent and symptomatic cSDHs

Methods

MMA embolization was performed in 10 patients with therapy refractory cSDH or multimorbid patients using angiography, selective microcatheterization of the MMA, and embolization using microspheres (Embozene) different sizes and coils. The outcome was assessed clinically and with individually indicated follow-up cCT imaging. Coronal cCT images were used to measure the thickness of haematomas, hyperdens areas, chronic parts and membranes.

Results

MMA embolization was performed successfully in 10 patients with cSDH. The indications were 1. treatment for new (not previously treated) cSDH in 3 patients, 2. recurrent cSDH in 5 Patients, and 3. Prophylactic treatment (soon after surgical evacuation) in 2 patients. No patient needed additional surgical evacuation after the treatment, and 70 % had a reduction in size >50% of SDH at longest follow-up. Long term follow-up cCT imaging is outstanding. One patient had one new neurological deficit (abducens paresis) after MMA which was recurrent after long-term follow up. 60% were treated with MMA embolization under anticoagulation.

Conclusion

MMA embolization may represent a minimally-invasive alternative or additional procedure to surgery for new or recurrent chronic SDH, especially in patients with a high risk cardiovascular profile or when cardiovascular disease does not allow pausing anticoagulation. Additionally, patients with therapy refractory recurrent and symptomatic cSDHs could benefit from this procedure

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P005

Effektivität und Kostenanalyse des Cell-saver Einsatzes in der chirurgischen Behandlung zerebraler Aneurysmen

Efficacy and cost effectiveness of intraoperative blood salvage in cerebral aneurysm clipping

B. Behmanesh, E. Adam, F. Geßler, J. Konczalla, V. Seifert, C. Senft

Universitätsklinikum Frankfurt am Main, Neurochirurgie, Frankfurt am Main, Germany

Objective

The use and effectiveness of intraoperative cell salvage has been introduced in many surgical specialties. Until now no data exists evaluating the efficacy of intraoperative cell salvage in cerebral aneurysm surgery.

Aim of the present study is to evaluate the efficacy and cost effectiveness of intraoperative cell salvage in cerebral aneurysm surgery.

Methods

Data were collected retrospectively for all the patients who underwent cerebral aneurysm surgery at our institution. All cases were divided in ruptured cerebral aneurysm group and unruptured cerebral aneurysm group

Results

A total of 212 patients underwent cerebral aneurysm clipping. 102 treated aneurysms were ruptured and 110 were unruptured and clipped electively. The mean preoperative hemoglobin levels of both groups were 13.7 g/dl and 12.8 g/dl respectively, $p = 0.9$. The mean intraoperative

blood loss was 204.5 ml and 633 ml, $p = 0.0001$. Retransfusion of salvaged blood could only be facilitate in 2 cases with ruptured cerebral aneurysms and in none being clipped electively. Of the 212 patients, 31 patients with ruptured cerebral aneurysms and one patient with unruptured cerebral aneurysm required transfusion after surgery and 64 vs. 2 units of blood were transfused, $p = 0.001$. The mean postoperative hemoglobin levels were 11.5 g/dl and 10.7 g/dl respectively, $p = 0.03$.

In terms of cost effectiveness, a total of 42,400 € in 2012 patients were spend to run the cell saver. Additional 26,400 € were spent for allogenic blood transfusion.

Conclusion

The use of cell salvage in cerebral aneurysm clipping is neither efficient nor cost effective.

Pädiatrische Neurochirurgie & neurovaskuläre Chirurgie/Paediatric neurosurgery & neurovascular surgery

P006

Einzelzentrische Analyse des funktionellen Outcomes bei Patienten mit arteriovenöser Malformation *Single-centre analysis of functional outcome in patients with arteriovenous malformation*

I. Hostettler, B. Meyer, M. Wostrack

Klinikum rechts der Isar München, Neurochirurgische Klinik und Poliklinik, München, Germany

Objective

Arteriovenous malformations (AVM) are vascular malformations. Functional outcome differs depending on whether an AVM has bled or not and which treatment modality was used. We evaluated all AVMs treated at our institution.

Methods

Retrospective analysis of a prospectively collected database of all consecutive patients seen in our neurosurgical department between 2006 and 2018. We measured functional outcome using the modified Ranking Scale (mRS) and defined favourable functional outcome as an mRS of 0-2.

Results

A total of 183 patients with cerebral AVMs were included. Mean age was 44.42 years (SD 17.7), 37.7% were female. 112 (61.2%) patients presented with a haemorrhage due to the AVM. 71 (38.3%) patients were treated surgically-only, 10 (5.5%) with embolization-only, 12 (6.6%) with radiosurgery-only and 69 (37.7%) with a combination. In the univariable analysis age, female sex and haemorrhage vs no haemorrhage were associated with favourable outcome on follow-up. In the multivariable analysis age (OR 0.96; 95%CI 0.93-0.98; p-value=0.002), Spetzler Martin Grade (OR 0.64; 95%CI 0.42-0.97; p=0.04) and haemorrhage from AVM (OR 0.14; 95%CI 0.04-0.55; p=0.005) were all inversely associated with functional outcome on follow-up. Surgery did not negatively influence functional outcome on follow-up (p=0.85). 73/181 patients (40.3%) improved the mRS subgroup, 6 demonstrated a decline in mRS subgroup. Of 126/183 where a detailed follow-up was available, 92.1% indicated a complete recovery or improvement of symptoms.

Conclusion

Most patients with AVMs improve considerably during follow-up. Patients undergoing surgery do not have worse functional outcome compared to other modalities.

Pädiatrische Neurochirurgie & neurovaskuläre Chirurgie/Paediatric neurosurgery & neurovascular surgery

P007

Hohe Inhomogenität in der frühen Perfusions-Computertomographie – ein Prädiktor für ein schlechtes Therapieergebnis bei Patienten mit Subarachnoidalblutung

High inhomogeneity of early perfusion computerised tomography measurement – a predictor for poor outcome in patients with subarachnoid haemorrhage

B. B. Hofmann¹, I. Fischer², C. Rubbert³, J. F. Cornelius¹, S. Muhammad¹, D. Hänggi¹, M. A. Kamp¹

¹Heinrich-Heine-Universität Düsseldorf, Abteilung für Neurochirurgie, Düsseldorf, Germany

²Heinrich-Heine-Universität Düsseldorf, Abteilung für Informatik und Statistik, Abteilung für Neurochirurgie, Düsseldorf, Germany

³Heinrich-Heine-Universität Düsseldorf, Institut für Diagnostische und Interventionelle Radiologie, Düsseldorf, Germany

Objective

Impairment of tissue oxygenation caused by inhomogeneous micro- and macroscopic blood flow distribution, the so-called capillary transit time heterogeneity (CTH) was considered to contribute to delayed cerebral ischemia (DCI). Therefore, increased inhomogeneity of parenchymal perfusion can potentially contribute to the development of tissue hypoxia and DCI and ultimately may influence clinical outcome. Aim of the present study was to assess the value of inhomogeneity in early perfusion computerized tomography measurement (PCT) in predicting poor outcome.

Methods

121 patients underwent an early PCT measurement within the first 24 hours after SAH. Inhomogeneity of the mean transit time (MTT) and the time to peak of the residue function (Tmax) in individual patients were correlated with the dichotomized functional outcome initially upon admission (good grade, World Federation of Neurosurgeons Scale (WFNS)^o 1-3 vs. Poor grade, WFNS^o4-5) and at 3 months (unfavorable, Glasgow Outcome Scale (GOS) 1-3 vs. favorable, GOS 4-5). Inhomogeneity of cerebral perfusion was measured as the coefficient of variation (CV) of MTT and Tmax of a representative CAT-scan slice of the entire brain circumference.

Results

Upon admission, 64 patients (53%) were good and 57 patients (47%) poor neurological grade. After three months 46 patients (38%) had an unfavourable and 75 patients (62%) a favourable clinical outcome. The CV of MTT and Tmax did not correlate with the WFNS grade upon admission (CV of MTT: p = 0.9; CV of Tmax: p = 0.6). Also, the CV of MTT did not correlate with the GOS after three months. Contrary to this, CV of Tmax showed a highly significant correlation with the GOS after three months (p=0,002). A high inhomogeneity of Tmax values in the initial PCT scan correlated with a poor functional outcome.

Conclusion

Tmax-CV significantly correlated with the dichotomized clinical outcome of patients 3 months after discharge, whereby a high inhomogeneity of Tmax values in the initial PCT scan correlated with a poor functional outcome. The inhomogeneity of Tmax in early PCT therefore seems to be a potent predictor for the outcome in patients with subarachnoid hemorrhage.

Pädiatrische Neurochirurgie & neurovaskuläre Chirurgie/*Paediatric neurosurgery & neurovascular surgery*

P008

Neuronavigierter STA-M4 Bypass zur Behandlung von fusiformen MCA Aneurysmen – eine Serie von 6 Patienten

Use of neuronavigation for superficial temporal artery to cortical branch of middle cerebral artery (STA-M4) revascularisation in the treatment of fusiform aneurysms of middle cerebral artery (MCA) – a series of 6 patients

A. Tortora¹, J. F. Cornelius², H. J. Steiger², D. Hänggi², A. Petridis²

¹Kantonsspital Aarau AG, Neurochirurgie, Aarau, Schweiz

²Heinrich-Heine-Universität Düsseldorf, Klinik für Neurochirurgie, Düsseldorf, Germany

Objective

STA-M4 bypass combined with trapping is a versatile technique in the treatment of fusiform aneurysms of MCA. Intraoperative identification of the right cortical recipient artery originating from the lesion located in the distal fissure may be demanding. Furthermore, the exploration of the aneurysm prior to revascularization is risky in ruptured cases. We present a series of 6 patients with fusiform MCA aneurysm in which the revascularization was performed with guidance of neuronavigation.

Methods

The preoperative CTA or DSA were uploaded on neuronavigation system. After intraoperative laser surface-based registration of the patient, the donor STA branch, the recipient artery and the craniotomy were located on the skin surface the perform a tailored skin incision. After dissection of STA branch, craniotomy and dura opening, the recipient M4 branch distal to aneurysm was localized by neuronavigation. After vascular reconstruction the aneurysm was excluded from the circulation.

Results

Between January 2016 and November 2019 we treated 6 patients with fusiform MCA aneurysm and therefore STA-M4 bypass and trapping. The mean age was 38.14 years. The aneurysm was located in M2 segment in 5 cases and in M3 segment in one patient. The aneurysm was ruptured in 3 patients, caused epilepsy in 2 patients and was an incidental finding in the 1 case. In all patients the neuronavigation was used to plan the skin incision after localizing the course of STA branches without need of Doppler and according to the site of craniotomy. Only in one case a standard pterional craniotomy was sufficient. In all other cases the location of the lesion in the distal Sylvian fissure or the distal location of the recipient M4 branch on angular or supramarginal Gyri required a tailored approach. In all patients the cortical recipient artery for the anastomosis was correctly localized on the brain surface and prepared for bypass prior of aneurysm dissection. Furthermore in four cases neuronavigation was used to localize the aneurysm in the distal Sylvian fissure allowing just a selective opening.

Conclusion

Neuronavigation is a useful tool for this complex surgery. It allows straightforward identification of the recipient artery, tailored Sylvian dissection and increased safety of the procedure.

Pädiatrische Neurochirurgie & neurovaskuläre Chirurgie/*Paediatric neurosurgery & neurovascular surgery*

P009

Lebensqualität bei Patienten nach rupturierten und inzidentellen intrakraniellen Aneurysmen *Quality of life after ruptured and unruptured intracranial aneurysms*

N. Grübel¹, R. König², T. Kapapa², C. R. Wirtz², A. Pala¹

¹Bezirkskrankenhaus Günzburg, Neurochirurgie, Günzburg, Germany

²Bezirkskrankenhaus Günzburg, Neurochirurgie, Günzburg, Germany

Objective

Aneurysmal subarachnoid haemorrhage (SAH) can lead to permanent neurological, psychosocial and neurocognitive deficits and can decisively influence the subsequent quality of life (QoL). These potential sequelae after the treatment of unruptured intracranial aneurysms (UIA) is similarly an important factor in the decision making for the intervention and further counselling. The aim of our study was to compare QoL data including anxiety and depression as well as cognitive deficits in patients after treatment of UIA and patients after SAH.

Methods

Retrospectively, we compared the QoL of patients after endovascular and surgical treatment of UIA with patients after SAH using standardized questionnaires; 36- Item Short Form Health Survey (SF-36), Hospital Anxiety and Depression Scale (HADS), German questionnaire for self-perceived deficits in attention (FEDA) and not standardized questionnaire analyzing personal job-related situation, family circumstances and chronic illnesses.

Results

Based on SF-36 all patients with treated UIA showed reduced QoL compared to the normal control cohort. Both physical and psychological scales showed decreased QoL. In detailed comparison of patients after SAH and UIA all parameters of SF-36, except for pain are higher in patients with UIA. Return to work is a great indicator for complete recovery and an excellent tool to decrease potential depression periods. However, chronic illnesses and current job situations and not treatment itself had the most relevant influence on QoL in patients with UIA.

Conclusion

The concept of the QoL as an evaluation criterion of outcome has to be seen differentiated for SAH and UIA patients. The different initial situation in both patient collectives seems to lead to different individual assessments of QoL with different influencing factors.

Fig 1

Table 1. Results of Short Form 36 Health Survey for Patients with Unruptured Intracranial Aneurysm Compared with Patients After Spontaneous Subarachnoid Hemorrhage

	Mean (SE)	Mean (SE) Normal Population	P	Mean (SE)
Physical functioning (n = 78)	72.94 (25.04)	85.41 (25.85)	<0.001	89.79 (23.28)
Role physical (n = 78)	58.06 (46.28)	82.38 (32.85)	<0.001	58.37 (41.85)
Body pain (n = 78)	63.00 (31.12)	87.38 (25.87)	0.386	70.53 (28.90)
General health (n = 78)	54.46 (22.42)	80.42 (18.10)	<0.001	69.44 (22.70)
Vitality (n = 78)	68.96 (21.87)	89.02 (11.80)	<0.001	49.48 (21.94)
Social functioning (n = 78)	71.84 (25.99)	88.28 (19.92)	<0.001	71.28 (27.81)
Role emotional (n = 73)	63.47 (44.15)	88.11 (28.88)	<0.001	67.18 (40.84)
Mental health (n = 78)	64.50 (20.67)	72.48 (18.88)	0.007	64.58 (12.88)
Physical component summary (n = 73)	43.73 (12.98)	48.36 (9.42)	0.002	49.08 (12.89)
Mental component summary (n = 73)	48.06 (12.98)	58.87 (8.82)	<0.001	44.48 (11.75)

SE, standard error.
 *p < 0.05.

Pädiatrische Neurochirurgie & neurovaskuläre Chirurgie/*Paediatric neurosurgery & neurovascular surgery*

P011

Hunt und Hess Grad V aneurysmatische Subarachnoidalblutung – Effekt der aggressiven Behandlung auf das klinische Ergebnis

Hunt and Hess grade V aneurysmal subarachnoid haemorrhage – the effect of aggressive care on clinical outcome

L. M. Schenk, A. Hadjiathanasiou, S. Brandecker, P. Schuss, H. Vatter, E. Güresir

Universitätsklinikum Bonn, Klinik und Poliklinik für Neurochirurgie, Bonn, Germany

Objective

Patients presenting with Hunt and Hess grade V aneurysmal subarachnoid hemorrhage (aSAH) are in extremely critical condition at admission, resulting in the assumption of a generally poor prognosis.

To gain further insight into the effect of instantaneous and straightforward treatment this study assessed the clinical outcome of 238 patients with aSAH Hunt and Hess grade V using our prospectively conducted database.

Methods

A total of 238 patients admitted into the authors' clinic between January 2002 and November 2018 and were analyzed in regards of treatment and clinical outcome.

This period of time was divided into three terms, specifically 2002-2007, 2008-2012 and 2013-2018.

Clinical outcome was assessed using the modified Rankin Scale (mRS) and dichotomized into favorable (mRS score 0-3) versus unfavorable outcome (mRS score 4-6) at time of discharge, at 6 months and at 1 year after ictus.

Results

Data was available for a total of 238 patients at discharge, 225 patients at 6 months and 195 patients at 1 year after ictus.

In the time period from 2002-2007, 5.6% achieved favorable outcome at time of discharge, 4.9% after 6 months and 5.8% after 1 year.

Patients in 2008-2012 achieved favorable outcome in 1.4% at discharge, 5.6 % at 6 months and 6.3% after 1 year.

In contrast, patients treated from 2013-2018 achieved favorable outcome in 12.6% at discharge, 17.2% at 6 months, and 17.7% after 1 year.

Comparing the rates of favorable outcome in the cohort of patients treated between 2002-2012 and the cohort treated between 2013-2018, the rates of favorable outcome differed significantly early as well as late during the treatment course with $p=0.009$ at discharge, $p=0.006$ at 6 months and $p=0.02$ at 1 year respectively.

Conclusion

Poor grade SAH patients Hunt and Hess grade V may achieve favorable outcome in the modern era in a significant number when treated in terms of aggressive care.

Neurovaskuläre Chirurgie/*Neurovascular surgery*

P013

Die Rolle der spannungsgesteuerten Ca²⁺-Kanäle (VGCCs) im Rahmen der neurovaskulären Kopplung – eine Evaluation mittels kontaktloser, retinaler Gefäßanalyse (rGA)

The role of voltage-gated Ca²⁺-Channels (VGCCs) in neurovascular coupling – an evaluation using non-contact retinal vessel analyzer (RVA)

W. Albanna¹, K. Kotliar², M. Weiss³, T. P. Schmidt³, C. Conzen³, U. Lindauer³, H. R. Clusmann³, T. Schneider⁴, G. A. Schubert³

¹Rheinisch-Westfälische Technische Hochschule Aachen, Neurochirurgie, Aachen, Germany

²Fachhochschule Aachen, Medizintechnik und Technomathematik, Aachen, Germany

³Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neurochirurgie, Aachen, Germany

⁴Universitätsklinikum Köln, Institut für Neurophysiologie, Köln, Germany

Objective

Metabolic demand increases with neuronal activity; adequate supply is then ensured by neurovascular coupling (NVC), adapting cerebral blood flow accordingly. Impairment of NVC was recently reported in the context of clinical and experimental aneurysmal SAH and is thought to correlate with both disease severity and outcome. Voltage-Gated Ca²⁺-Channels (VGCCs) are key regulators in vasomotor tone. In the present study, we investigate the role of VGCCs in the context of NVC using a non-contact retinal vessel analysis in wildtype (WT) and Cav2.3-deficient (KO) mice

Methods

Wildtype (WT) and Cav2.3-deficient mice (KO) were dark-adapted overnight. Anesthesia was performed by intraperitoneal injection and unilateral application of a mydriaticum achieved pupillary dilatation. An adapted prototype of a non-contact retinal vessel analyzer (RCrodent, Imedos Sytems UG) was used to assess retinal vessel diameter. Dynamic vessel analysis (DVA) using flicker light impulses allowed quantification of vessel reactivity (NVC) as characterized by a change in vessel diameter. The following parameters were calculated: area under curve (AUC) during flicker, mean maximal arterial and venous dilatation (mMAD & mMVD) and constriction (mMAC & mMVC) in response to flicker (%), time until maximal dilation (tMAD & tMVD) and constriction (tMAC & tMVC) in (s)

Results

A total of 57 retinal scans was conducted in 42 male mice (WT n=28, KO n=14, 12-15 weeks old, 25-31 g). Assessment of murine retinal arteries was technically feasible only in 15 animals whereas venous reaction to flicker light was observed in all animals. VGCC-depleted mice were characterized by attenuated functionality of NVC. AUC in artery responses was significantly reduced in Cav2.3 deficient mice: AUC_{art-KO}-6.2 (-11 - -4) %*s vs. AUC_{art-WT}0.3 (-1.9 - 11.8) %*s, (p = 0.04) and the venous mean maximal dilation (mMVD) was significantly lower: mMVD_{KO}0.4 (0.1 - 0.8) % vs. mMVD_{WT}1.0 (0.6 - 1.7) %, (p = 0.046). A trend towards attenuated AUC in veins was also observed in KO vs. WT (p=0.132). Comparable results were observed in tMAD, mMAC, tMAC, tMVD, mMVC, tMVC

Conclusion

To the best of our knowledge, this is the first study using a novel, non-contact analysis technique to document impairment of NVC in VGCC-deficient mice. Modulation of Cav2.3/R-type-Ca²⁺-channels may contribute to the pathophysiological changes of NVC in general and may be considered as a novel therapeutic target for vasomotor related ischemic complications as in the context of SAH

Neurovaskuläre Chirurgie/*Neurovascular surgery*

P014

Risikofaktoren für unvollständigen Aneurysma-Verschluss nach Clipping auf der Basis einer morphometrischen Analyse und Vorschlag eines Risiko-Scores

Risk factors for aneurysm remnants after microsurgical clipping determined by morphometric analysis and proposal of a risk sum score

L. Goertz, M. Pflaeging, C. Kabbasch, G. Brinker, R. H. Goldbrunner, B. Krischek

Universitätsklinikum Köln, Köln, Germany

Objective

Microsurgical clipping provides more durable aneurysm occlusion than endovascular therapy. Albeit the risk of aneurysm remnants after microsurgical clipping is relatively low, complete aneurysm occlusion cannot always be guaranteed. Some aneurysms with incomplete clip occlusion may carry a residual rupture risk and may therefore require retreatment. The objective was to perform a morphometric analysis of intracranial aneurysms to identify predictors for aneurysm remnants and to propose a novel risk score.

Methods

This is a retrospective, single-center analysis of consecutive patients with ruptured and unruptured aneurysms that underwent microsurgical clipping and postoperative digital subtraction angiography between 2010 and 2018. Based on preoperative rotational angiography, distinct morphological aneurysm characteristics (e.g. ruptured status, location, size, neck width, aneurysm and vessel geometry) were determined and correlated with postoperative angiographic results. Factors predictive in the univariate and multivariate analyses were weighted to establish a risk sum score for postoperative remnants after aneurysm clipping. Performance of the score was evaluated by receiver operating characteristic analysis.

Results

A total of 140 patients with 166 clipped aneurysms were included. Postoperative angiography revealed aneurysm remnants in 19.9%. In the multivariate analysis, ruptured aneurysm status (OR: 7.8, 95% CI: 1.7 – 36; $p < 0.01$) and increased aspect ratio (OR: 1.9, 95% CI: 1.0 – 4.0; $p = 0.07$) were associated with postoperative aneurysm remnants. Anterior communicating artery location ($p = 0.02$), internal carotid artery location ($p = 0.06$), increased aneurysm inclination angle ($p < 0.01$) and irregular aneurysm shape ($p = 0.07$) were further predictors for aneurysm remnants in the univariate analysis. These factors were weighted and included into a risk sum score for postoperative aneurysm remnants (range: 0 – 8 points), which performed with good accuracy in the same cohort (AUC = 0.807).

Conclusion

After external validation of the proposed risk score, it could help identify cases requiring angiographic control after aneurysm surgery.

Neurovaskuläre Chirurgie/*Neurovascular surgery*

P015

Ein neues Bewertungssystem für die Wirksamkeit der Behandlung bei zerebralen Aneurysmen
A new scoring system for the efficacy of intracranial aneurysm treatment and outcome

A. Haj

Universitätsklinikum Regensburg, Regensburg, Germany

Objective

The most employed outcome score for the evaluation of aneurysm treatment is the Glasgow Outcome Score (GOS), but this score solely displays the safety of treatment while disregarding its efficacy (i.e. neck remnant). An incomplete occluded aneurysm, however, is a major cause of distress to the patient, reducing the quality of life (lifelong control or re-treatment, risk of rupture). Consequently, we propose a new outcome scoring system (**Grade of Aneurysm Occlusion and Outcome – GAOO score**) based on the conventional GOS, now additionally including the degree of aneurysm occlusion.

Methods

We consulted our institutional database and we identified 286 patients in whom at least one unruptured cerebral aneurysm were treated, with either clip or coil. We extracted all specific data necessary for the new assessment (GAOO - combined score: GOS + grade of occlusion): neurological performance and degree of aneurysm occlusion due to the post-procedural rotational angiography (grade of occlusion: complete = A; small remnant $\leq 3\text{mm}$ = B; large remnant $> 3\text{mm}$ = C).

Results

GOS, clipping group: 5=98.8% (n=166), 4=1.2% (n=2). GOS, coiling group: 5=95.9% (n=139), 4=4.1% (n=6). GAOO score, clipping group: 5A=79.2% (n=133), 4A=1.2% (n=2), 5B=15.5% (n=26), 5C=4.2% (n=7). GAOO score, coiling group: 5A=64.8% (n=94), 4A=0.7% (n=1), 5B=14.5% (n=21), 4B=2.1% (n=3), 5C=17.9% (n=26). Compared to the GOS, the GAOO score had a significantly higher sensitivity and specificity to predict the treatment efficacy (range from 97.8-100%, and 81.6-100%, resp.). According to the GAOO score significantly more patients achieved the best grade (5A) after clipping than after coiling (79.2% vs 64.8%, $p<0.05$).

Conclusion

The GAOO score combines the neurological performance and the radiographically confirmed occlusion. The new GAOO score is an easy applicable score to predict precisely the outcome after aneurysm treatment, at least for unruptured cerebral aneurysms.

Neurovaskuläre Chirurgie/*Neurovascular surgery*

P016

Die Behandlung eines Riesenaneurysma der *Arteria carotis interna* kombiniert mikrochirurgisch und endovaskulär

Treatment of a giant paraclinoid internal carotid artery aneurysm with partial clip ligation, followed by flow diverter implantation – case report and literature review

A. Haj

Universitätsklinikum Regensburg, Regensburg, Germany

Objective

A 53-year-old female patient presented with progressive visual loss of her left eye due to an atrophy of the optic nerve. Computed tomography (CT), magnetic resonance imaging (MRI), and digital subtraction angiography (DSA) showed a giant paraclinoid aneurysm of the internal carotid artery (ICA) on the left hand side, approximately measuring 35 x 23 mm, with consecutive compression of the left optic nerve.

Methods

Parent artery occlusion without bypass surgery did not appear possible, given the poor collaterals to the left anterior circulation. Primary flow diversion alone was turned down for the known risk of aneurysm rupture. Stent- or flow diverter-assisted coiling would both have been technically feasible but would have failed to reduce instantaneously the compression of the optic pathway. After interdisciplinary contemplation of these options microsurgical partial clipping of the aneurysm was chosen with the expectation to reduce the mass effect of the aneurysm. A subsequent need to reconstruct the parent artery by endovascular means was anticipated. We planned the craniotomy for partial clipping in deep hypothermia with circulatory arrest.

Results

No new permanent focal neurological deficit had occurred. The subsequent endovascular treatment was tolerated without clinical issues. Control DSA confirmed complete occlusion of the aneurysm with reconstruction of the left ICA

Conclusion

Each giant aneurysm presents its own unique characteristics and should be approached individually. Benefits are best weighed in a multidisciplinary discussion, after which we used a combination of microsurgical partial clipping and endovascular flow diversion. This staged treatment concept illustrates the potential benefit of joined efforts of vascular neurosurgeons and interventional neuroradiologists, depending on their skills, field of expertise, and preferences.

Neurovaskuläre Chirurgie/*Neurovascular surgery*

P017

Saisonale Variation aneurysmatischer Subarachnoidalblutung aus einer neuen Perspektive *A new perspective of seasonal variation of aneurysmal subarachnoid haemorrhage*

S. Kashefiolaj, N. Brawanski, V. Seifert, J. Konczalla

Universitätsklinikum Frankfurt am Main, Neurochirurgie, Frankfurt am Main, Germany

Objective

Assessed data about the relationships between seasonal determinants and the occurrence of aneurysmal subarachnoid hemorrhage (aSAH) are conflicting. Because hypovitaminosis D has been identified as a risk factor for other vascular diseases, according to seasonal difference of vitaminD level, we examined its association with aSAH.

Methods

We randomized vitaminD (VitD) levels (25-(OH)-vitaminD3) in patients admitted to our department 2007-2015. Mean values of VitD levels were demonstrated to detect 2 months with a peak (summer) versus decrease of VitD level (winter), annually. Therefore, we stratified clinical course and outcome analysis in SAH patients admitted between 2007 to 2015, seasonally.

Results

VitD levels of all registered patients during 2007-2015 (n=95036) were retrospectively analyzed. We stratified 2 patient groups, admitted in summer versus winter, annually. A total of 278 SAH patients were included in this cohort. Concerning aneurysm rupture, there is a significant higher rate of hemorrhage during winter ($p<0,01$;OR1,7) associated with a higher risk for aneurysm size $>5\text{mm}$ ($p<0,01$;OR1,9). We could detect a significant lower rate of neurological deficits indicated as Hunt&Hess grades ($p<0,0001$;OR7,9) and high blood volume described as Fisher3-blood-pattern ($p<0,05$;OR1,7) in patients admitted in summer. In addition, SAH patients in summer had a statistically significant lower rate of early hydrocephalus ($p<0,05$;OR1,8), cerebral vasospasm ($p<0,05$;OR1,7) and followed delayed ischemic neurological deficits ($p<0,01$;OR2). Delayed cerebral infarction and shunt implantation 6 months post SAH showed a higher rate in SAH patients admitted in winter without reaching a statistical significance. Concerning clinical outcome 6 months after SAH, patients with hemorrhage onset in summer had a higher chance for favorable outcome (modified Rankin Scale 0-2) ($p<0,05$;OR1,7).

Conclusion

We demonstrated a higher risk for aneurysm rupture, SAH-dependent complications and unfavorable outcome in patients admitted during winter season with the highest rate of VitD deficiency. However, further research is needed to develop a therapeutic scheme for VitD in aneurysm patients.

Neurovaskuläre Chirurgie/*Neurovascular surgery*

P019

Über den Einfluss der intraoperativen Magnetresonanztomographie (MRT) bei der Resektion zerebraler Kavernome – eine retrospektive Analyse

The impact of intraoperative magnetic resonance imaging (ioMRI) on cerebral cavernoma surgery – a retrospective, single-centre analysis

G. Durner¹, A. Knoll², C. R. Wirtz¹, R. König¹, A. Pala¹

¹Bezirkskrankenhaus Günzburg, Neurochirurgie, Günzburg, Germany

²Bezirkskrankenhaus Günzburg, Neurochirurgie, Günzburg, Germany

Objective

When treating cerebral cavernous malformation surgically, maximum safe resection is the desired goal. Factors like complex shape, multiple lesions or location can make this goal harder to achieve. The resection of hemosiderin might play a separate and important role when aiming for seizure reduction.

With all that in mind, we examined the effect of intraoperative magnetic resonance imaging (ioMRI) on the operative result of cavernoma patients.

Methods

For this study we retrospectively analyzed all consecutive cases of cavernous malformation resection operated in our department since 2009. Multiple parameters such as age, cavernoma volume, hemosiderin ring size, eloquence, location, outcome and additional resection after ioMRI were examined. Cavernoma volumetric analysis was performed using Brainlab Elements Software. Statistical analysis was performed by SPSS, significant level was set for $p < 0.05$.

Results

Out of 37 patients total, 31 (83.8%) underwent ioMRI assisted cavernoma resection. Mean age was 39 years (range 7-69 years), 51.6% (N=16) were male. Most common cavernoma location was frontal lobe (N=12, 38.7%). The Brainstem was affected in 3 patients (9.7%). In 9 patients (29.0%) had deep seated lesions. Irregular shaped lesions were found in 21 cases (67.7%). Familiar history of cavernoma was noted in 8 patients (25.8%). Mean tumor volume was 4.2 cm³ (SE 0.91). Mean ring diameter was 3.08 mm (SE 0.40). Excellent outcome was achieved in 27 patients (87.1%). Only 1 patient had a bad outcome due to a surgery related complication. Engel I grade was achieved in 28 patients (90.3%). After ioMRI, additional tumor resection was performed in 15 cases (48.4%). The most common reasons were infratentorial location (40%, N=6/15), cavernomatosis (40%, N=6/15) and macrobleeding (20%, N=3).

Conclusion

ioMRI might be a useful tool for cavernoma resection especially in complex deep seated infratentorial lesions or in the case of cerebral cavernomatosis. Furthermore, ioMRI might offer special value in achieving gross total resection including hemosiderin ring which could be a potential epileptogenic focus.

Neurovaskuläre Chirurgie/*Neurovascular surgery*

P020

Erste Erfahrungen mit einem High-Definition-3-Dimensional-Exoskop in der zerebralen Bypass-Chirurgie bei Moyamoya-Patienten

First surgical experience with a high-definition 3-dimensional exoscope for cerebral bypass surgery in moyamoya patients

F. Diesner¹, B. Steinhilber², F. Ebner¹

¹Alfried Krupp Krankenhaus, Neurochirurgie, Essen, Germany

²Universitätsklinikum Tübingen, Arbeitsmedizin, Tübingen, Germany

Objective

Cerebral bypass surgery is the treatment of choice for Moyamoya patients with diminished cerebral perfusion. The standard superficial temporal artery to middle cerebral artery bypass (STA-MCA) is a technically demanding procedure which requires excellent optical visualisation and magnification. The current gold standard are high-end operating microscopes (OM). However, they have well known ergonomic drawbacks. Exoscope (EX) systems have been proposed as an alternative in microsurgery with the potential to improve ergonomics and offer digital features. The Objective is to report surgical and ergonomic aspects of our first experience using a robotic-assisted High-Definition (HD) 3-Dimensional (3D) EX system for cerebral bypass surgery

Methods

Over a 2 months period we operated Moyamoya patients who received cerebral bypass surgery at our institution utilising the HD 3D EX. For objective assessment the surgeon completed the Nordic questionnaire and a six items questionnaire including aspects of usability, body posture, working precision, mental and physical effort. The same was done for bypass surgeries performed with the high-end OM. Technical and ergonomic aspects of the visualisation systems and clinical outcome of the patients were assessed and compared.

Results

A total of 5 patients underwent STA-MCA bypass surgery with the exoscope system. No complications occurred and all bypasses were patent. The slim design of the EX promoted a simple surgical set up and application of surgical instruments was no problem. Ergonomics for the surgeon were comfortable. In our set up the screen position limited the ergonomics for the cosurgeon. Operation time was longer due to a new procedure (mean operation time (min) EX / OM: 194 / 129). The 3D-effect was very impressive. However, digital picture quality seems to have slight disadvantages relating to colour discrimination in high resolution.

Conclusion

The 3D optic of the EX is suitable for cerebral bypass surgery. The evolution of digital picture quality is still in progress and provides unlimited possibilities. Therefore digital microscopes have the potential to become the next step in microsurgery.

Neurovaskuläre Chirurgie/*Neurovascular surgery*

P021

Zusammenhang zwischen Thrombus und Aneurysmawand partiell thrombosierter intrakranieller Aneurysmen in der 7 Tesla MPAGE

Relationship between thrombus and aneurysm wall in partially thrombosed intracranial aneurysms visualised with 7T MPAGE

B. Chen¹, T. Sato^{1,2}, O. Gembruch¹, R. Jabbarli¹, P. Dammann¹, M. Darkwah Oppong¹, D. Pierscianek¹, K. Saito², U. Sure¹, K. H. Wrede¹

¹Universitätsklinikum Essen, Klinik für Neurochirurgie, Essen, Germany

²Fukushima Medical University, Department of Neurosurgery, Fukushima, Japan

Objective

Thrombosed intracranial aneurysms (ICA) are often associated with increased aneurysm wall instability. Recently, contrast enhancement in the aneurysm wall of thrombosed ICAs could be visualized in vivo using high-resolution gadolinium-enhanced 7 Tesla (T) magnetic resonance imaging (MRI). This in-vivo study aimed to investigate the relationship between thrombus characteristics and the aneurysm wall in partially thrombosed intracranial aneurysms using MPAGE at 7T MRI.

Methods

The study cohort included fifteen patients (7 males, 8 females) with sixteen partially thrombosed ICAs. All subjects were evaluated utilizing a 7T whole-body MR system (MAGNETOM 7T, Siemens Healthcare GmbH, Erlangen, Germany) equipped with a 1/32-channel Tx/Rx head radiofrequency coil (Nova Medical, Wilmington, USA). The gradient system provides 40 mT/m maximum amplitude and a slew rate of 200 mT /m/ms. A modified 7T MPAGE sequence was implemented. The signal intensity ratio in the thrombus was defined as the highest signal intensity in the thrombus divided by the signal intensity in the anterior corpus callosum. The signal intensity ratio in the thrombus was compared to the thickness of the aneurysm wall at 7T MPAGE. Histopathological findings in six tissue samples were correlated with 7T MRI.

Results

The mean signal intensity ratio of thrombus was 0.97 (standard error of the mean 0.14, range 0.27-2.28). The mean thickness of the aneurysm wall was 1.25 mm (standard error of the mean 0.08, range 0.84-1.55 mm). The signal intensity ratio of thrombus significantly correlated with the thickness of the aneurysm wall ($p < 0.01$) (Fig. 1). The aneurysm walls with the highest signal intensity ratio of thrombus were significantly thicker. In the histopathological examinations, three cases with hypointensity of the thrombus in MPAGE showed only a few macrophages in the thrombus and a thin, degenerated aneurysmal wall (Fig. 2). On the other hand, three cases with hyperintensity of the thrombus in the MPAGE showed abundant macrophages in the thrombus.

Conclusion

In MPAGE at 7T MRI, the signal intensity ratio of thrombus in partially thrombosed intracranial aneurysms correlates with aneurysm wall thickness and histologic features indicating wall instability.

Fig 1

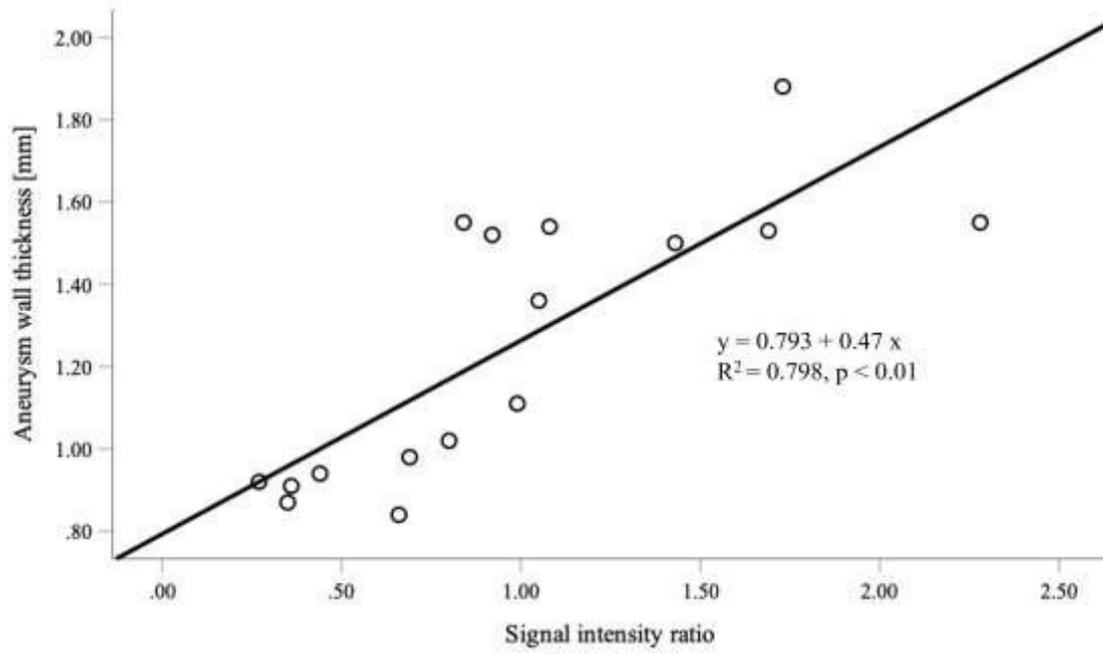
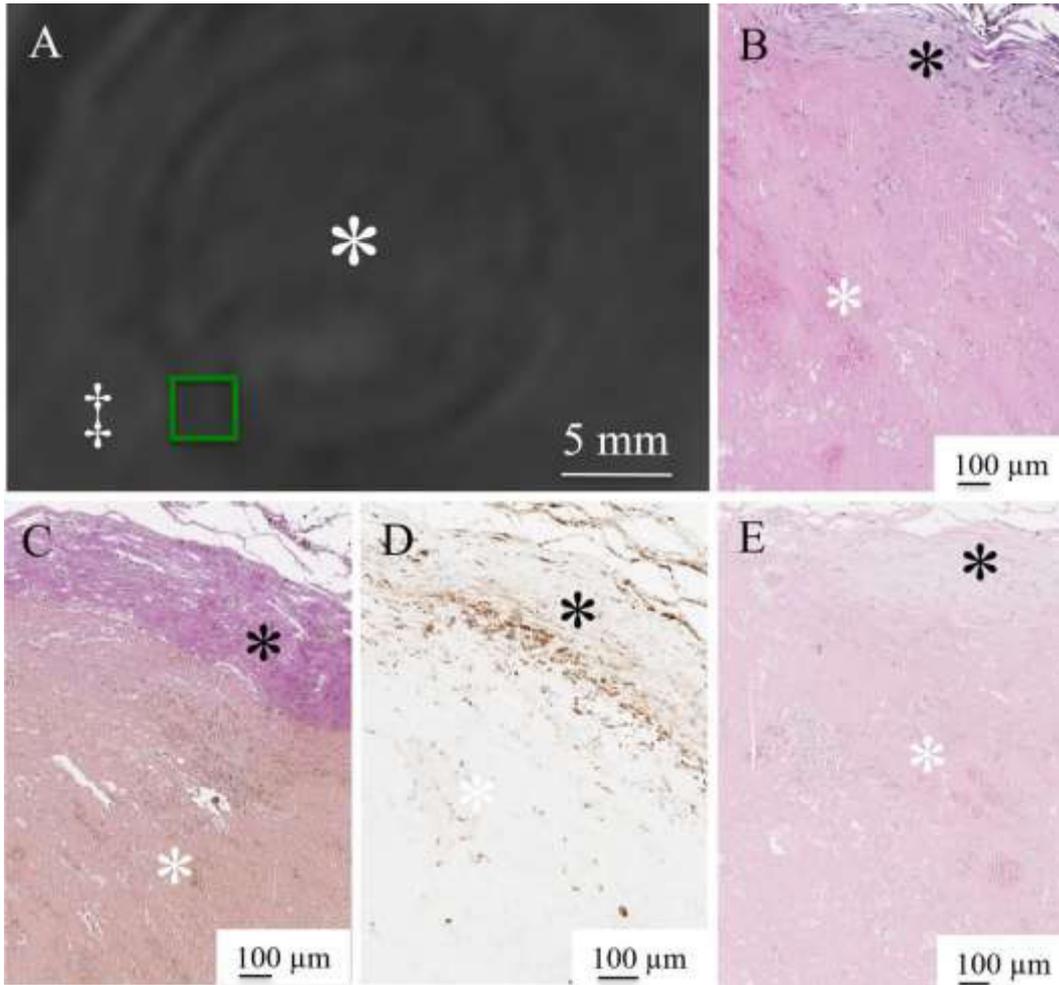


Fig 2



Neurovaskuläre Chirurgie/*Neurovascular surgery*

P022

Radiologische Merkmale, Behandlung und klinisches Ergebnis von AICA-Aneurysmen – eine Fallserie aus der Helsinki-Aneurysmadatenbank

Radiological characters, treatment and clinical outcome of anterior inferior cerebellar artery (AICA) aneurysms – a case series from Helsinki aneurysm data bank

S. Muhammad¹, A. Hafez², B. R. Jahromi², D. Hänggi¹, M. Niemelä²

¹Heinrich-Heine-Universität Düsseldorf, Abteilung für Neurochirurgie, Düsseldorf, Germany

²University of Helsinki, Department of Neurosurgery, Helsinki, Finland

Objective

Anterior inferior cerebellar artery (AICA) aneurysms are rare posterior circulation lesions and are challenging to treat. Here we present morphological/ anatomical characteristics, treatment and clinical outcome of AICA aneurysms in a series of 15 patients from Helsinki aneurysm data bank.

Methods

A retrospective analysis of DSA and CT angiography images of 15 consecutive patients harboring AICA aneurysms who were treated between 1968 to 2017 at Helsinki University Hospital. Different anatomical characteristics including morphology, location, length, width, neck width, aspect ratio, and bottleneck factor were quantified. Moreover, treatment modality and clinical outcome at 1 year was analyzed

Results

Of the 15 AICA aneurysm patients studied, 12 (80%) were female and the mean \pm SD age was 52.4 ± 9.6 years. Seventy-three percent of patients were smokers. Ten out of fifteen patients (67%) had a saccular aneurysm; the remaining 33% had a fusiform aneurysm. Ten out of fifteen AICA aneurysms (67%) were located in the proximal segment, 20% in the meatal segment, and the remaining 13% in the distal segment. The mean \pm SD size of AICA aneurysms was 14.8 ± 18.9 mm. The mean \pm SD aspect ratio was 0.92 ± 0.47 and the mean \pm SD bottleneck factor was 1.66 ± 1.65 . Eleven out of fifteen (73%) patients presented with subarachnoid hemorrhage (SAH); 82% of SAH patients had a good-grade SAH (Hunt and Hess grade 1-3). Eleven patients (73%) were treated surgically, 3 (20%) were treated conservatively, and 1 (7%) had coil embolization. In 27% of patients, a sub-temporal approach with anterior petrosectomy was performed. A retrosigmoid approach was used in the remaining 73%. In 18% of the patients, a parent vessel occlusion was necessary to occlude the aneurysm. Five out of eleven (47%) of the patients developed post-operative cranial nerve deficits. All patients who presented with an unruptured AICA aneurysm had good clinical outcome (mRS 1-2) at one year follow-up. In patients with SAH, 82% achieved good clinical outcome (mRS 1-2) and 18% had poor clinical outcome (mRS 3-6) after 1 year.

Conclusion

AICA aneurysms are mostly large and are more often fusiform in the distal segment. Although surgical treatment of AICA aneurysms has a high rate of cranial nerve deficits, most of patients achieved a good long-term clinical outcome. Currently, surgical treatment could still be an alternative treatment option in selected cases of AICA aneurysms.

Neurovaskuläre Chirurgie/*Neurovascular surgery*

P024

Epilepsie bei temporal gelegenen Kavernomen – Management und Anfallsoutcome *Cavernoma-related epilepsy in cavernous malformations located within the temporal lobe – surgical management and seizure outcome*

P. Schuss¹, J. Marx¹, V. Borger¹, S. Brandecker¹, $\hat{\imath}$ Güresir¹, A. Hadjiathanasiou¹, M. Hamed¹, M. Schneider¹, R. Surges², H. Vatter¹, E. Güresir¹

¹Universitätsklinikum Bonn, Klinik und Poliklinik für Neurochirurgie, Bonn, Germany

²Universitätsklinikum Bonn, Klinik für Epileptologie, Bonn, Germany

Objective

Cavernoma-related epilepsy (CRE) is a frequent symptom in patients with cerebral cavernous malformation (CCM). Reports on surgical management and seizure outcome of epileptogenic CCM often focus on CCM in general. Therefore, data on CCM within the temporal lobe is scarce. We therefore analyzed our institutional data.

Methods

From 2002 to 2018, 52 patients suffering from CCM located within the temporal lobe underwent surgery for CCM-associated epilepsy in our institution. Information on patient characteristics, preoperative seizure history, preoperative evaluation, surgical strategies, postoperative complications, and seizure outcome were assessed and further analyzed. Seizure outcome was assessed 12 months after surgery according to the International League Against Epilepsy (ILAE) classification and stratified into favorable (ILAE class I) versus unfavorable (ILAE classes II–VI).

Results

Overall, 47 of 52 patients (90%) with CCM located temporal and CRE achieved favorable seizure outcome. Pure lesionectomy was performed in 5 patients, extended lesionectomy with resection of hemosiderin rim in 38 patients, and anterior temporal lobectomy in 9 patients with temporal CCM. In detail, 36 patients (69%) suffered from drug-resistant epilepsy (DRE), 3 patients from chronic CRE (6%), and 13 patients sustained sporadic CRE (25%). In patients with DRE favorable seizure outcome was achieved in 32 of 36 patients (89%). Patients with DRE were significantly older than patients with CCM-associated chronic or sporadic seizures ($p=0.02$). Furthermore, patients with DRE underwent more often additional amygdalohippocampectomy following the recommendation of pre-surgical epileptological evaluation.

Conclusion

Favorable seizure outcome is achievable in a substantial number of patients with epileptogenic CCM located temporal, even if patients suffered from drug-resistant CRE. For adequate counseling and monitoring, patients with CRE should undergo thorough pre- and post-surgical evaluation in dedicated epilepsy surgery programs.

Wirbelsäulenchirurgie I/Spine surgery I

P025

Adhäsionscharakteristika von Bakterien und Biofilmbildung auf verschiedenen Implantatmaterialien für intervertebrale Cages

Bacterial adhesion characteristics and biofilm formation on implant materials for intervertebral cages

T. Krätzig¹, S. Weisselberg², K. C. Mende¹, M. Mohme¹, S. Von Kroge², M. Stangenberg³, H. Rohde², S. O. Eicker¹

¹Universitätsklinikum Hamburg-Eppendorf, Klinik für Neurochirurgie, Hamburg, Germany

²Universitätsklinikum Hamburg-Eppendorf, Institut für Mikrobiologie, Hamburg, Germany

³Universitätsklinikum Hamburg-Eppendorf, Klinik für Unfallchirurgie und Orthopädie, Hamburg, Germany

Objective

Infections of the spine are a rare but increasing pathology. Surgical intervention with intercorporeal stabilization is increasingly recommended. However, there is no guideline which material for intervertebral cages should be used. The aim of this study was to compare titanium and PEEK cages according to their adhesion characteristics of different bacteria *in vitro*.

Methods

Platelets made from PEEK, polished titanium (Ti) and polished/porous structured titanium (TiMe) as well as original PEEK and porous trabecular structured titanium (TiLi) cages were inoculated with *S.aureus* (MSSA, MRSA), *S.epidermidis* and *E.coli*. Growth characteristics of serial dilutions of bacteria suspensions after sonication were analysed. Biofilms and bacteria were visualized under a confocal laser scanning and a crossbeam electron microscope.

Results

Platelets: Platelets showed significant differences between PEEK/Ti ($p=0.04$) and Ti/TiMe ($p=0.004$) after 80h for *S.epidermidis* with 67.7 vs. 7.0 and 7.0 vs. 40.3 colony-forming units (CFU). In MSSA significant differences were seen for PEEK/TiMe after 32h with 1.3 vs. 22.7 CFU ($p=0.006$). After 80h additional growth differences were found for PEEK/Ti (118.7 vs. 37.0 CFU; $p=0.03$), PEEK/TiMe (118.7 vs. 49.7 CFU; $p=0.04$). In MRSA significant differences could be detected for PEEK/TiMe (1.0 vs. 6.3 CFU; $p=0.02$) at 56h and PEEK/TiMe (40.3 vs. 6.3 CFU; $p=0.009$) at 72h as well as PEEK/Ti (83.3 vs. 33.3 CFU; $p=0.007$) and Ti/TiMe (33.3 vs. 96.7 CFU; $p=0.003$) at 80h. *Cages*: For PEEK and TiLi cages significant differences were found at 72h for *S.epidermidis* (2913 vs. 230 CFU; $p<0.001$), *E.coli* (398 vs. 836 CFU; $p<0.001$) and MRSA (14.9 vs. 8.3 CFU; $p<0.001$). For MSSA a significant difference could be seen at both time points (8 and 72h; $p<0.001$) with 1.4 vs. 0.22 and 2.6 vs. 0.9 CFU. Electron microscopy demonstrated enhanced adhesion in transition areas of material structure. No increased adhesion could be shown in porous compared to polished areas.

Conclusion

For *S.epidermidis* MSSA and MRSA PEEK cages showed a significantly higher count of CFU, whereas for *E.coli* PEEK seemed to be advantageous over titanium. Interestingly, electron microscopic visualization could show that bacteria did not adhere at the titanium mesh structure, but at the border zones of polished material to rougher parts.

Wirbelsäulenchirurgie I/*Spine surgery I*

P026

Relevanz der Amyloidose des *Ligamentum flavum* und der paravertebralen Muskulatur für die Behandlung lumbaler Spinalkanalstenose

Relevance of amyloid deposits in the ligamentum flavum and the spine muscle for the treatment of lumbar spinal stenosis

B. Pintea¹, S. Amur¹, A. K. Güttsches², K. Gousias^{1,3}, M. Vorgerd², P. Zahn⁴, R. Martínéz-Olivera¹

¹Berufsgenossenschaftliches Universitätsklinikum Bergmannsheil, Neurochirurgie, Bochum, Germany

²Berufsgenossenschaftliches Universitätsklinikum Bergmannsheil, Neurologie, Bochum, Germany

³Katholisches Klinikum Lünen-Werne, Neurochirurgie, Lünen, Germany

⁴Berufsgenossenschaftliches Universitätsklinikum Bergmannsheil, Anästhesie, Bochum, Germany

Objective

To evaluate the relevance of the amyloid deposits in the ligamentum flavum and the spine muscle for the microsurgical treatment of lumbar spinal stenosis.

Methods

We prospectively collect data regarding the extent of lumbar spine degeneration (evidence of scoliosis, Cobb angle, evidence of spondylolisthesis, the number of lumbar segments with spinal stenosis), the health related quality of life (Oswestry Disability Index/ODI and the EQ-5D questionnaire) and the pain intensity on the visual analog scale (VAS) from patients assigned for microsurgical decompression of lumbar spinal stenosis. Biopsy of the ligamentum flavum and spine muscle tissue were taken during surgery. Histochemical examination of the tissue was subsequently performed for amyloid deposits. The patients were divided into two groups depending on the presence of amyloid deposits in the ligamentum flavum and monovariant analysis was performed to detect significant differences.

Results

50 patients were included in the trial, 32 patients had amyloid deposits in the ligamentum flavum and 3 patients had amyloid deposits in the ligamentum flavum and the spine muscle. The extent of scoliosis/cobb angle tended to be higher in the group of patients with amyloid deposits in the ligamentum flavum (patients with amyloid deposits in the ligamentum 8° vs patients without amyloid deposits in the ligamentum flavum 4°; p= 0,089). The preoperative health related quality of life was significantly lower for the patients with amyloid deposits in the ligamentum flavum (patients with amyloid deposits in the ligamentum ODI: 48% and EQ-5D: 2,8 vs. Patients without amyloid deposits in the ligamentum flavum ODI: 38%; p=0.005 and EQ-5D: 2,4; p=0.014). The pain intensity (VAS) did not differ significantly between patients with or without amyloid deposits in the ligamentum flavum.

Conclusion

Amyloid deposits in the ligamentum flavum are associated with a lower health related quality of life and a higher extent of degenerative deformity.

Wirbelsäulenchirurgie I/Spine surgery I

P027

Extreme lateral interbody fusion (XLIF) in einer konsekutiven Serie von 68 Patienten *Extreme lateral interbody fusion (XLIF) in a consecutive series of 68 patients*

M. Pojskic¹, B. Saß¹, B. Völlger¹, D. Jankovic², C. Nimsky², B. Carl²

¹Universitätsklinikum Gießen und Marburg, Klinik für Neurochirurgie, Marburg, Germany

²Philipps-Universität Marburg, Klinik für Neurochirurgie, Marburg, Germany

Objective

Extreme lateral interbody fusion (XLIF) has become the standard of minimally invasive therapy of lumbar scoliosis due to minimally invasive access to the spine, less blood loss compared to open procedures, decreased operative times, shorter hospital stays, and less postoperative pain. Our objective is to determine the safety and efficacy of extreme lateral lumbar interbody fusion (XLIF) with supplemented instrumentation in degenerative spinal canal stenosis and spondylodiscitis.

Methods

Patients who were treated with XLIF at our department in the period 2012-2018 were retrospectively analysed. Patient records with clinical and radiographical data were evaluated.

Results

There were 38 male and 28 female patients. 43 patients had spinal canal stenosis and 25 patients had spondylodiscitis. The mean follow up was 17.8 months. Indications included segmental lumbar scoliosis and the bilateral stenosis of the neuroforamen. One level XLIF was performed in 45 patients, 2 levels in 13 and 3 levels in 10 patients. All but one patient received an additional dorsal stabilization. The pain was present in all patients preoperatively with medium VAS of 7.6 ± 2.3 . Postoperatively VAS was significantly improved at 3.4 ± 2.1 ($p < 0.05$). A preoperative neurological deficit was found in 14 patients. Only three patients had a neurological deterioration, 11 patients improved and 54 patients remained unchanged. Complications occurred in 8 patients: in 2 patients screw displacement, in 3 patients wound healing deficit, in 2 patients pneumothorax and in 1 patient retroperitoneal hematoma. There were two cases of cage sintering. Non-union occurred in 5 cases. There were no outcome differences with regard to pain and neurological outcome between patients with spinal canal stenosis and spondylodiscitis as well as between patients with one level vs. multilevel surgery.

Conclusion

Extreme lateral interbody fusion (XLIF) with supplemented instrumentation is a safe method for surgical therapy of spinal canal stenosis and spondylodiscitis with segmental scoliosis and bilateral neuroforamen stenosis.

Wirbelsäulenchirurgie I/*Spine surgery I*

P028

90-Tage-Morbiditäts- und Mortalitätsrate bei über 90-jährigen Patienten, die an einer atlantoaxialen Fusion bei akut traumatischen odontoiden Typ-II-Frakturen mit Hilfe der intraoperativen spinalen Navigation operiert wurden

90-day morbidity and mortality rate in nonagenarians undergoing intraoperative spinal navigation based atlanto-axial fusion for acute traumatic odontoid type II fractures

M. Issa^{1,2}, B. Ishak¹, K. Kiening¹, A. W. Unterberg¹

¹Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

²Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

Objective

Odontoid type II fractures are the most common cervical spine injury in the elderly. Recent studies confirm that external stabilization is associated with high complication and mortality rates. The decision for surgical treatment in the very elderly is still controversial, particularly with regard to comorbidities and poor bone quality. The aim of this study was to assess early morbidity and mortality in nonagenarians.

Methods

15 patients with an acute traumatic odontoid type II fracture who underwent posterior CT-guided atlanto-axial instrumentation at our institution between February 2010 and October 2019 were retrospectively analysed. Complication, morbidity and mortality rate, as well as length of ICU and hospital stay were determined.

Results

Average age was 91 years (range 90 – 96 y). In-hospital mortality was non-existent and no patient showed new permanent neurological deficits after surgery. One C2 screw was misplaced into the vertebral canal without any symptoms. Average length of hospital stay was 13.4 days and 2 days for ICU. Blood transfusion was necessary in three patients. Two patients (13%) developed urinary tract infection. One patient (7%) developed pulmonary embolism with fully recovery within several weeks.

Conclusion

Our current study confirms that atlanto-axial fusion by using intraoperative CT-navigation in nonagenarians is a safe and effective procedure with few complications. Implant-related complications occurred in one patient (7%). 90-day mortality rate was 0%

Wirbelsäulenchirurgie I/*Spine surgery I*

P029

Hohe Rate an pulmonalen Zementembolien bei Patienten mit zementaugmentierten Pedikelschrauben und intraoperativem perivertebralem Zementaustritt – Übersicht der letzten 10 Jahre
High rate of pulmonary cement embolism (PCE) in patients with cement augmented pedicle screw placement with intraoperative perivertebral cement leakage –10-year single-centre experience

K. Klumbies, K. Kiening, A. W. Unterberg, B. Ishak

Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

Objective

To assess morbidity, mortality and pulmonary cement embolism in patients who had undergone cement augmented pedicle screw placement of the thoracic and lumbar spine.

Methods

35 patients who had received CT-navigated pedicle screws with cement augmentation for degenerative or traumatic conditions were analyzed retrospectively between June 2009 and July 2019. Only patients with perivertebral cement leakage verified by a CT scan of the thoracic or lumbar spine and additional thoracic CT-scan were analyzed. Complications, mortality and pulmonary cement embolism were determined.

Results

Average age was 72.5 years (range: 47-68 years). A total of 169 vertebral bodies with 337 screws were inserted, of which 238 were cement-augmented. The screws were placed in the lumbar (63%), thoracic (9%) or both lumbar and thoracic (28 %) spine. Perivertebral cement leakage occurred in all patients. PCE occurred in 10 patients (29%). 24 patients (69%) were asymptomatic whereas 11 patients (31%) had symptoms like dyspnea or thoracic pain. In-hospital mortality due to PCE was 9% (3 patients). Mean hospital stay was 15 days.

Conclusion

Our study confirms that cement application for pedicle screw placement leads to PCE in 29% of patients with pulmonary symptoms in 31% of patients. Early mortality related to PCE was 9%.

Wirbelsäulenchirurgie I/Spine surgery I

P030

CFR-PEEK Instrumentierung bei Spondylodiszitis – eine monozentrische Studie *CFR-PEEK instrumentation for spondylodiscitis – a single-centre experience*

A. K. Jörger¹, E. Shiban¹, S. Krieg¹, B. Meyer²

¹Universität Augsburg, Neurochirurgie, Augsburg, Germany

²Technische Universität München, Neurochirurgie, München, Germany

Objective

The advantage carbon-fiber-reinforced (CFR) polyethyl-ether-ether-ketone (PEEK) material is its radiolucency. CFR-PEEK has been established in spinal instrumentation for primary bone tumors and metastases. Laboratory data showed that CFR-PEEK shows even reduced bacterial adhesion as titanium does.

Thus, the idea to use CFR-PEEK spinal instrumentation for spondylodiscitis cases was to gain artifact free follow-up imaging, so therapeutic success can be evaluated. This study therefore evaluates the first consecutive series of spondylodiscitis patients who underwent CFR-PEEK instrumentation.

Methods

We conducted a prospective single center study. From June 2018 till March 2019 patients with thoracic or lumbar spondylodiscitis and CFR-PEEK instrumentation were included. Follow-up imaging of at least three months after surgery was evaluated in terms of screw loosening. A matched-pair analysis was then performed using data of spondylodiscitis cases from January 2014 till December 2016 with titanium instrumentation for equal localization, operative strategy and type of germ.

Results

23 patients with CFR-PEEK and 23 with titanium instrumentation were included. Concerning the CFR-PEEK group, in six cases no follow-up imaging was performed. Of the remaining 17 cases, six cases (35%) showed loosening while only 14% of cases with titanium instrumentation were loosened ($p=0.004$). There was no difference in the rate of 360° fusion in both groups.

Conclusion

As opposed to other indications like tumors etc., for reasons unknown to date CFR-PEEK screws show a higher rate of screw loosening than titanium screws in spinal infections. Until factors related to this are elaborated, we advice caution when implanting CFR-PEEK screws in infectious cases.

Wirbelsäulenchirurgie I/*Spine surgery I*

P031

Tear-Drop-Technik in Platzierung von Ilium-Schrauben – eine technische Analyse *Tear-drop technique in iliac screw placement – a technical analysis*

S. Nowak, J. Müller, M. E. Weidemeier, H. W. S. Schroeder, J. U. Müller

Universitätsmedizin Greifswald, Neurochirurgie, Greifswald, Germany

Objective

Instrumentation of the lumbosacral region is due to the complex anatomical structures and biomechanical forces one of the more challenging techniques. It could already be demonstrated that in order to enhance the fusion rate of the lumbosacral junction additional iliac screw placement is necessary. Numerous techniques have been described for iliac screw placement. Not only open surgical techniques with anatomic guidance, but also navigated or robotic supported placement have been described. These techniques, if applied correctly, have the advantage to give the surgeon an extra reference for safety at the cost of prolonged operative time and cost. That is why we adapted at our neurosurgical spine-center a fast and simple radiological controlled open placement technique for iliac screw fixation.

Methods

Between October 2016 and August 2019 48 patients underwent sacropelvic fixation in tear-drop-technique. To indicate surgery generally applied world standards were used in every specific case. Screw position was verified with a 3d x-ray-scan intra-operatively. Follow-up x-ray was performed before discharge and 3 months after surgery. The data was collected prospectively. The chart review was done retrospectively. The statistical analysis was done by using excel and SPSS for Windows.

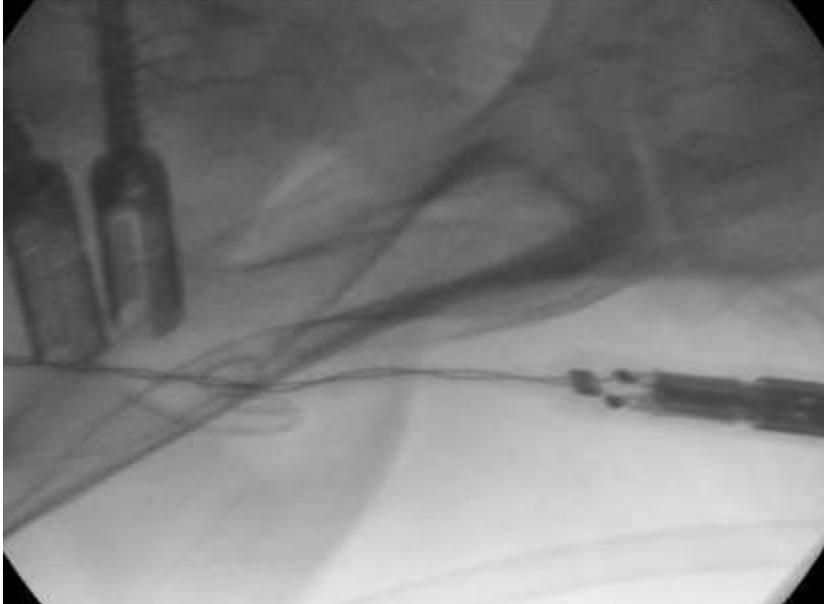
Results

Between October 2016 and August 2019 we included 48 patients. The mean age was 64 years (27-81 years). In total, 95 iliac screws were placed in tear-drop-technique. Only in one side (1.04%) navigated placement was performed due to tumor deformed iliac anatomy. The mean follow-up was 9.8 months. Spinal instrumentation was performed due to degenerative spinal scoliosis in 22 cases (45.8%), in equal number (22 cases; 45.8%) a revision surgery after previous spinal instrumentation necessitated a spinopelvic fusion. All these cases received a multi-level spinal instrumentation. In all cases (98.9%) but one the 3d x-ray scan after tear-drop screw placement confirmed a correct position of the screw. Only in one case there was a lateral breach of the screw head. In the three-month follow up there were no complications regarding the iliac screws. Other surgical complications included post-operative infection in 4 cases (8.3%), non-fusion of the upper and mid-level in 4 cases (8.3%) and fractured pedicle screw on level L2 in one case (2.1%).

Conclusion

The tear-drop-technique for iliac screw placement in spinal surgery is a fast, reliable and safe method only utilizing single x-ray imaging and minimal exposure.

Fig 1



Wirbelsäulenchirurgie I/Spine surgery I

P032

Hyperextensionsverletzungen der thorakolumbalen Wirbelsäule – Inzidenzentwicklung, typische Verletzungsmorphologien und deren differenzierte Behandlung *Hyperextension injuries of the thoracolumbar spine – shift of incidence, typical fracture morphologies and treatment options*

T. M. Heintel, F. Gilbert, M. C. Jordan, S. Jovic, H. Jansen, R. H. Meffert

Universitätsklinikum Würzburg, Klinik und Poliklinik für Unfall-, Hand-, Plastische und Wiederherstellungschirurgie, Würzburg, Germany

Objective

Hyperextension injuries [HEIs] of the thoracolumbar spine are supposed to be rare. Their frequency of occurrence ranges from 0.2 to 2.5 %. Corresponding to this, the literature only contains small numbers of case reports and studies with small numbers of participants. In the last 25 years a striking increase in the frequency of HEIs was noticed. Different treatment concepts are proposed. Aim of this study was to investigate incidence, localization, typical fracture morphologies, treatment options and outcome.

Methods

Between 01/1997 and 12/2018 our prospective data base included 154 patients with 165 HEIs of the thoracolumbar spine (41 women and 113 men, average age at the time of the accident 71.3 ± 13.5 years, range 25 – 93 years). The data were analyzed retrospectively. Computed tomographic scans and MRI scans were evaluated. The injury patterns of the anterior column were differentiated into 3 groups: transosseous, transdiscal and combined forms, in which both the disc space and the vertebral body were affected. At the posterior column, osseous and ligamentous injuries were differentiated. A classification system with 6 different types of HEIs resulted from the combinations of these groups (figure 1). Values were expressed as the mean and standard error of the mean.

Results

In the last 25 years, more than a tenfold increase in patients with HEIs has been registered in our institution. 154 patients with 165 HEIs of the thoracolumbar spine were analyzed. 122 (74%) HEIs were associated with DISH, 23 (14%) with ankylosing spondylitis, and 11 (7%) with Spondylosis deformans. Only 9 (5%) of these injuries involved patients without ankylosing spinal disease. HEIs in ankylosing spondylitis and DISH showed in part highly significant differences in the injury morphology. 45 HEIs, all patients with type 1, 2 or 3 injuries without neurological deficit received non-operative treatment. 14 of the 154 patients (8%) died within the first 12 months after injury. 121 of the 140 surviving patients were followed up for an average of 31.3 ± 12.7 months after injury. Within the first year, 96% of surgically treated and 98% of conservatively treated extension injuries recovered and attained stability.

Conclusion

To our knowledge, this study is by far the largest cohort of patients with HEIs of the thoracolumbal spine. The study provides important data for epidemiology, localization, accompanying pathologies, fracture morphology and the need for therapy.

Fig 1

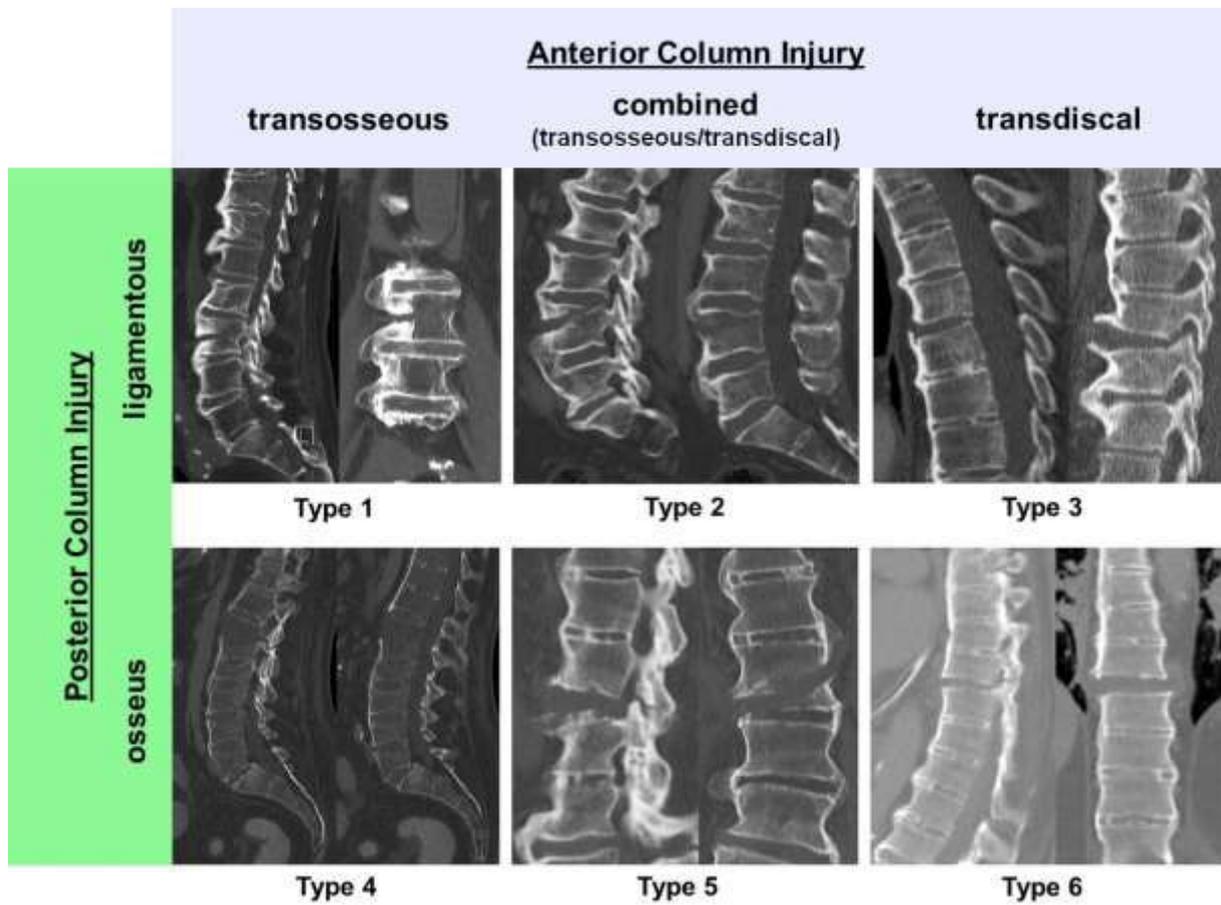


Fig 2



Wirbelsäulenchirurgie I/Spine surgery I

P033

PICA mit extra-duralem Abgang aus dem V3 Segment

Posterior inferior cerebellar artery with an extradural origin from the V3 segment – higher incidence on the nondominant vertebral artery

M. Yasuda

Ichinomiyanishi Hospital, Neurological Surgery, Ichinomiya, Japan

Objective

The posterior inferior cerebellar artery (PICA) and the vertebral artery (VA) often show anatomical variations at the craniovertebral junction (CVJ). PICA originating extradurally from the V3 segment of the VA is one example, but its incidence and relationship to the VA and the atlas have not been discussed. This study evaluated the prevalence of PICAs originating from V3. We also analyzed other variations of the atlas and the VA.

Methods

We analyzed the computed tomography (CT) images from a series of 153 patients who underwent 3-dimensional CT angiography and investigated variations of the PICA, VA and atlas.

Results

Finally, 142 patients (284 sides) were analyzed and 11 patients (7.7%) were excluded due to poor image quality. The most common VA variation was PICA originating from V3. It was more frequently observed on the lesser VA than on the dominant VA (22.5% versus 6.25%; $p=0.0005$). The VA with PICA end was identified in 4 patients (1.41%); the incidence was the same as that observed in the persistent first intersegmental artery (1.41%).

VA fenestration was only found in one patient (0.35%). Regarding the atlas, a ponticulus posticus (PP) was observed in 24 sides (6.0%). There was no relationship between the incidence of PP and the variations of the VA.

Conclusion

The PICA from V3 was the most common VA variation at the CVJ and was more frequent on the lesser VA. Surgeons should take care of this variation during operations.

Wirbelsäulenchirurgie I/Spine surgery I

P034

Die Anlage einer Redondrainage ist nur von der Länge dorsaler, zervikaler Instrumentation abhängig, ohne Einfluss auf die Komplikationsrate

Placement of redon drainage solely depends on length of posterior cervical instrumentation without significant impact on complication rate

C. Wolfert, B. Sommer, C.Von der Brelie, V. Rohde, I. Fiss

Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Complication rates up to 19% had been reported after dorsal fusion for cervical instability. Postoperative pain and cardiopulmonary difficulties are wide-spread. Spinal epidural hematoma (SEH) and surgical site infections (SSI) are rarer, but are possibly leading to long-term sequela, are more dreaded with ranges up to 1.5% (SEH) and 4.7% (SSI). Redon drainage (RD) is frequently used to avoid these complications, without definitive guidelines. For this reason, this study aims to examine the relationship between placement of a RD and complication rate of SSI and SEH.

Methods

Monocentric, retrospective review of 319 consecutive patients who underwent first-time cervical fusion from 2012 to 2018. Demographic, clinical, operative and follow up characteristics were compared between patients with/without RD placement using uni- and multivariate regression models (UR, MR) to identify independent predictors of RD placement (Statistic Software R Version 3.4.0; R Core Team 2018; $p < 0.05$ was considered statistically significant).

Results

Of 319 patients (44.8% f), with mean age 66.4 years (22-98), 208 (65.2%) had a RD placed. Overall, fifteen patients (4.7%) developed SSI, which lead to revision surgery, while revision due to SEH was necessary in seven patients (2.2%). These events occurred independently of RD placement ($p=1.0$). Furthermore, total number of operated levels had no significant impact on the occurrence of complications ($OR=1.3$; $p=0.07$).

Stabilization of one or two segments was performed most frequently (one: $n=125$; 39.2%, two: $n=102$; 32.0%), while three ($n=43$; 13.5%) and four or more segments were treated less frequently ($n=49$; 15.4%). UR identified duration of surgery ($OR=1.0$; $p=0.00001$), total number of operated levels ($OR=1.5$; $p=0.00016$), and simultaneously performed decompression ($OR=1.8$; $p=0.01$) as independent predictors of RD placement. MR solely confirmed "total number of levels operated" ($OR 1.1$; $p=0.009$) as independent predictor, with significant increase with more than three operated levels ($OR=1.7$; $p=0.001$).

Conclusion

Placement of a RD solely depends on the length of posterior cervical instrumentation. Separate analysis of patients with and without placement of a RD did not reveal any differences in re-operation rate due to SSI and SEH. Regarding these results, a clear recommendation towards routine placement of a RD cannot be made.

Wirbelsäulenchirurgie I/*Spine surgery I*

P035

Periphere Nervenkompressionssyndrome der oberen Extremität – postoperativer Verlauf nach Dekompression unter besonderer Berücksichtigung zusätzlicher degenerativer Erkrankungen der Halswirbelsäule

Surgical therapy for peripheral nerve compression syndromes of the upper extremity – results of a single centre with special reference to additional degenerative disease of the cervical spine

D. Keiner, J. Oertel

Universitätsklinikum des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

Objective

The presented study focuses on surgical results for treatment of common nerve entrapment syndromes of the upper extremity in a single center with special attention on patients with diagnosed carpal tunnel and cubital tunnel syndrome and additional degenerative disease of the cervical spine with and without previous surgery.

Methods

Between 01/2011 and 05/2018, 170 patients (195 hands) were surgically treated for carpal tunnel syndrome (CTS) and 202 patients (220 elbows) were treated surgically for cubital tunnel syndrome (CuTS). Data of surgery and possible peculiarities, the postoperative course regarding objective improvement of symptoms and patient satisfaction was analyzed retrospectively.

Results

Cervical spine degeneration including severe disease such as myelopathy was diagnosed in 39.9% of CTS cases and in 32.4% of CuTS cases. In CTS, brachialgia resolved completely / improved markedly in 97.1% of cases with additional spine degeneration and in 96.9% of cases without this diagnosis. The improvement of sensory function in CTS patients with or without cervical spine disease was equal ($p = 0.39$). Improvement of motor function was significantly better in patients with cervical spine disease ($p = 0.01$), whereas preoperative comparison did not show a significant difference. In patients treated for CuTS, symptom relief was good in patients with and without cervical spine disease. Advanced symptoms were observed in a higher proportion of patients without a history of cervical spine disease. Postoperatively, results were favorable in patients with cervical spine disease showing a complete or marked recovery of motor symptoms in 80.6% of cases ($p = 0.01$), and of sensory symptoms in 72% of cases ($p = 0.3$). In the remaining patients, a complete or marked recovery of motor symptoms was found in 72.9% of cases, and a complete or marked recovery of sensory symptoms was observed in 54.9% of cases.

Conclusion

Patients with additional degenerative disease of the spine had a marked improvement after surgery for CTS or CuTS. Degenerative disease of the spine did not seem to affect the outcome in a negative way. With thorough preoperative diagnosing, the results are favorable. Surgical decompression of the nerve was not connected to inferior results or special risks.

Wirbelsäulenchirurgie I/*Spine surgery I*

P036

Zervikale Bandscheibenprothesen als Therapie der degenerativen Erkrankung der Halswirbelsäule – klinische und MRT-basierte Daten einer Serie von 24 Patienten mit einem mittleren Verlaufsuntersuchungszeitraum von 11 Jahren

Anterior cervical disc arthroplasty for the treatment of degenerative disorders – clinical outcome and MRI-based findings of series of 24 patients with a mean follow-up of 11 years

B. Burkhardt, L. Baumann, J. Oertel

Universität des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

Objective

The ideal surgical technique for the treatment of degenerative disorders of the cervical spine has not been determined yet. Cervical disc arthroplasty (CDA) has been evolved to reduce the development of adjacent segment degeneration which might become symptomatic (sASD) and lead to repeated procedure. Studies with long-term clinical outcome and MRI data following CDA are rare.

Methods

A retrospective file review of all patients who underwent CDA for degenerative disorder between 2005 and 2010 was performed. Inclusion criteria for further evaluation were a complete set of preoperative, postoperative and follow-up documentation of the neurological status and documentation of repeated procedures. At final follow-up with a personal examination was performed and clinical outcome was assessed via Odom's criteria, Neck disability index (NDI). Degeneration of the cervical spine was assessed via a five step grading system (range 0 -1) based on the MRI scan.

Results

A total of 95 patients were identified and 82 among those fulfilled inclusion criteria. 1- and 2-level CDA was performed in 61 and 21 patients respectively. In nine (10.9%) patients repeated procedures was performed. In seven (8.5%) for sASD and in two (2.4%) due to failure of the CDA. The mean interval between initial CDA and repeated procedure was 52 months (range: 5-107 months). Prior to preparation of this abstract, 24 patients (10 male und 14 female) with a mean age of 58 years attended the final follow-up examination. The mean follow-up was 11 years (range 9-14 years), mean NDI score was 18%, eighteen patients (75%) reported clinical success according to Odom's, and 22 (91%) patients reported that they would choose CDA as treatment again. The grade of degeneration at the adjacent segments to CDA was moderate, with a mean of 0.45 and 0.35, respectively.

Conclusion

The clinical success rate following CDA for the treatment of degenerative disorders reached only 75% within 11 years. The repeated procedure rate was 10.9%. The MRI based grade of degeneration of the cervical spine was moderate.

Wirbelsäulenchirurgie II/*Spine surgery II*

P037

Operative Therapie der zervikalen Myelopathie – Wann sollten wir operieren? *Surgery for cervical spondylotic myelopathy? – when to operate?*

O. Gembruch, R. Jabbarli, M. Chihi, Y. Ahmadipour, U. Sure, P. Dammann, N. Oezkan

Universitätsklinikum Essen, Abteilung für Neurochirurgie, Essen, Germany

Objective

Cervical spondylotic myelopathy (CSM) is the most common reason for spinal cord injuries in elderly patients. Up to now, timing of surgical treatment is still various.

In this study we analysed demographic data, comorbidities, surgical treatment, number of treated levels and radiological findings such as high signal intensity (SI) on MRI to evaluate the association on the postoperative neurological outcome.

Methods

Patients treated in our department between 2007 until 2016 with CSM were analysed retrospectively. The modified Japanese Orthopaedic Association Score (mJOA), the mJOA Score improvement and the Minimum Clinically Important Difference (MCID) were used to define the pre- and postoperative neurological function. Multivariate Analysis was performed for sex, age, comorbidities, high SI on MRI, surgical approach.

Results

The study group comprised 411 (36.0 % female, mean age: 62.6 years (range: 31 - 96years). Surgical treatment and the number of treated levels did not influence the postoperative outcome. There was a significant improvement of the functional study endpoints after evaluation of the postoperative mJOA Score and the MCID ($p < 0.001$). In the multivariate analysis, patients' age, CCI and high SI on T2-weighted MRI ($p=0.0005$) were independently associated with a lower pre- and postoperative mJOA Score and the lower postoperative MCID.

Conclusion

Surgical treatment and the number of treated levels did not affect the neurological outcome. Age, Comorbidities, high SI on MRI are negatively associated with the preoperative status and the postoperative neurological outcome (postoperative mJOA Score and MCID). Therefore, surgery should be performed before a high SI on MRI is present to prevent irreversible damage of the spinal cord.

Wirbelsäulenchirurgie II/*Spine surgery II*

P038

Genauigkeit beim Einsetzen von bildgestützt navigierten Pedikelschrauben mithilfe der intraoperativen Computertomographie – eine Serie von 608 Schrauben

Pedicle screw insertion accuracy using intraoperative computed tomography image-guided navigation – a series of 608 screws

B. Stemmer, B. Trnovec, E. Shiban, V. Heidecke

Universitätsklinikum Augsburg, Klinik für Neurochirurgie, Augsburg, Germany

Objective

The goals of this study were to assess the accuracy of pedicle screw insertion using an intraoperative computed tomography (iCT), and to analyze potential risk factors for screw misplacement.

Methods

A retrospective analysis of all patients following iCT navigated spinal pedicle screw placement between November 2016 and February 2019 was performed. Navigated drilling of the pedicle was followed by screw placement. Screw position was checked by a further iCT scan. Screw position was assessed according to the Gertzbein-Robbins classification.

Results

109 consecutive patients were identified (52,3 % male, 47,7 % female). Median age was 71 years. Screws were placed in all spinal regions : cervical and cervico-thoracal (68), thoracic (118), thoracic-lumbar (126), lumbar (206) and lumbosacral (90). Degenerative spine disease was the most common diagnosis (49,0%). There were 75,3%, 12,0%, 7,4%, 2,5% and 3,1% screws classified as Gertzbein-Robbins A, B, C, D and E, respectively. 30 screws (4,93%) were revised intraoperatively. Lumbar spine, thoracic spine, tumor and infection diagnosis were associated with highest rates of screw misplacement. None of the patients suffered from any neurovascular damage.

Conclusion

The all-over revision rate was 4,93%. The highest revision rates were observed for tumor (6,38 %), infection patients (6,86 %), lumbar spine (6,30 %) and thoracic spine (5,90 %). None of the patients suffered from any neurovascular damage. No secondary operation to revise the misplaced screws was required.

Wirbelsäulenchirurgie II/*Spine surgery II*

P039

Die Operation in halbsitzender Lagerung bei Patienten über 70 Jahren *Surgery in semi-sitting position in patients older than 70 years*

H. Elkayekh, S. Al-Afif, D. Scheinichen, T. Palmaers, E. J. Hermann, J. K. Krauss

Medizinische Hochschule Hannover, Neurochirurgie, Hannover, Germany

Objective

The semi-sitting position is used by many neurosurgeons dealing with pathologies in the posterior cranial fossa. However, hypotension and venous air embolism (VAE) are potential issues in this position. Older patients often have limited cardiovascular and respiratory compensatory capacities compared to younger patients. Here we investigated, if elderly patients are exposed to more risk for complications when operated in semi-sitting position.

Methods

Clinical data were analysed retrospectively in a consecutive series of 755 patients who were operated between 1996 and 2016 in the semi-sitting position. From the 755 patients there were 66 patients who are older than 70 years. The incidence of VAE, severe hypotension (drop of blood pressure by more than 20 mmHg) and the postoperative course were compared between patients older than 70 years and patients who were younger.

Results

There were no significant differences for the incidence of the air embolism between the two groups (12% vs. 18% $P=0.15$). There were also no differences for the occurrence of a marked decrease of $PtCo_2$ (5% vs. 4% $P=0.73$) or severe hypotension (4,6% vs. 3% respectively, $P=0.57$). The surgical time in minutes (240 ± 116 vs. 254 ± 120 $P=0.34$) as well as hospital stay in days were comparable (16 ± 10 vs. $18, 8 \pm 11$ $P=0.07$). However, the time spent in the intensive care unit in days after surgery was significantly longer in patients older than 70 years (2 ± 6 vs. 6 ± 10 $P=0.01$).

Conclusion

There was no increase in complication rates in elderly patients operated in the semi-sitting position. Our results suggest that age per se should not be considered a factor excluding patients from being operated in the semi-sitting position.

Wirbelsäulenchirurgie II/*Spine surgery II*

P040

Endoskopische zervikale und lumbale Wirbelsäulenchirurgie – klinische Ergebnisse einer konsekutiven Serie von 260 Patienten mit einem mittleren Verlaufsuntersuchungszeitraum von 52 Monaten

Endoscopic cervical and lumbar spine surgery – clinical results of a consecutive series of 260 patients with a mean follow-up of 52 month

B. Burkhardt, J. Oertel

Universität des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

Objective

The primary idea of endoscopic spine surgery (ESS) was to reduce muscle trauma. In this work the authors present their experience in ESS for the treatment of cervical and lumbar degenerative disorders.

Methods

Clinical data about neck and back pain, arm and leg pain, intra- and perioperative complication, and reoperation was prospectively collected for all patients who underwent ESS over the past 10 years. All patients who underwent ESS via a paramedian approach for degenerative cervical or lumbar disorders who were followed for at least 3 month postoperatively were included for further final follow-up assessment. At final follow-up a personal examination and a standardized questionnaire was performed including the Oswestry disability index (ODI), neck disability index (NDI), and the modified MacNab/Odoms Criteria.

Results

A total of 319 out of 502 patients fulfilled inclusion criteria, and 260 out of those 319 patients attended the final follow-up examination (82%). Sixty patients underwent ESS for posterior cervical foraminotomy (PCF), 18 for lumbar synovial cyst (LSC), 66 for decompression of lateral recess (LRS) or central canal stenosis (LSS), and 116 for lumbar disc herniation (LDH). The mean follow-up was 52 months. The rate for radicular pain relief in LDH, LSC, LRS/LSS and PCF procedure were 92%, 90%, 93%, and 86% respectively. No weakness was documented in 85% of lumbar and 86% cervical spine cases. The mean ODI was 14.0% and mean NDI was 12%. According to MacNab/Odoms criteria clinical success was noted in 91% and 89%, respectively. The dural tear rate varied from 1.1% in LDH to 21% in LSC procedures and all were closed endoscopically. The recurrent disc herniation rate was 6.1%. The mean surgical time decreased from 71 to 54 minutes.

Conclusion

ESS is a safe and effective technique to treat degenerative cervical and lumbar spine disorders. The rates for pain relief, clinical success, intraoperative complication, and reoperation are similar to established open procedures.

Wirbelsäulenchirurgie II/Spine surgery II

P041

Ist der Grad der Degeneration der Halswirbelsäule nach zervikaler Fusion unterschiedlich in Bezug auf das klinische Ergebnis, die Diagnose und bei Reoperationen? – eine MRT-Studie von 102 Patienten mit einem mittleren Verlaufuntersuchungszeitraum vom 25 Jahren

Is there a difference in the grade of degeneration at the cervical spine following anterior cervical fusion with respect to clinical outcome, diagnosis and repeated procedure? – a magnetic resonance imaging study of 102 patients with a mean follow-up of 25 years

B. Burkhardt¹, A. Simgen², M. Dehnen¹, G. Wagenpfeil³, W. Reith², J. Oertel¹

¹Universität des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

²Universität des Saarlandes, Klinik für Neuroradiologie, Homburg, Germany

³Universität des Saarlandes, Institut für Medizinische Biometrie, Epidemiologie und Informatik, Homburg, Germany

Objective

Accelerated degeneration of the adjacent segments (ASD), loss of disc height (DH) and loss of segmental alignment (SSA) following anterior cervical fusion (ACDF) is still discussed controversially. It is unclear if the grade of ASD, DH and SSA correlates with clinical outcome, the initial diagnosis, or number of fused levels. The purpose of the present study was to assess the grade of segmental degeneration as well as the clinical outcome and to analyse if they are related.

Methods

Retrospectively, a total of 102 patients who underwent ACDF at a minimum of 18 years ago were identified. At final follow-up, the clinical outcome according to Odoms, Neck disability index (NDI), and reoperation for symptomatic ASD (sASD) were assessed. A five step grading system (SDI) was used for evaluation; it includes disc signal intensity, anterior and posterior disc protrusion, narrowing of the disc space and foraminal stenosis. Further, the disc height (DH) and the sagittal segmental angle (SSA) of fused levels were measured. MRI findings were compared with respect to clinical outcome (NDI: 0-20 vs. >20, Odom's: clinical success vs. no clinical success), the event of reoperation for sASD, the initial diagnosis (soft disc herniation [SDH] vs. myelopathy [CSM] and spondylosis), and fused levels (1 vs. 2-4 levels).

Results

The mean follow-up was 25 years (range: 18-45). Initial diagnosis was a CDH in 74.5%, and CSM or spondylosis in 25.5% of patients. At follow-up, the mean NDI was 12.4% (range: 0-36%), clinical success was reported by 87.3% of patients, and reoperation rate for sASD was 15.7%. For SDI no significant differences were seen with respect to NDI, Odoms and sASD. Patients diagnosed with CDH had significant more degeneration at the adjacent segments ($p=0.015$, $p=0.017$). Patients with 2-4 level procedure had less degeneration at the caudal adjacent and adjoining segments ($p=0.011$, $p=0.019$). The mean DH at the 1. cranial adjoining segment was significantly lower in patients operated on for CSM or spondylosis and without clinical success. No further significant differences were seen for DH. No significant differences in clinical outcome were seen in patients with lordotic and straight or kyphotic SSA.

Conclusion

The grade of SDI does not differ with respect to clinical outcome. The SDI was lower in patients with multilevel procedures and fusion for SDH. The degree of SSA was not different and DH was hardly different with respect to clinical outcome, diagnosis and number of fused levels.

Wirbelsäulenchirurgie II/Spine surgery II

P042

Sekundäre Deformität des Sagittalprofils nach instrumentierter Operation mit und ohne Korpektomie zur Behandlung der pyogenen Spondylodiszitis

Secondary deformity of sagittal profile following instrumented surgery with and without corpectomy for treatment of pyogenic spondylodiscitis

P. Melich^{1,2}, B. Schatlo¹, C. Bettag¹, V. Malinova¹, D. Mielke¹, V. Rohde¹, T. Abboud¹

¹Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

²Universitätsklinikum Köln, Neurochirurgie, Köln, Germany

Objective

Pyogenic spondylodiscitis is associated with significant morbidity and mortality. Secondary spinal deformity may arise due to vertebral body collapse. Despite growing number of studies on the subject, there is no consensus on the threshold for 360° fusion compared to stand-alone posterior approach. The aim of the current study is to assess secondary deformity of sagittal profile and evaluate the difference between 360° fusion and posterior stabilization in this regard.

Methods

We retrieved radiological data of 90 patients who underwent instrumented surgery for pyogenic spondylodiscitis at our institution between 2010-2017. Kyphosis angle in the thoracic spine and lordosis angle in the lumbar spine were measured between the endplates above and beneath the involved discs and vertebrae. This measurement was performed using CT- imaging prior to the surgery, postoperatively and at follow-up. We applied paired T-test to compare measured angles and T-test to compare the angle changes between patients who received posterior instrumentation and those who received 360° fusion.

Results

Instrumentation was conducted in the lumbar spine in 65 patients, 14% of them received 360° fusion, and in the thoracic spine in 25 patients, 44% of them received 360° fusion. Mean follow-up period was 9±3 months. Mean lordosis angles pre- and postoperatively and at follow-up were 26.4±15.8°, 28.9±16° and 24.7±14.2°, respectively. Mean kyphosis angles pre- and postoperatively and at follow-up were 12.3± 6.7°, 11.1±7.1° and 16.3±9.1°, respectively. The deformity decreased significantly after surgery in the lumbar spine and increased at follow up (P=0.034 and P=0.001, respectively), while kyphosis correction after surgery in the thoracic spine was not significant and the kyphosis increased significantly at follow-up (P=0.211 and P=0.001, respectively).

When comparing posterior instrumentation with 360° fusion, the only significant difference was found in the lumbar spine where the positive change in the lordosis angle was higher at follow up in patients with 360° fusion than in those with posterior instrumentation (mean 3.6±7.2° and -2.5±8.5°, p=0.045)

Conclusion

Following instrumented surgery for treatment of pyogenic spondylodiscitis, secondary deformity of the sagittal profile occurred in the lumbar and thoracic spine. 360° fusion might be of higher value in the lumbar spine than in the thoracic spine. Larger and perhaps prospective series are needed to validate these results.

Wirbelsäulenchirurgie II/Spine surgery II

P043

Redundant nerve roots in der lumbalen Spinalkanalstenose – Validierung der Inter- und Intraobserver-Reliabilität einer MRT-basierten Klassifikation

Redundant nerve roots in lumbar spinal stenosis – inter and intra-rater reliability of an MRI-based classification

L. Papavero¹, C. Marques², J. Lohmann¹, T. Fitting³, K. Schawjinski¹, N. Ali¹, H. Hillebrand¹, R. Maas⁴

¹Schön Klinik Hamburg Eilbek , Klinik für Spinale Chirurgie, Hamburg, Germany

²Schön Klinik Hamburg Eilbek , Science Office, Klinik für Endoprothetik, Hamburg, Germany

³Schön Klinik Hamburg Eilbek , Radiologie, Hamburg, Germany

⁴Private MRT- und CT-Röntgenpraxis Raboisen 38 Hamburg , Hamburg, Germany

Objective

Patients with central lumbar spinal stenosis (LSS) have a longer symptom history, more severe stenosis, and worse postoperative outcomes if redundant nerve roots (RNRs) are evident in the preoperative MRI. An RNR classification in the MRI report could provide clinicians with clinically relevant information. This is a retrospective validation study to test the inter- and intra-rater reliability of an MRI-based classification for RNR.

Methods

This retrospective reliability study retrieved data from a central database. A neuroradiologist, an orthopedic surgeon, and a neurosurgeon (senior raters) and three orthopedic surgeons in training (junior raters) classified RNRs on 126 preoperative MRIs of patients with LSS admitted for microsurgical decompression. On sagittal and axial T2-weighted images, the following four categories were defined: Allocation (*A*) of the key stenotic level (KSL); Shape (*S*) of RNR (serpentine or loops); Extension (*E*) of RNR (less or more than one vertebral height); and Direction (*D*) of the RNR in reference to *A* (cranial, caudal, or cranio-caudal). A second read with cases ordered differently was performed four weeks later. Fleiss and Cohen's kappa procedures were used to determine reliability.

Results

The ASED classification showed moderate to almost perfect inter-rater reliability, with kappa values of $k= 0.86$ (0.83, 0.90), $k= 0.62$ (0.57, 0.66), $k= 0.56$ (0.51, 0.60), and $k= 0.66$ (0.63, 0.70) for Allocation, Shape, Extension, and Direction, respectively. Intra-rater reliability was almost perfect, with $k= 0.90$ (0.88, 0.92), $k= 0.86$ (0.84, 0.88), and $k= 0.84$ (0.81, 0.87) for Shape, Extension, and Direction, respectively. Intra-rater kappa values were similar for junior and senior raters. Kappa values for inter-rater reliability were similar between the first and second reads ($P= 0.06$) among junior raters and improved among senior raters ($P= 0.008$).

Conclusion

The MRI-based classification of RNRs showed moderate to almost perfect inter-rater and almost perfect intra-rater reliability. The classification is easy to learn and easy to document in the MRI report.

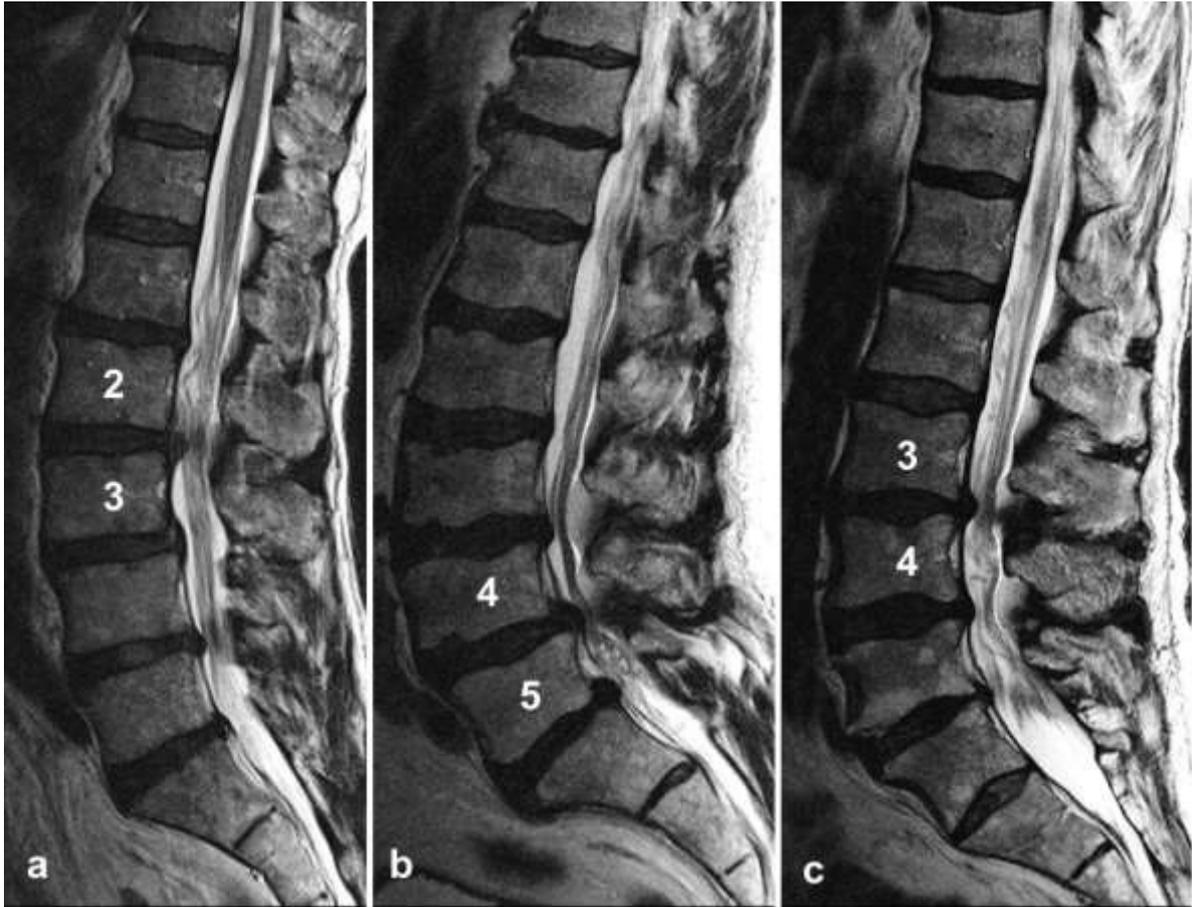
Tab. 1 Instructions for using the ASED Classification

Fig. 1 Examples of ASED-classification: a) RNR+: L2/L3. S. 1+.cr; b) RNR+: L4/L5.L.1.ca; c) RNR+: L3/L4.L.1+.cc

Fig 1

ASED	Category definition	Items	Item definition	Notation
A llocation	Refers to the key stenotic level (KSL). The KSL shows the switch between straightened cauda nerve roots (CNR) and RNR or, shows adjacent cranio-caudal RNR. When in doubt between two potential KSL the most stenotic level (with the smallest CSA) is defined as KSL.	L1/L2		KSL (i.e. L3/L4)
		L2/L3		
		L3/L4		
		L4/L5		
		L5/S1		
S hape	Refers to the shape of RNR. This category comprises two items.	Serpen- tines	Serpentines are present when a sinusoidal deflection (complete crest-trough wave) of the majority of CNR occurs within the height of a vertebral body without any horizontalization of the involved roots.	S
		Loops	Loops are present when at least in two different areas dots or horizontal roots in the sagittal T2WI-slice were combined with tortuous, coiled roots in the axial T2WI-slice. Mixed serpentine and loop findings are scored as loops.	L
E xtension	Refers to the length of RNR. This category comprises two items.	1	When RNR extend up to one vertebral height adjacent to the KSL they are notated with "1".	1
		1+	When RNR extend beyond one vertebral height they are notated with "1+". Cranio-caudal RNRs are always notated as "1+".	1+
D irection	Refers to the localization of RNR in relation to the KSL. This category comprises three items.	cranial	RNR are only present cranially from the KSL.	cr
		caudal	RNR are only present caudally from the KSL.	ca
		cranial- caudal	RNR are present cranially and caudally from the KSL.	cc

Fig 2



Wirbelsäulenchirurgie II/*Spine surgery II*

P044

Extrafokale perkutane dorsale Stabilisierung zur Therapie der pyogenen Spondylodiscitis **Extrafocal percutaneous transpedicular fixation for the treatment of pyogenic spondylodiscitis**

H. Abdelrahman^{1,2}, E. Sadaat¹, A. Shawky^{1,2}, K. Branko¹, A. Ezzati¹

¹Helios-Klinikum Erfurt, Wirbelsäulenchirurgie, Erfurt, Germany

²Assiut University, Assiut, Egypt

Objective

Pyogenic spondylodiscitis (PS) is a challenging disease with poor prognosis that requires immediate diagnosis and treatment. It can be treated non-surgically with antibiotics and immobilization with an external orthosis for several weeks to months. If surgical intervention is required, a combined anterior and posterior approach is usually performed. We report on our experience with a minimally invasive percutaneous transpedicular fixation (PTPF) procedure for the treatment of patients with PS.

Methods

We reviewed data of 32 patients, between 06/2013 and 06/2018, treated for PS, without extensive bone destruction or significant neurological deficit, with PTPF. Demographic, operative, and perioperative data were collected and analysed.

Results

The study included 17 women and 15 men with mean age of 73.6 years (56-90). Renal insufficiency was found in 27 and DM in 19 cases. Five cases were class II ASA-Score und 27 were class III and IV. The lumbar spine was affected in 20 patients, thoracic: 12, cervical: 2 and four patients had multifocal PS (33%). More than three segments were fixed in 18 patients. The average operative time was 88 minutes. The average blood loss was 160 ml. Intraop. biopsy for microbiological and histopathological examination was obtained in 33 patients; organisms could be isolated in 26 cases (70%). There were no intraop. complications, one patient died two days postop. due to cardiac infarction. 10 patients had been reoperated for shortening of the fixation after autofusion of the infected segments; occurred in 27 patients within 6 months. Preop. VAS of 6/10 reduced to 2 at the last FU. 10 cases had ASIA-D, 9 improved postop. to ASIA-E with neurological improvement rate of 90%. Preop. CRP and WBC were 83.2 and 10.7 reduced to 32.5 and 8.8 at the last FU respectively.

Conclusion

The internal immobilization and antibiotic therapy without touching the infected tissue is sufficient to completely resolve the spondylodiscitis. Short and midterm outcomes are promising. A larger series and continuing follow-up examinations are necessary in order to clarify and define benefits and limitations of the presented technique.

Wirbelsäulenchirurgie II/*Spine surgery II*

P046

Entwicklung spinaler Liquorfisteln nach inzidenteller Durotomie bei spinal dekompensiven Eingriffen *Development of cerebrospinal fluid fistula after incidental durotomy in decompressive spine surgery*

C. Hohenberger¹, A. Brawanski², F. Zeman³, K. M. Schebesch²

¹Universitätsklinikum Regensburg, Klinik und Poliklinik für Neurochirurgie, Regensburg, Germany

²Universitätsklinikum Regensburg, Klinik und Poliklinik für Neurochirurgie, Regensburg, Germany

³Universitätsklinikum Regensburg, Zentrum für Klinische Studien, Regensburg, Germany

Objective

Incidental durotomy (ID) during spinal surgery is a risk factor for the development of cerebrospinal fluid (CSF) fistula. The rates of ID with or without consecutive CSF fistula vary according to the extent of the surgical procedure. Revision surgery has the highest rates of dural tears. However, not every case of ID leads to CSF fistula requiring revision surgery. The objective of this study was to analyze the predictors for the development of CSF fistula after ID.

Methods

This retrospective study included 6024 consecutive patients who had been surgically treated for degenerative spinal disease at our clinic over the past 15 years. Patients who had undergone surgical revision for CSF fistula were assigned to the CSF fistula group. A matched 3:1 control group (ID group) was formed of patients with ID but without CSF fistula. Charts, surgical reports, and radiographic data were reviewed and statistically analyzed for demographics, duration of symptoms, co-morbidities, surgical strategy, and pre- and postoperative neurological performance.

Results

The 15-year incidence of CSF fistula in the overall population was 0.36% (n=22). The following anatomic locations were affected: n=18 lumbar (81.8%), n=2 cervical (9.1%), and n=2 thoracic (9.1%). The extent of ID was similar in both groups. The two groups did not significantly differ with regard to the intraoperative management of dural repair with primary suturing (p=0.345), dural patches, sealant, or collagen matrix (p=0.228; p=0.081; p=0.081). In the postoperative period, bed rest in supine position for 48 hours (p=0.037) and laxative therapy (p=0.034) were the most beneficial treatment modalities for preventing CSF fistula. Patients with CSF fistula were hospitalized significantly longer (21 days vs. 10 days in the control group; p<0.001).

Conclusion

This large test group showed a low incidence of postoperative CSF fistula after intraoperative ID. Bed rest and laxative treatment were important approaches towards preventing CSF fistula.

Wirbelsäulenchirurgie II/*Spine surgery II*

P047

Postoperative Veränderungen der sagittalen Balance nach Behandlung mit kraniokaudal expandierbarem Implantat zur minimal-invasiven Rekonstruktion von osteoporotischen Kompressionsfrakturen – 4 Jahre Erfahrungen mit 120 Patienten

Postoperative changes in sagittal balance after therapy with new craniocaudal expandable implant for the minimally invasive reconstruction of osteoporotic vertebral body compression fractures – 4 years of experience with 120 patients

J. Assaf, M. J. Fritsch

Dietrich-Bonhoeffer-Klinikum Neubrandenburg, Klinik für Neurochirurgie, Neubrandenburg, Germany

Objective

We present the surgical technique and patient data of 120 patients with 4 years follow up treated for osteoporotic compression fractures of the thoracic and lumbar spine. Patient data were collected prospectively. The aim of this study is to evaluate the restoration of sagittal balance with this technique and the clinical outcome for the patients.

Methods

We treated 120 patients for 133 spinal osteoporotic fractures with an age ranging from 46-88 years. OF-Classification of osteoporotic vertebral body fracture (OF 0-5) was type OF 0 (23), OF 1 (30), OF 2 (24), OF 3 (22), OF 4 (31) and OF 5 (3). All implants were percutaneous transpedicular. For augmentation PMMA or a combination of PMMA / hydroxyapatite was used. All patients had a preop clinical examination, spine x-ray, CT and MRI as well as a postop clinical examination and x-ray after 1 month, 1 year and 3 years. For each patient we measured the height of the vertebral body as well as the kyphosis angle of the fractured vertebral body. Restoration of the spinal profiles was assessed with spine x-ray. All included patients had a 4-year follow up.

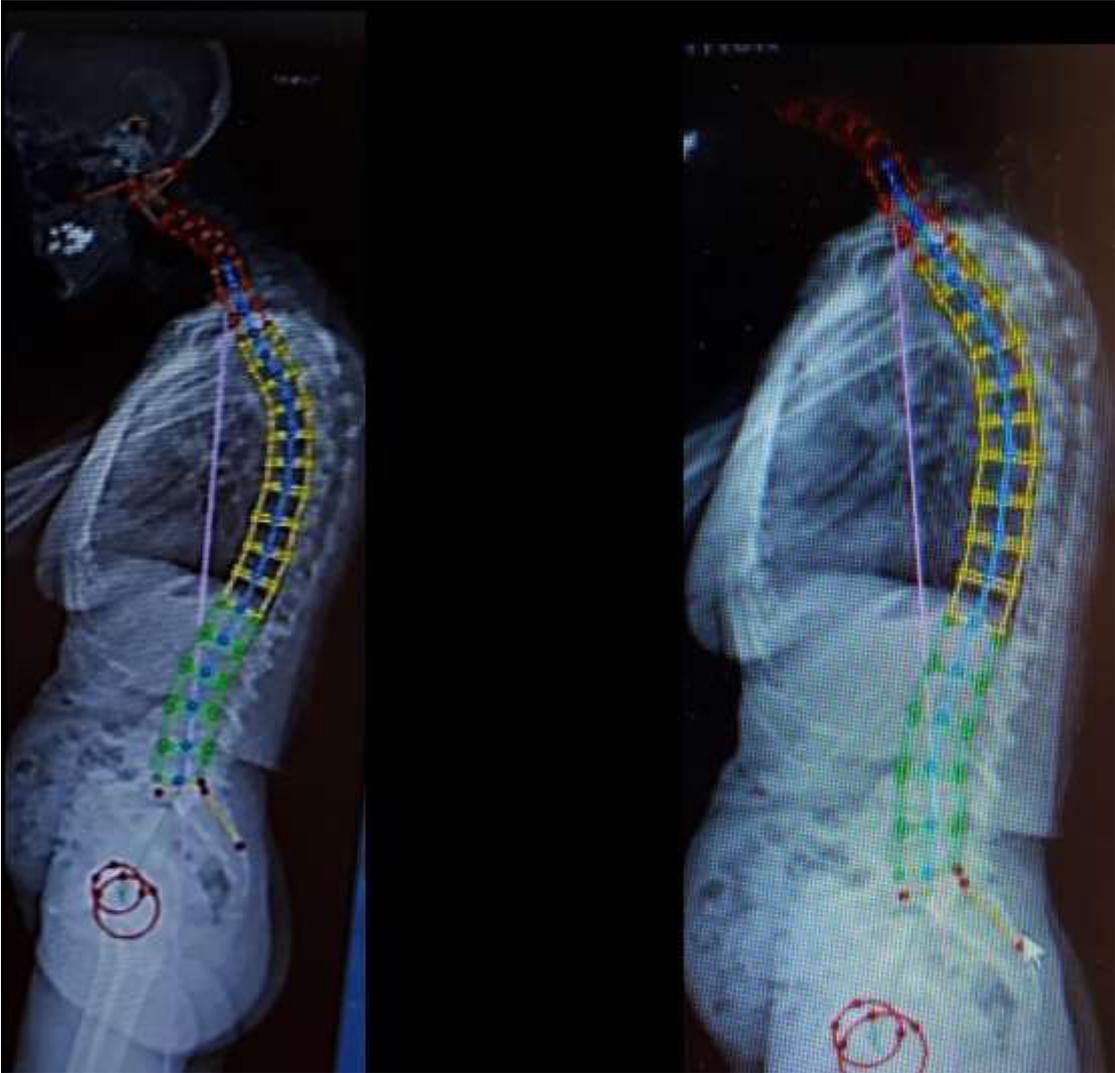
Results

Within the 4 years follow-up period, the reduction of pain according to VA-scale was 77%. Increase of vertebral body height was 15% after the procedure and 11% after 3 years. The kyphosis angle was -6° prior to surgery and $-4,5^\circ$ 3 year later. The restoration of the sagittal balance was detectable in 89% of the cases. Cement leak was seen in 40,6%, in all of them without neurologic deficits except for one case. There was no reoperation in the same segment within 4 years. Sagittal vertical axis (SVA): Pre-op: $6,98 + 3,0$ cm, Post-op: $5,01 + 2,98$ cm.

Conclusion

The presented method with a craniocaudal expandable implant is efficient and is providing excellent results after 4 years follow up. We achieved long lasting reduction of pain and pain medication in our patients. This technique allows a restoration of sagittal balance in most cases.

Fig 1



Wirbelsäulenchirurgie II/*Spine surgery II*

P048

Intraoperative Beurteilbarkeit der Lage von Pedikelschraubenlage mittels digitaler Volumentomographie *Intraoperative assessability of pedicle screw placement using digital volume tomography*

J. Woitzik¹, L. Wolter², N. Hecht², P. Vajkoczy², S. H. Bayerl²

¹Evangelisches Krankenhaus Oldenburg, Universitätsklinik für Neurochirurgie, Oldenburg, Germany

²Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

Objective

Navigated pedicle screw placement can be performed using intraoperative computerized tomography (CT) or digital volume tomography (DVT). An additional benefit of using high-resolution intraoperative imaging, such as DVT, is the possibility to immediately assess screw placement with the chance of direct intraoperative revision, if needed. However, information on the intraoperative assessability of navigated pedicle screws using DVT remains lacking. Therefore, we evaluated the intraoperative assessability of navigated pedicle screws across the entire spine using DVT-based intraoperative imaging compared to postoperative CT.

Methods

Between March 2017 and February 2019, 944 subaxial pedicle screws were inserted in 174 consecutive patients using DVT-based spinal navigation with the O-arm. Intraoperative image data sets underwent multiplanar 3-dimensional reconstruction and were analyzed regarding to pedicle screw accuracy and screw assessability in comparison to postoperative CT in 105 cases. In addition, unexpected adverse events (UAEs) were documented.

Results

Of all implanted screws, only 0.4% (4/944) were rated 'not-assessable' due to artifacts (3/944 cervico-thoracic, 1/944 lower thoracic spine). Further, 7% (67/944) of all screws were rated 'poorly assessable' due to the following reasons: 79% (53/67) due to artifacts, 10% (7/67) due to difficult distinction between bone and surrounding tissue and 10% (7/67) due to grade II or III obesity. Specifically, 29% of screws in the lower cervical spine (C6-7), 18% in the upper thoracic spine (T1-4), 20% in the middle thoracic spine (T5-8), 3% in the lower thoracic spine (C9-12), 3% in the lumbar spine (L1-5) and 4% in the sacrum (S1) were rated 'poorly accessible'. 44/944 pedicle screws (4.7%) were intraoperatively corrected in 31/174 cases (18%).

Conclusion

Intraoperative pedicle screw assessment with DVT is feasible but inferior to conventional CT imaging at the cervico-thoracic level and in obese patients due to anatomically associated artifact susceptibility. Overall, however, DVT permits reliable and clear intraoperative screw assessment.

Fig 1

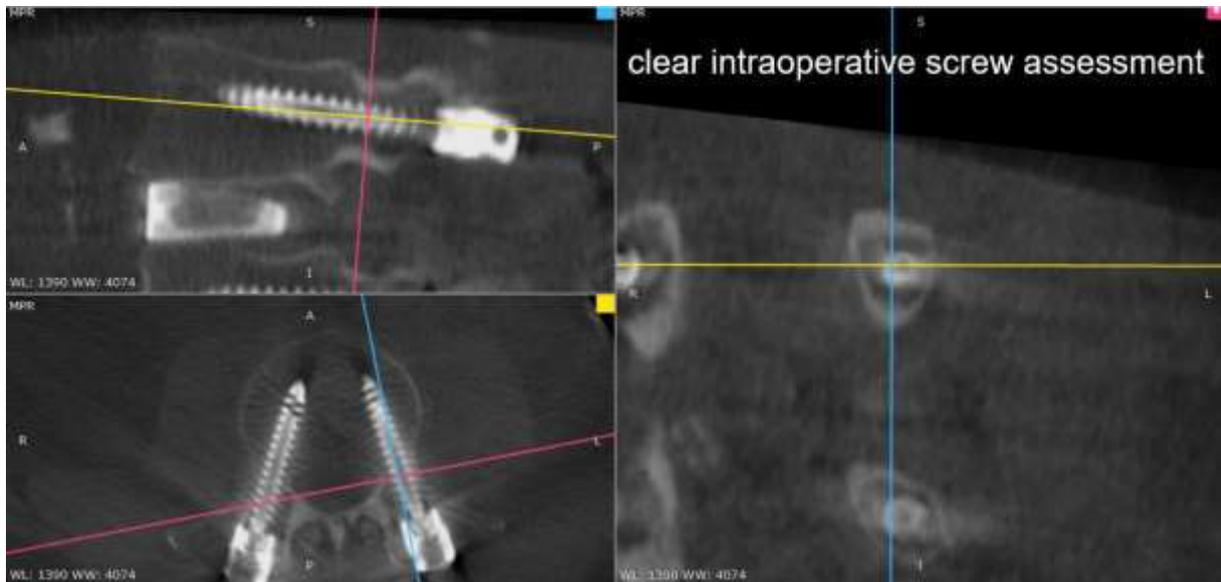
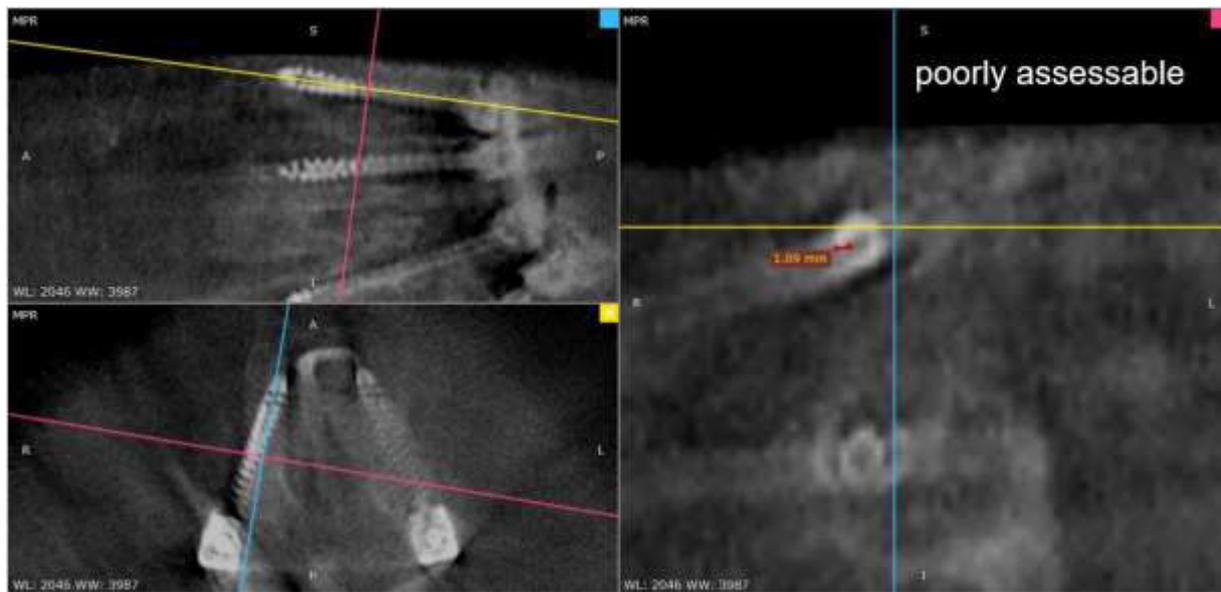


Fig 2



Spinale und zerebrale Metastasen I / *Spinal and cerebral metastases I*

P049

Ex-vivo Gewebeanalyse von Metastasen verschiedener Tumorentitäten mittels optischer Kohärenztomographie

Ex vivo tissue analysis of metastases from different tumour entities using optical coherence tomography

L. A. Bartsch¹, J. Möller², M. Lenz², R. Krug¹, I. Tischoff³, H. Welp⁴, M. Hofmann², K. Schmieder¹, D. Miller¹

¹Universitätsklinikum der Ruhr-Universität Bochum , Neurochirurgie, Bochum, Germany

²Universitätsklinikum der Ruhr-Universität Bochum, Lehrstuhl für Photonik und Terahertztechnologie, Bochum, Germany

³Universitätsklinikum der Ruhr-Universität Bochum , Pathologie, Bochum, Germany

⁴Technische Hochschule Georg Agricola, Bochum, Germany

Objective

Brain metastases (BM) are the most common brain tumours. During the resection of BM, it is essential to precisely distinguish between tumour and surrounding brain tissue (BT) as tiny tumour remnants might lead to local recurrence. Optical coherence tomography (OCT) is an imaging technique with a resolution of a few micrometres that might improve the detection of small tumour remnants. The objective of this study was to distinguish the necrotic and vital proportion of BM from healthy BT in an ex vivo setting by applying texture analysis and machine learning algorithms for tissue classification to OCT images.

Methods

Twenty-eight patients with suspected BM were included in the study. BM tissue samples were taken during resection using neuro-navigation and microsurgical techniques. BT was taken during the approach in subcortical lesions only. Fresh tissue samples were scanned using a spectral domain high-resolution OCT system. Volumetric OCT images were stored for further post-processing. Tissue samples were then evaluated histologically. The percentage of vital tumour tissue, necrosis and BT per sample was recorded. Texture feature-based post-processing as well as machine learning with principal component analysis (PCA) and support vector machines (SVM) were applied to the OCT scans. Ultimately, a classification using SVM was carried out, determining the accuracy with which BM tissue (sample with at least 60% of vital tumour, alternatively samples with 100% necrotic tissue) can be distinguished from BT (at least 90% healthy tissue).

Results

Every possible combination of used texture parameters according to the PCA and SVM was considered. 6 BM samples showed 100% of necrotic tissue. Those were compared to BT. The SVM enabled us to classify necrotic and healthy tissue with an accuracy of 99.07%. The best result was obtained for a combination of local binary pattern and Law's energy texture measure. The same procedure was applied for those samples of at least 60% vital tumour tissue (n=7). It was possible to classify vital tumour against healthy tissue with an accuracy of 95.75%.

Conclusion

This innovative method of OCT and texture-based classification enables us to precisely distinguish between healthy tissue on the one hand and tumorous necrotic and vital tissue on the other hand. This is a promising method to be tested in an intraoperative setting.

Spinale und zerebrale Metastasen I/*Spinal and cerebral metastases I*

P050

Multiparametrische Analyse von extrazellulären Vesikeln aus dem Liquor von Patienten mit intraspinalen Tumoren

Multiplex analysis of CSF extracellular vesicles of intraspinal tumours

F. L. Ricklefs¹, I. Stevic¹, C. Maire¹, J. Welsh², K. C. Mende¹, M. Westphal¹, K. Lamszus¹, S. O. Eicker¹

¹Universitätsklinikum Hamburg-Eppendorf, Neurochirurgie, Hamburg, Germany

²National Institutes of Health (NIH), Washington, WA, United States

Objective

Extracellular vesicles (EVs) play an important role in cell-cell communication in different types of tumors, carrying multiple layers of biological functional molecules, including proteins, RNA, DNA and lipids. We previously demonstrated that extracellular vesicles (EV) from central nervous system tumors reflect the molecular subtype of the original tumor and mediate an exchange of pro-oncogenic signals. Their implication as biomarkers in tumor disease is under current investigation. It is unclear, however, to what extent cerebrospinal fluid (CSF) EVs from intraspinal tumors are utilizable for diagnostic purposes and how their marker profiles overlap with EVs derived from non tumorous EVs. We analyzed CSF EVs of intraspinal tumors to define CSF EV profiles that allow tumor subtype classification.

Methods

EVs were isolated from CSF of patients suffering from intraspinal meningioma (n=5), ependymoma (n=7) and neurinoma (n=5). Patients suffering from normal pressure hydrocephalus were used as controls (n=5). EVs were analyzed by multiplex bead based assay, immunoblotting, electron microscopy and NTA.

Results

CSF EVs were 97.21 ± 3.37 nm (tumor patients) and 101.6 ± 3.68 nm (controls) in sizes and showed vesicular structures by electron microscopy. Particle number were not significantly different between both groups ($p = 0.103$). Using our 37 protein multiplex EV profiling kit we found 29 proteins to be expressed in a sufficient manner on CSF EVs. CSF EVs of intraspinal meningioma showed elevated CD62P, HLA-DR, CD40, CD42a and CD45 expression levels, while ependymoma showed decreased levels of CD9, CD63, CD81, whereas neurinomas had elevated levels of SSEA-3 and CD25.

Conclusion

This is the first comprehensive analysis of CSF EV of intraspinal tumor patients. CSF EV display distinct subpopulations that may allow tumor classification and long-term surveillance. However as tumor-specific EVs may be rare, there is still the need to identify markers that can enrich tumor-specific EVs for molecular profiling.

Spinale und zerebrale Metastasen I/*Spinal and cerebral metastases I*

P051

Kolorektales Karzinom und Hirnmetastasen – eine retrospektive Analyse von 59 Patienten

Colorectal carcinoma is not a rare primary in patients suffering from brain metastases – a retrospective analysis of 59 patients

D. Keiner, J. Stürmer, J. Oertel

Universitätsklinikum des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

Objective

Colorectal carcinoma (CRC) is often describes as a rare cause for brain metastases (BM). Few studies focus on the neurosurgical therapy. BM tend to occur late in the course of CRC and surgical removal in general is performed in a minority of patients. In this retrospective analysis, patients with surgically treated BM caused by CRC were followed up in terms of clinical outcome, morbidity, and survival.

Methods

A retrospective analysis of 608 patients with BM of different primary tumours having tumor resection at the Department of Neurosurgery, Saarland University Medical Center, between 01/2007 and 03/2016 was conducted. Clinical and patient-related data as well as histopathological, radiological and neurosurgical data were collected from the patients' records.

Results

Fifty-nine patients (9.7%) had been diagnosed with CRC. Twenty-eight (47.5%) patients were female and 31 (52.5%) patients were male. Mean age was 66.9 years. A singular metastasis was present in 42 (71.2%) patients whereas in 27 (28.8%) patients multiple metastases occurred. Mean follow-up time was 179.4 days (5.6 months). Tumor resection was performed in all patients without having special primary exclusion criteria such as advanced age, poor general condition, extracranial tumour activity, neurological symptoms or number and size of tumors. Supratentorial metastases occurred in 37 patients (67.7%), and infratentorial metastases occurred in 19 (32.2%) patients. In 6 (10.2%) patients, combined supra- and infratentorial metastases were present. Mean overall survival of the present cohort was 138.4 days (4.6 months) and up to 36 months. Mean survival of patients with posterior fossa BM was 6.1 months compared to patients with supratentorial BM (4.2 months). If case of supra- and infratentorial BM, the outcome was poor with a mean survival of 6 weeks.

Conclusion

BM developing from CRC were diagnosed frequently and were treated with surgical removal without general preclusion of certain factors such as old age. Surgical resection seemed to have a positive impact in many patients. Overall survival of patients with infratentorial BM was best despite the prevailing opinion in the literature of a less favourable prognosis due to posterior fossa metastases. Surgical removal might be beneficial at an advanced tumor stage of CRC disease as well. In many patients, surgical tumor resection is crucial to preserve quality of life. A more generous indication should be considered in many patients suffering from CRC brain metastases.

Spinale und zerebrale Metastasen I/*Spinal and cerebral metastases I*

P052

Quantifizierung der PpIX-Fluoreszenz von zerebralen Brustkrebs-Metastasen *Quantification of PpIX-fluorescence of cerebral breast cancer metastases*

J. Knipps, M. Rapp, D. M. Donaldson, D. Hänggi, M. Sabel, M. A. Kamp

Universitätsklinikum Düsseldorf, Neurochirurgische Klinik, Düsseldorf, Germany

Objective

Introduction of the 5-ALA technique is one major advance in neuro-oncological surgery. Protoporphyrin IX (PpIX)-fluorescence was observed in about half of cerebral metastases. For now, no study found a correlation between the dichotomized PpIX-fluorescence of breast cancer metastases and neither the receptor status nor the histological subtype of breast cancer metastases. Aim of the present pilot study was to quantify PpIX-induced fluorescence of breast cancer metastases and correlate this with the hormone receptor status.

Methods

5-ALA induced fluorescence intensity was quantified in 14 patients suffering from cerebral breast cancer metastases. A systematic spectrometric evaluation of tumor specimen and the resultant PpIX-induced fluorescence was performed using a spectrometer connected by optic fiber to a handheld probe. The difference between maximum PpIX-fluorescence at 635 nm and baseline fluorescence was considered as PpIX fluorescence intensity of the metastasis. In addition, results were correlated with receptor status (PD-L1, estrogen receptor, progesteron receptor, HER-2/neu) and histopathological examinations.

Results

All 14 patients had breast cancer with cerebral metastases. The mean age was 58 year (32 – 80 years). All patients were female. All 14 cerebral breast cancer metastases were considered as ALA fluorescent by the surgeon. A PpIX fluorescence over 1.1×10^6 AU was observed as "ALA-positive" by the surgeon. The mean PpIX fluorescence of analyzed cerebral breast cancer metastases was 3.5×10^6 AU (2.3×10^6 – 6.3×10^6 AU). After quantification we observed no significant difference in the levels of 5-ALA fluorescence in cerebral breast cancer metastases with different hormone receptor status.

Conclusion

Firstly, PpIX fluorescence over 1.1×10^6 AU was observed as "ALA-positive" by the surgeon.

Secondly, all cerebral breast cancer metastases were tested as "ALA-positive" by the spectrometer.

Thirdly, quantification of 5-ALA fluorescence showed no significant difference between cerebral breast cancer metastases with different hormone receptor status in our cohort.

Spinale und zerebrale Metastasen I/*Spinal and cerebral metastases I*

P053

Hypofraktionierte Radiochirurgie bei Hirnmetastasen *Multisession radiosurgery (msRS) for brain metastases – a single-centre series*

S. Fichte, H. U. Herold, G. Surber, K. Hamm

Cyberknife Centrum Mitteldeutschland, Erfurt, Germany

Objective

Radiosurgery (RS) is a well-accepted therapeutic option for brain metastases and increasingly used even for multiple metastases. However, large brain metastases or those in critical locations may not be amenable to single-session treatment. In these cases, multisession radiosurgery (msRS) in 3-5 fractions may be an alternative. We present our series of patients treated with multisession image-guided robotic radiosurgery.

Methods

Patients treated for brain metastases with multisession radiosurgery between November 2012 and March 2019 were analyzed retrospectively. Metastases with prior local therapy (surgery and/or focal radiotherapy except whole-brain radiotherapy) were excluded from analysis. Patient data, planning details and imaging were analyzed. For follow-up, contrast-enhanced MRI was fused to the initial imaging. Tumor response was evaluated and local control rate was assessed. Additionally, regional progression (new brain metastases) was documented. Kaplan-Meier estimation was used for statistical analysis of survival and local progression-free survival.

Results

70 patients underwent 72 courses of multisession radiosurgery in 3-5 fractions (median 3). Mean time of follow-up after the first treatment was 13,1 (0,2-82,7) months. Overall survival was 63 % and 37% at 6 and 12 months, respectively. At least one radiographic follow-up was available for 45 treatments. Local control rate was 95%, 92% and 74% at 3, 6 and 12 months. 23 patients had regional progression after a mean time of 10,2 (1,6-39,4) months of whom 12 were treated with repeated radiosurgery.

Conclusion

msRS is a treatment option for brain metastases with a good rate of local control when single-session radiosurgery is not feasible, avoiding or postponing WBRT.

Spinale und zerebrale Metastasen I/*Spinal and cerebral metastases I*

P054

Frühes motorisches Outcome nach intraoperativer Strahlentherapie in hoch-eloquenten Gehirnarealen *Early motor function outcome in patients receiving intraoperative radiotherapy (IORT) in highly eloquent brain areas*

S. Brehmer¹, A. Delhey¹, F. Schneider², S. Clausen², M. Seiz-Rosenhagen¹, N. Etminan¹, F. A. Giordano²

¹Universitätsklinikum Mannheim, Klinik für Neurochirurgie, Mannheim, Germany

²Universitätsklinikum Mannheim, Klinik für Strahlentherapie und Radioonkologie, Mannheim, Germany

Objective

Intraoperative radiotherapy (IORT) is a routine procedure in gynecological oncologic surgery. However, IORT gains increasing interest as an innovative approach to reach local tumor control in the treatment of intracranial pathologies. This therapy enables the concomitant radiotherapy of the resection cavity-which is the golden standard- in a single session in patients receiving surgical treatment for brain metastases, which results in shorter length of hospitalization and potentially earlier salvages cancer therapy. The role of IORT in eloquent brain areas is uncertain due to the mere size and thereby local pressure of the radiation applicator and the high single dose. We here report a subgroup analysis of our prospective phase II INTRAMET (intraoperative radiotherapy after the resection of brain metastases) trial for patients undergoing surgical treatment for metastases in the motorcortex area.

Methods

Since 7/2017 6 patients were treated with IORT following resection of lesions in the motorcortex area (3 left and 3 right). Resection was performed using intraoperative neuromonitoring. All patients had frozen section confirmed metastasis and were treated with a single dose of 30 Gy. Neurological outcome was assessed before surgery, immediately after as well as 2 weeks, 6 weeks and 3 months after surgery and IORT.

Results

All patients had preoperative paresis (1 with a complete hemiparesis M4, 3 with arm palsy ranging from M3 to M4, 1 with a facial nerve palsy and 1 with leg palsy M4). Intraoperative neuromonitoring showed no change in MEP or SSEP during surgery and IORT. In all patients complete resection was achieved. Immediately, after treatment 2 patients had a drop of muscle strength of 1 to 5 points, 3 patients had no change in function and 1 improved to full strength. After 2 weeks another patient improved to full strength and 1 to preoperative level. After 6 weeks 3 patients had full strength. After 3 months 5 patients improved to full strength and 1 remained at baseline level. Those patients who suffered from postoperative worsening of motor function improved back to baseline function at 6 weeks after treatment.

Conclusion

In this INTRAMET subgroup analysis no patient receiving tumor resection combined with IORT suffered from a new permanent deficit. Applicator insertion and applicator pressure whilst radiation does not seem to have a detrimental effect in functional outcome. Thus, IORT is a safe and feasible adjunct to metastases resection in eloquent brain areas.

Spinale und zerebrale Metastasen I/*Spinal and cerebral metastases I*

P057

Komplikationen nach stereotaktischer Radiochirurgie bei zerebralen Metastasen – Befunde und Behandlungen

Delayed complications after stereotactic radiosurgery for brain metastases – neuro-imaging findings and treatments

H. Aiyama^{1,2}, M. Yamamoto³, E. Ishikawa², T. Kawabe⁴, S. Watanabe², T. Koiso⁵, Y. Sato⁶, A. Matsumura², Y. Shibata^{1,2}

¹Mito Kyodo General Hospital, Neurosurgery, Mito, Japan

²University of Tsukuba Hospital, Neurosurgery, Tsukuba, Japan

³Katsuta Hospital Mito Gamma House, Neurosurgery, Hitachinaka, Japan

⁴Rakusai Shimizu Hospital, Neurosurgery, Kyoto, Japan

⁵Hitachi General Hospital, Neurosurgery, Hitachi, Japan

⁶Keio University School of Medicine, Tokio, Japan

Objective

Stereotactic radiosurgery (SRS) has been widely applied to the management of brain metastasis (BM) patients. We have already presented our incidences of and factors correlating with post-SRS complications and this paper was published in Radiotherapy and oncology in October 2018. We will present these results focusing on neuro-imaging findings and treatments.

Methods

This was an institutional review board-approved, retrospective cohort study using our prospectively accumulated database including 3519 patients (2100 males, 1419 females, mean age; 65 [range; 19-96] years) who underwent gamma knife SRS for BMs during the 1998-2018 period. The most common original tumor site was the lung (2300) followed by the gastro-intestinal tract (392), breast (399), kidney (139) and others (289). Median and mean tumor numbers were 3 and 7 (maximum; 89, IQR; 1-8). Median cumulative tumor volume was 5.4 (range; 0.01-126.2, IQR; 1.8-12.8) cc and median volume of the largest tumor was 3.6 (range; 0.01-94.2, IQR; 1.0-8.9) cc. The median maximum dose was 35 (range; 15-60, IQR; 30-40) Gy.

Results

The overall median survival time after SRS was 8.3 (95% CI; 8.0-8.8) months. Post-SRS complications occurred in 105 patients (3.0%) 0.5-135.6 (median; 13.9, IQR; 5.8-30.0) months after treatment. Cumulative incidences determined with a competing risk analysis were 0.8%, 1.7%, 2.4%, 2.6% and 2.8% at the 12th, 24th, 36th, 48th and 60th post-SRS month, respectively. Radiation necrosis was most commonly seen (77.9%) and was treated by steroid administration. The second finding was delayed cyst formation (11.6%) with/without a growing enhanced mass lesion which were treated by surgical intervention.

Conclusion

The post-SRS complication incidence is considered to be acceptably low (3.0%). Most complications could be managed by steroid treatment. However, cyst formation should be carefully followed up and surgical intervention should be for this condition, by which good treatment outcome could be expected.

Spinale und zerebrale Metastasen I/*Spinal and cerebral metastases I*

P058

Sicherheit und Resektabilität von Hirnmetastasen kombiniert mit intraoperativer Radiotherapie – eine monozentrische Studie mit 34 Fällen

Safety and feasibility of resection of brain metastases combined with intraoperative radiotherapy – a single-centre experience with 34 cases

S. Ertl¹, H. Kahl², N. Balagiannis², G. Stüben², U. Grossert¹, V. Heidecke¹, E. Shiban¹

¹Universitätsklinikum Augsburg, Klinik für Neurochirurgie, Augsburg, Germany

²Universitätsklinikum Augsburg, Klinik für Strahlentherapie, Augsburg, Germany

Objective

The utility of intraoperative radiotherapy (IORT) has been demonstrated in many and diverse surgical fields. However, Data for the utility for brain metastases (BrM) is scarce.

Methods

A retrospective study of nonconsecutive patients following surgical resection and IORT of BrM between January 2013 and October 2019 was performed. Surgical and Oncological outcome was evaluated.

Results

34 patients were identified. 56% were Female. Median Age was 61 (range 39 – 82). Breast Cancer was the most common Primary and was found in 26% of cases. IORT delivered a mean of 20 Gy (Range 13 – 20). Mean Follow up was 8 Months (range 1 -60). Local tumor control was seen in 82% of all cases. Surgical complications were seen in 15% of cases (2 neurological deterioration, 2 wound healing disorder and one case of postoperative hemorrhage)

Conclusion

IORT is a safe and effective method to achieve sustainable local tumor control for patients with brain metastases.

Spinale und zerebrale Metastasen I/*Spinal and cerebral metastases I*

P059

Die 30-Tage Mortalität bei chirurgisch behandelten Patienten mit spinalen Metastasen – kritische Analyse von 237 Patienten

The 30-day mortality in patients with surgically treated spinal metastases – a critical analysis of 209 patients

A. Abusamha, J. Gliemroth, V. M. Tronnier, L. Graumüller, J. Küchler

Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Lübeck, Germany

Objective

Spinal metastasis is a major cause of morbidity in cancer patients, leading to severe pain syndromes, spinal instability and neurological deficits. In this context, surgery for patients with spinal metastasis provides a promising benefit. But the treatment success is difficult to predict and the morbidity and mortality of surgical procedures is high. Established clinical prediction rules focus on the life expectancy and not on the short term follow up. The aim of this study was to determine the 30-day mortality rate and to assess the ability of different CPR to predict the short term mortality in patients with spinal metastasis.

Methods

A retrospective analysis of surgically treated patients of spinal metastasis was performed in a six-year period. We extracted various clinical variables from the patients' medical charts and our database. The CPR of Tomita and Tokuhashi were determined. A chi-square test was used to compare the 30-day mortality among different diagnoses. Multivariate logistic regression assessed whether Tomita and Tokuhashi score were independent predictors of 30-day mortality.

Results

We identified a 30-day mortality rate of 0.10 (21/209). The leading cause of death was a rapid progress of the primary tumor (nine cases), followed by respiratory insufficiency (six cases), for the other six patients we found no cause of death in the documentation. Minor surgical complications were present in one case. Among the different diagnoses, patients with lung cancer had a significant ($p < 0.05$) higher rate of 30-day mortality (8/47) than patients with non-lung cancer (13/162). Multivariate logistic regression show that Tokuhashi Score (OR 0.34; $p < 0.001$) but not the revised Tomita score was a predictor for 30-day mortality.

Conclusion

Spine surgery might appear promising from the surgeon's point of view in the context of spinal metastasis. But it must be explained to the patient that even the short term mortality is high after surgery for spinal metastasis, notably in case of lung cancer. A briefly evaluation of the individual situation might help to stratify the patients risk and to avoid futile treatment.

Spinale und zerebrale Metastasen I/*Spinal and cerebral metastases I*

P060

Der Wert der Resektion symptomatischer Metastasen von malignen Melanomen aus dem Blickfeld der molekularen Therapien – eine retrospektive Analyse

The value of resection of symptomatic metastases from malignant melanoma in the spotlight of molecular treatment – a retrospective analysis

C. A. Hamisch¹, C. Mauch², M. Proescholdt³, W. Dietmaier⁴, M. Wittersheim⁵, M. Montesinos-Rongen⁶, A. Brunn⁶, M. Deckert⁶, M. Kocher⁷, C. Baues⁸, R. H. Goldbrunner^{9,1}, M. I. Ruge^{9,7}, S. Grau^{9,1}

¹Universitätsklinikum Köln, Zentrum für Neurochirurgie, Klinik für Allgemeine Neurochirurgie, Köln, Germany

²Universitätsklinikum Köln, Klinik für Dermatologie, Köln, Germany

³Universitätsklinikum Regensburg, Klinik für Neurochirurgie, Köln, Germany

⁴Universitätsklinikum Regensburg, Institut für Pathologie, Regensburg, Germany

⁵Universitätsklinikum Köln, Institut für Pathologie, Köln, Germany

⁶Universitätsklinikum Köln, Institut für Neuropathologie, Köln, Germany

⁷Universitätsklinikum Köln, Zentrum für Neurochirurgie, Klinik für Stereotaxie und funktionelle Neurochirurgie, Köln, Germany

⁸Universitätsklinikum Köln, Klinik für Strahlentherapie, Köln, Germany

⁹Universitätsklinikum Köln, Centrum für Integrierte Onkologie (CIO), Köln, Germany

Objective

Prognosis for patients with metastatic melanoma has substantially changed due to novel medical and radiosurgical approaches. In this context, a cerebral metastectomy is rarely performed compared to other tumor entities, but is still indicated in large and/or symptomatic tumors or tumor associated hemorrhages. We evaluated the oncological course of patients after resection of symptomatic MBM in the context of the novel systemic treatment regimens

Methods

We retrospectively evaluated patients with MBM undergoing resection of at least one metastasis. Post-surgical survival was calculated using Kaplan-Meier-estimates. Prognostic factors for survival were identified using the log-rank test and Cox proportional hazards analysis.

Results

Seventy-one patients (singular/solitary metastasis: 45.1%, 2-4 metastasis: 39.4%, > four metastasis: 15.5%) were included. Almost all patients were neurologically impaired by the metastasis. Surgery improved neurological status in these patients (median Karnofsky Performance Score (KPS) 70% pre- and 90% postoperatively). The frequency of adjuvant systemic therapy correlated with postoperative KPS (Pearson's r 0.304, $p=0.01$). Median survival (OS) and local control (LC) after surgery were significantly influenced by any postoperative systemic therapy (OS: 5.2 (95%CI 3.9-6.1) vs. 22.1 (95%CI 10.6-33.4) months; $p<0.0001$, 6- and 12-months LC: 51 vs. 89% and 36 vs. 87%; $p=0.028$); the number of metastases was not decisive ($p=0.528$).

Conclusion

In patients with an impaired clinical status caused by MBM, metastectomy may improve the clinical status and thus facilitate further systemic therapy, which in turn increases survival.

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P074

"Minimal intensiv" – fehlende Vorwegnahme des Wissenschaftsprozesses oder wissenschaftlicher Terminus?
"Minimally invasive" – *incorrect anticipation of science or scientific term?*

A. Aschoff

Ruprecht-Karls-Universität Heidelberg, Neurochirurgische Klinik (ehemals), Heidelberg, Germany

Objective

In 1966 the term "minimally invasive" (MI) was coined for carcinomas in situ (Barter). For 18 years MI was used in this precise original meaning 0-4 times per year only. Later on the term spreaded arbitrarily in the overall medicine into 81,107 papers (PUBMED 11/2019). Unfortunately the term "minimally invasive" has a threefold semantic: 1. local malignomas, 2. a normative meaning closed to the ultimate aim of every medicine ("nil nocere"), 3. as inaccurat substitute of precise terms such as endoscopic, endovascular, etc. Procedures. The term oscillates uncontrollably between 2 and 3.

Methods

The terms MI/ MIN (minimally invasive neurosurgery) were systematically screened in PubMed.

Results

MI was created in 1966, remained a rarity over 15 years and increased slowly in the 80ties. From 1990 to 2018 MI-articles exploded from 53 to 7806 per year and reached now 81,107. - In neurosurgery MIN was created in 1985 (stereotactic removal of ventricular catheter. Blacklock) followed by Ascher (LASER .. in minimally invasive treatment ... 1991) and Hellwig/Bauer (Minimally invasive neurosurgery by means of ultrathin endoscopes.1992). From 1991 to 2018 the MIN-papers increased from 2 to 544/per year; now 5025. - Old, but precise terms such as stereotaxy (Goodlee 1885), endoscopy (Desormeaux 1865), endovascular (Grüntzig 1979) were substituted by the diffuse euphemistical term MI, which suggests, but not confirms less sideeffects, dangers and pain. Paradoxical effects are common: The ETV has a lethality of 0.28% (8/2985; Bouras 2011; 0.4% Tefre 2018), but is "minimally invasive"; shunts with a peri-operative mortality of 0.1% are "invasive" (diRocco 94)

Conclusion

Scientific language requires precision, unambiguity and a crystal-clear distinction between descriptive and normative terms. The apriori-declaration of a treatment as MI anticipates any empiric evaluation and should be avoided. MI belongs in the world of advertizing, not of science. MI disturbs and delays critical evaluations.

Keywords: Minimally invasive, scientific language, advertizing

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P079

Der klinische Verlauf nach "end of life" Entscheidung auf einer neurochirurgischen Normalstation – was wir lernen und verbessern können

Clinical course after end of life decisions on a neurosurgical ward – much to learn and improve

X. Hautmann, V. Rohde, C. Von der Brölie

Georg-August-Universität Göttingen, Göttingen, Germany

Objective

End-of-life (EoL) decisions are, unfortunately, a routine part in neurosurgical care due to frequent devastating diagnoses resulting in a severely impaired prognosis. Patients' provision, discussions with patients' representatives and evaluation of the alleged will play an increasing role in decision making. Institutional standards, ethics climate, different ethnical backgrounds and individual physicians' values, experiences and emotions might impact judgements and decisions, thus the clinical course after EoL decisions is challenging. The aim of this study is to characterize the clinical course of moribund patients on a neurosurgical general ward with special emphasis on sufficiency of palliation care.

Methods

This is a retrospective observational analysis. All patients who died between 2014 and 2019 on a neurosurgical general ward were included. Baseline parameters were analyzed. It was checked if an active EoL decision was made and if it was in-line with either a patient's provision or the alleged patient's will. The clinical course was further analyzed with regard to palliation therapy and support. Analyzing documentations it was categorized if a palliation therapy was carried out sufficiently. Consequential palliation was categorized if care contained withdrawal of medication, food and a restrictive thirst-oriented fluid management.

Results

168 patients were included. Given a mean annual caseload of 3000/year this accounts for 0.1%. 79.9% had a cranial diagnosis (20.1% spinal). Only 22.6% of all patients suffered from oncological diagnoses. 62.6 % of all patients died because of intracranial diagnoses (22% due to systemic sepsis, 15.4% due to cardiocirculatory deficiency).

EoL decisions were made in 84.1%. Of those patients, only 33.6% had a patient's provision. EoL was consented with the patients' relatives in 87.4%. Medication withdrawal (WD) was performed in 82.1% (food WD in 86.8%, permanent fluid WD in only 39.1%). Sufficient control for dyspnea was achieved in 51.4%, pain control in 90.9% and agitation control in 66.7%. It took a mean duration of 2.1 days (range 0 – 20 days) from the EoL until the patient died. Consequential palliation lead to a shorter duration until death (2.4 ± 2.3 vs. 1.2 ± 0.9 days, $p = 0.001$).

Conclusion

Even though symptoms are carefully watched for sake of palliation, dyspnea and agitation are difficult to control. If an EoL decision is reached, consequential palliation should be carried out in order to limit suffering of moribund patients.

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P061

***In vivo* Darstellung mikroanatomischer Strukturen und Pathologien des menschlichen Hirns mittels optischer Kohärenz-Tomographie**

In vivo visualisation of human microanatomical brain structures and pathologies using optical coherence tomography

K. P. Stein¹, K. Hartmann², B. Neyazi¹, I. E. Sandalcioglu¹

¹Otto-von-Guericke-Universität Magdeburg, Universitätsklinik für Neurochirurgie, Magdeburg, Germany

²KRH Klinikum Nordstadt, Klinik für Neurochirurgie, Hannover, Germany

Objective

Imaging of anatomical microstructures with optical coherence tomography (OCT) proves to correlate with histological findings. The present work summarises the possibilities and limits of three-dimensional microscope integrated OCT as a suitable intraoperative imaging modality during microsurgical procedures.

Methods

We performed OCT-Scans during supratentorial micro-neurosurgical procedures with a microscope-integrated OCT camera. Using a standardized protocol, the scans were post-processed with ImageJ2 and Fiji. The surgeon defined the region of interest depended on surgical approach, target and conditions. All patients gave written informed consent and the local ethics committee approved the study

Results

Scans of the dura mater (n=20), the gyral and sulcal subarachoid space (n=26), arteries (n=10) and veins (n=6) of the anterior circulation and unruptured aneurysms of the anterior circulation (n=16) and their parent vessels were generated. OCT allowed depicting, identifying and measuring the anatomical microstructure of the dura mater, the subarachnoid space and the vessel wall of arteries and veins in most cases. The scans of aneurysms identified the transition zone of the aneurysm neck from the physiological 3-layer structure of the parent vessel to the thin mono-layer of the aneurysm wall. Furthermore, irregularities of both aneurysm and parent vessel wall such as calcification, residual tunica media and atherosclerotic plaque could be visualized.

Conclusion

OCT allows in-vivo imaging especially of those structures, vulnerable to artefacts during histopathological slide preparation (e.g. subdural and subarachnoid space, vessel wall) with high image quality, approaching the spatial resolution of histopathology. Additional information of vessel and aneurysm wall structure might be of relevance during intraoperative manipulation and clip positioning.

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P062

Resting-state fMRI – Robustheit der Bestimmung von Sprachnetzwerken bei Tumorpatienten *Resting-state fMRI – robustness of language assessment in tumour patients*

C. Ott¹, K. Rosengarth¹, M. Goldhacker¹, J. Höhne¹, E. Lang², A. Brawanski¹, N. O. Schmidt¹

¹Universitätsklinikum Regensburg, Klinik und Poliklinik für Neurochirurgie, Regensburg, Germany

²Universität Regensburg, Experimentelle Psychologie, Regensburg, Germany

Objective

In recent years, resting-state functional magnetic resonance imaging (RS-fMRI) has been shown to be a promising and feasible method for preoperative language assessment. The use in preoperative language assessment remains a controversial subject due to mass effect and edema caused by the tumor. This study examines whether the results for the language-related resting-state components obtained using an independent data-driven component-based identification algorithm based on a template derived from healthy volunteers compared to the results using the same algorithm but excluding the tumor area and the displaced tumor surrounding areas are substantially different.

Methods

20 patients with brain lesions close to supposedly language-relevant cortical areas were included in the study.

Preoperative language assessment was performed with RS-fMRI. The best fitting independent component analysis (ICA) component for the resting-state language network (RSLN) referential to a template for the language network derived from healthy volunteers were subsequently identified using an algorithm based on the Dice index. The same procedure was performed using an additional individual template (a sphere) to mask the tumor and its potentially displaced surroundings.

Results

RSLNs associated with both methods seemed to be reasonable. There was no significant difference in the results with or without masking the tumor and its surroundings.

Conclusion

Using an independent data-driven component-based identification algorithm based on a predefined template seems to be robust enough for clinical purposes for language assessment in tumor patients regardless of mass effect and edema due to the lesion.

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P063

Deterministische klinische Traktographie ist äußerst genau in der Nähe von eloquenten Gliomen – eine Studie mittels IONM und elastischer Fusion basierend auf intraoperativen MRT-Daten
Deterministic clinical tractography is highly accurate in the vicinity of eloquent gliomas – a study by IONM and elastic fusion based on intraoperative MRI data

S. Ille¹, A. Schröder¹, A. Wagner¹, B. Wiestler², K. Kreiser², B. Meyer¹, S. Krieg¹

¹Technische Universität München, München, Germany

²Technische Universität München, München, Germany

Objective

Intraoperative neuromonitoring (IONM) is the gold standard technique for a safe resection of motor eloquent gliomas. To get an impression of the corticospinal tract (CST), diffusion tensor imaging fiber tracking (DTI FT) can be used. The study evaluates the correlation of IONM and DTI FT with the postoperative motor outcome by intraoperative magnetic resonance imaging (iMRI)-based elastic fusion (IBEF).

Methods

Of 154 patients with motor eloquent gliomas between July 2018 and July 2019, we performed a matched-pair analysis of five patients with (A) and without (B) an intraoperative amplitude loss of motor evoked potential (MEP) monitoring during resection, respectively. Preoperatively, we performed DTI FT of the CST in all patients. Intraoperatively, we performed an IBEF, which enables to adjust preoperative fiber objects to new conditions such as brain shift and resection cavity.

Results

The postoperative motor status correlated with the results of IONM in both groups. The mean correction of the CST by IBEF was 5.1 ± 2.3 mm (A) vs. 5.6 ± 3.1 mm (B) ($p = .84$). With a threshold of < 5 mm distance between resection cavity and fiber objects, all patients of group A showed CST lesions after IBEF while no patient of group B showed lesions of the CST after IBEF. Before the application of IBEF, two patients of group A and 1 one patient of group B showed lesions of the CST.

Conclusion

Based on the visualization of subcortical pathways after IBEF, the present matched-pair analysis approves the reliability of DTI FT of the CST by its correlation to IONM and the postoperative clinical status of patients. The results prove the relevance of applying IBEF with the aim of adjusting preoperatively determined subcortical fiber objects.

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P064

Identifikation von Prädiktoren für ein schlechtes Behandlungsergebnis nach der chirurgischen Evakuation von chronischen Subduralhämatomen in 755 Patienten mittels maschinellen Lernens
Identification of predictors for an unfavourable outcome after surgical treatment of chronic subdural haematomas in 755 patients using machine-learning

A. Younsi, L. Riemann, C. Habel, J. Fischer, K. Zweckberger, A. W. Unterberg

Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

Objective

Chronic subdural hematomas (cSDH) are expected to become the most frequent neurosurgical disease by the year 2030. Although often perceived as a "benign" condition, considerable rates of mortality and poor outcome have been reported. We therefore evaluated factors associated with an unfavorable outcome after surgical treatment of cSDH patients by developing a predictive model using machine-learning.

Methods

Consecutive patients treated for cSDH with surgical evacuation between 2006-2018 at a single institution were retrospectively analyzed. Potential demographical, clinical, imaging and laboratory predictors were assessed and a decision-tree predicting unfavorable outcome (GOS 1-3) was subsequently developed using the Classification and Regression Tree (CART) algorithm. Hereby, the complexity parameter was set at 0.02 and at least 25 observations were required at every split or node. Out-of-sample model performance was evaluated using repeated cross-validation (5-fold with 200 repetitions).

Results

755 eligible patients were analyzed. The median age was 75 (IQR 68-81) years and 69% were males. The mortality rate was 1.6% and the rate of unfavorable outcomes was 14.3%. The developed decision-tree to predict unfavorable outcome had 5 splits and included the following 4 clinical variables (in descending order of calculated importance): GCS, comorbidities, Hb, and age. After cross-validation, the following model performance metrics were obtained: a model accuracy of 0.88 (0.85-0.90), sensitivity of 0.35 (0.19-0.51), and specificity of 0.96 (0.94-0.99).

Conclusion

GCS, comorbidities, Hb, and age were identified as the most important clinical predictors for an unfavorable outcome in cSDH patients after surgery. The developed model was simple and still displayed a high accuracy and very high specificity, the sensitivity was however rather low. Our results might help clinicians to better assess the prognosis in patients with cSDH.

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P065

Ultrahochfeld 7 Tesla MRT in der Neurochirurgie – Erfahrungen von 335 Fällen *Ultra-high-field 7 Tesla MRI in neurosurgery – lessons from 335 cases*

O. Gembruch¹, B. Chen¹, P. Dammann¹, T. Schoemberg¹, R. Jabbarli¹, H. H. Quick², U. Sure¹, K. H. Wrede¹

¹Universitätsklinikum Essen, Abteilung für Neurochirurgie, Essen, Germany

²Universität Duisburg-Essen, Erwin L. Hahn Institute for Magnetic Resonance Imaging, Essen, Germany

Objective

To report on clinical application as well as the advantages and disadvantages of ultra-high-field 7T MRI in a neurosurgical setting.

Methods

Since 2008 eligible neurosurgical patients were prospectively examined on a 7T whole-body MR system (Magnetom 7T, Siemens Healthcare Sector) equipped with gradient coils capable of delivering 45 mT/m of maximum amplitude and a slew rate of 220 mT/m/ms. Three different 8-channel and 32-channel radiofrequency transmit/receive head coils were used and a custom-built 8-channel radiofrequency transmit/receive array body coil was used. Peripheral nerves were scanned with a custom-built 8-channel radiofrequency transmit/receive meander coil. Pulse sequences included optimized MPRAGE, FLASH-TOF, SWI, T2*, PD, T2, VIBE and TWIST sequences.

Results

The study group comprised 335 patients (161 males) with age ranging between 18 and 82 years. The majority of all patients suffered from cavernomas (n=67) and aneurysms (n=81) as well as other vascular pathologies (n=57). For anatomical scans, the best results were achieved with SWI, T2, T2*, SWI, and the modified MPRAGE pulse sequences. Arterial vasculature was best depicted with the modified FLASH-TOF pulse sequence (0.21 mm in-plane and 0.42 mm through-plane resolution) including the possibility of venous saturation pulses. All but 7 patients could be scanned successfully in 36 to 75 minutes. In 4 cases the scans had to be aborted before the scanning protocol was finished because of claustrophobia. In 3 cases the scan had to be aborted due to technical failure of the scanner. The occasional need of rebooting the scanner and long preparation phases are the main disadvantages in application of 7T MRI for neurosurgical patients. The strength of ultra-high-field MRI was especially seen when depicting the vasculature in cavernomas, aneurysms, AVMs and Moyamoya angiopathy patients.

Conclusion

Clinical applicability of 7T MRI as well as the advantages and disadvantages are shown in the worldwide largest neurosurgical cohort. Seven Tesla MRI has clinical potential for dedicated diagnostic questions.

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P066

Venöse 3D-Phasenkontrastangiographie als valides Tool in der Diagnostik von Shunt dysfunktionen *Optimising the evaluation of shunt malfunction with 3D venous phase contrast angiography MRI*

M. Huhndorf¹, G. Cohrs², N. Margraf³, M. Synowitz², O. Jansen¹

¹Universitätsklinikum Schleswig-Holstein, Neuroradiologie, Kiel, Germany

²Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Kiel, Germany

³Universitätsklinikum Schleswig-Holstein, Neurologie, Kiel, Germany

Objective

In the situation of suspected shunt malfunction MRI is widely accepted as a primary evaluation tool, especially in paediatric patients. Clinical symptoms can be unspecific, and the presence or absence of ventricular enlargement does not reliably predict raised intracranial pressure (ICP) in these patients. Therefore, we aimed to investigate the utility of 3D venous phase contrast angiography (PCA) in the situation of shunt failure and suspected raised intracranial pressure.

Methods

We retrospectively analysed MRI studies of shunted children presenting with symptoms of elevated ICP and therefore receiving surgery due to shunt malfunction. Patients were included when pre- and postoperative MRI was performed including an axial T2-weighted image and 3D venous PCA. We assessed Evans' index on T2 weighted images for assessment of ventricular enlargement and evaluated venous PCA for signs of compression of the sagittal superior sinus and the left and right transverse sinus. Sinus compression was defined as reduction in diameter and/or reduced/missing signal. Elevated intracranial pressure was defined as compression of at least two sinuses.

Results

We included 19 (11 male) shunted patients who had clinical symptoms of raised intracranial pressure and received surgery for shunt dysfunction, on whom pre- and postoperative MRI was performed. All three sinuses were compressed in 12 patients, of which 11 showed normalization after shunt revision. Only two sinuses were compressed in 6 children. 3D venous PCA showed normalization after shunt revision in all cases. Of 18 patients with compression of 2 or 3 sinuses 15 showed no significant change in Evans' Index. The only patient who did not show any sinus compression showed significant change in Evans' Index.

Conclusion

In accordance with the current literature our results confirm that ventricular morphology alone is not a reliable marker for elevated ICP in shunt malfunction. Our results show that sinus compression might serve as a predictor for elevated ICP. In order to confirm indication for revision surgery, the addition of 3D venous PCA is a helpful tool. This could especially be useful to identify paediatric patients with elevated ICP in which assessment of clinical symptoms can be challenging.

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P067

Erhöhung des Brain Natriuretic Peptide Serumspiegels bei Patienten mit symptomatischen chronischen Subduralhämatomen – vorläufige Ergebnisse einer laufenden prospektiven Studie *Elevation of brain natriuretic peptide serum levels in patients with symptomatic chronic subdural haematoma – preliminary results of an on-going prospective study*

M. Chihi¹, H. Maslehaty², B. O. Hütter¹, R. Jabbarli¹, U. Sure¹, K. H. Wrede¹

¹Neurochirurgische Universitätsklinik Essen, Germany

²KRH Klinikum-Nordstadt, Hannover, Germany

Objective

Brain Natriuretic Peptide (BNP) is a reliable biomarker for cardiac insufficiency (CI). However, elevation of BNP serum levels in patients with other intracranial pathologies in absence of CI is also observed. The purpose of the current prospective study was to analyse BNP serum levels in patients with chronic subdural hematoma (cSDH) and its clinical implication.

Methods

In this prospective study design, we included patients with cSDH, who underwent surgery at our department between November 2016 and October 2019. We excluded patients with recurrent bleedings, traumatic brain injury, cSDH associated with other intracranial pathologies and with a history of congestive heart failure, renal or endocrine disease, from analysis. We measured BNP serum levels pre- and postoperatively and at discharge. BNP values were analysed in view of the patients' medical history and neurological condition. The cut-off for the BNP values was 35 pg/ml. The Glasgow coma score (GCS) and the modified Rankin scale (mRS) classified the clinical and the neurological condition at time of admission and discharge respectively. We used SPSS 25.0 for Windows® for statistical analysis.

Results

We analysed the data of 94 patients with cSDH (mean age 73.4 ± 12 years, male/female 3.5:1). The BNP-level in serum was preoperatively elevated in 68% of the patients (n=64; mean=136.8 pg/ml; range 35.3 – 546.7 pg/ml; Mann-Whitney U Test $p < 0.01$). The serum levels increased after surgery (Wilcoxon signed-rank test $p < 0.001$) and decreased in the continuing course ($p < 0.001$), reaching the preoperative level at discharge. Indeed, BNP serum levels at discharge did not significantly differ from the preoperative levels ($p = 0.202$). Preoperative BNP levels showed a further significant statistical association with patient's age, sex and antiplatelet and/or anticoagulant therapy (AAT) ($p < 0.01$), but not with GCS and mRS at admission.

Conclusion

Our preliminary results showed an elevation of BNP serum levels in patients with cSDH independently from CI. Moreover, BNP levels were significantly higher in females, old patients and in patients under AAT. Whether BNP values could predict functional outcome of patients with cSDH is part of the on-going prospective study.

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P068

Codman Certas – Verlust der Genauigkeit und Druckstufen, Sicherheitsrisiken *Codman Certas – collaps of accuracy, loss of pressure ranges, safety risks*

A. Aschoff

Ruprecht-Karls-Universität Heidelberg, Neurochirurgische Klinik (ehemals), Heidelberg, Germany

Objective

In 2011 the Codman-Certas was launched, in 2013 recalled and in 2015 relaunched. We found in PubMed with Certas 8 und CertasPlus 3 papers only. The often combined SiphonGuard (SG) has 6 Journal titels.

Methods

Since 1988 we tested in vitro 195 adjustable valves, 34 new and 163 explanted. 118 were adjustable Codman-Medos, 10 Codman adjustable MicroValve, 2 MicroValve with SG, 41 Miethke ProGAV, 2 ProSA, 13 Sophysa SU 8+3, 3 Polaris, 3 Mini 8+3, and 2 Kuffer-Strub. Simultaneously we made clinical experiences with 1388 adjustable valves in 1127 patients. Due to closed lab of Certas and CertasPlus we could worked with demo-spezimen, but made an exhaustive analysis of 5 Certas-patents, company-data and related literature.

Results

In contrast to the excellent precision of the adjustable Medos (± 10 mmH₂O!) Certas showed tolerances of ± 20 to ± 50 mm, fivefold poorer. Eklund measured (2012) in range 400 mmH₂O deviations of 51-156 mmH₂O. - The 18-stepped Medos allows a subtle fine regulation. Certas has only 7 steps, 3 of those in the seldom used high pressure (145-215 mm). - Safety: During puncture the chamber needle tip can penetrate the valve mechanism. - With strong magnets it is possible to elevate the rotor and to adjust every position. Using an iPhone 5S the mechanism can be switched-off (Ozturk 2017). According to own measurements SGs with 8-15 cmH₂O pressure allow flow up to 150 ml/h, leading to a high quote of chronic subdural hematomas (cSAD) in iNPH-patients (19.3%, Sundström 2017); between 20-50 cmH₂O the flow is critically low. The helictical bottleneck has a diameter of 0.4 mm, ergo is at risk for occlusion and underdrainage.

Conclusion

Certas/Plus has solved the Medos-problems of X-rays after adjustments and MRIs. The price is a massive deterioration of precision, loss of fine tuning options and safety deficits (missing needle guard; disturbance by electromagnetic apparatus). In iNPH-patients the risk of cSDHs counted with Certas 16.7% and with SG combined with the adjustable Medos 19.6% (Sundström 2017).

Keywords. Hydrocephalus shunt, Codman Certas, Codman SiphonGuard

Ethik in der Medizin & freie Themen/*Ethics in medicine & free topics*

P069

Sekundäre Verschlechterung bei NPH Patienten nach VP-Shuntimplantation – Vorschlag eines Behandlungsalgorithmus

Secondary deterioration in patients with normal pressure hydrocephalus after ventriculoperitoneal shunt placement – a proposed algorithm of treatment

P. Gutowski¹, S. Rot¹, M. Dweek¹, M. J. Fritsch², U. Meier¹, J. Lemcke¹

¹Unfallkrankenhaus Berlin, Klinik für Neurochirurgie, Berlin, Germany

²Dietrich-Bonhoeffer-Klinikum Neubrandenburg, Neurochirurgie, Neubrandenburg, Germany

Objective

After ventriculoperitoneal shunt surgery for idiopathic normal pressure hydrocephalus (iNPH) with adjustable gravitational valves, a certain proportion of patients develop secondary clinical worsening after initial improvement of clinical symptoms. The aim of this study was to analyze this group of patients with secondary deterioration and to evaluate the performed shunt management.

Methods

We retrospectively reviewed our prospective NPH registry. Patients who showed equal or worse Kiefer scores (KS) in the first year of follow up compared to the preop score were defined as "primarily deteriorated". "Secondary deterioration" was defined as a decrease by the min of 2 points in the KS in the first year of follow-up and an increase of 2 points in the KS between the second and the fifth year after shunt surgery.

Patients with secondary deterioration resulting from a treatable shunt issue (adaption of the pressure setting, shuntography, surgical revision) were defined as "shunt insufficiency". Patients with secondary deterioration and unsuccessful shunt management were assigned as "secondary non-responder". Then, we searched for risk factors.

Results

Out of 353 patients, 53 (15 %) patients showed secondary deterioration on an average of 2,7 years after shunt surgery. Fourteen (26%) patients with secondary deterioration improved after shunt / valve management, 58% remained without clinical benefit after taking action of the VPS. We had a drop-out rate of 15% due to incomplete datasets. Our shunt management reduced the rate of secondary deterioration from 15% to 8%. On the basis of our findings, we developed an algorithm to decrease the rate of "secondary non-responder". Risk factors for becoming "secondary non-responder" patient's age at the time of shunting, newly diagnosed neurodegenerative diseases and overdrainage requiring adjusting the valve to higher-pressure levels.

Conclusion

Fifteen percent of patients with NPH are at risk for secondary clinical worsening about 3 years after shunt surgery. About one fourth of these patients benefit for additional years from pressure level management and / or shunt valve revision. Our findings underline the need for long-term follow-ups and intensive shunt management to achieve a favorable long-term outcome for patients with NPH and VPS.

Digitale Medizin/Digital medicine

P073

Auf dem Weg zu einer automatisierten Erkennung von Hirntumorgewebe mittels optischer Kohärenztomographie

Towards automated brain tumour detection with optical coherence tomography

P. Streng¹, B. Lange¹, V. Danicke¹, D. Theisen-Kunde¹, C. Grill², W. Draxinger², R. Huber², E. Ducho³, M. M. Bonsanto³, H. Handels⁴, C. Hagel⁵, R. Brinkmann^{1,2}

¹Medizinisches Laserzentrum Lübeck GmbH, Lübeck, Germany

²Universität zu Lübeck, Institut für Biomedizinische Optik, Lübeck, Germany

³Universitätsklinikum Schleswig-Holstein, Abteilung für Neurochirurgie, Lübeck, Germany

⁴Universität zu Lübeck, Institut für Medizinische Informatik, Lübeck, Germany

⁵Universitätsklinikum Hamburg-Eppendorf, Institute for Neuropathology, Hamburg, Germany

Objective

Optical coherence tomography (OCT) is a non-invasive technique that can capture 3-dimensional images with micrometer resolution. Prior studies of several groups have shown that OCT has the potential to detect glial tumors by evaluating changes in tissue structure and / or optical properties compared to healthy brain tissue. The aim of our project is the *in vivo* identification of brain tumours with OCT as a guidance for the surgeon to increase the neurosurgical tumor resection efficiency. The basis for the realization of this goal are segmented datasets, which enable the training of an AI-based classification of tissue.

Methods

Three different OCT systems were used for imaging human glial tumors *in vivo* (830nm spectral domain (SD) OCT integrated into a surgical microscope) and *ex vivo* (940nm SD-OCT and 1310nm swept-source MHz-OCT using a Fourier domain mode locked (FDML) laser). Overall, more than 140 human brain samples with different infiltration grades were taken from 20 patients diagnosed with glioblastoma multiforme or other malign brain tumors. For the *ex vivo* image acquisition, the brain tissue was embedded in a negative agar cuboid. This step simplifies creating H&E stained histological sections in the same orientation as the OCT scans. From every sample, several sections were segmented by a neuropathologist.

Transferring the information of the histological sections to the OCT data set was possible by using structures visible in both image modalities (e.g. blood vessels, hemorrhages) for registration. The segmented OCT data set gained from this process was used to evaluate supervised classification algorithms and start training of neural networks. For tissue discrimination, optical properties such as the attenuation coefficient, but also texture features related to tissue structure were considered

Results

First examples of the clinical study show that a registration of histological and OCT images was possible to define the ground truth of the tumor segmentation in the OCT images. Furthermore, a spatially resolved representation of the attenuation coefficient provides a good image contrast and confirm that white matter shows a higher signal and more homogeneous signal structure than tumor tissue.

Conclusion

Intraoperative high speed OCT has the potential for *in situ* tissue monitoring analysis and detection of residual tumor. Thus, intraoperative OCT with real-time data evaluation by AI algorithms may be used for guidance of the neurosurgical resection.

Digitale Medizin/Digital medicine

P075

Beurteilung intrakranieller Aneurysmen mithilfe von CFD – Stabilität hämodynamischer Parameter *Assessment of intracranial aneurysms using CFD – stability of haemodynamical parameters*

C. Doenitz¹, T. Wagner^{1,2}, L. Krenkel^{3,2}, D. Deuter¹, N. O. Schmidt¹, A. Brawanski¹

¹Universitätsklinikum Regensburg, Klinik für Neurochirurgie, Regensburg, Germany

²Regensburg Centre of Biomedical Engineering (RCBE), Regensburg, Germany

³Ostbayerische Technische Hochschule Regensburg, Biofluid-Mechanik, Regensburg, Germany

Objective

Hemodynamic parameters and the flow situation inside intracranial aneurysms have great influence on the risk of rupture. Therefore, computational fluid dynamics (CFD) is a frequently used tool for rupture risk assessment [1]. However, there are great differences between different studies regarding CFD strategy, like spatial and temporal resolution or the extent of considered geometry.

Methods

3D rotational angiography data of a middle cerebral artery (MCA) aneurysm was segmented using a threshold-based method. For the first investigation, five meshes with different spatial resolution were created. The second study applied a modular meshing approach to investigate the impact of increasing inlet vessel lengths. Frequency analyses was conducted to ensure, that the applied time step size of 0.001 s is sufficient. Wall shear stress (WSS) and oscillatory shear index (OSI) as defined by Xiang et al. (2011) were calculated, since they were identified as significant parameters for aneurysm rupture [2]. CFD computations were performed using ANSYS Fluent V18.2.

Results

Table 1a shows the mesh statistics and the resulting WSS and OSI for the first study. While the coarsest mesh seems to be sufficient for an accurate computation of the WSS, this is not applicable to the OSI. A comparison of the OSI distribution between the coarsest and the finest mesh can be seen in figure 1. The results of the inlet vessel variation study are shown in table 1b. It is noticeable, that including the carotid siphon in the geometry greatly influences the resulting OSI. Frequency analyses showed, that the highest occurring frequencies were at approximately 150 Hz. Furthermore, it was found, that including the carotid siphon greatly increases the occurrence of higher frequencies.

Conclusion

The presented results show the great importance of including enough inlet vessel geometry and choosing a sufficient mesh resolution, in order to calculate hemodynamic parameters reliably. Especially the OSI shows a great dependence of mesh resolution and the presence of the carotid siphon, since it induces flow instabilities.

References

¹Chung, and Cebal, Annals of Biomedical Engineering, 43:122–138, 2015.

²Xiang et al, Stroke, 42:144–152, 2011.

Fig 1

Table 1

WSS and OSI for different mesh resolutions (a) and different inlet vessel length (b).

a)

#El	mV [mm ³]	nPL	WSS	OSI
747000	1.29e-7	4	0.5665	0.006094
1260000	6.94e-8	6	0.7872	0.005102
1886000	3.42e-8	8	0.7843	0.006746
4208000	1.87e-8	10	0.7808	0.008577
6591000	1.06e-8	12	0.7727	0.009605

b)

IVL [mm]	WSS	OSI
5	0.6112	0.003979
10	0.7996	0.003622
18	0.8703	0.005274
25	0.7897	0.005535
84	0.7808	0.008577

#El: Number of elements
mV: mean element volume
nPL: number of prism layers
IVL: inlet vessel length

Fig 2

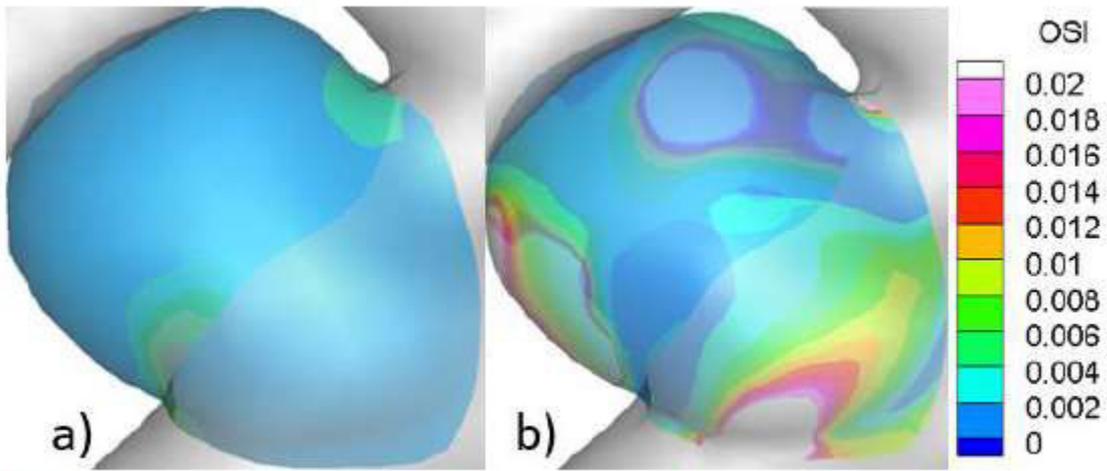


Fig. 1
OSI distribution for the coarsest (a) and finest mesh (b).

Digitale Medizin/*Digital medicine*

P076

Voll-digitale 3D4k-Videoskopie in der Neurochirurgie – eine prospektive Kohortenstudie zur Evaluation der technischen und klinischen Implementierbarkeit

Fully digital 3D4k videoscopes in neurosurgery – a prospective cohort study addressing device implementation and clinical feasibility

A. L. Roethe¹, S. Georgiev¹, U. C. Schneider¹, M. Misch¹, P. Vajkoczy¹, T. Picht^{1,2}, J. Onken¹

¹Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

²Humboldt-Universität zu Berlin, Excellence Cluster »Matters of Activity. Image Space Material«, Berlin, Germany

Objective

Fully digital exoscopes (videoscopes) consist of a camera mounted on a robotic arm and a high resolution 3D video monitor positioned independently. Exoscopic surgery in general promises alleviation of physical strain and improved intraoperative visualization. This study investigates the clinical usability of a novel 3D4k videoscope in neurosurgical routine interventions.

Methods

Based on a previous randomized trial on exoscopic neurosurgery, a documentation protocol comprising quantitative and qualitative data has been established. Intracranial, spinal and peripheral nerve procedures of low to intermediate complexity were included prospectively. All participating neurosurgeons (n=10) received initial device training. A complementary eyepiece as well as a conventional surgical microscope were available during surgery. Observational parameters, clinical data and scale instruments for user feedback were analyzed using descriptive statistics.

Results

Within 8 weeks, 29 cases were performed with the 3D4k videoscope (22 cranial, 6 spinal and 1 peripheral procedures), including 72% tumors, 14% epilepsy surgery and 10% nerve decompression/spinal stabilization. The overall experience was rated good by 70% of surgeons. Primary reasons for conversion to ocular-based surgery in 48% of cases were the discrepancy of working and viewing direction, impaired hand-eye coordination and limited depth perception in critical areas. The grading of image quality was high (resolution, sharpness, contrast, color fastness, luminance) to excellent (magnification). The videoscope allowed for an upright head position in 95% of the surgical time. Most surgeons used both hand and foot control for camera repositioning. Despite satisfactory robotics, the usability and speed of the foot panel was rated overall low. Surgical results of the exoscopic surgery (including the conversion rate) were non-inferior to historic matched-controls. Across all cases, setup integratability has been rated favorable due to device size and versatility.

Conclusion

The 3D4k videoscope investigated in this study can be integrated in established neurosurgical workflows. Surgical ergonomics improved compared to standard setups while hand-eye coordination required additional training. Mainly the good image quality and the direct single-hand control of the camera head added to overall user satisfaction. For experienced surgeons, the incentive to switch from conventional microscopy to next generation videoscopes greatly varies.

Digitale Medizin/*Digital medicine*

P077

Barcode-unterstützte Dokumentation von Bluttransfusionen mittels mobilem Device – prospektive Pilotstudie

Introduction of a novel mobile electronic bar code-based documentation of blood component transfusions – a prospective pilot study

J. E. Scorzin, M. Banat, H. Vatter

Universitätsklinikum Bonn, Klinik für Neurochirurgie, Bonn, Germany

Objective

Ever since the introduction of electronic patient charts, documentation of blood product transfusions remains a manual process on paper, in most clinics. National guidelines require detailed documentation according to the German Transfusion Act. A number of studies revealed that manual pretransfusion check and documentation on paper is inappropriate in daily transfusion medicine practice. Misidentification of patient and mismatch to the blood product are the most frequent factors for transfusion errors. We introduced an electronic documentation process and have conducted a pilot study to examine the accuracy and compliance in daily blood transfusion process in our clinic since 4/2019.

Methods

Patients were allocated an ID wristband at admission to our clinic by standard. The blood product and the accompanying note were labelled with bar codes which provided the transfusion relevant information. The bar code scanning, pre- and posttransfusion check and signed documentation was performed bedside via a mobile device (iPad) App by the transfusion practitioner. The App provides several plausibility notifications if incompatibility between patient's ID, crossmatched blood parameters and the blood product occurs. The data was directly transferred to the patient's electronic medical chart (ORBIS, AGFA HealthCare) via the hospital WLAN. Close audits were provided according to PDCA quality improvement cycle.

Results

103 blood component units (13 FFP, 22 TC, 68 PRC) were transfused between April and November 2019. A total of 55 (53.4%) inaccurate or incomplete electronic documentations were observed through the audits. After re-training of the staff members, the rate of incorrect documentation dropped from 66.1% in the first 4 months to 34.1% in the 3 months after the re-training. In total an incomplete documentation was counted in 33 cases (32.0%), missing Rh-group documentation was observed in 14.6%, inappropriate documentation of transfusion time occurred in 9.7% and incorrect ABO-/Rh-group was entered in 5.8%. In 5 transfusion cases, electronic documentation could not be achieved because of malfunction of the mobile devices.

Conclusion

Electronic bar code-based documentation has been reported to be beneficial in reducing blood administration errors. The presented process was not as robust as expected. However, regular audits and periodical re-training of the practitioners have proven to be crucial and efficacious.

Digitale Medizin/Digital medicine

P078

Der Einsatz von Roboter-Technologie zur Bestimmung der *in vitro* Antwort von Hirntumoren auf Substanzapplikation

A robot-technology for the acquisition of large-scale in vitro pharmacology-response of brain cancer

A. Vargas-Toscano, A. C. Nickel, M. Hewera, M. A. Kamp, I. Fische¹, H. J. Steiger, D. Hänggi, U. D. Kahlert

Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany

Objective

In vitro pharmacology testing is an assay in early stage in drug development and fundament of various *in vitro*-diagnostic technologies. Liquid handling systems allow large-scale and highly reproducible allocation of solved components and is a standard assay in industry and routine diagnostics. We implement this technology for the identification of chemo resistance therapies of *in vitro* processed tumor samples focusing on a stem cell model of glioblastoma. Stem-like cells in cancer are involved in tumor progression and mediating resistance to therapy.

Methods

A drug library composing 167 FDA-approved, molecularly diverse compounds with reported brain tissue penetration capacity was assembled. A pipetting scheme was developed and programmed to instruct a BiomekFXP robotic workstation perform a high resolution (≥ 5 concentrations/substance) drug response testing. Cellular growth was used as reporter assay. The GSC model was expanded under neurosphere conditions. Statistical significant responses result in ranking the test substances according to therapeutic potential using IC50 values.

Results

Repetitive drug-dose response profiles were generated. Out of the tested compounds, 22 exhibited a homogeneous decrease on cellular growth in the nm concentration range compared to the vehicle treatment control ($P < 0,001$) indicating physiological meaningfulness therapeutic potential against this tumor model. Twelve of which had intermediate potency (between 50-25% viability decrease) and 10 showed high potency ($>75\%$ viability decrease). These compounds include prominent mTOR-pathway inhibitor Everolimus or cytostatics Doxorubicin but also identified novel repurposed compounds such as Trihexyphenidyl (muscarinic receptor antagonist used in symptomatic treatment of Parkinson), Clonidine (anti-hypertensive) and Rizatriptan (anti-migraine).

Conclusion

We established an automated test platform for reproducible medium-throughput *in vitro* pharmacology which could be useful in personalized medicine of neuro oncology. *Mode of Action* characterization and validation of therapeutic meaningfulness of the *in vitro* results by *in vivo* trial are underway. Given the assembly of FDA approved drugs this efforts support clinical translation. Moreover, applying cell models equipped with reporter constructs, this screening tool is suitable to identify pharmacological modulators of transcriptional activity.

Digitale Medizin/Digital medicine

P080

TMS Sprachmapping – Analyse von 90 Patienten im MNI-Raum mit anschließender Klassifizierung durch maschinelles Lernen

TMS language mapping revisited – analysis of 90 patients in MNI space and machine learning classification

Z. Wang¹, L. Fekonja¹, F. Dreyer², P. Vajkoczy¹, T. Picht¹

¹Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

²Freie Universität Berlin, Brain Language Laboratory, Berlin, Germany

Objective

Non-invasive repetitive navigated transcranial magnetic stimulation (rnTMS) is increasingly used for preoperative cortical language mapping. While in recent years knowledge about the healthy human language network has constantly improved, the effect of language eloquent brain tumors on the language network remains largely unclear. Several studies investigated tumor-induced neuro-reorganization, but the reorganization pattern still needs to be analyzed. This study aims to examine the language network in regard to the impact of pathology by applying group analysis methods.

Methods

We retrospectively reviewed a cohort of 90 right-handed patients with left perisylvian WHO grade II-IV gliomas. All patients underwent preoperative rnTMS-language- mapping. The patients were classified into an aphasic and non-aphasic group. All TMS spots were registered from individual space into MNI space and parcellated using the automated anatomical labeling (AAL) template to obtain the error rate (ER) of each anatomical volume of interest (AVOI). Subsequently, univariate statistical analysis was performed for each ER of AVOI and biometric data between the two groups. The significant results were fed as features, e.g. input variables, into the support-vector machine (SVM), a supervised machine learning model, to classify aphasic and non-aphasic patients.

Results

30 of 90 (33.3%) patients suffered from aphasia. Univariate analysis revealed 11 perisylvian AVOIs' ERs (8 left, 3 right hemispheric) that were significantly higher in the aphasic than non-aphasic group ($p < 0.05$), depicting a broad, bihemispheric language network. After feeding the significant AVOIs into the SVM model, it showed that additional to age ($w = 2.95$), the ERs of right Frontal_Inf_Tri ($w = 2.06$) and left SupraMarginal ($w = 2.05$) and Parietal_Inf ($w = 1.80$) contributed more than other features to the model. The model's sensitivity was 89.7%, the specificity was 82.0%, the overall accuracy was 81.1% and AUC was 88.7%.

Conclusion

SVM based group analysis revealed a distinct pattern of perisylvian language-network reorganization with especially the right inferior frontal gyrus showing a significantly higher ER in aphasic patients than in non-aphasic patients. Moreover, the model demonstrated that aphasic patients were significantly older than non-aphasic patients, indicating a reduced potential for language reorganization in elderly patients.

Digitale Medizin/Digital medicine

P081

Hemisphärenasymmetrie bei gesunden Kontrollprobanden – eine Vergleichsstudie zwischen Diffusio-Kurtosis- und Diffusions-Tensor-Bildgebung

Hemispheric asymmetry in healthy volunteers – a comparative study of diffusion kurtosis imaging and diffusion tensor imaging

X. Liu, M. Bopp, B. Carl, C. Nimsky

Universitätsklinikum Gießen und Marburg, Klinik für Neurochirurgie, Marburg, Germany

Objective

Asymmetry of microstructure in brain has been demonstrated in fiber tracts using diffusion tensor imaging (DTI). Due to the inherent drawbacks of DTI such as limited capability of resolving fanning and crossing fibers, limited modeling of diffusion profiles and characteristics, more sophisticated approaches are needed such as diffusion kurtosis imaging (DKI). However, only a few studies investigated asymmetry of fiber tracts applying DKI. In this study, the effect of DTI vs. DKI regarding detection and evaluation of hemispheric asymmetry is evaluated.

Methods

20 healthy (10 / 10 male / female, mean age 24 ± 1.2 years, 3 / 17 left-/right-handed) volunteers were included. For each volunteer DWI data (incorporating the possibility of analysis applying DTI as well as DKI) were acquired at a 3T MRI. Data was processed for DTI and DKI using the Diffusion Kurtosis Estimator (DKE) gaining diffusion parameters such as mean kurtosis (DKI_MK), fractional anisotropy (DTI_FA, DKI_FA), mean diffusivity (DTI_MD, DKI_MD). Data analysis was performed using Tract-based spatial statistics (TBSS) incorporating voxel-wise statistical analysis applying FSL Randomize. For nine major white matter tracts (CST = corticospinal tract, SLF = superior longitudinal fascicle, ILF = inferior longitudinal fascicle, UF uncinated fascicle, IFOF = inferior frontooccipital fascicle, CB = cingulate bundle, ATR = anterior thalamic radiation, Fmi = Forceps minor, Fma = Forceps major) a laterality index (LI) was calculated.

Results

Regarding DTI_FA and DTI_DKI leftward asymmetry was seen in CST, SLF, CB, ATR (LI: 0.19, 0.81, 0.31, 0.08), rightward asymmetry in Fmi, Fma, IFOF, UF (LI -0.56, -0.15, -0.27, -0.37), while the distribution of asymmetric regions was comparable between DTI and DKI. DTI_MD showed global rightward asymmetry in the Fmi, CB and ATR (p : 0.008, 0.008, 0.001) whereas DKI_MD revealed rightward asymmetry along the ILF and ATR (p : 0.024, 0.003). DKI_MK resulted in global leftward asymmetry for Fmi and ATR (p : 0.024, p : 0.002), as well as rightward asymmetry for ILF and SLF (p : 0.020, 0.041).

Conclusion

Only few previous studies have shown the location of asymmetric regions in fiber tracts. This study provides an overview of asymmetric regions in healthy young adults, especially within nine major white matter tracts. DTI_FA and DKI_FA are sensitive detecting hemispheric asymmetry. DKI_MK allows for a more accurate positional information on asymmetry not seen in DTI and DKI derived FA and MD.

Digitale Medizin/Digital medicine

P071

Optimales Zeitfenster für kortikales Mapping bei der Wachkraniotomie – eine Zwei-Center Studie *Optimal time window for cortical mapping in awake craniotomy – a two-center study*

D. Meskelevicius¹, A. Schäfer¹, L. Haddad¹, M. A. Kamp¹, B. Mainzer², H. J. Steiger¹, M. Rapp¹, D. Hänggi¹, V. Singh³, M. Sabel¹

¹Universitätsklinikum Düsseldorf, Klinik für Neurochirurgie, Düsseldorf, Germany

²Universitätsklinikum Düsseldorf, Klinik für Anästhesiologie, Düsseldorf, Germany

³Tata Memorial Centre, Department of Neurosurgery, Mumbai, India

Objective

In our previous study we have demonstrated that the optimal time window for cortical mapping in a Sleep-Awake-Awake (S-A-A) craniotomy might begin 20 minutes after extubation of the Patient, however the assessment of time window beyond 40 minutes after extubation was not possible due to the lack of data. During the last year we have accumulated additional data in order to assess a longer intraoperative time window. Moreover, in cooperation with Tata Memorial Hospital in Mumbai, India, we have acquired the data about intraoperative reaction speed during Awake-Awake-Awake (A-A-A) craniotomy.

Methods

Reaction speed was assessed in 62 Patients in S-A-A and 18 Patients in A-A-A group. Pathology operated was primary or metastatic brain tumors. All patients in S-A-A Group underwent surgery following a "Sleep-Awake-Awake" protocol, whereas patients in A-A-A group underwent "Awake-Awake-Awake" anesthesia protocol. The registration was done with an application Reaction Time Sampler in both groups. Reaction times were determined at least once every 10 minutes. Reaction time determination was performed in parallel with our standard methods for evaluation of language and cognitive functions. Statistical analysis was performed using SPSS v24.0 (IBM, New York, U.S.).

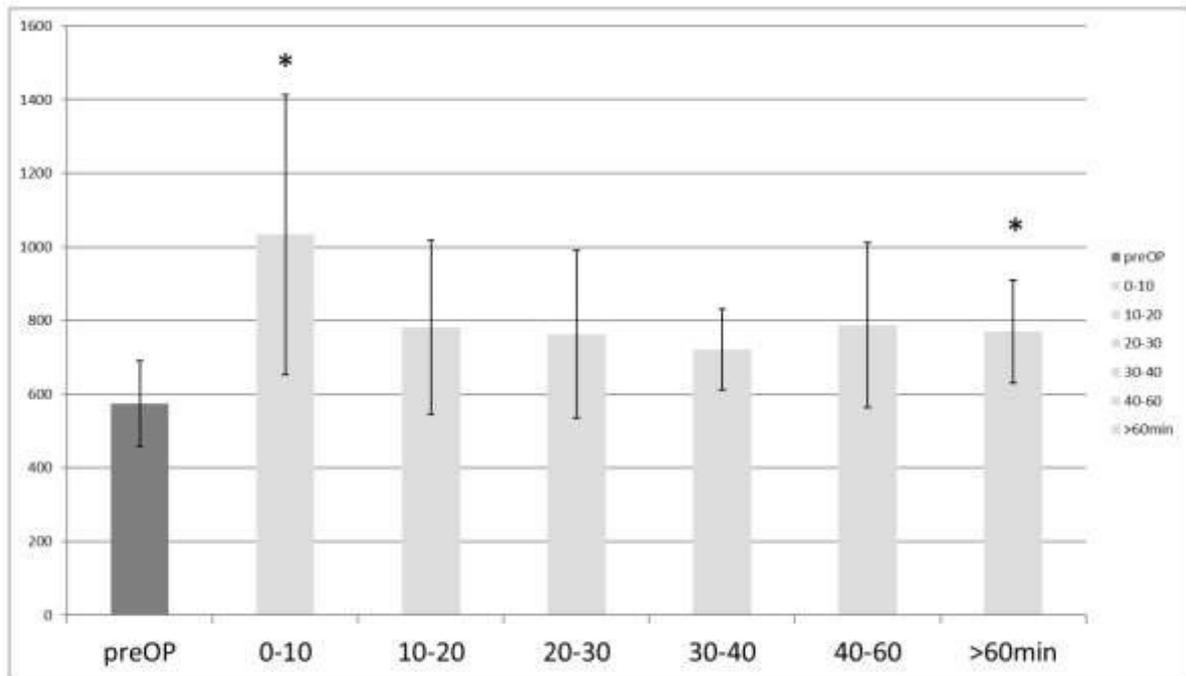
Results

The data is presented as mean \pm standard deviation. The preoperative response times of S-A-A patient cohort (574 ± 116 ms) were significantly shorter than those measured during surgery (810 ± 75 ms; $p < 0,001$). No factors correlated with intraoperative reaction speed. Patient age was the only factor that correlated with the preoperative reaction speed in S-A-A cohort, $r = .562$, $p < 60$ minutes after extubation. In the A-A-A cohort, the difference between the pre- and intraoperative reaction speed was insignificant. Interestingly, the preoperative and intraoperative reaction times are significantly longer in the A-A-A cohort, namely PreOP: A-A-A (1343 ± 918 ms) vs. S-A-A (609 ± 326 ms), IntraOP: A-A-A (1112 ± 374 ms) vs. S-A-A (815 ± 260 ms).

Conclusion

Patients in the S-A-A cohort react 34% slower during surgery than the day before surgery. The intraoperative reaction times were not significantly longer than preoperative in A-A-A cohort. Furthermore, the reaction time in S-A-A cohort was significantly longer during the first 10 and >60 intraoperative minutes than preoperatively. Hence, according to our data the optimal time window for cortical mapping in Sleep-Awake-Awake craniotomy possibly starts 10 minutes and ends 60 minutes after extubation of the patient.

Fig 1



Digitale Medizin/*Digital medicine*

P072

Untersuchung von Unterschieden in der Lokalisation von Sprachfunktion zwischen verschiedenen Sprachen durch navigierte repetitive transkranielle Magnetstimulation und Traktographie von subkortikalen Faserbahnen

Examining differences in the localisation of language function between various languages using nrTMS and subcortical pathway tractography

C. Börner, A. Schröder, B. Meyer, S. Krieg, [S. Ille](#)

Technische Universität München, München, Germany

Objective

The anatomical location of language is highly variable across individuals. The location of language can be identified cortically using navigated repetitive transcranial magnetic stimulation (nrTMS) and subcortically using diffusion tensor imaging fiber tracking (DTI FT). This study investigates how nrTMS-based cortical locations of language function and DTI FT tractographies of language-eloquent subcortical pathways differ between various languages.

Methods

We included 40 patients with language-eloquent brain lesions speaking various languages. Preoperative nrTMS using an object-naming task identified language-related brain sites. nrTMS-based DTI FT visualized subcortical language tracts. Cortical language error rates and subcortical language pathway volumes were compared between Slavic and Indo-Germanic languages within bilingual patients.

Results

Error rates related to stimulations in the mSFG, pMFG, mPoG, pSFG, and pSTG differed significantly between Slavic and Indo-Germanic languages. Error rates related to stimulations in the pSTG, pMTG, mSFG, trIFG, mMFG, vPoG, and anG differed significantly between bilingual individuals. No differences were found in the subcortical language pathway volumes between Slavic and Indo-Germanic languages nor between bilingual patients. The subcortical language pathway volumes correlated moderately with error rates related to stimulations in the opIFG, mMFG, mSFG, PrG, SMG, dPoG, mSTG, pMTG, and anG in Slavic and Indo-Germanic languages.

Conclusion

Even though the underlying subcortical structure may be similar across languages, there are significant differences in the pattern of cortical location of language between various languages depending on the semantic processing. This is important for indication but also the resection of language-eloquent brain lesions since the location of language cannot be generalized across languages or individuals.

Neurointensivmedizin I/Neurocritical care I

P083

Nicht-invasives Autoregulations-Monitoring bei wachen Patienten während Karotisendarterektomie *Non-invasive autoregulation monitoring in awake patients during carotid endarterectomy in relation to neurological status*

J. Zipfel¹, M. U. Schuhmann¹, M. Lescan², S. Bantle²

¹Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

²Universitätsklinikum Tübingen, Klinik für Herz-/Thorax- und Gefäßchirurgie, Tübingen, Germany

Objective

Carotid endarterectomy (CEA) is well-established for patients at risk for stroke with carotid artery disease. Selective shunting has been proposed with NIRS (Near-infrared spectroscopy) as a non-invasive tool for monitoring cerebrovascular autoregulation with the cerebral oximetry index (COx) and the hemoglobin volume index (HVx).

Methods

We performed NIRS in 59 consecutive patients, who underwent awake CEA. Regional SO₂ and THb, as well as invasive arterial blood pressure were captured via ICM+ software (Cambridge Enterprise) and COx and HVx were calculated continuously. In case of neurological deterioration, a shunt was inserted.

Results

6 of 51 (11.8%) patients needed intraoperative shunting. The drop in ipsilateral rSO₂ was significantly larger in the shunt-group (5.31 vs. 13.50%) with increased contralateral values. ODA increased bilaterally, whilst significantly only on the non-operated side (1.62 to 1.678, p=0.056 vs. 1.63 to 1.68; p=0.016). In patients with neurological deficit during clamping no significant change in ODA during clamping was found, whereas in the patients without neurological deficit we detected a significant bilateral increase (1.59 to 1.65; p=0.022 vs. 1.60 to 1.66; p=0.01). In neurologically intact patients, COx decreased significantly on the operated side after clamping (0.18->0.12 (0.13, 0.02) p=0.024). In patients with deterioration of the neurological status, COx increased significantly (0.13 to 0.32±0.05; p=0.048). When pooling ipsi- and contralateral data, patients with neurological deficit showed a significant increase in HVx as compared to patients without deficit, where the trend was even negative (no shunt: 0.073 to 0.037 ±0.014) p=0.123, shunt: 0.05 vs 0.15 ±0.02) p<0.001). Comparable observation was made for COx (no shunt: COx 0.17 vs 0.10 (± 0.01) p=0.002, shunt: 0.18 vs 0.23±0.01; p=0.039). This autoregulation works up to mean arterial pressures of 110mmHg and higher, leading to impaired cerebrovascular reactivity contralaterally. When no shunt was needed, changes of autoregulation parameters remained non-significant.

Conclusion

Neurological deficit during awake CEA is associated with a significant decrease in ipsilateral rSO₂ plus impaired contralateral autoregulation. Thus, the additional calculation of NIRS based autoregulation parameters makes it possible to identify patients, in whom a critical reduction of CBF has occurred. This is especially of importance, when general anesthesia is needed, and awake CEA is not possible.

Fig 1

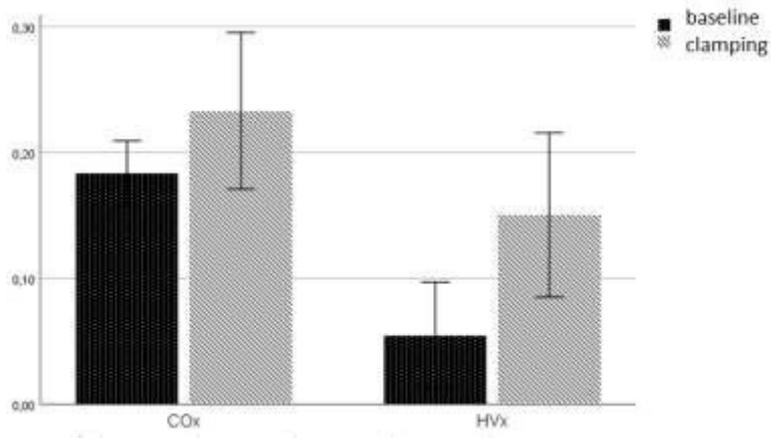
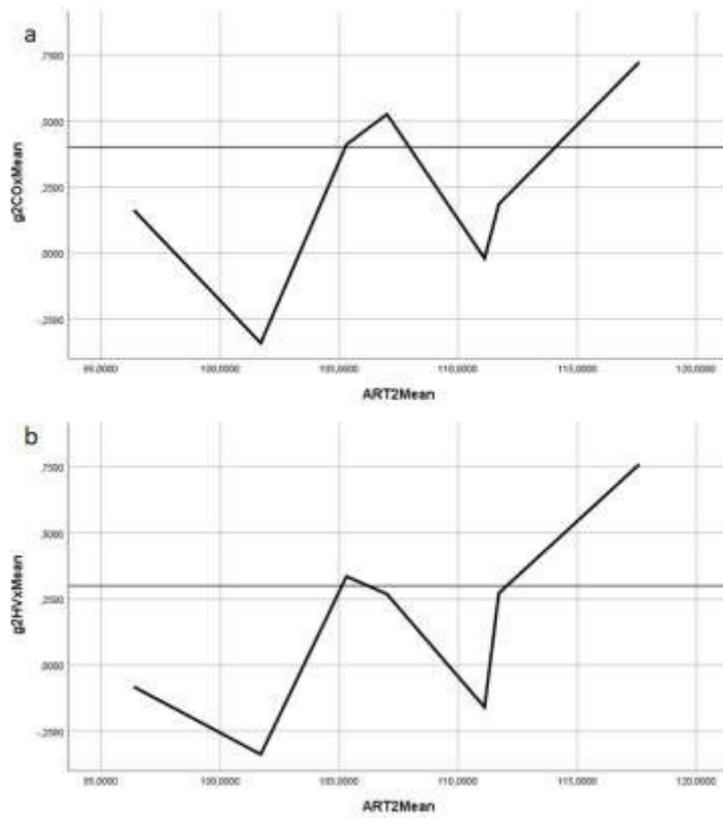


Fig 2



Neurointensivmedizin I/Neurocritical care I

P084

Die Neuropsychological Assessment Battery (NAB) ist ein wertvolles Untersuchungstool zur Evaluation des neuropsychologischen Outcomes nach aneurysmatischer Subarachnoidalblutung
The Neuropsychological Assessment Battery (NAB) is a valuable tool for evaluating neuropsychological outcome after aneurysmatic subarachnoid haemorrhage

J. Walter¹, M. Grutza¹, L. Vogt¹, A. W. Unterberg¹, K. Zweckberger²

¹Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

²Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

Objective

Detecting and treating neuropsychological deficits after aneurysmatic subarachnoid hemorrhage (aSAH) play a key role in regaining independence; however, detecting subtle deficits has been difficult and optimal timing of assessments remains unclear. Therefore, we evaluated the feasibility of administering the Neuropsychological Assessment Battery screening module (NAB-S) to patients with aSAH and characterized clinical as well as neuropsychological recovery over 24 months.

Methods

A total of 72 consecutive patients treated for aSAH were recruited. After acute treatment, follow up visits were conducted at 3, 12 and 24 months after hemorrhage. NAB-S, Montreal Cognitive Assessment (MoCA) and physical examination were performed at each follow up visit. Neuropsychological follow up was only scheduled if patients were able to understand and follow simple commands. Otherwise, outcome parameters (i.e. Extended Glasgow Outcome Score (GOSE) and Modified Rankin Score (mRS)) were assessed via telephone interview.

Results

The NAB-S could be administered to 40.0%, 77.8% and 94.1% of the patients at 3, 12 and 24 months, respectively. Severe impairment of one or more neuropsychological domains (e.g executive function, etc.) significantly correlated with inability to return to work at 12 months. Moderate impairment of two or more domains significantly correlated with poor outcome assessed by GOSE at 3 and 12 months. The number of patients with favorable outcomes increased from 30.9% to 36.8% and 46.7% at discharge, 3 and 12 months, respectively, and significantly increased to 87.5% after 24 months.

Conclusion

The NAB-S can be administered to the majority of patients with aSAH and can effectively detect clinically relevant neuropsychological deficits. Clinical recovery after aSAH continues for at least 24 months after the hemorrhage which should be considered in the design of future clinical trials.

Neurointensivmedizin I/*Neurocritical care I*

P085

Antiinflammatorische Antwort von Vitamin D auf extrakranielle Gefäße nach Subarachnoidalblutung *Anti-inflammatory response of vitamin D on extracranial vessels after subarachnoid haemorrhage*

S. Kashefiolas¹, K. Schröder², V. Seifert¹, R. Brandes², J. Konczalla¹

¹Universitätsklinikum Frankfurt am Main, Neurochirurgie, Frankfurt am Main, Germany

²Johann Wolfgang Goethe-Universität Frankfurt am Main, Kardiovaskuläre Physiologie, Frankfurt am Main, Germany

Objective

Vitamin D has been promoted to vascular regeneration in non-cerebral arteries because of its anti-inflammatory properties. Systemic inflammatory reaction as a multifactorial complication after subarachnoid hemorrhage (SAH), correlated with higher mortality and poor outcome, is the result of a multifactorial mechanism with vasoactive inflammation on extracranial vessels. We therefore hypothesized that vitamin D attenuates the systemic vascular inflammatory reaction.

Methods

We investigated the effect of vitamin D pretreatment (100 ng/kg/d; 5 days) in a blood injection SAH model in adult male C57BL6 mice. Vasomotor function (via wire myograph) of carotid and femoral artery and neurological deficits were measured. Different inflammatory factors such as tumor necrosis factor α (TNF- α), interleucin 6 (IL-6), vascular cell adhesion molecule (VCAM) and intercellular adhesion molecule (ICAM), were also tested.

Results

A significantly enhanced vasorelaxation was identified in Vitamin D pretreated mice (SAH-VitD versus SAH-control: $p < 0,001$; $n=10$). Missing a relevant difference in vasoconstriction of carotid and femoral artery comparing SAH mice with and without vitamin D treatment, there was a significantly higher endothelial related vasorelaxing effect in treated SAH mice ($p < 0,01$, $n=5$). Neurological deficits in vitamin D pre-treated SAH mice were significantly decreased ($p < 0,05$; $n=10$). All tested inflammatory factors were down-regulated in vitamin D pre-treated mice (SAH-VitD versus SAH-control: $p < 0,0001$; $n=10$).

Conclusion

Extracranial vascular Inflammation after SAH, as one of the influencing components in the follow-up after SAH onset, was significantly attenuated by Vitamin D pretreatment. Furthermore, the anti-inflammatory effect of vitamin D resulted in a decrease of extracranial vasoconstriction and neurological deficits. Further research should be focused on vitamin D to optimize therapeutic strategies for SAH patients in critical care units.

Neurointensivmedizin I/Neurocritical care I

P086

Einfluss von Interleukin-4 auf den sekundären Hirnschaden nach experimentellem Schädel-Hirn-Trauma im Mausmodell

Influence of interleukin-4 on secondary brain damage after experimental traumatic brain injury in mice

J. Walter¹, O. Kovalenko¹, A. Younsi¹, C. Maurer², J. Kirsch², A. W. Unterberg¹, K. Zweckberger¹

¹Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

²Ruprecht-Karls-Universität Heidelberg, Anatomisches Institut, Heidelberg, Germany

Objective

Recent focus of experimental research in traumatic brain injury has been directed towards the role of inflammatory processes. Proinflammatory pathways have become the focus of interest; however, in models of ischemic stroke and spinal cord injury it has been shown that anti-inflammatory pathways, especially the interleukin-4 (IL-4) pathway, play an important role in the evolution of secondary brain injury as well. Therefore, we aimed to assess the role of the interleukin-4 pathway on secondary brain damage following experimental traumatic brain injury.

Methods

C57/Bl6 wildtype as well as C57BL/6-*Il4tm1Nnt/J* interleukin-4 knockout mice were subjected to controlled cortical impact (CCI) injury (tip diameter 2mm, impact depth 1mm, velocity 8m/s, contact time 150ms). Neurological function was assessed using hole board, video open field and CatWalk XT gait analysis tests 24 hours as well as three and seven days after CCI. In addition, contusion volume was determined by Nissl staining and pericontusional distribution of IL-4 and IL-4 receptor assessed by immunohistochemistry at the same timepoints.

Results

Exploration (33.9 +/- 2.4 vs. 24.8 +/- 3.7 hole board explorations per 10 minutes on day 3, p= 0.008), locomotion (154.1 +/- 18.6 seconds vs. 100.9 +/- 15.3 seconds to visit all open field sections on day 1, p=0.033) and motor function (i.e. difference in left hindpaw print area on day 3: -0.017 +/- 0.012 cm² vs. -0.050 +/- 0.015 cm², p=0.04) was significantly more impaired in interleukin-4 knockout mice. Contusion volume was significantly higher (81.0 +/- 7.8 vs. 123.3 +/- 7.7 on day 3, p=0.04) and pericontusional distribution of IL-4 and IL-4 receptor significantly lower in IL-4 knockout mice.

Conclusion

Interleukin-4 plays an important role in the evolution of secondary brain damage after experimental traumatic brain injury as lack of interleukin-4 in the pericontusional area leads to larger contusion volumes and to deterioration in neurological outcome. The current results provide the basis for future studies examining a potential positive therapeutic effect of interleukin-4 in CCI.

Neurointensivmedizin I/Neurocritical care I

P087

Kann künstliche Intelligenz (KI) frühe prädiktive Serum-Biomarker für post-aneurysmatische Komplikationen identifizieren?

Can artificial intelligence (AI) identify early predictive serum biomarkers of post-aneurysmal SAH complications?

J. Fischer¹, S. R. Chaudhry², D. Hänggi¹, S. Muhammad^{1,2}

¹Heinrich-Heine-Universität Düsseldorf, Klinik für Neurochirurgie, Düsseldorf, Germany

²Rheinische Friedrich-Wilhelms-Universität Bonn, Klinik für Neurochirurgie, Bonn, Germany

Objective

Both systemic and local inflammation in the brain parenchyma play a critical role during early brain injury (EBI) and delayed cerebral ischemia (DCI). Multiple biochemical markers are known to be associated with cell damage and post-SAH inflammation and hence contribute to the pathophysiology of aSAH. We investigated whether machine learning methods can identify those biomarkers to predict post-aSAH complications.

Methods

Blood concentration of eleven potential blood markers (Cytochrome B, D-loop, Cox-1, CCL5, CRP, leukocytes, IL-6, IL-10, IL-23, sIL-17, and HMGB1) for 81 SAH patients were recorded on day 1, together with demographic and clinical data. Five potential complications—cerebral vasospasms (CVS), delayed ischemic neurologic deficit (DIND), shunt dependent hydrocephalus, convulsive epilepsy and delayed cerebral ischemia (DCI)—were considered. If one or more complications occurred, the day of the earliest occurrence was recorded. Missing values were imputed as medians or the most frequent value.

The data were randomly split into a training and a test set, in the 60:40 ratio. Two machine learning algorithms, Random Forest (RF) and Support Vector Machine (SVM), were trained to predict whether (classification) and when (regression) a patient will develop complications during his or her stay. All combinations of the blood markers, together with the Hunt & Hess score were systematically tested. For SVMs, the radial (Gaussian) kernel with the default width was used. For classification, the performance was quantified as sensitivity, specificity, and F1. For predicting the complications' onset day (regression), ICC (3,k) was used.

Results

63 patients (78%) developed post-aSAH complications. Most epilepsies (88%) occurred on days 1 or 2, and other complications mostly on days 4 or 5. Age (31-85, median 56) and sex did not correlate with complications. The SVM classifier achieved 100% sensitivity and 71% specificity (F1=0.96) on the test set. For Random Forest sensitivity was 100%, specificity 57% and F1=0.95. SVM regression reached an ICC (3,k) of 0.3 (p=0.19), while RF regression achieved ICC=0.34 (p=0.15).

Conclusion

Despite the small but high-dimensional training sets (48 observations for classification, 34 for regression), good performance was achieved for classification. Due to the small data set size we are cautious in regard to the potential of machine learning to identify serum predictive biomarkers for post-aSAH complications in intensive care.

Neurointensivmedizin I/Neurocritical care I

P088

Frühe Prädiktoren zur Vorhersage eines guten, funktionellen Outcomes bei Patienten mit intrazerebraler Blutung und fibrinolytischer Therapie *Early predictors of good functional outcome in patients with intracerebral haemorrhage and fibrinolytic therapy*

C. Wolfert¹, B. Iliev^{1,2}, D. Mielke¹, V. Rohde¹, V. Malinova¹

¹Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

²Westpfalz-Klinikum, Neurochirurgie, Kaiserslautern, Germany

Objective

Intracerebral hemorrhage (ICH) is associated with high morbidity and mortality. Minimally invasive surgery with neuronavigated intrahematoma catheter placement and subsequent application of recombinant tissue Plasminogen Activator (rtPA) facilitates a faster hematoma resolution. The assessment of early predictors for achieving a good functional outcome is of great clinical relevance and could be supportive during the decision-making process for further therapy. In this study we aimed to evaluate early predictors of good functional outcome in ICH-patients, who survived the acute phase after the acute incident.

Methods

We performed a retrospective analysis of patients with supratentorial ICH back to 2010. The following factors were included: age, arterial hypertension (aHT), diabetes mellitus (DM), serum glucose (GLU) and Glasgow coma scale (GCS) at admission, initial hydrocephalus (HC), anticoagulation (AC), duration of sedation (DoS), duration of ventilation (DoV), duration of intensive care unit stay (ICU-stay) and intraventricular hemorrhage (IVH). Volumetric analysis of initial ICH volume and volume after every dose of rtPA was performed (brainlab). The functional outcome was calculated according to the modified Rankin scale (mRS), whereas mRS≤3 was considered as good functional outcome.

Results

A total of 100 patients (54%; n=54 male) with mean age 65.8 years (range: 30-93 years), were enrolled. Mean initial ICH volume was 51.5 mL (range: 19-108 mL), with deep-seated ICH in 58% (n=58). The mean administered rtPA dose was 10.8 mg rtPA (range: 3.0-22.0 mg) in up to 5 single doses. Good functional outcome was achieved by 7 patients (7%). Most patients (n=74, 74%) had mRS 4. DM ($p=0.75$), sex ($p=0.70$), quantity of lysis ($p=0.64$), aHT ($p=0.22$), initial ICH volume ($p=0.16$), localization of the bleeding ($p=0.15$), infections ($p=0.11$), intraventricular bleeding ($p=0.10$) and GCS at admission ($p=0.066$) reached no significance for the prediction of functional outcome. In contrast to that, HC ($p=0.026$), GLU ($p=0.018$) and residual volume after second rtPA dose ($p=0.005$) were significant predictors of functional outcome.

Conclusion

Good functional outcome is still rarely achieved by ICH-patients. Unexpectedly, initial GCS and preexisting comorbidities were not predictive of functional outcome after ICH. The achievement of a smaller residual ICH-Volume within the first 48 hours after onset of hemorrhage seems to be a relevant goal of fibrinolytic therapy, which might lead to a better functional outcome after ICH.

Neurointensivmedizin I/*Neurocritical care I*

P089

Der Nutzen der kraniellen MR Bildgebung während des frühen Therapieverlaufs bei Patienten mit poor-grade aneurysmatischer Subarachnoidalblutung

The value of cranial MRI during the early treatment course in patients with poor-grade aneurysmal subarachnoid haemorrhage

S. Brandecker, A. Hadjiathanasiou, L. M. Schenk, P. Schuss, H. Vatter, E. Güresir

Universitätsklinikum Bonn, Klinik und Poliklinik für Neurochirurgie, Bonn, Germany

Objective

The aim of this study was to present the value of cranial MRI during the early treatment course in patients with poor-grade (WFNS grade IV and V) aneurysmal subarachnoid hemorrhage (aSAH) in view of decisions for therapy limitation resulting from this.

Methods

Between 10/2012 and 04/2019 a total number of 146 patients with poor-grade aSAH (WFNS grade IV and V) were treated at our institution. Patient data were prospectively entered into a computerized database.

Patients underwent cranial MRI in the first 10 days, when there was no trend in clinical improvement. We retrospectively analysed the data of radiological MRI findings in these after SAH patients and analysed the decisions for therapy limitation resulting from this. Outcome was analysed according to modified Rankin Scale (mRS) and dichotomized into favourable (mRS 0-4) versus unfavourable (mRS 5-6) outcome after 6 months.

Results

Of the 146 patients with poor-grade aSAH treated at our institution between 10/2012 and 04/2019, 33 patients (22.6 %) underwent cranial MRI in the first 10 days after SAH for evaluating general prognosis. In 10 patients (30.3 % of patients with cMRI) a decision for therapy limitation was made because of the radiological findings, which had been brain stem infarction (20.0 %), mesencephalic infarction (30.0 %), hemispheric infarction (20.0 %), multi-infarction (20.0 %) and disseminated micro bleeding / septic embolism (10.0 %). In patients with an early cMRI and without limitation of therapy a favourable outcome could be achieved in 21.7 %.

Conclusion

In a relevant number of patients receiving a cMRI in order to evaluate general prognosis, a decision for therapy limitation was made following the radiological findings in cMRI. Furthermore, in patients with an early cMRI and without limitation of therapy, a relevant number of patients were able to achieve a favourable outcome. Therefore cranial MRI in the early treatment course of patients with poor-grade aSAH seems to be important and should not be omitted in these severely ill patients.

Neurointensivmedizin I/*Neurocritical care I*

P090

Komplette hemispherische Entdeckung versus *Sinus sagittalis superior* schonende Kraniotomie – Inzidenz von Scheerblutung und Shunpflichtigkeit – die Größe zählt
Complete hemispheric exposure versus superior sagittal sinus sparing craniectomy – incidence of shear bleeding and shunt dependency – size matters

M. Vychopen

Universitätsklinikum Bonn, Klinik und Poliklinik für Neurochirurgie, Bonn, Germany

Objective

Decompressive hemicraniectomy (DC) has been established as a standard therapeutic procedure for raised intracranial pressure. However, the size of the DC remains unspecified. The aim of this study is to determine the ideal boundary of the craniectomy in relation to the superior sagittal suture.

Methods

306 patients, who underwent DC for elevated intracranial pressure were analyzed. Anteroposterior and craniocaudal DC size was measured according to the postoperative CT scans. Patients were divided into two groups with 1. exposed superior sagittal sinus (ES) and 2. covered superior sagittal sinus (CS). DC related complications e.g. shear-bleeding at the margins of craniectomy and hydrocephalus were evaluated and compared between the two groups.

Results

Craniectomy size was large in both groups according to the anteroposterior diameter, and did not differ between the groups (mean size: 136,8 mm). The ES group had significantly lower rates of shear-bleeding (20 of 176 patients; 11%), compared to patients of the CS group (36 of 130 patients, 27%; $p=0,0003$, OR 2.9, 95% CI 1.6-5.5).

There was no significant difference in the incidence of shunt-dependent hydrocephalus between the two groups (19 of 130 patients, 14,6%, vs. 24 of 176 patients, 13,6%; $p=0,9$).

Conclusion

Complete hemispheric exposure, and therefore larger DC size, seems to be associated with a smaller likelihood of shear bleeding, without the elevation of the incidence of shunt-dependent hydrocephalus and should therefore be performed whenever deemed possible during decompressive craniectomy.

Neurointensivmedizin I/*Neurocritical care I*

P091

Pilzabszesse des Gehirns – nicht länger ein Todesurteil ***Fungal brain abscess – not longer a death sentence***

N. Lange¹, A. K. Jörger¹, A. Wagner¹, F. Liesche¹, N. Wantia², B. Meyer², J. Gempt²

¹Technische Universität München, Neuropathologie, München, Germany

²Technische Universität München, Neurochirurgie, München, Germany

Objective

Cerebral aspergillosis is a rare but severe and life threatening condition. The aim of this case series was, to provide a modern cohort of patients with cerebral aspergillosis, assess the clinical characteristics and reveal the relevant aspects for future therapy for such a condition.

Methods

In a 10 years period from January 2009 to January 2019, we identified 10 patients (6 male, 4 female) who underwent surgery or frameless stereotactic drainage of a cerebral aspergilloma at our center. Patients' and disease characteristics were recorded, including age, mortality, dates and types of surgical procedures, neurological symptoms and length and type of antifungal treatment, germ spectrum and immunosuppressive conditions were also assessed.

Results

The median age was 65 (range 45 to 83). We conducted 133 cranial surgeries in 100 patients due to cerebral brain abscess (BA) during that time, resulting in a percentage of 10% of aspergilloma within BAs in our patient sample. We performed 3.1 surgeries per patient followed by antifungal treatment for 6 months (=median) according to the microbiological findings. Regarding comorbidities, mean CCI at the time of admission was 5, representing an estimated 10-year survival of 21%. Six of 10 patients (60%) had conditions of immunosuppression, one suffered endocarditis after replacement of aortic valves. 4 patients showed associated frontobasal bone destruction, mycotic aneurysms or thromboses. Mean duration of hospital stay was 37 days. Mortality was much lower than in the literature. 60% of the patients died during the follow-up period. Outcome of the two immunocompetent patients was more favorable.

Conclusion

Cerebral aspergillosis is a rare, but still life threatening condition, which predominantly occurs in immunosuppressive conditions. Due to radical surgical removal of infected tissue and antifungal therapy for several months, mortality can be reduced dramatically.

Neurointensivmedizin I/Neurocritical care I

P093

Das endogene Melatonin nach aneurysmatischer Subarachnoidalblutung (aSAH) – eine prospektive Analyse *Endogenous melatonin after aneurysmal subarachnoid haemorrhage (aSAH) – a prospective analysis*

W. Albanna¹, M. Weiss², T.P. Schmidt², C. Conzen², M. Veldeman², H. R. Clusmann², G. A. Schubert²

¹Universitätsklinikum Köln, Institut für Neurophysiologie, Köln, Germany

²Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neurochirurgie, Aachen, Germany

Objective

An acute increase in intracranial pressure and reduction of cerebral blood flow are thought to initiate Early Brain Injury (EBI) after SAH, a crucial contributor to overall outcome. In this period, oxidative stress, inflammatory factors, and neuronal apoptosis are triggered. After experimental SAH, the circadian molecule melatonin showed both antioxidant and anti-inflammatory impacts. We prospectively assessed the endogenous melatonin level in SAH patients in the context of disease severity and outcome.

Methods

We prospectively enrolled 30 consecutive adult patients (57.9±12yrs) with acute aSAH from 02/2015 to 05/2017. Thirty adult patients undergoing elective aortic surgery (56.9±11.7yrs) served as a control group (cG). All relevant demographic data, modified Fisher score (mFS), clinical course and complications (including DCI, infarcts) as well as outcome (GOS) after three months were recorded. Samples of serum were collected from each patient (from 11:00 am to 05:00 pm) at different time points: after ictus (d0), early (EPd1-4), in the critical (CPd5-8, CPd9-12, CPd13-15) and in late phase (LPd16-21). For measuring of melatonin, ELISA kits from IBL International GmbH were used. The lower limit of quantification (LLOQ) was set by 3pg/ml.

Results

In 80 out of 183 samples (43.7%), melatonin remained below the LLOQ (46.7% in cG, 41.7% in d0, 55.2% in EPd1-4, 72% in CPd5-8, 38% in CPd9-12, 32% in CPd13-15, 14.8% in LPd16-21), indicating a predominant decrease of melatonin in the critical phase. Cases with LLOQ in CPd5-8 showed significantly more infarcts ($p < 0.05$). Higher levels of melatonin initially (EP) were associated with a lower incidence of DCI ($p < 0.05$). Samples in patients with ruptured anterior communicating artery aneurysms (ACoM) showed significantly increased melatonin levels in the early and the critical phase ($p = 0.05$, $p < 0.05$).

Conclusion

To our knowledge, this is first clinical data detailing a characteristic course of melatonin levels after aSAH. In the acute/critical phase melatonin levels are decreased, whereas higher levels initially are associated with a more benign clinical course, possibly due to its antioxidant and anti-inflammatory impact. The close proximity of the melatonin-controlling suprachiasmatic nucleus to the ACoM-complex may explain the significant elevation of melatonin in these cases.

Neurointensivmedizin I/Neurocritical care I

P094

Der CatWalk XT ist eine valide Methode zur Beurteilung von Gleichgewicht und motorischer Funktion nach experimentellem Schädel-Hirn-Trauma im Mausmodell

The CatWalk XT is a valid tool for objective assessment of gait and motor function after controlled cortical impact in mice

J. Walter, O. Kovalenko, A. Younsi, M. Grutza, A. W. Unterberg, K. Zweckberger

Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

Objective

In order to further elucidate the pathophysiology of traumatic brain injury (TBI) and test new treatment options different animal models are available, the controlled cortical impact (CCI) model being one of the most frequently used. However, objectively assessing functional outcome after CCI in animals is challenging; therefore, we evaluated the value of the CatWalk XT in assessing gait and motor function after CCI in mice.

Methods

C57/Bl6 wildtype mice were subjected to either right parietal craniotomy followed by controlled cortical impact (tip diameter 2mm, impact depth 1mm, velocity 8m/s, contact time 150ms) or craniotomy only. A total of 103 parameters of motor function and gait were automatically analyzed using the CatWalk XT test one, three and seven days after CCI.

Results

Gait and motor function were significantly more impaired and contusion volumes significantly higher in animals subjected to CCI compared to animals that underwent craniotomy alone (i.e. change in left hindpaw maximum intensity on day 3: 15.8 +/- 5.1 vs. -3.2 +/- 6.0, p=0.02; change in left hindpaw print area on day 3: 0.062 +/- 0.039 cm² vs. 0.002 +/- 0.041 cm², p=0.004; change in left frontpaw maximum intensity on day 3: 13.8 +/- 3.5 vs. 1.2 +/- 4.3, p=0.04). Although CCI is a model for focal injury, the effect on gait and motor function was bilateral and diffuse. Impairments of static parameters were most severe within the first three days after CCI and resolved thereafter while impairments of dynamic parameters persisted until day seven after trauma induction.

Conclusion

CatWalk XT is a valuable tool for observer-independent and automated assessment of gait and motor function after CCI in mice. Spatial and temporal profiles of impairments of gait and motor function induced by CCI with the chosen parameters are similar to the ones seen in human patients after TBI; therefore, CCI is a valid model for preclinical evaluation of the effect of possible new treatment strategies on functional motor outcome.

Neurointensivmedizin II/*Neurocritical care II*

JM–JNS07

Einige Überlegungen der dekomprimierenden Kraniektomie für schwere traumatische Hirnverletzungen von Säuglingen

Some considerations of decompressive craniectomy for severe traumatic brain injury of infants

T. Kim, Y. S. Park, Y. Motoyama, H. Nakase

Nara Medical University, Neurosurgery, Kashihara, Japan

Objective

Brain edema after severe traumatic brain injury (sTBI) is a common occurrence in infants resulting in elevated intracranial pressure (ICP), and causing a severe or fatal state. Because of infant brain plasticity, however, appropriate treatments to improve ICP can lead to positive outcomes. Decompressive craniectomy (DC) is an effective strategy in adults for cases of high ICP that are refractory to medication, but it is important to specify the treatment for the unique complications in infants, such as bone resorption and infections. To avoid such complications, we have taken some intraoperative steps and strictly controlled the ICP in the postoperative phase for a better outcome.

Methods

From January 2013 to December 2017, four patients with sTBI underwent DC and hypothermia barbiturate (HB) therapy. The mean age of the patients was 9.75 months (range, 2–20 months) and the mean follow-up period was 26 months (range, 12–50.5 months). We retrospectively reviewed information regarding bone resorption, ICP movements, HB therapy complications and clinical outcomes of the four patients. DC was conducted under the following rules: (1) do not remove the bone flap unless its infected, (2) make a vascularized bone flap with a hinge using the temporal muscle, (3) do not use an artificial material, but an autologous fascia or periosteum instead for duroplasty, (4) place the bone flap "floating" on the brain, do not fix it to the cranial bone, (5) attach absorbable cranial fix plates only to the bone flap to prevent sinking, and (6) strictly control ICP in the Intensive Care Unit by HB therapy.

Results

All four patients survived with sufficient lowering of ICP following complete DC and HB therapy. None of the patients exhibited bone resorption or other severe complications. Two patients recovered well, while two patients, who experienced child abuse, were severely disabled (SD).

Conclusion

Appropriate treatment can change the outcome of an infant with sTBI. Our DC technique was effective in decreasing ICP and avoiding severe complications. Bone formation was adequate so that subsequent cranioplasty was not necessary.

Neurointensivmedizin II/Neurocritical care II

P095

Zeitlicher Verlauf von eRNA (extrazellulärer RNA) im Rahmen der aneurysmatischen SAB (Subarachnoidalblutung)

Time course of eRNA (extracellular RNA) expression in aneurysmal SAH (subarachnoid haemorrhage)

R. Xu¹, S. Fischer², S. Liu¹, K. Tielking¹, U. C. Schneider¹, K. Preissner², P. Vajkoczy¹

¹Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

²Justus-Liebig-Universität Gießen, Gießen, Germany

Objective

Previous research hypothesizes that eRNA is released upon tissue injury and subsequently activates inflammatory signaling. Previous data from our laboratory showed that eRNA is released into the subarachnoid space in an animal model of experimental SAH, and is associated with an activation of the innate immune system. This study aims to quantify eRNA release and investigate RNase activity in patient samples.

Methods

CSF and EDTA samples from patients with aneurysmal SAH (n=20) were collected within the scope of a prospective study after acquiring approval by the ethics committee board. Control samples (n=5) were acquired from pseudotumor cerebri patients and healthy individuals. Sampling was conducted at four time points after bleeding onset (day 1,4,7,14). CSF and blood samples were spun down twice at 500g for 5min at 4°C to remove debris and blood. For eRNA quantification, 80U/ml RNase Inhibitor was added. Isolation of RNA was conducted with the Master Pure RNA Purification Kit; quantification was done with the Qubit™ RNA Assay Kit (Invitrogen) and measured with the fluorometer. For RNase activity, supernatant was added to poly(c)solution, RNase buffer, and BSA solution and incubated at 37°C for 15min. Substrate degradation was determined by measuring the absorbance of the supernatant at 280nm.

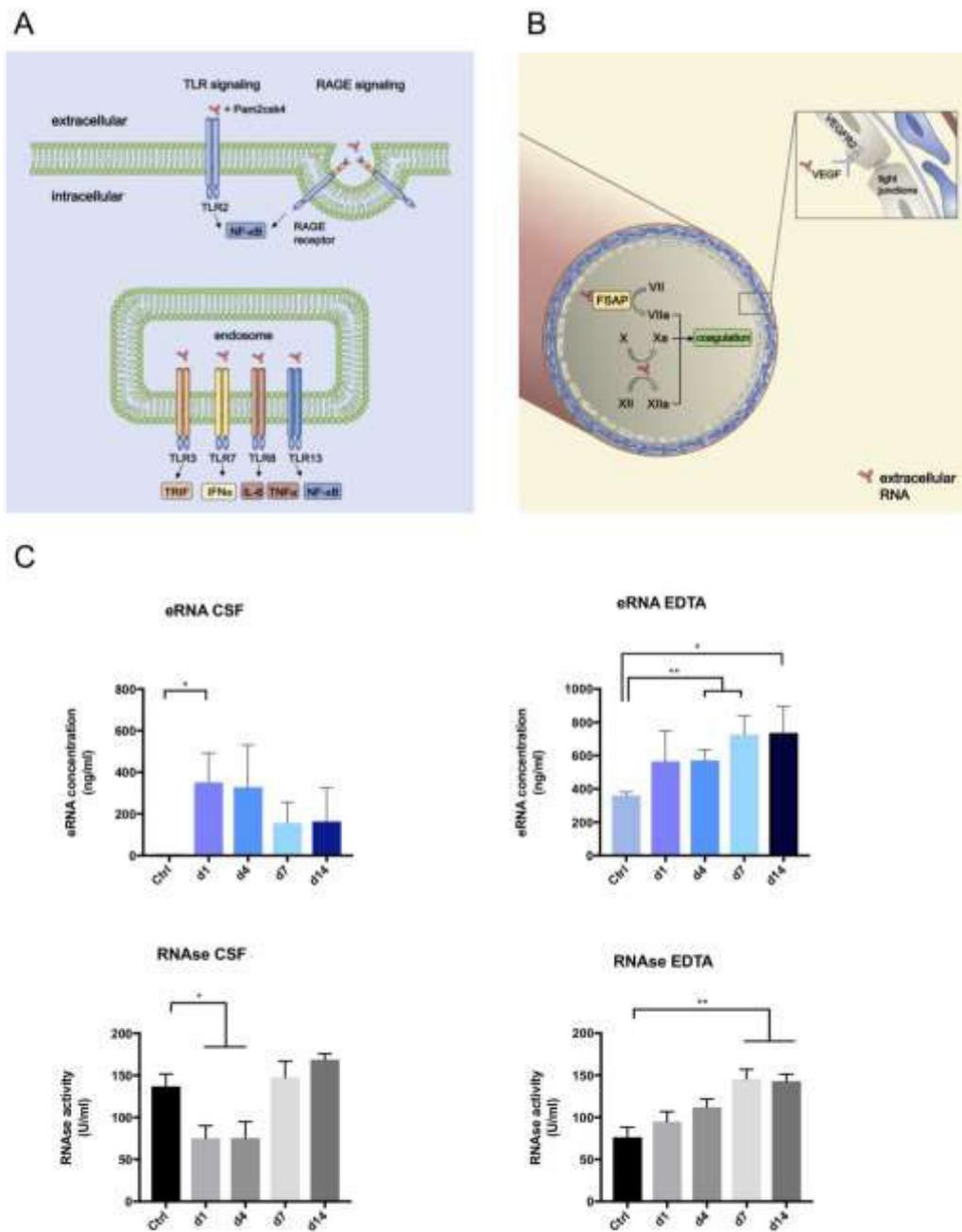
Results

In the acute stage of SAH, we found a significant increase of eRNA in the CSF on day 1 (Ctrl vs. SAH: 2ng/ml vs. 351.4ng/ml;p=0.033). In concomitance, RNase activity was significantly decreased in the CSF of SAH patients (Ctrl. Vs. SAH: 136.9U/ml vs. 75.23 U/ml; p=0.045). In peripheral blood samples, an eRNA peak was observed at a later time point on day 14 (Ctrl. Vs. SAH: 361ng/ml vs. 736.5ng/ml;p=0.039). This was paralleled by a significant increase of RNase activity in EDTA blood (Ctrl. Vs. SAH: 76.44U/ml vs. 143.1U/ml; p=0.004).

Conclusion

Aneurysmal SAH is associated with a significant increase in eRNA in the CSF, paralleled by a decrease in RNase activity, underpinning previously described mechanistic data on our mouse model. Hence, inhibition of eRNA may represent a potential strategy in modulating neuroinflammatory signaling but further ex vivo studies are needed to understand the underlying pathway mechanism.

Fig 1



Neurointensivmedizin II/*Neurocritical care II*

P096

Betablocker und Subarachnoidalblutung

The effects of the usage of betablockers on subarachnoid haemorrhage

M. Strey, J. Küchler, C. Ditz, V. M. Tronnier, K. Krajewski

Universitätsklinikum Schleswig-Holstein, Neurochirurgie, Lübeck, Germany

Objective

Previous studies have shown that preadmission betablockers (BB) could possibly be associated with cardioprotective and vasospasm-reducing benefits. Nebivolol has specifically been shown to increase nitric oxide levels and decrease oxidative stress after SAH. The aim of this study was to elucidate whether betablockers have an effect on vasospasm and/or vasospasm-related infarction, mortality and unfavorable outcome.

Methods

A retrospective analysis of all SAH patients treated at our single university center from 2007-2017 was performed. Data were obtained from the electronic patient chart, discharge summaries and questionnaires sent to all patients to determine the administration of beta blockers before the SAH. The following variables were dichotomized: Hunt and Hess grade and outcome according to the modified Rankin scale (mRS). Chi-squared and multiple logistic regression were performed with SPSS. $P < 0.05$ was considered significant.

Results

Among the 397 patients, data on medication prior to admission was available for 148 patients (37 with BB, 110 without BB). 109 patients had an angiographic confirmation of aneurysm (aSAH), 38 were non-aneurysmal (naSAH). 394 patients (129 with BB, 265 without BB) were included for analyses on BB usage on discharge. Among these, 306 patients had an angiographic confirmation of aneurysm, 81 were non-aneurysmal. Most aneurysmal patients had pretreatment with metoprolol ($n=20$) and in naSAH patients, metoprolol ($n=2$) and bisoprolol ($n=2$) were the most common preadmission BB. Nearly all patients were discharged with metoprolol ($n=98/105$ in aneurysmal, $n=18/22$ in naSAH). Preadmission BB were a significant factor for mortality in univariate analysis ($p=0.00$) in aSAH. Preadmission BB usage was also associated with an increased OR for mortality in multiple logistic regression analyses after correcting for age and Hunt & Hess grade (OR 3.19, CI: 1.0-10.0, $p=0.046$), whereas discharge with BB was associated with a lower OR for mortality (OR 0.046, CI: 0.01-0.13, $p=0.00$) and a higher OR for good outcome at 6 months (OR 3.17, CI: 1.51-6.65, $p=0.002$). Preadmission BB had no effects on vasospasm and/or associated infarction. For the naSAH group, no effects were found between BB use and vasospasm, vasospasm-associated infarction, death or outcome.

Conclusion

The role of preadmission BB is unclear. BB use on discharge may lower the risk of mortality and may be associated with a better outcome in aSAH patients.

Neurointensivmedizin II/Neurocritical care II

P097

Klinischer Einfluss der präoperativen Faktor XIII Aktivität beim chronischen und subakuten Subduralhämatom – eine retrospektive Studie

Clinical impact of preoperative factor XIII activity in chronic and subacute subdural haematoma – a retrospective study

P. Gutowski, S. Rot, U. Meier, J. Lemcke

Unfallkrankenhaus Berlin, Klinik für Neurochirurgie, Berlin, Germany

Objective

We analyzed the preoperative activity of factor XIII in patients with subdural hematoma (SDH) in the subacute and chronic stage. The purpose was to determine the predictive value of factor XIII deficiency regarding the recurrence rate and the incidence of postoperative complications. A factor XIII activity of > 70% activity is considered to be physiological.

Methods

We included patients after surgery (burr hole trepanation or craniotomy) for SDH. We excluded patients with acute subdural hematomas. Retrospective data assessment obtained the preoperative factor XIII activity, baseline characteristics (age, sex, oral anticoagulants and antiplatelet, co-morbidities), radiological findings (recurrence of SDH, postoperative acute subdural hematoma) and the neurological outcome (Glasgow Outcome Scale) on discharge. For the analysis we dichotomized the patients into two groups – chronic SDH and SDH in subacute stage.

Results

One hundred and sixty five (165) patients with chronic/subacute subdural hematoma were treated from January 2018 until October 2019. We had a dropout of 54 patients due to missing laboratory examination of factor XIII activity in the preoperative setting. Ninety patients were treated for chronic SDH and 21 patients for subacute SDH. Twenty (18%) patients had a recurrence of the SDH with the need for surgery. Twelve (10%) patients developed a postoperative complication requiring surgery. In 22 (19%) patients the preoperative factor XIII activity was equal or less than 70%. In 3 (15%) of the patients with recurrence of the SDH, factor XIII activity was equal or less than 70%. In 5 (41%) of the patients with postoperative complications decreased factor XIII activity was measured. Before operation, 59 (52%) patients had oral anticoagulants or antiplatelet therapy.

Conclusion

Factor XIII deficiency is a common finding (19% of the patients) in the preoperative laboratory examination. Although it does not seem to play a role in the risk of recurrence of SDH, it does have an impact on the clinical course regarding postoperative complications.

Neurointensivmedizin II/*Neurocritical care II*

P099

Lungenembolie in Patienten mit aneurysmatischer Subarachnoidalblutung *Pulmonary embolism in aneurysmal subarachnoid haemorrhage*

D. Dubinski¹, S. Y. Won¹, F. Keil², B. Behmanesh¹, N. Brawanski¹, F. Raimann³, V. Seifert¹, C. Senft¹, J. Konczalla¹

¹Universitätsklinikum Frankfurt am Main, Neurochirurgie, Frankfurt am Main, Germany

²Universitätsklinikum Frankfurt am Main, Klinik für Neuroradiologie, Frankfurt am Main, Germany

³Universitätsklinikum Frankfurt am Main, Anästhesiologie, Frankfurt am Main, Germany

Objective

Pulmonary embolism (PE) is a dreaded complication with high morbidity and mortality rates. Patients with aneurysmal subarachnoid hemorrhage constitute a critically ill cohort with often strict contraindications to conventional embolism treatment. The aim of the present study is to identify risk factors for pulmonary embolism in this demanding cohort.

Methods

Retrospective analysis of patients with suspected PE and thoracic CT scan included: Age, gender, admission status, treatment modality, the presence of deep vein thrombosis, resuscitation, in-hospital mortality, present anticoagulation, coronary artery disease, diabetes mellitus, smoking status, hypertension, ABO blood type, antidepressants, migraine, hematological analysis, early hydrocephalus, Glasgow outcome scale at 6 months and mRS at 6 months, VP-Shunt at 6 months, cerebral vasospasm, delayed ischemic neurological deficit.

Results

A total of 60 patients had a thoracic CT scan suspected pulmonary embolism. Computer tomography confirmed 25 cases (42%). Smoking ($p<0.02$) and deep vein thrombosis ($p<0.02$) were identified as significant risk factors for pulmonary embolism. Patients with PE had a statistically significant lower Karnofsky, and higher extended Glasgow outcome scale values at 6 months than patients without PE ($p<0.001$, and $p<0.02$) respectively. The presence of vitamin K antagonists at admission and the development of cerebral vasospasm in the clinical course were protective against PE ($p<0.05$, and $p<0.02$) respectively.

Conclusion

Patients with aneurysmal subarachnoid hemorrhage that present with a history of tobacco use are at an elevated risk for PE which in turn is associated with poor outcome. This cohort should therefore be put under intensified monitoring.

Neurointensivmedizin II/*Neurocritical care II*

P100

Kombinierte Anwendung von Nimodipin und Amilorid verstärkt neuronalen Zelltod in einem *in vitro* Modell der Hirnischämie

Combination of nimodipine and amiloride increases neuronal cell death in an in-vitro brain ischemia model

J. Ort¹, B. Kremer¹, L. Grüßer², R. Blaumeiser-Debarry², M. Coburn², H. R. Clusmann¹, A. Höllig¹, U. Lindauer¹

¹Universitätsklinikum RWTH Aachen , Klinik für Neurochirurgie, Aachen, Germany

²Universitätsklinikum RWTH Aachen , Klinik für Anästhesiologie und Intensivmedizin, Aachen, Germany

Objective

Effective ways of pharmacological neuroprotection are one of greatest goals in modern medicine. The influx of calcium is widely regarded as a final common pathway in neuronal cell death. We postulated that combined inhibition of L-type calcium channels and the acid-sensing ion channel 1a (ASIC1a) using the two clinically established drugs nimodipine and amiloride may result in neuroprotection and thus reduced cell death using a well-established in-vitro model of cerebral ischemia.

Methods

Hippocampus-slices from 4-7 days old mice pups (C57BL/6N) were prepared and cultivated in growth medium at 37°C and 5% CO₂ for 14 days. Baseline images for cell death assessment were obtained using propidium iodid (PI) staining and fluorescence microscopy. Slices then underwent oxygen-glucose deprivation (with 95% N₂, 5% CO₂) for 60 minutes. Afterwards slices received no treatment (control group; n=101), 2 Vol.% dimethyl-sulfoxide (DMSO) (solvent control; n=45) or treatment consisting of either 100µM amiloride alone (n=43) or a combination with 10µM (n=47) or 20µM (n=46) nimodipine. After incubation for 72h cell death was assessed using the pre-described PI staining and fluorescence microscopy. We used a Kruskal-Wallis test to calculate p-values and posthoc Dunn's Test (using GraphPad Prism Version 8.2.0) to correct for multiple comparisons, with p<0.05 regarded as statistically significant

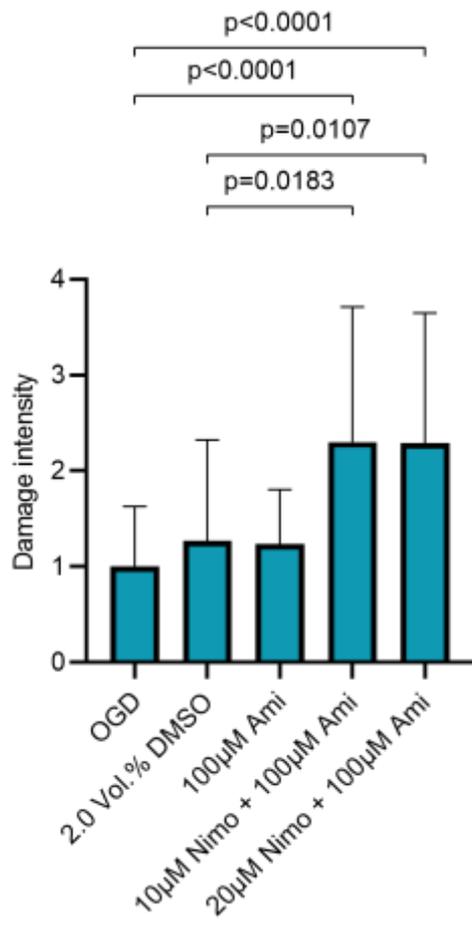
Results

Slices receiving only DMSO as vehicle or additional amiloride did not show any statistically significant differences in levels of cell death. Slices receiving the combination of 100µM amiloride and 10µM or 20µM nimodipine respectively at 2.0 Vol.% DMSO displayed a significant increase in cell damage levels at 72 hours after OGD compared to the OGD control group (p=0.0001 for both).

Conclusion

No effective neuroprotection could be observed using a combination of nimodipine and amiloride. Interestingly, the combination of the two drugs statistically impaired cell outcome after OGD. A possible explanation might be unspecific effects of amiloride combined with increased extracellular calcium levels through L-type calcium blockage. Our results suggest that the simultaneous administration of nimodipine and amiloride (e.g. during the treatment of delayed cerebral ischemia) should be critically evaluated.

Fig 1



Neurointensivmedizin II/*Neurocritical care II*

P102

Zusammensetzung der Hämatomflüssigkeit von chronischen Subduralhämatomen – Ergebnisse der prospektiven TOSCAN Studie

Composition of chronic subdural haematoma content – results of the prospective TOSCAN trial

C. Fung¹, D. H. Heiland¹, P. Schucht², A. Raabe², J. Beck¹

¹Universitätsklinikum Freiburg, Neurochirurgie, Freiburg, Germany

²Universitätsspital Bern, Neurochirurgie, Bern, Switzerland

Objective

To evaluate the fluid content in chronic subdural hematoma (cSDH) patients and analyze their effect on the outcome of patients.

Methods

In the setting of the prospective trial we evaluated the fluid content. Hematoma fluid was withdrawn during initial evacuation and analyzed with respect to protein amount, specific weight, albumin, osmolarity, hemoglobin, erythrocytes and leucocyte amount. Principal component analysis and dimensional reductions as well as Partitioning Around Medoids clustering was used to identify subgroups based on similarities across all patient's hematoma fluid. Outcome was assessed 6 months after evacuation of cSDH and dichotomized into favorable (mRS 0-3) and unfavorable (mRS 4-6).

Results

361 patients were included in the trial. Hematoma fluid was available for analysis in 283 patients. Cluster analysis revealed two subgroups of patients based on differences in hemoglobin (cluster 1 2.73 mg/dl vs cluster 2 12.2 mg/dl, $p < 0.001$) and erythrocyte count (cluster 1 0.7 mio/dl vs cluster 2 4.1 mio/dl, $p < 0.001$). The remaining parameters did not show a significant difference between the two groups. Patients of cluster 2 showed a significantly worse outcome with respect to mRS 6 months (mRS 4-6 cluster 1 4.4% cluster 2 13.2% $p = 0.024$) after evacuation of cSDH. In addition, a significantly higher risk of recurrence was observed in cluster 2 (cluster 1 20% vs cluster 2 26.5%).

Conclusion

Cluster analysis yields two distinct groups of cSDH patients. The groups were defined by significant differences in hemoglobin and erythrocytes. Patients with higher amounts of hemoglobin and erythrocytes in their hematoma fluid more often had an unfavorable outcome.

Neurointensivmedizin II/*Neurocritical care II*

P103

Elektrolytstörungen nach Schädel-Hirn-Trauma *Electrolyte disorders after traumatic brain injury*

A. Wagner, J. Heim, L. Mikhina, M. C. Simonstadt, N. Lange, M. Wostrack, B. Meyer, J. Gempt

Klinikum rechts der Isar München, Neurochirurgische Klinik, München, Germany

Objective

To examine the incidence and risk factors for the occurrence of electrolyte disorders after traumatic brain injury (TBI).

Methods

A retrospective analysis of hospital records and digital imaging was conducted for patients admitted to our intensive care unit for mild, moderate or severe TBI for a minimum of 4 days. Demographic variables, modified Rankin Scale (mRS) scores and serum chemistry panels were reviewed and used in regression models to predict outcome.

Results

Between September 2008 and September 2018, 420 patients with TBI and complete records were included in our analysis. On admission, a mild TBI was noted in 26.6% of patients, a moderate TBI in 12.0% and a severe TBI in 61.4%. While the mild TBI subgroup presented with an mRS >1 in 35.9% of cases, the moderate (75.9%) and severe (98.0%) TBI groups presented significantly more often with a substantial neurological deficit. These proportions decreased non-significantly to 29.6% for mild TBI ($p=0.629$), significantly to 51.7% for moderate TBI ($p=0.008$) and significantly to 72.7% for severe TBI ($p<0.001$) by discharge. Patients with a severe TBI underwent at least one surgical intervention in 82.4%, which was significantly more frequent than patients with mild (32.8%; $p<0.001$) and moderate TBI (58.6%; $p<0.001$). Hyponatremia represented the most common electrolyte disorder and was noted in 23.7% of all patients, without significant difference between TBI grades. Hypernatremia was seen significantly more often among patients with severe TBI (48.0%) versus both mild (17.2%) and moderate TBI (20.7%; $p<0.001$). The binary logistic regression model revealed that patients with severe TBI (OR 3.15; $p=0.005$) and at least 2 surgical interventions (OR 3.11; $p=0.024$) were more likely to develop hyponatremia, while the presence of intraventricular hemorrhage or symptomatic vasospasms did not contribute to the model. When controlling for age, TBI grade and number of surgical interventions, the presence of hyponatremia prolonged the hospital stay by an average of 10 days ($p<0.001$).

Conclusion

Hyponatremia represents the most common electrolyte disorder occurring after TBI and is associated with a delayed hospital discharge. Patients with severe TBI and multiple surgical interventions are more likely to develop hyponatremia.

Neurointensivmedizin II/*Neurocritical care II*

P104

Entwicklung eines Monitors zur Detektion von reduzierter intrakranieller Compliance und gestörter Autoregulation

Development of a bedside monitor to detect reduced intracranial compliance and impaired autoregulation

M. Proescholdt¹, S. Wolf², S. Bele¹, A. Brawanski¹, R. Faltermeier¹

¹Universitätsklinikum Regensburg, Neurochirurgie, Regensburg, Germany

²Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

Objective

In neurocritical care, it is crucial to detect pathophysiological conditions such as reduced intracranial compliance or impaired cerebral autoregulation as early as possible. To achieve this goal, an array of different brain monitoring techniques was established. However, focusing on specific parameters with fixed thresholds may not be adequate for finding the optimal treatment algorithm. In contrast, it is necessary to integrate the multimodal monitoring data into a platform making it possible to unmask critical changes in intracranial dynamics. We therefore developed a point of care system, which allows the detection of brain swelling and impairment of autoregulation, based on model simulations that predict specific correlation between ABP and ICP under the above mentioned pathophysiological conditions.

Methods

Initially, we developed a mathematical toolkit called selected correlation analysis (sca) that reliably detects negative and positive correlations between arterial blood pressure (ABP) and intracranial pressure (ICP) data. To identify slow homeostatic positive or negative correlations between isochronic segments of ABP and ICP, we utilized coherence and power spectra calculations (lsc) with the multi-taper method (MTM). In addition, we calculated the mean Hilbert phase difference between these segments (mhpd). If mhpd is higher or equal to 110 degree a correlation is called negative (scn) and indicates reduced intracranial compliance without loss of autoregulation. Conversely if the mhpd is lower or equal 70 degree, the correlation is defined as called positive (scp) and therefore suggests an impaired autoregulation. Finally, we established a method that detects the rate of false positives for fixed pairs of thresholds (lsc,lmhpd), to determine a valid significance level for all future patients.

Results

We calculated the error rates as a function of the predefined thresholds for each individual out of a patient cohort of 52 patients in a retrospective way. We subsequently incorporated these results into an analytical software platform, which has now been applied in four test patients. Our preliminary experience indicates a robust and stable detection of reduced intracranial compliance and / or impaired cerebral autoregulation.

Conclusion

Our data demonstrate that an integrated real time analysis tool to process brain multimodal monitoring data may be useful for the early detection and management of pathophysiological events.

Neurointensivmedizin II/*Neurocritical care II*

P105

Dekompressive Kraniektomie nach aneurysmatischer Subarachnoidalblutung – Risiko-Score für frühe Vorhersage

Decompressive craniectomy after aneurysmal subarachnoid haemorrhage – a risk score for early prediction

R. Jabbarli^{1,2}, M. Darkwah Oppong¹, R. Rölz², D. Pierscianek¹, M. J. Shah², K. H. Wrede¹, J. Beck², U. Sure¹

¹Universitätsklinikum Essen, Klinik für Neurochirurgie, Essen, Germany

²Universitätsklinikum Freiburg, Klinik für Neurochirurgie, Freiburg, Germany

Objective

The prognosis of patients with aneurysmal subarachnoid hemorrhage (SAH) requiring decompressive craniectomy (DC) is usually poor. Proper selection and early performing of DC might improve the patients' outcome. We aimed at developing a risk score for the prediction of DC after SAH.

Methods

All consecutive SAH cases treated at the University Hospital of Essen between January 2003 and June 2016 (test cohort) and the University Hospital of Freiburg between January 2005 and December 2012 (validation cohort) were eligible for this study. Various parameters collected within 72 hours after SAH were evaluated through univariate and multivariate analyses to predict separately primary (PrimDC) and secondary DC (SecDC).

Results

The final analysis included 1376 patients. The constructed risk score included the following parameters: intracerebral ("**Parenchymal**") hemorrhage (1 point), "**Rapid**" vasospasm on angiography (1 point), **E**arly cerebral infarction (1 point), aneurysm **S**ack > 5 mm (1 point), clipping ("**Surgery**", 1 point), age **U**nder 55 years (2 points), Hunt&Hess grade ≥4 ("**Reduced consciousness**", 1 point) and **E**xternal ventricular drain (1 point). The **PRESSURE** score (0-9 points) showed high diagnostic accuracy for the prediction of PrimDC and SecDC in the test (AUC=0.842/0.818) and validation cohorts (AUC=0.903/0.823) respectively. 63.7% of the patients scoring ≥6 points required DC (vs. 12% for the PRESSURE<6 points, p<0.0001). In the subgroup of the patients with the PRESSURE≥6 points and absence of dilated/fixed pupils, PrimDC within 24 hours after SAH was independently associated with a lower risk of an unfavorable outcome (modified Rankin Scale >3 at 6 months), than in individuals with later or no DC (p=0.02).

Conclusion

Our risk score was successfully validated as a reliable predictor of DC after SAH. The PRESSURE score might present a background for a prospective randomized clinical trial addressing the utility of early prophylactic DC in SAH.

Funktionelle Neurochirurgie & Neurointensivmedizin / *Functional neurosurgery & neurocritical care*

P106

Drahtlose Spinal Cord-Stimulation zur Behandlung von neuropathischen Schmerzen – eine Single-Center Erfahrung

Wireless spinal cord stimulation technology for the treatment of neuropathic pain – a single-centre experience

M. M. Hajiabadi¹, B. Campos¹, C. Geist², A. W. Unterberg¹, R. Ahmadi¹

¹Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

²Universitätsklinikum Heidelberg, Anästhesie, Heidelberg, Germany

Objective

Spinal cord stimulation (SCS) is an effective method to treat therapy-resistant neuropathic pain. A new wireless SCS technology, which was introduced in recent years, promises minimal invasive SCS as well as additional advantages such as a wide range of stimulation paradigms and 3-Tesla MRI compatibility. Here, we report on our single-center experience with this new wireless SCS technology and focus our report on handling of the device as well as on potential advantages and disadvantages of wireless SCS compared to conventional SCS.

Methods

We retrospectively evaluated 12 patients suffering from therapy-resistant neuropathic pain, who were implanted with a wireless Stimwave® SCS system from 2017 to 2019. Potential issues related to handling and usability of the SCS device were evaluated from a patients' as well as from a surgeon's perspective. Any surgical complications were recorded. To evaluate treatment response, we assessed changes in pain ratings according to a visual analogue scale (VAS) after SCS.

Results

Mean follow-up was 228 d (95% CI, 20 d – 518 d). After an average test period of 52 d (95% CI, 11 d – 104 d), n=9/12 patients (75%) had reached pain relief greater than 50% with an average pain relief of 69.5 % (95% CI, 50.0 % – 85.0 %). On average, patients tested 2.2 different stimulation paradigms, with frequencies ranging from 60 Hz to 10 kHz but there was no preferred stimulation paradigm. There were no surgical complications and no reported incidents with the 3-Tesla MRI-compatibility. N = 3/12 patients reported discomfort from wearing the SCS antenna and one patient complained about a short battery life of the controller device. Other than that, we did not record any handling issues nor did we record any relevant local discomfort associated with the implanted SCS device. Hardware complications were seen in one patient, who suffered an epidural electrode displacement.

Conclusion

Minimally invasive implantation of wireless Stimwave® SCS systems was feasible. The device offered a broader range of stimulation paradigms compared to conventional SCS devices, an allowed for a prolonged testing phase and continuous adjustment of SCS programs.

Funktionelle Neurochirurgie & Neurointensivmedizin /*Functional neurosurgery & neurocritical care*

P107

Der Effekt funktioneller Konnektivität des motorischen Systems auf die Ruhemotorschwelle – eine Replikationsstudie

The impact of functional connectivity of the motor system on the resting motor threshold – a replication study

M. Engelhardt^{1,2}, D. Komnenić³, L. Fekonja^{1,4}, F. Roth¹, L. Kawelke¹, C. Finke^{2,3}, T. Picht^{1,4}

¹Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

²Charité – Universitätsmedizin Berlin, Einstein Centre for Neurosciences, Berlin, Germany

³Humboldt-Universität zu Berlin, Berlin School of Mind and Brain, Berlin, Germany

⁴Humboldt-Universität zu Berlin, Cluster of Excellence Matters of Activity, Berlin, Germany

Objective

Cortical excitability measured with the resting motor threshold (RMT) shows large inter-individual variability. Several anatomical factors contributing to this variability have been suggested, however recent evidence also suggests an impact of functional connectivity of the motor system on the RMT. The aim of this study was to validate findings on the impact of functional connectivity between the primary motor cortex (M1) and dorsal premotor cortex (PMd) as well as other motor areas on the RMT. The impact of the above-mentioned predictors is compared to the coil-to-cortex distance (CCD) as a known predictor of the RMT.

Methods

The RMT was measured bi-hemispherically in 35 healthy right-handed subjects (38.7 ± 13.7 years, 19 females) without any neurological or psychiatric condition using navigated TMS. Resting-state functional connectivity was assessed inter-hemispherically on M1 and intra-hemispherically between M1 in relation to primary somatosensory cortex (S1), dorsal and ventral premotor cortex (PMd, PMv), supplementary motor area (SMA) and pre-SMA. Other factors included in the analysis were age, sex and CCD. The relationship between each predictor and the RMT was assessed with a linear mixed model to account for non-independence of observations within the same subjects. Further, we evaluated the added impact of a combined model.

Results

Functional connectivity between M1 and PMd did not significantly predict the RMT ($b = 0.05$, $t(34) = 0.02$, $p = 0.99$). In addition, functional connectivity between further regions did not predict the RMT either. Singularly CCD showed a significant impact on the RMT ($b = 1.64$, $t(34) = 6.29$, $p < .001$). The model with CCD explained 51% of the variance of the RMT and was advantageous over a simpler model containing only the random effect for subjects ($\chi^2(1) = 28.48$, $p < 0.001$). A model containing all variables explained only 56% of the variance and thus, did not prove better than the previous model ($\chi^2(9) = 6.60$, $p = 0.68$).

Conclusion

We could not replicate previous findings on the impact of functional connectivity to non-primary motor areas on the RMT in a larger sample. The distance between stimulation coil and cortex remains the most important and well-established predictor for the RMT.

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P109

Etablierung eines an die *in vivo* Bedingungen angepassten *in vitro* Modells zur Untersuchung des Einflusses der elektrischen Stimulation auf inflammatorische Mediatoren

Establishment of an *in vivo* adapted *in vitro* model of deep brain stimulation and investigations regarding the influence of electric stimulation on inflammatory mediators

H. Molkewehrum, C. Kubelt, M. Synowitz, J. Held-Feindt, A. K. Helmers

Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Kiel, Germany

Objective

Deep brain stimulation (DBS) is a neurosurgical therapy especially for movement disorders but also psychiatric diseases as depressions with a therapy-refractory course are rising. Even if the therapeutic results are mostly satisfactory, the mechanism of action is not completely understood. Possibly the effect of DBS is partly based on changed cytokine/ chemokine concentrations of the surrounding brain cells. Thus, in this study we established an *in vivo* adapted *in vitro* model of DBS and analyzed the influence of an electric stimulation on different brain cells.

Methods

According to conditions used in DBS patients, we established an *in vitro* model to electrically stimulate SVGA- (Astrocytes), HMC3- (Microglia) and SH-SY5Y-cells (Neurons). To exclude an influence on apoptosis or proliferation rates, cells were stained by TUNEL-Assay and proliferation rates were determined by cell counting compared to control samples, respectively. Additionally, we stimulated brain cells with 2mV for 24 hours and measured the expression of different cytokines and chemokines (CXCL12, CXCL16, CCL2, CCL20, IL1 β , IL6) by qrtPCR and verified significant expression differences by fluorescence staining.

Results

The *in vivo* adapted *in vitro* DBS-model was established successfully. An influence on cell proliferation and apoptosis rates was not observed. mRNA expression of IL1 β in SH-SY5Y-cells and CXCL12 in SVGA-cells were significantly induced, and these results were confirmed by fluorescence staining.

Conclusion

The mechanism of action of DBS seems to be very complex and its influence on the expression of cytokines and chemokines should be further explored. The establishment of this DBS-model could lead to a better understanding of these effects.

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P110

Rezidivierende Trigeminusneuralgie nach mikrovaskulärer Dekompression – Ergebnisse der mikrochirurgischen Reoperation in einer Serie von 27 Patienten
Microsurgical re-decompression for recurrent trigeminal neuralgia after previous microvascular decompression in a series of 27 patients

G. Hatipoglu Majernik, S. Al-Afif, H. E. Heissler, J. K. Krauss

Medizinische Hochschule Hannover, Klinik für Neurochirurgie, Hannover, Germany

Objective

Microvascular decompression (MVD) is a well-accepted treatment modality for trigeminal neuralgia (TN). The initial success rate is high, however, in a subset of patients TN might recur in the long-term. Recurrent TN after MVD might be due to several causes and treatment algorithms remain unclear. Here, we present the surgical findings and clinical outcome of patients with recurrent TN after MVD who underwent microsurgical re-decompression.

Methods

Twenty-seven patients with recurrent TN who underwent microsurgical re-decompression over a period of 10 years were analysed. There were 14 women (54%) and 13 men (46%) with a mean age of 60 years (range, 35-82 years). Patients with multiple sclerosis were excluded. All patients had magnetic resonance imaging before surgery. Microsurgical re-decompression included dissection of the previously inserted Teflon and of scar tissue avoiding any damage to the trigeminal nerve. In no case the trigeminal nerve was lesioned, "combed" or dissected. New Teflon felt was placed in case an offending artery was found. There was no operative morbidity or mortality. All patients were available for postoperative follow-up. The outcome of the repeat intervention was graded according to the Barrow Neurological Institute (BNI) Pain intensity score. Follow-up was analysed postoperatively at 3, 12 and 24 months and at long-term (mean 48.1 months).

Results

Recurrent TN was associated with the following findings as identified intraoperatively: arachnoid adhesions/scar tissue at the trigeminal entry zone (23/27), deformation of the trigeminal nerve/Tefloma (14/27), new nerve/vein contact (15/27), new nerve/artery contact with marked pulsations (1/27) and compression of the trigeminal nerve by the electrode in cavum Meckeli used for treatment of neuropathic pain (1/27). 23/27 patients had a combination of findings. Early postoperative pain relief was achieved in all patients. 23 patients were available for 24- month follow-up or longer. Of these, 16/23 patients (69%) had BNI I, 5/23 patients (22%) had BNI IIIa, and 2 patients (9%) had a BNI pain score of IV or V.

Conclusion

Microsurgical re-decompression was highly successful for recurrent TN. There were no serious side effects and the frequency of postoperative hypaesthesia was low. We conclude that microsurgical re-decompression completely preserving the trigeminal nerve is a feasible and beneficial treatment option in this context. Manoeuvres such as dissecting or combing the trigeminal nerve may be avoided.

Funktionelle Neurochirurgie & Neurointensivmedizin /*Functional neurosurgery & neurocritical care*

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Eine Kombination aus 3D-Computertomographischer und elektromagnetischer Navigation im Hybrid-Operationsaal für perkutane Trigemini-Eingriffe

Combination of 3D-CT and electromagnetic navigation in the hybrid suite for percutaneous trigeminal procedures

C. Ugas, F. Roser, L. Rigante, E. Francois

Cleveland Clinic Abu Dhabi, Neurosurgery, Abu Dhabi, United Arab Emirates

Objective

Trigeminal percutaneous ablative procedures for trigeminal neuralgia have been widely used for large groups of patients, including such methods as alcohol or glycerol injections, balloon compression, and radiofrequency thermocoagulation of the gasserian ganglion. These procedures require cannulation of the foramen ovale and its precise visualization using fluoroscopy is frequently difficult, and it might affect the length of the procedure. We describe our experience about the accuracy, safety and simplicity of using electromagnetic neuronavigation and cone-beam CT in the hybrid OR suite as a guiding technique for cannulation of the foramen ovale in percutaneous trigeminal procedures.

Methods

We retrospectively analysed data from patients with trigeminal neuralgia who had clinical indications for percutaneous trigeminal pain procedures in our hospital from June 2016 to November 2019. Electromagnetic navigation-assisted trigeminal nerve blocks, balloon compression or radiofrequency ablations were performed by using pre-operative brain MRI and/or CT scans. Additionally, intraoperative DynaCT and/or fluoroscopy was used for foramen ovale cannulation confirmation.

Results

Fourteen patients had 21 procedures during the study period. Most patients were male (n=8, 57.14%) and the age range was from 28-80 years old. Interventions performed consisted of nine balloon compressions, 9 radiofrequency ablations and 3 nerve blocks. The mean duration of the surgical procedure was 31.28 ± 19.85 minutes. Average radiation exposure was 104.22 mGy. Foramen ovale cannulation was successful in all cases and there were no complications.

Conclusion

The combination of electromagnetic neuronavigation and intraoperative DynaCT is a simple, fast, accurate and effective alternative for percutaneous trigeminal nerve procedures.

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P112

Neuromodulative Behandlung chronischer Cluster-Kopfschmerzen (Platten- versus Stabelektrode) – retrospektive Analyse von 5 Fällen

Neuromodulatory treatment of chronic cluster headache (surgical lead versus percutaneous lead) – a retrospective analysis of 5 cases

P. Haas, M. Tatagiba, M. Morgalla

Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

Objective

Cluster headache (CH) is a rare entity of the trigeminal autonomic cephalgias, which remains difficult to treat. Neuromodulatory procedures such as bilateral greater occipital nerve stimulation (ONS), sphenopalatine ganglion stimulation (SPG) or spinal cord stimulation (SCS) represent promising surgical approaches. However, the use of percutaneous leads in the high cervical area during SCS often leads to dislocations due to the increased mobility and the small target region (C2/3). Surgical leads may offer advantages in this situation. In the literature only case reports or studies with low case numbers on SCS in CH exist so far. We report our results from 5 patients treated with SCS by percutaneous or surgical leads.

Methods

We treated 5 patients (5 males, median age 52 [31-56]) with drug-resistant CH using SCS (level C2/3; 4 percutaneous, 1 surgical lead) in our clinic between 07/2017 and 04/2019 after a successful test stimulation (50% reduction in attack frequency). A retrospective descriptive analysis was performed with pre- and postoperative assessment of the Brief Pain Inventory (BPI), Pain Disability Index (PDI), Pain Catastrophizing Scale (PCS), Beck Depression Inventory II (BDI-II), Short Form 36 (SF-36), Symptom Check List (SCL-90-R) and Cluster Headache Severity Scale (CHSS).

Results

CHSS improved from pre- to postoperative by median 5/12 [0-12]. The BPI [median improvement 41.7% [0-100]], PDI (median improvement PR 69 [1-81]), PCS (median improvement PR 81 [2-94]), BDI (median improvement 8/63 [0-31], SCL-90 [median improvement t-value GSI 5 [0-36]) and SF-36 (emotional well-being median improvement t-value 28 [48-100]) also showed improvements. Overall, 4 out of 5 patients showed improvement in all scores, 3 of them with clinical symptom clearance and one with slight symptom reduction. In one case, neither a clear change of the score results nor of the symptoms was achieved. Relevant side effects did not occur in any patient. One patient had to have a probe repositioned one month after implantation. Another patient with implanted and recurrently defective percutaneous leads was already revised four times ex domo before a surgical lead was inserted in domo. This was revised once in the case of a probe defect and the patient has been symptom-free since then.

Conclusion

Cluster headaches can be well treated with SCS as a neuromodulatory procedure. However, percutaneous leads showed a tendency to dislocation. In this case, surgical leads can offer a possible advantage.

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P113

Invasives Neuromonitoring in gut gradige Subarachnoidalblutungen

Role of invasive neuromonitoring in good-grade subarachnoid haemorrhage patients

M. Veldeman¹, W. Albanna¹, M. Weiss¹, C. Conzen¹, T. P. Schmidt¹, H. Schulze-Steinen^{1,2}, M. Wiesmann^{1,2,3}, H. R. Clusmann¹, G. A. Schubert¹

¹Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neurochirurgie, Aachen, Germany

²Universitätsklinikum RWTH Aachen , Operative Intensivmedizin, Aachen, Germany

³Universitätsklinikum RWTH Aachen , Klinik für Neuroradiologie, Aachen, Germany

Objective

In aneurysmal subarachnoid hemorrhage (SAH), good-grade patients (H&H Grade I-II) tend to have a more favorable prognosis. Nonetheless, a relevant proportion of patients may still develop delayed cerebral ischemia (DCI) and worsening of outcome. If secondary deterioration occurs, invasive neuromonitoring (INM) may help to identify additional waves of DCI events and guide treatment.

Methods

We performed a prospective cohort analysis of all good-grade SAH patients referred to a single tertiary care center between 2010 and 2018. A total of 135 patients were enrolled in this observational trial. The cohort was separated into two groups, one before (pre-INM; n=60) and one after the introduction of invasive neuromonitoring in 2014 (post-INM; n=75). Secondary worsening prohibiting neurological examination occurred in 26 cases in the pre-INM group and in 28 cases in the post-INM group. In the latter group, patients received INM with either parenchymal oxygen saturation measurement (ptiO₂), cerebral microdialysis (CMD) or both.

Results

There was a significant reduction in the rate of silent infarction after the introduction of INM (15.0 % vs. 4.0% p=0.026), with lower rates of overall DCI related infarctions and overall DCI related mortality, though the difference was not statistically significant (20.0% vs. 13.3%; p=0.297; 14.6% vs. 10.6%; p=0.265). In patients with secondary deterioration, the rate of favorable outcome was higher in the post-INM group (85.2% vs. 68.4%; p=0.252), but the difference was not statistically significant.

Conclusion

The majority of good-grade SAH patients eventually recover with favorable outcome. However, in patients with secondary deterioration, invasive neuromonitoring may help to guide DCI treatment and reduce the rate of silent infarction.

Aneurysmen experimentell/*Aneurysms experimental*

V111

Expression von Cyclooxygenase 2 (COX-2) in der Wand zerebraler Aneurysmen in Korrelation zur MRT-Bildgebung

Expression of cyclooxygenase 2 (COX-2) in the wall of human cerebral aneurysms and correlation to MRI

J. Rodemerk¹, A. Junker², B. Chen^{1,3}, D. Pierscianek¹, P. Dammann¹, A. Radbruch⁴, H. H. Quick^{5,3}, S. Maderwald³, Y. Zhu⁶, R. Jabbarli¹, U. Sure¹, K. H. Wrede^{1,3}

¹Universitätsklinikum Essen, Neurochirurgie, Essen, Germany

²Universitätsklinikum Essen, Neuropathologie, Essen, Germany

³Universität Duisburg-Essen, Erwin L. Hahn Institute for Magnetic Resonance Imaging, Essen, Germany

⁴Universitätsklinikum Essen, Institut für Diagnostische und Interventionelle Radiologie und Neuroradiologie, Essen, Germany

⁵Universitätsklinikum Essen, Erwin L. Hahn Institute for Magnetic Resonance Imaging, Essen, Germany

⁶Universitätsklinikum Essen, Molekulare Neurochirurgie, Essen, Germany

Objective

The pathophysiology of development, growth and rupture of cerebral aneurysms is only partially understood. Cyclooxygenase 2 (COX-2) converts arachidonic acid to PGH₂ which in turn is isomerized to PGE₂. COX-2 plays an important role in the inflammatory pathway of the human body. Expression of COX-2 seems to be related to aneurysm instability and might serve as a future target for medical treatment and rupture prevention. The aim of this feasibility study was to investigate COX-2 expression in the wall of cerebral aneurysms and correlation to image features in clinical (1-3 Tesla) MRI and ultra-high field 7 Tesla MRI.

Methods

The study group comprised 5 patients with partly thrombosed saccular intracranial Aneurysms (IAs), one ruptured, 4 unruptured which underwent microsurgical treatment. Formaldehyde fixed paraffin embedded samples were immunohistochemically (IHC) stained with a monoclonal antibody against COX-2 (DAKI, Clone: CX-294). Perls's Prussian blue staining and MRI images were correlated to the IHC, that was analysed with the "Trainable Weka Segmentation" (doi:10.1093/bioinformatics/btx180).

Results

Aneurysm dome size ranged between 5 to 40 millimetres. Proportion of COX-2 positive cells ranged between 3.7 % to 79.98 %. The expression of COX-2 correlated positively with aneurysm size, but in the smallest aneurysm which had a relatively high expression of 47.85 % COX-2 positive cells. At all field strength, MRI shows a wall hypointensity due to iron deposition (Figure 2 A, B).

Figure 1. 27-millimetre Aneurysm. A, Circulus 3T TOF-MRI shows a hypointensity surrounding the aneurysm, asterisk indicating the aneurysm wall. B in situ. C, 0.5x magnification IHC COX-2 staining (48.54 % coverage of positive cells), asterisk indicating in both slides positive stained aneurysm wall. D, 0.5x magnification Perls's Prussian blue.

Figure 2. Largest (40-millimetre) aneurysm. SWI MRI at 1T a with hypointensity (A), not as strong as in the SWI 7T MRI (B), asterisk indicating the aneurysm wall. This hypointensity correlates with the high iron deposition in the Perls's Prussian blue staining (C, 40x magnification). COX-2 positive cells cover 79.98 % of the 40x magnification IHC slide (D).

Conclusion

As COX-2 could be a future molecular target for aneurysm treatment the hypointense signal patterns in TOF and SWI have a potential to serve as a biomarker for treatment stratification and treatment response monitoring.

Fig 1

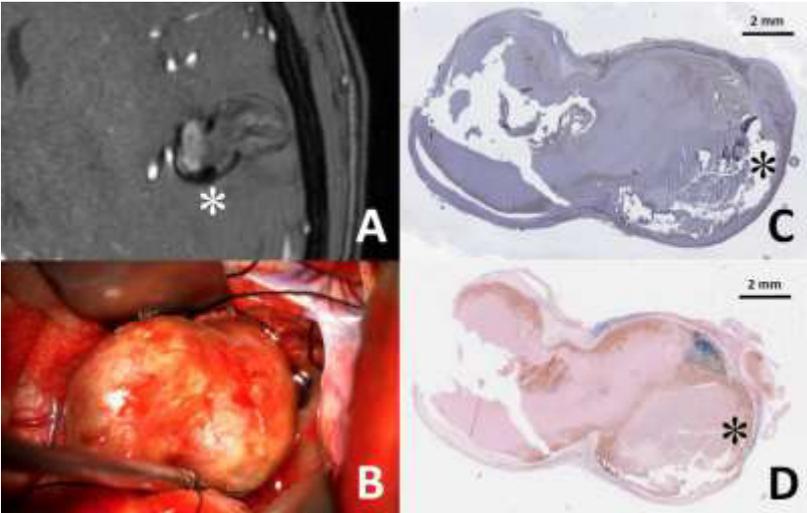
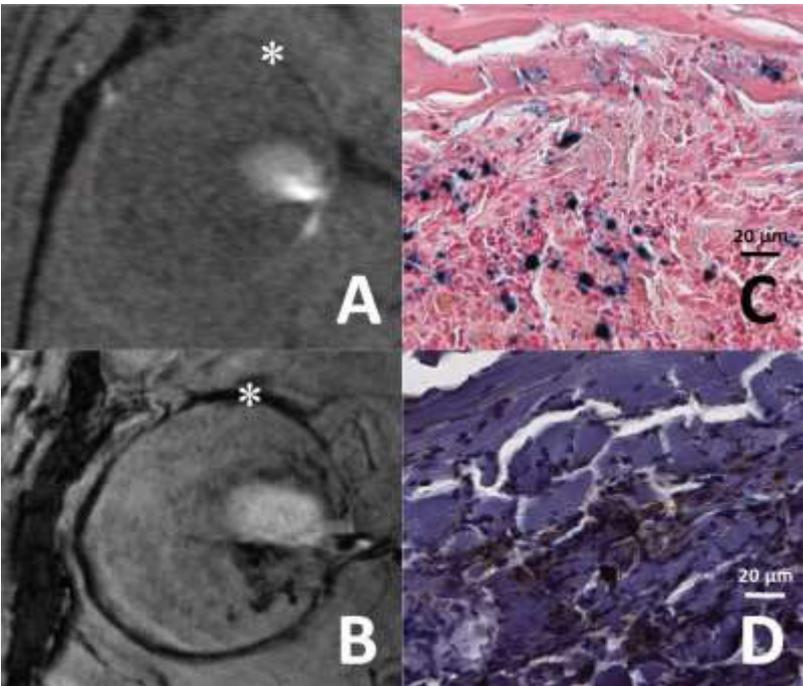


Fig 2



Aneurysmen experimentell/*Aneurysms experimental*

V112

Kollagen-Abbauprodukte als serologische Marker für strukturelle Instabilität von intrakraniellen Aneurysmen *Collagen breakdown products as biomarkers for structural instability in intracranial aneurysms*

K. Hackenberg¹, P. Richter¹, A. Abdulazim¹, J. Böhme², M. Neumaier³, E. Neumaier-Probst², M. M. Alzghoul², C. Groden², N. Etmian¹

¹Universitätsklinikum Mannheim, Neurochirurgie, Mannheim, Germany

²Universitätsklinikum Mannheim, Neuroradiologie, Mannheim, Germany

³Universitätsklinikum Mannheim, Klinische Chemie, Mannheim, Germany

Objective

The estimation of the individual rupture risk of intracranial aneurysms (IA) remains challenging. Structural integrity of IA is predominantly determined by collagen type I, the main molecular constituent in IA. A hallmark of the pathogenesis of IA is ongoing collagen remodelling in the IA wall and synthesis of immature/structural deficient collagen. To date, *in vivo* biomarkers for molecular instability in IA are lacking. We endeavoured to detect breakdown products of collagen derived from human IA in serum as potential surrogates for the instability of the IA wall.

Methods

Two blood samples from intra-aneurysmal (intra-IA) and the femoral artery were obtained during catheter angiography from patients undergoing endovascular repair of their IA. Additionally, venous blood samples were obtained from IA patients as well as control subjects (no known presence of IA). Detection of collagen breakdown products cross-linked C-telopeptide of collagen type I (CTx) was performed by serum immunoassay. Recently grown or ruptured IA were defined as unstable. T-test, correlation, logistic regression and receiver operating characteristic (ROC) analyses were performed.

Results

Between 10/2018 and 11/2019 27 IA patients (15 female, 12 male) with 57.3±12.2 years were included. There were 8 unruptured, 19 ruptured and 5 stable, 22 unstable IA. 18 control subjects (7 female, 11 male) with 45.4±16.6 years were included. Intra-IA CTx levels were higher in ruptured compared to unruptured IA (0.63±0.28ng/ml vs. 0.35±0.24ng/ml, p=0.02) and higher in unstable compared to stable IA (0.62±0.28ng/ml vs. 0.27±0.10ng/ml, p=0.01). Intra-IA CTx levels predicted IA rupture in univariate analysis (likelihood ratio (LR) 6.6, p=0.01; OR 275.4, 95% CI 1.1-72395.9) and after including age, smoking, hypertension in multivariate analysis (LR 5.6, p=0.02; OR 223.0, 95% CI 0.8-63843.5). ROC analysis demonstrated a good test accuracy (AUC 0.72, 95% CI 0.45-0.98) for intra-IA CTx levels with a threshold ≥ 0.464 ng/ml for IA rupture. Venous CTx levels were higher in IA patients compared to controls (0.33±0.18ng/ml vs. 0.20±0.08ng/ml, p=0.004). There was a strong correlation between intra-IA and venous CTx levels (r=0.53, p=0.004) and between CTx levels from intra-IA and femoral artery (r=0.95, p<0.001).

Conclusion

Our pilot study indicates that arterial and potentially venous CTx levels could serve as a novel indicator for increased instability in IA patients for assessment of their IA.

Aneurysmen experimentell/*Aneurysms experimental*

V113

Kollagenmarkierung zur Darstellung der strukturellen Stabilität von intrakraniellen Aneurysmen – eine Pilotstudie

Collagen labelling for visualisation of structural instability in intracranial aneurysms – a pilot study

K. Hackenberg¹, N. Willett¹, A. Abdulazim¹, R. Dreier², D. Hänggi³, B. Wängler⁴, C. Wängler⁴, N. Etminan¹

¹Universitätsklinikum Mannheim, Neurochirurgie, Mannheim, Germany

²Universitätsklinikum Münster, Institut für Physiologische Chemie und Pathobiochemie, Münster, Germany

³Universitätsklinikum Düsseldorf, Neurochirurgie, Düsseldorf, Germany

⁴Universitätsklinikum Mannheim, Institut für Klinische Radiologie und Nuklearmedizin, Mannheim, Germany

Objective

The estimation of the individual rupture risk of intracranial aneurysms (IA) remains challenging. Structural integrity of IA is predominantly determined by collagen type I, which is the main molecular constituent in IA. A hallmark of IA pathogenesis is ongoing collagen remodelling in the IA wall and synthesis of immature/structural deficient collagen; the latter cannot be visualized with existing imaging modalities to date. Here, we report our pilot data on a novel Positron Emission Tomography contrast agent to investigate radiolabelling of immature/novel collagen in human IA as a marker for instability.

Methods

Unruptured and ruptured IA samples derived from patients undergoing surgical repair, were used for radio- and immunolabelling. A peptide called collagelin was synthesised, conjugated to NODAGA as a chelator and radiolabelled with ⁶⁸Gallium (⁶⁸Ga-NODAGA-Collagelin). Longitudinal cryosections of the IA including the dome and the transition zone (between dome and neck) were performed. 12µm cryosections were incubated with ⁶⁸Ga-NODAGA-Collagelin for 90 minutes and visualised by autoradiography. 9µm cryosections were used for immunolabelling of collagen alpha 1 chain type I and visualised by confocal laser microscopy. Qualitative assessment was performed by 2 independent investigators. IA regions with unstructured collagen fibres were defined as immature, structured collagen as mature. t-Test was performed as statistics.

Results

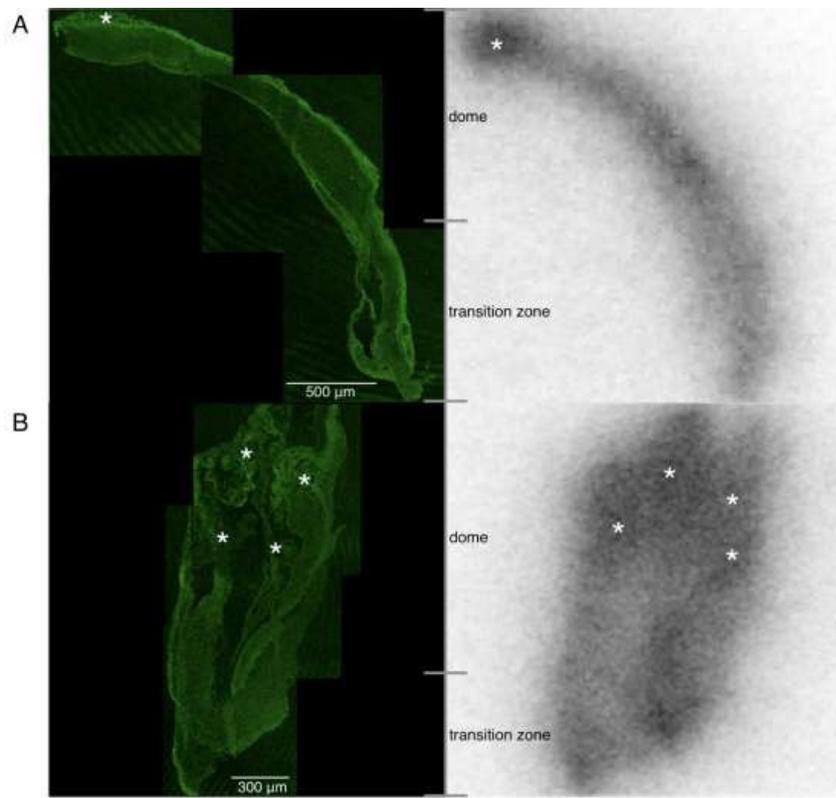
Within a pilot study radio- and immunolabelling were performed in 6 IA samples (3 unruptured, 3 ruptured) from 6 female patients. Immunolabelling demonstrated regions of mature collagen, which were predominantly localized in the transition zone of the IA and predominantly in unruptured compared to ruptured IA. Regions of immature collagen were predominantly found in IA domes and especially in ruptured IA (figure 1). Radiolabelling demonstrated increased uptake in IA regions with immature collagen and less uptake in the regions with mature collagen (figure 1). Radioactivity per area was higher in ruptured compared to unruptured IA (178.7±45.0 kBq/cm² vs. 145.7±38.2 kBq/cm², p=0.03).

Conclusion

Our novel collagen radiotracer seems to specifically label IA regions with immature/structurally deficient collagen, which we found especially in ruptured IA. These findings will be underlined in a larger patient sample.

Figure1: Immuno- (left) and radiolabelling (right) of an unruptured (A) and ruptured (B) IA. Regions with immature collagen are labelled (*).

Fig 1



Aneurysmen experimentell/*Aneurysms experimental*

V114

Periinterventionelle Bedeutung von Neutrophilen-Lymphozyten-Ratio in Patienten mit intrakraniellen Aneurysmen

Peri-interventional behaviour of neutrophil to lymphocyte ratio in patients with intracranial aneurysms

A. Cho, T. Czech, W. T. Wang, P. Dodier, A. Reinprecht, G. Bavinzski

Medizinische Universität Innsbruck, Universitätsklinik für Neurochirurgie, Wien, Austria

Objective

The Neutrophil-to-Lymphocyte-Ratio (NLR) has already been investigated as an independent predictive marker for clinical outcome in vascular diseases. This study aimed to investigate the peri-interventional behavior of NLR in patients with ruptured and unruptured intracranial aneurysms (IAs).

Methods

117 patients with IAs, who were treated in our department and had available completed data, were retrospectively identified during a ten-year period. Routine laboratory parameters, including neutrophil and lymphocytes, were measured at baseline and follow-up (FUP) visits.

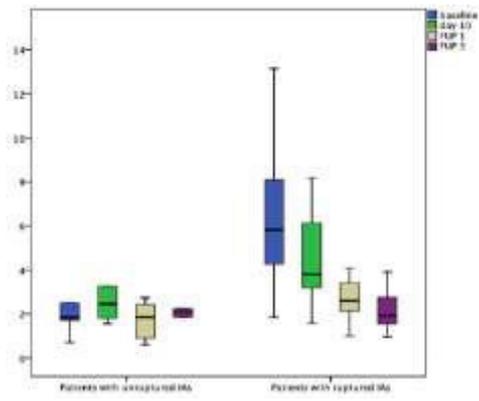
Results

The baseline NLR showed significant differences between patients with ruptured and unruptured IAs [6.3 (IQR 4.2-9.0) vs. 1.8 (IQR 1.6-2.3), $p<0.001$]. In patients with ruptured IAs, baseline NLR significantly decreased during the FUP visits, while in unruptured IAs, the NLR remained low. In patients with ruptured IAs, higher baseline NLR values could be observed in patients with fatal outcome, in comparison to surviving patients [8.0 (IQR 5.2 - 9.1) vs. 5.4 (IQR 4.0-9.0); $p=0.220$]. In patients with poor functional outcome, defined as modified Rankin Score (mRS) ≥ 3 , NLR was significantly higher before treatment [7.2 (IQR 4.7-9.6) vs. 5.3 (IQR 3.5-8.1); $p=0.047$], but also at day 10 [5.4 (IQR 3.9-6.8) vs. 4.2 (IQR 3.3-5.9); $p=0.025$] and one month after treatment [3.5 (IQR 2.5-5.8) vs. 2.3 (IQR 1.7-2.9); $p=0.001$].

Conclusion

The peri-interventional NLR was significantly different between patients with ruptured and unruptured IAs. In patients with ruptured IAs, elevated baseline NLR levels was associated with poor postoperative functional outcomes and decreased postoperatively, implying the potential prognostic importance of NLR in patients with IAs.

Fig 1



Aneurysmen experimentell/*Aneurysms experimental*

V115

Periphere T-Zellen Polarisation und deren therapeutische Implikationen nach aneurysmatischer Hirnblutung *Peripheral blood T-cell polarisation and their therapeutic implications after aneurysmal subarachnoid haemorrhage (aSAH)*

S. Muhammad^{1,2,3}, S. R. Chaudhry³, D. Hänggi¹

¹Heinrich-Heine-Universität Düsseldorf, Abteilung für Neurochirurgie, Düsseldorf, Germany

²University of Helsinki, Department of Neurosurgery, Helsinki, Finland

³Universitätsklinikum Bonn, Abteilung für Neurochirurgie, Bonn, Germany

Objective

Aneurysmal subarachnoid hemorrhage (aSAH) is associated with significant morbidity and mortality even after successful treatment of the bleeding aneurysm. Devastating complications occurring after SAH contribute mainly to poor clinical outcome. The current state of the knowledge suggests the indispensable role of sterile inflammation during early and delayed brain injury phases over which these complications arise. T-cells are fundamental part of adaptive immunity that can polarize to different sub-populations with different functional roles. Here, we investigate the role of different CD4+ T cell subsets and Treg cells during early and delayed brain injury after SAH.

Methods

Peripheral venous blood anticoagulated with EDTA was obtained from 15 SAH patients on day 1 and day 7, and once from healthy controls for multicolour flowcytometry. After erythrocyte lysis and a single cell wash, 1 million cells in 100 µL of FACS buffer were stained with different anti-human mouse monoclonal antibodies for 20 mins on ice. Cells were washed and final volume was adjusted to 500 µL. Cells were then acquired on LSR Fortessa (BD Biosciences, CA, USA). Lymphocytes were gated based on their low side scatter and high CD45 expression. Different subsets of CD3+ CD4+ T cells were characterized by differential cell surface expression of CXCR3 and CCR6 into Th1, Th2, Th17, whereas Tregs by CD25hi and CD127lo.

Results

Total number of CD4+ T cells was significantly increased after SAH. Interestingly, **T helper-2** (Th2) cells were significantly decreased on day 7, whereas Th17 cells were increased compared to day 1 post-SAH. Regulatory T (Tregs) cells were significantly increased on both assessment days compared to controls. All T cell sub-populations (assessed by CD38 and HLA-DR expression) revealed a distinct activation state during the phases of early brain injury and delayed phase.

Conclusion

Subarachnoid hemorrhage leads to imbalance of anti-inflammatory T helper-2 (Th2) and pro-inflammatory T helper-1 (Th1) cells. Increase in Th1 cells and decrease in Th2 cells may exacerbate inflammation and contribute to post-SAH complications. T cell polarization could be potential target to ameliorate sterile inflammation after aSAH.

Aneurysmen experimentell/*Aneurysms experimental*

V116

Expression von Relaxin in Arteriolen des Großhirns *Relaxin expression in adult cerebral cortex arterioles*

C. Gewiss¹, C. Hagel¹, K. Krajewski²

¹Universitätsklinikum Hamburg-Eppendorf, Institut für Neuropathologie, Hamburg, Germany

²Universitätsklinikum Schleswig-Holstein, Neurochirurgie, Lübeck, Germany

Objective

Relaxin is a peptide hormone of the insulin superfamily which has recently been shown to stimulate expression of VEGF *in vitro*. Once thought to be strictly a reproductive hormone, relaxin has been found to be a potent vasodilator via NO-mediated mechanisms in many other organs. However, relaxin expression in cerebral vessels has not been studied to date in humans and a deeper understanding of its role in the brain is still lacking. We recently published our data on relaxin expression in pediatric and adult cavernoma and now focus on relaxin expression in adult cerebral cortex arterioles. As clinical trials for the treatment of acute heart failure with relaxin have been promising, we hypothesize that relaxin may even be a new target for treatment of vasospasm and/or ICP therapy.

Methods

Temporal lobe tissue obtained during epilepsy surgery served as controls in a previously published study on pediatric and adult cavernoma. Immunohistochemical staining for Relaxin 1/2/3 and VEGF-R1/R2 were performed. Relaxin 1, 2, and 3 staining was deemed "positive" or "negative" within the endothelium of the veins and arterioles in controls.

Results

A total of n= 5 patients, mean age: 43y; range: 23 – 67y were analyzed. The control specimens were found to have positive relaxin 1 and 3 expression in intraparenchymal arterioles and leptomeningeal arterioles in all 5 cases, respectively. For veins, staining was as follows: relaxin 1: 4/5 positive, relaxin 2: 0/5 positive, relaxin 3: 5/5 positive. In veins, 4/5 cases stained positively for VEGF-R1. In veins, 2/5 cases stained positive for VEGF-R2.

Conclusion

Relaxin 1 and 3 expression in normal human cerebral arterial vasculature is a novel finding and needs further exploration, in particular regarding its binding site, as it may represent a potential target for vasospasm and increased intracranial pressure.

Spinale und zerebrale Metastasen/*Spinal and cerebral metastases*

V117

8-Jahres Ergebnisse der robotergestützten SRS/SRT mit zentraler Dosisoptimierung für einzelne und multiple Hirnmetastase

8-year results of robotic-guided SRS/SRT with central dose optimisation for single and multiple brain metastases

D. Krug^{1,2}, S. Stera³, S. Wurster^{4,2}, R. Wolff^{2,5}, V. Seifert⁵, V. M. Tronnier⁶, M. Synowitz⁷, H. W. S. Schroeder⁸, R. Breitsprecher⁴, D. Rades⁹, C. Rödel³, G. Hildebrandt¹⁰, J. Dunst¹, O. Blanck^{1,2}

¹Universitätsklinikum Schleswig-Holstein, Klinik für Strahlentherapie, Kiel, Germany

²SAPHIR Radiochirurgie Zentrum, Güstrow, Germany

³Universitätsklinikum Frankfurt am Main, Klinik für Strahlentherapie, Frankfurt am Main, Germany

⁴Universitätsmedizin Greifswald, Medizinische Klinik IV Endokrinologie, Greifswald, Germany

⁵Universitätsklinikum Frankfurt am Main, Klinik für Neurochirurgie, Frankfurt am Main, Germany

⁶Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Lübeck, Germany

⁷Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Kiel, Germany

⁸Universitätsmedizin Greifswald, Klinik für Neurochirurgie, Greifswald, Germany

⁹Universitätsklinikum Schleswig-Holstein, Klinik für Strahlentherapie, Lübeck, Germany

¹⁰Universitätsmedizin Rostock, Klinik für Strahlentherapie, Rostock, Germany

Objective

We retrospectively evaluated robotic-guided stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (SRT) with central dose optimization for single and multiple brain metastases (BM).

Methods

We treated 197 patients (m/w=102/95, age=28-86, lung=73, melanoma=57, breast=35, other=32) with 674 BM (75 with 1, 63 with >3, 29 with >5 and 10 with >10 BM) in 253 SRS/SRT series with median PTV of 0.6cc (0.01-78.8cc). Median PTV-BED10 was: D98% 50.8Gy10 (20.1-63.5Gy10), D2% 97.4Gy10 (27.8-135.4Gy10) and D50% 73.1Gy10 (24.8-96.1Gy10). Whole brain irradiation (WB) before SRS/SRT or simultaneous immune-/targeted-therapy (TT) was performed in 65 (33%) and 62 (31.5%) patients.

Results

Mean follow-up was 13.2 months (1-86 months) with median OS of 9.0 months. 6, 12, and 24-month OS was 64.2%, 40.3%, and 18.7% (1-year OS breast 44.1%, lung 39.7%, melanoma 39.6%, others 38.7%, ≤3 BM 44.9%, >3 BM 32.7%, TT 43.3%, no TT 38.8%, WB 37.1%, no WB 42.1%). 6, 12 and 24-month PFI was 52.4%, 26.2% and 9.0% and in 69.6% the progression was intracerebral (1-year PFI ≤3 BM 35.3%, >3 BM 9.5%, WB 31.0%, no WB 23.9%). 6, 12 and 24-month LC was 99.4%, 93.3% and 76.1%, with 98.4% absolute LC (1-year LC TT 95.4%, no TT 91.4%, WB 91.0%, no WB 94.4%) 1-year LC was better with higher PTV D98% (96.2% vs. 84.6%), which corresponded to the BM border recurrence pattern. 2.4% showed toxicity grade ≥3 (operated radionecrosis) and one patient died of intracerebral hemorrhage after local re-SRS concomitantly with BRAF inhibitors.

Conclusion

Robotic-guided SRS/SRT with central dose optimization w/wo TT/WB is safe and effective for new brain metastases. However, caution is advised when re-treating recurrences previously treated with SRS/SRT concomitant to TT. Further, close follow-up in patients with >3 brain metastases without WB is important in order to detect and treat new metastases early. To increase local control only the PTV prescription dose may be raised, however this may result in higher rates of radionecrosis.

Spinale und zerebrale Metastasen/*Spinal and cerebral metastases*

V118

Einfluss der mikrochirurgischen Resektion auf fokale neurologische Defizite bei Patienten mit Hirnmetastasen

Impact of microsurgical resection on focal neurological deficits in patients with brain metastases

P. Schödel, K. M. Schebesch, J. Falter, C. Doenitz, L. Ramsz, A. Brawanski, M. Proescholdt

Universitätsklinikum Regensburg, Regensburg, Germany

Objective

About 30% of all cancer patients develop brain metastases (BMs). Surgical resection is an important element in the multidisciplinary treatment pursuing three main objectives: a. tissue acquisition to establish a histological and molecular diagnosis b. removal of mass lesion to improve overall survival c. improvement of neurological status by decompression of eloquent brain regions. In this study we analyzed the frequency of focal neurological deficits and the impact of resection on these impairment groups.

Methods

We analyzed 366 patients (52.7 % male; 47.3% female; median age 62.3 years) consecutively treated for BM in our department. The most frequent primary tumor was lung cancer (33.9%), followed by malignant melanoma (16.1%) and breast cancer (13.9%). Solitary BM were diagnosed in 23.7%, singular in 33.9% and multiple in 42.4% of all cases; the majority of BM (64.2%) occurred metachronously. Intratumoral hemorrhage occurred in 18.6% of all patients, while BM originating from MM displayed a significantly higher frequency of intratumoral hemorrhage (49.1%; $p = 0.001$). RPA classes were distributed as follows: 12.1% class 1, 76.8% class 2 and 11.1% class 3. To assess the functional status, we determined Karnofsky performance index (KPI), the neurological performance status (MRC – NPS), as well as three neurological deficits: Aphasia, hemiparesis and visual field deficits.

Results

KPI and MRC – NPS was significantly improved following surgery ($p = 0.001$; and $p = 0.020$, respectively); 16.7% of all patients presented with seizures, which were improved in all cases (100%). Aphasia was present in 16.9% of all cases, with an improvement rate of 54.2%; hemiparesis occurred in 14.8% with an improvement rate of 51.8%; vision field deficits were detected in 13.4% with an improvement rate of only 22.4%. We did not detect any difference in improvement rates between complete and incomplete resection, primary tumor or age. Interestingly, patients with improvement of hemiparesis and better RPA class following surgical resection showed significantly longer overall survival ($p = 0.034$).

Conclusion

Resection of brain symptomatic metastases improves focal neurological deficits and thereby improved RPA class can lead to longer overall survival.

Spinale und zerebrale Metastasen/*Spinal and cerebral metastases*

V119

Klinische Merkmale und prognostische Faktoren bei Patientinnen mit Hirnmetastasen mehr als 10 Jahre nach Erstdiagnose eines Mammakarzinoms

Clinical characteristics and prognosis of breast cancer patients with brain metastasis more than 10 years after initial diagnosis

A. Michel, T. F. Dinger, M. Darkwah Oppong, M. Chihi, Y. Ahmadipour, R. Jabbarli, N. El Hindy U. Sure, D. Pierscianek

Universitätsklinikum Essen, Klinik für Neurochirurgie, Essen, Germany

Objective

Breast cancer (BC) is the most common cancer in women. Routinely, patients are followed up for 10 years, but there is a subgroup of patients with brain metastasis (BM) occurring after this follow up period. We therefore sought to assess the clinical characteristics and prognosis between patients with BM during (≤ 10 years) and after (> 10 years) the routine follow-up period.

Methods

All patients with BM of BC that were treated in our department from January 2008 to December 2018 were eligible for our study. Patients' records were analysed regarding age, receptor status, location of BM, histological subtype of BC, receptor conversion, extracranial metastasis, adjuvant therapies and overall survival (OS). Statistical analyses were carried out using SPSS version 25. Categorical data was analysed using chi-square test and for continuous data the Mann-Whitney-U test was applied. Survival analysis was conducted with Kaplan-Meier analysis and log-rank test.

Results

72 patients were included into our study. 58 patients experienced BM during 10 years (group 1) after diagnosis whereas 14 patients (group 2) had very late BM (> 10 years). Patients in group 2 were significantly younger at the time of first diagnosis of BC than patients in group 1 ($p=0.007$) and presented more frequently with multiple BM ($p=0.010$). However, there was no significant difference regarding age at BM diagnosis and BM location between both groups. Invasive lobular BC was significantly more frequent in group 2 ($p=0.010$) and patients in group 2 showed significantly more often a receptor conversion ($p=0.035$). When analysing the different receptors, we detected a significant difference between both groups for HER2 receptor conversion ($p=0.001$) but not for progesterone ($p=0.641$) or estrogen receptor conversion ($p=0.059$). There was a significant difference in OS after diagnosis of BC ($p=0.0001$), but not after the occurrence of BM ($p=0.730$). For both groups, we found a better survival for patients with identical HER2 receptor status.

Conclusion

In our patients' cohort we identified a subgroup of patients with very late BM. These patients are characterized by a younger age at diagnosis of BC, have more frequently an invasive lobular BC, multiple BM and frequent receptor conversion, especially for HER2 receptor status. In both groups, a better survival was found for patients with identical HER2 receptor status.

Spinale und zerebrale Metastasen/*Spinal and cerebral metastases*

V120

Spielt der Operationszeitpunkt eine Rolle in Patienten mit Paraparesen metastatischer epiduraler Rückenmarkskompression?

Does timing of surgery matter in patients suffering from paraparesis due to metastatic epidural spinal cord compression?

C. Wiplinger, C. Orban, J. Klingenschmid, S. Lener, A. Stocsits, L. Grassner, C. Thomé, S. Hartmann

Medizinische Universität Innsbruck, Universitätsklinik für Neurochirurgie, Innsbruck, Austria

Objective

While it is known that surgical decompression of the spinal cord improves neurological outcomes in patients suffering from paraparesis or paraplegia from metastatic epidural spinal cord compression (MESCC), there is still controversy about the appropriate timing. To evaluate the impact of timing from symptom onset until surgical intervention, we performed a retrospective analysis of patients with MESCC treated with surgical decompression in our institution.

Methods

The medical records of 51 patients with a preoperative ASIA Score between A and D treated with a decompressive procedure included sufficient timing data and were retrospectively reviewed. Procedures performed included decompression, corpectomy as well as epidural resection, with or without instrumentation. We evaluated demographics, treatment modalities, time from symptom onset to surgery, amount of affected vertebrae as well as surgical time, blood loss, and perioperative complications. These parameters were analyzed for a correlation with neurological improvement.

Results

The mean age among the patient population was 62 ± 14 years, including 32 males and 19 females. Twenty-nine patients presented with an ASIA score of D, 16 patients with C, four patients with B and two patients with A. The mean follow-up was 14 ± 20 months. During the follow-up period, we observed neurological improvement in 23 patients. Nine patients (31%) improved from ASIA D to E, ten patients (63%) from C to D, one patient from C to E (6%), two patients from B to C (50%) and one patient from A to C. (50%) Among the patients with neurological improvement, six patients died after 25 ± 28 months, while eight patients without postoperative improvement died after 7 ± 8 months. When comparing all evaluated factors, only the time from symptom onset to surgery showed a significant correlation with neurological recovery ($p < 0.01$). Patients who showed neurological improvement were operated within 6 ± 8 days while patients without postoperative improvement were operated on average 16 ± 33 days after symptom onset.

Conclusion

Apparently, the time from symptom onset to surgical decompression is a critical factor for neurological recovery in patients with paraparesis after MESCC. Interestingly, first neurologic symptoms are present many days prior to surgery, although development of severe paraparesis or paraplegia may then happen rapidly. Moreover, we observed a trend towards prolonged survival in patients who recovered after surgery.

Spinale und zerebrale Metastasen/*Spinal and cerebral metastases*

V121

Die prognostische Genauigkeit des revised Tokuhashi Scores in chirurgisch behandelten Patienten mit spinalen Metastasen

Prognostic accuracy of the revised Tokuhashi score in patients undergoing surgical treatment for spinal metastasis

C. Wipplinger, C. Orban, J. Klingenschmid, S. Lener, A. Stocsits, L. Grassner, S. Hartmann, C. Thomé

Medizinische Universität Innsbruck, Universitätsklinik für Neurochirurgie, Innsbruck, Austria

Objective

Due to recent advances in cancer therapy and subsequent prolonged survival, spinal metastases are an increasingly common finding in cancer patients. One of the most critical factors for treatment decisions is the estimated life expectancy. In our institution, treatment decisions in cancer patients are made individually in an interdisciplinary board meeting. The revised Tokuhashi score (rTS) has been described as a useful tool for estimating a patient's life expectancy. In order to determine the prognostic accuracy, we performed a retrospective analysis of patients treated surgically for spinal metastasis at our institution.

Methods

According to Tokuhashi et al., patients with an rTS of 0-8 (group I) have an estimated survival of <6 months and should be treated non-surgically. For patients with an rTS of 9-11 (group II) the estimated survival is assumed between six and 12 months, and palliative surgery such as decompression and stabilization only is recommended. Potentially curative treatment with surgical resection is recommended only in patients with an rTS between 12-15 (group III), and an estimated life expectancy of ≥ 12 months. In this retrospective analysis, we included patients if they had complete medical records and a sufficient follow-up for evaluating their predicted survival according to Tokuhashi et al.

Results

Sixty-four patients, 19 females and 45 males with an average age of 60 ± 14 years, were analyzed. Thirty patients were in group I, 25 patients in group II and nine patients in group III. All patients underwent decompressive surgery with or without stabilization. Additionally, tumor resection was performed in 18 patients (60%) in group I, in 14 patients (25%) in group II and in nine patients (100%) in group III. In group I, six patients died within six months, while 24 patients survived longer than six months. Therefore, the predictive accuracy of the rTS was 20%. In group II, the rTS predicted accurately in four patients (16%) while three patients died before six months, and seven patients survived longer than 12 months. In group III, one patient died before 12 months resulting in an accuracy of 89%. The overall accuracy of the rTS was 28%.

Conclusion

In our patient population, the accuracy of the rTS was especially low in patients with a limited estimated life expectancy and we did not adhere to the rTS recommendations. Treatment decisions should always be made on an individual basis, and not solely based on a single scoring system.

Spinale und zerebrale Metastasen/*Spinal and cerebral metastases*

V122

Operative Versorgung spinaler Metastasen des zervikothorakalen Übergangs *Surgical treatment of spinal metastases of the cervicothoracic junction*

V. Hubertus¹, M. Mariño¹, A. Wagner², N. Lange², A. K. Jörger², J. Gempt², B. Sommer³, S. O. Eicker⁴, M. Stangenberg⁵, V. Rohde³, P. Vajkoczy¹, J. Onken¹, B. Meyer²

¹Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

²Technische Universität München, Neurochirurgie, München, Germany

³Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

⁴Universitätsklinikum Hamburg-Eppendorf, Neurochirurgie und Universitäres Wirbelsäulenzentrum, Hamburg, Germany

⁵Universitätsklinikum Hamburg-Eppendorf, Unfallchirurgie und Universitäres Wirbelsäulenzentrum, Hamburg, Germany

Objective

Spinal metastases of the cervicothoracic junction pose a challenge for treatment due to the region's anatomical condition, their rarity and a high complication rate. The aim of our multicentric study is to compare surgical strategies for metastases of this anatomical region (C7-Th2) with respect to their complexity and associated complications.

Methods

216 patients were surgically treated with spinal metastases of segments C7-Th2 in 2005-19 in 4 university neurosurgical units in Germany. Spinal instability neoplastic score (SINS), clinical and operation data were assessed. Patients were divided into 4 surgical groups: Patients with high comorbidities were only decompressed(1), decompression and instrumentation from dorsal(2) or ventral(3) was performed in case of instability according to SINS and dependent on location of myelon compression(2/3). A 360° ventro-dorsal instrumentation was performed in extensive lytic lesions and in patients with lower comorbidity rate(4).

Results

33 patients were included in (1)(15%), 114 patients were included in (2)(53%), 16 patients received treatment in (3)(7%) and 53 patients received treatment in (4)(25%). Medium SINS was (1)7, (2)10 and (3+4)12. In (1-2) patients presented with worse neurological function than in (3-4), whereas in (1) systemic tumor burden was highest. In (3-4)83-89% suffered from mechanical pain, in (1)45%. The mean duration of surgery was (1)144 min, (2)229min, (3)187min and (4)308min. Surgical complications occurred in (1)11%, (2)32%, (3)25% and (4)15%, mostly being internistic. Mortality associated with surgery was 0%. Hardware failure (HwF) occurred exclusively in(2) and led to surgical revision in 6 cases. HwF occurred exclusively in monocortically placed massa lateralis screws (mMLS) in the cervical spine. In case of bicortical massa lateralis screws (bMLS) or pedicle screws (PS), no HwF was observed at 10 months follow up.

Conclusion

The biomechanical loading capacity of dorsal instrumentation alone seems to have a decisive influence on the revision rate in metastases of the cervicothoracic junction. In patients with favorable comorbidity rate, the continuous extension of life expectancy through new therapy options should play a crucial role in choosing the right surgical strategy. Hereby, special attention should be paid to the biomechanical properties of the cervicothoracic junction, with 360° stabilization and placement of bMLS or PS preferable to mMLS in our multicentric cohort.

Psychoonkologie/Psychooncology

V123

Wie werden psychosoziale Belastung, gesundheitsbezogene Lebensqualität und Neurokognition in neurochirurgischen Kliniken erfasst? – eine Umfrage der Sektion Neuroonkologie der DGNC
Assessment of psychosocial burden, health-related quality of life and neurocognition in German neurosurgical departments – a survey from the neurooncological section of the DGNC

M. Rapp¹, M. Renovanz², D. Wiewrodt³, C. Weiß Lucas⁴

¹Universitätsklinikum Düsseldorf, Neurochirurgie, Düsseldorf, Germany

²Universitätsklinikum Tübingen, Neurochirurgie, Tübingen, Germany

³Universitätsklinikum Münster, Neurochirurgie, Münster, Germany

⁴Universitätsklinikum Köln, Neurochirurgie, Köln, Germany

Objective

The preservation of health-related quality of life (HRQoL) as well as the assessment and treatment of increased distress are defined therapeutic aims in neurooncological treatment. However, despite the increasing number of certified neurooncological centres, these patient-reported outcomes are not yet part of the regular assessment. Therefore, we aim to develop a standardized assessment approach. In a first step, we perform a survey supported by the neurooncological section of the DGNC to evaluate the status quo. A suggestion for a standard protocol will be developed thereafter.

Methods

We conduct a survey of 140 neurosurgical departments (registered by the DGNC) comprising 1) the structure of neurooncology, 2) the personnel infrastructure in the field of psychooncology, palliative care as well as neuropsychology and 3) applied assessment tools to evaluate psychooncological distress, HRQoL and neurocognition.

Results

So far, data from n=32 surveys (university hospitals (n=19); certified neurooncological centres (n=20)) were included. Three centres refused to participate. HRQoL and psychooncological distress assessment is performed in most departments on a regular basis (n= 18 departments, 56%). HRQoL was mostly assessed using the EORTC-QLQ C30 + BN20 (72%). However, the evaluation of neurooncological distress is quite variable. The following instruments are applied: Distress Thermometer (DT, 66%), Hospital Anxiety and Depression Scale (HADS, 33%), Beck-Depressions-Inventar (BDI, 27%). Neurocognitive assessment is performed mostly in the framework of clinical studies (48%). Only six departments (18%) use at least the Mini Mental Status Test (MMST) on a regular basis.

Conclusion

Our preliminary results reflect that 1) the EORTC-QLQ C30 + BN20 is widely used to evaluate the HRQoL, and 2) there is no consistency in the assessment of distress. Moreover, our data demonstrate that 3) the assessment of neurocognition is only performed sporadically in clinical routine, using poorly sensitive tools. The assessment of patient-reported outcomes is overall poorly standardized across German neurooncological centres. Achieving a common sense regarding a standard protocol seems advisable – not only to encourage the routine assessment of important patient-related parameters in the disease and treatment monitoring but also in order to unify the outcome parameters and thus make study results better comparable.

Psychoonkologie/Psychooncology

V124

Psychische Belastung bei Patienten mit Meningeom unter Beobachtung verglichen mit Patienten nach kompletter Resektion – eine prospektive Beobachtungsstudie

Psychological burden under watchful waiting versus after complete meningioma resection – prospective observational study

D. Kalasauskas¹, S. Abu Ajaj¹, L. Von Cube¹, N. Keric¹, F. Ringel¹, M. Renovanz^{1,2}

¹Universitätsmedizin Mainz, Klinik und Poliklinik für Neurochirurgie, Mainz, Germany

²Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

Objective

The diagnosis of a brain tumor is usually a life changing event. But what if the tumor is a small and benign one, or if it is totally removed? In this study, we aim to investigate psychological burden in patients with meningiomas with recommendation of watchful waiting compared to patients with a good outcome after complete resection.

Methods

Patients with small asymptomatic meningiomas under watchful waiting strategy and patients after complete meningioma resection, demonstrating no focal neurological deficits who gave informed consent were included. Exclusion criteria were any other known malignancies. Patients were evaluated for psychological burden using Hospital Anxiety and Depression Scale (<8 - no anxiety/depression, 8-10 - borderline case, 11-21 - anxiety/depression) and Distress Thermometer (DT) (score ≥ 6 indicated significant burden) during an outpatient visit. A follow-up survey was sent to the patients 3 months after the interview. Demographic, tumor-related and performance data were using Chi-Square as well as univariate and multivariate regression analyses.

Results

Out of n=55, n=48 patients (mean age 59.3(SD 12.8), 83.3% women) were included so far. Conservatively managed patients comprised 41.7%. We found a high prevalence of anxiety (no symptoms 8.3%, borderline 45.8%, anxiety 45.8%) and depression (no symptoms 4.2%, borderline 25.0%, depression 70.8%) among the study population. Depression was more prevalent in the watchful waiting cohort (90%, n=18, vs. 57.1%, n=16; p=0.001). No difference in the prevalence of anxiety was found (35%, n=7 vs. 53.6%, n=15; p=0.242). 43.8%, n=21 patients indicated significant burden on DT. The proportion of distressed patients in the watchful waiting group was as high as 55.0%. The psychological burden did not decrease with time: 40.9% (n=9) of patients reported DT score ≥ 6 , 52.2% (n=12) had depressive and 43.5% (n=10) anxiety symptoms 3 months after the interview.

Conclusion

Taken into account the small patient sample, the data show that the prevalence of psychological distress is high in non-operated meningioma patients. Both, patients under watchful waiting and after complete meningioma removal should be offered a psychooncological support.

Psychoonkologie/Psychooncology

V125

Hin zu einer optimierten klinisch-neuropsychologischen Testung bei Glioblastompatienten – Konzept und Interimanalyse einer prospektiven, multizentrischen Studie

Towards an optimised clinical neuropsychological assessment for glioblastoma patients – concept and interim analysis of a prospective multi-centre study

C. Weiß Lucas¹, R. H. Goldbrunner¹, C. Jungk², M. Löhr³, M. Renovanz⁴, N. 1. Studiengruppe^{1,2,3,4,5,6,7,8,9,10,11,12}

¹Universitätsklinikum Köln, Zentrum für Neurochirurgie, Köln, Germany

²Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

³Universitätsklinikum Würzburg, Neurochirurgische Klinik und Poliklinik, Würzburg, Germany

⁴Universitätsmedizin Mainz, Neurochirurgische Klinik und Poliklinik, Mainz, Germany

⁵Universitätsklinikum Carl Gustav Carus Dresden, Klinik und Poliklinik für Neurochirurgie, Dresden, Germany

⁶Donau Isar Klinikum, Neurochirurgie, Wirbelsäulenchirurgie, Interventionelle Neuroradiologie, Deggendorf, Germany

⁷Universitätsklinikum Regensburg, Neurochirurgie, Regensburg, Germany

⁸HELIOS Kliniken Schwerin, Neurochirurgie und Wirbelsäulenchirurgie, Schwerin, Germany

⁹Klinikum Chemnitz gGmbH, Klinik für Neurochirurgie, Chemnitz, Germany

¹⁰Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

¹¹Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Lübeck, Germany

¹²Universitätsklinikum Heidelberg, Klinik für Neurochirurgie, Freiburg, Germany

Objective

Neurocognitive deficits are a common and burdening sequela of brain lesions often remain undetected due to the lack of time-efficient, easily administrable and reliable tests, validated for this specific patient collective. We set up this study to investigate the use of a comprehensive neurocognitive test battery in a representative cohort of glioblastoma patients with respect to (i) clinical feasibility, (ii) tumour-location-related test sensitivity and specificity, (iii) test-parallel-test-reliability and to assess the influence of factors like the neurosurgical intervention on specific cognitive domains.

Methods

A total of n=250 previously untreated patients with suspected single supratentorial glioblastoma lesions will be allocated to this multicenter study throughout Germany. MRI scans, parallel neurocognitive test versions and patient surveys (SF-12, BDI) are performed pre- and postoperatively as well as every three months until the date of first tumour recurrence. Assessment time and motivation of the patients to participate in repeated testing are assessed as feasibility measures. As an addition to the calculation of sensitivity and specificity, a voxel-based lesion symptom mapping is performed. Intraclass correlation coefficients (ICC) are calculated as a measure of test-parallel-test-reliability. The average postoperative test results are compared to the paired preoperative baseline assessments.

Results

The interim analysis based on n=128 glioblastoma patients shows encouraging results with regard to the logistical feasibility (mean administration time: 39 ± 10 min) and usually excellent acceptance by the patients (8/10 on the numeric rating scale). Reliability was good to excellent (ICC=0.6–0.9), depending on the specific test, except for the short form of the trail-making-test C (ICC=0.51).

Conclusion

The study introduces an easily administrable, reliable and validated tool for a comprehensive assessment of neurocognitive functions in glioblastoma patients, offering the opportunity of longitudinal follow-up due to five parallel versions. Moreover, the final study results will allow to tailor location-specific (shortened) test sets in order to further improve the clinical feasibility.

Psychoonkologie/Psychooncology

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Bedarfserfassung optimieren – die Adaptation des Belastungsthermometers für Hirntumorpatienten in Deutschland (HEAT-Studie)

Holistic needs assessment in brain tumour patients – optimisation of the Distress Thermometer in Germany (HEAT-study)

M. Renovanz¹, C. Knuth², M. Damm¹, D. Linden¹, J. Coburger³, G. Tabatabai¹, F. Ringel⁴, M. Mehdorn⁵, S. Goebel²

¹Universitätsklinikum Tübingen, Tübingen, Germany

²Christian-Albrecht-Universität zu Kiel, Psychologie, Kiel, Germany

³Universitätsklinikum, Neurochirurgie, Ulm, Germany

⁴Universitätsmedizin Mainz, Neurochirurgische Klinik, Mainz, Germany

⁵Mehdorn Konsilium, Kiel, Germany

Objective

Holistic Needs Assessment (HNA) is widely used in cancer patients to determine needs. However, generic HNA tools may not reflect the unique symptom profile of brain tumor patients (BTPs) limiting their usability. Therefore, we aim to adapt the Distress Thermometer (DT) for BTPs, which is a screening tool including a numerical rating scale (1-10, cut-offs indicating relevant distress $\geq 4-6$) and a 40-item problem list.

Methods

The multicenter study included four university hospitals. We first performed an analysis with regard to frequency of indicated topics and evaluated their relevance for patients' psychosocial wellbeing via Pearson correlations with the DT score. Second, a qualitative interview with BTPs and experts, as well as an online expert survey were performed in order to search for missing but relevant items. Combining these results, we created a preliminary adapted version of the tool for HNA in BTPs.

Results

In the first part, data of $n = 670$ BTPs were analyzed. A total of 14/40 (35%) of the items was endorsed by less than 10% of the BTPs. However, some of these rarely reported problems were of relevance for patients' psychosocial wellbeing as indicated by significant correlations between the respective item and the DT score (e.g. breathing, $r = .125$; $p = .001$).

In the second part, intensive literature search, qualitative interviews (QI) conducted with $n = 10$ BTPs revealed the following missing topics: "inability to work, isolation, dizziness, dependency on others". In QI with $n = 4$ experts inter alia the following items were noticed: "social isolation, dependency on others, future uncertainty, loss of sensory functions".

A total of $n = 63$ doctors and $n = 39$ psychologists participated in the online expert survey including $n = 44$ items. Most relevant new topics were: "dependency, planning, social isolation, mood swings, shock/trauma, swallowing". Simultaneously to BTPs results, a bimodal distribution of the topic "breathing", "opstipation" and "nutrition" was observed indicating that these items may be applicable only for specific situations (e.g. under chemotherapy).

Conclusion

Overall, the problem list of the DT was adapted for BTPs, aiming to enable the targeted assessment of patients' specific problems and needs. In the next step, a multicenter application as well as a tumor entity specific and cross-cultural validation is necessary to meet the requirements of clinical daily praxis and different social systems.

Psychoonkologie/Psychooncology

V127

Die Rückkehr ins Berufsleben nach Gliom-OP

The ability to return to work following glioma surgery

C. Senft¹, M. Behrens², P. Baumgarten¹, I. Lortz¹, K. Wenger-Alakmeh³, V. Seifert¹, M. T. Forster¹

¹Universitätsklinikum Frankfurt am Main, Klinik für Neurochirurgie, Frankfurt am Main, Germany

²Universitätsklinikum Frankfurt am Main, Klinik für Neurologie, Frankfurt am Main, Germany

³Universitätsklinikum Frankfurt am Main, Institut für Neuroradiologie, Frankfurt am Main, Germany

Objective

Maximum safe tumor resection is the first step in the multimodal treatment of gliomas. Aside from improving overall survival, patient centered outcome parameters are gaining importance. Among others, the occupational status represents one such parameter. Our aim was to report the proportion of patients who are able to return to work (RTW) following glioma surgery and to identify factors influencing occupational status.

Methods

We retrospectively analyzed our prospectively collected database of glioma patients operated upon between 2013 and 2018. All patients received treatment according to interdisciplinary tumor board recommendation.

Patients with WHO grade IV tumors were excluded from the analysis. Clinical data were retrieved from the database. Details on occupational status before and after surgery were obtained by structured telephone interviews. All patients gave informed consent to participate in this study.

Results

69 patients were included in the analysis. Median age was 38 years (range: 21-70). The majority of patients (n=56) had WHO grade III tumors, followed by grade II (n=10) and grade I tumors (n=3). Most patients received adjuvant treatment (n=59). Median follow-up time was 38.7 months (range: 5.4-77.8 months). At diagnosis, 59 patients (85.6%) were working. Later, 40 patients (67.8%) were able to RTW. The median time to RTW was 8.0 months. Multivariable analysis showed that age at diagnosis, employment status at diagnosis, KPS at diagnosis and at follow up as well as extent of tumor resection were associated with the ability to RTW ($p < 0.001$, $p < 0.01$, $p < 0.05$, $p < 0.001$, and $p < 0.05$, respectively). While the proportion of patients able to RTW was higher after awake than after non-awake surgery (63.2 vs. 51.6%), this difference was not statistically significant ($p = 0.46$). Likewise, tumor histology or WHO grade were not statistically significantly associated with the ability to RTW ($p > 0.05$ for both).

Conclusion

Social interaction and self-sustainment affect personal well-being. Following tumor surgery, a large proportion of patients is able to RTW, even when tumors are eloquently located. Maximizing the extent of resection while preserving function is of paramount importance for maintaining patients' quality of life.

Psychoonkologie/Psychooncology

V128

Progredienzangst bei Patienten mit neu diagnostizierten Hirntumoren und ihren Angehörigen *Fear of progression in patients with new diagnosed brain tumours and their caregivers*

M. Rapp¹, A. Kusic², C. Quente¹, M. A. Kamp¹, M. Sabel¹, P. Pilcher², A. Karger²

¹Universitätsklinikum Düsseldorf, Neurochirurgie, Düsseldorf, Germany

²Universitätsklinikum Düsseldorf, Klinisches Institut für Psychosomatische Medizin und Psychotherapie, Düsseldorf, Germany

Objective

Despite therapeutic progress resulting in increased survival data, tumor recurrence is expected in all patients which is known by them as well as their caregivers. Fear of progression (FoP) refers to specific anxiety or concern about the recurrence or progression of cancer. Moderate to severe FoP are reported in 49% of patients and affects their QoL and social functioning. A correlation between FoP and increased incidence of anxiety, fatigue or pain and increased use of the health system has already been reported. Caregivers are also at risk for psychological distress. But less is known about FoP in brain tumor patients and the impact of cancer on their caregivers.

Methods

Since July 2019 consecutively all patients ($N = 82$) with a new diagnosis of brain tumor and their caregivers were asked to participate in a survey. Patients and their caregivers were assessed for FoP (Progression Anxiety-Questionnaire), anxiety and depression (Hospital Anxiety and Depression Scale, HADS), psychological distress (Distress Thermometer, (DT). Quality of life was assessed using the EORTC-QLQ-C30 and -B20. Psychological burden of patients and caregivers and group differences were calculated.

Results

30 patients (age: $M = 54.53$, range 22-76) and their caregivers (age: $M = 54.47$, range = 18-85) could be included. Regarding DT caregivers ($M = 5.43$, $SD = 2.80$) have a significant higher distress level than patients ($M = 7.23$, $SD = 2.38$; $p = .016$). This was reflected in the HADS results, where caregivers expressed significantly higher levels of anxiety ($M = 10.10$, $SD = 4.59$) and FoP ($M = 35.57$, $SD = 8.59$) compared with patients (anxiety: $M = 6.73$, $SD = 5.08$, $p = .004$; FoP: $M = 30.43$, $SD = 12.68$; $p = .001$). A significant correlation between the patients' and caregivers' expression of FoP ($p = .001$) was demonstrated: The higher the patient's expression, the higher the caregivers'.

Conclusion

Our first analysis clearly demonstrates a higher psychological burden for caregivers of brain tumor patients in relation to the patients and a positive correlation of patients and caregivers levels of FoP. These data underline the importance to offer further psychooncological support not only for the patients but also for the caregivers in the early phase of tumor therapy.

Chronische Subduralhämatome/*Chronic subdural haematomas*

V129

Absetzen der Antikoagulation bei Patienten mit chronischem subduralen Hämatom geht einher mit Thrombembolien und höherer Mortalität

Anticoagulation withdrawal in patients with chronic subdural haematoma is associated risk of thrombembolism and higher mortality

H. A. Hamou, H. Zaytoun, M. Alzaiyani, M. Veldeman, H. R. Clusmann, A. Höllig

Rheinisch-Westfälische Technische Hochschule Aachen, Neurochirurgie, Aachen, Germany

Objective

Chronic subdural hematoma (cSDH) is an entity with a high incidence particularly among the elderly (up to 8.2 per 100 000 per year in people above the age of 65). Due to the high average age the management of the patients is regularly hampered by the prior use of anticoagulant, especially as there are no specific guidelines for the treatment of this pathology. Here, we present a retrospective analysis of patients with cSDH with regards to the management of anticoagulant/antiplatelet use including the incidence of thromboembolic complications and the recurrence of the hematoma.

Methods

A total of 202 patients with cSDH (from October 2014 to July 2017) were included. Patient characteristics (age, sex, pre-existing conditions, use of anticoagulants/antiplatelets, 3 months follow-up) were noted. Management of anticoagulant, recurrence rate, mortality and incidence of thromboembolic complications until full recovery were documented. The variables were compared between the group with a history of prior anticoagulation/antiplatelets (AC+, N=97), which was discontinued after diagnosis of the cSDH, and the one without (AC-, N=105) using a t-Test/ Mann Whitney U Test and a Chi square test for categorical variables.

Results

Patients with cSDH and a prior history of anticoagulant had a similar age (77 ± 10 yrs.) compared to those without anticoagulant use (70 ± 15 yrs). There were slightly more male patients in the AC+ group compared to the AC- group (68% vs. 62%). Neither hematoma thickness nor frequency of surgical interventions differed between the two groups. Thromboembolic complications during the further course were significantly more prevalent in the AC+ group (N=12, 12.4% vs. 0%; $p < .0001$). All fatalities were related to thromboembolism and occurred exclusively in the AC+ group (N=9, 9.3% vs. 0%; $p < .001$).

Conclusion

So far, there are no specific guidelines for the anticoagulation management in cSDH. Here, we show that the common habit of anticoagulant/antiplatelet withdrawal results in a higher thromboembolic complication rate and related death. Further studies to balance the risk of anticoagulant continuation or withdrawal are required.

Chronische Subduralhämatome/*Chronic subdural haematomas*

V130

Prädiktoren des funktionellen Outcomes bei Patienten mit symptomatischen chronischen Subduralhämatomen – vorläufige Ergebnisse einer prospektiven Studie

Predictors of functional outcome in patients with symptomatic chronic subdural haematoma – preliminary results of a prospective study

M. Chihi¹, H. Maslehaty², B. O. Hütter¹, R. Jabbarli¹, U. Sure¹, K. H. Wrede¹

¹Neurochirurgische Universitätsklinik Essen, Germany

²Orthopädie & Unfallchirurgie, St. Vinzenz-Hospital Dinsklagen, Germany

Objective

Brain natriuretic peptide (BNP) is a reliable biomarker for congestive heart failure in the acute phase. In our ongoing prospective study, we demonstrated an independent increase of BNP serum levels in patients with chronic subdural hematoma (cSDH). The aim of the current study was to investigate, whether BNP can predict the long-term functional outcome of patients with cSDH.

Methods

In this study, we included patients with cSDH, which underwent surgery at our department between November 2016 and October 2019. We excluded patients with recurrent bleedings, traumatic brain injury, cSDH associated with other intracranial pathologies and with a history of congestive heart failure, renal or endocrine disease from analysis. We measured BNP serum levels pre- and postoperatively and at discharge. BNP values were analysed in view of the patients' medical history and clinical condition. The degree of disability of the patients was assessed using the modified Rankin scale (mRS) at admission, discharge and at 3 to 6 months follow up (FU) via a standardized telephone interview after surgery (n=86).

Results

In total, 94 patients were included in the study and underwent surgery (mean age 73.4 ± 12 years, male/female 3.5:1). 86 patients (91.5%) were available for the FU phone interview. 54 patients (53.5%) had a mRS score >3 (functional dependence, FD). FD was observed at discharge in 32 patients (34%) (McNemar-Test; $p < 0.05$) and in 13 patients (13.8%) at FU ($p < 0.05$). The BNP serum level was preoperatively elevated (> 35 pg/ml) in 68% of the patients (mean=136.8 pg/ml; range 35.3 – 546.7 pg/ml). The univariate analysis showed a significant statistical association between mRS at discharge and patient's age (Spearman's rank test, $p = 0.001$), preoperative BNP ($p = 0.009$) and mRS at admission (Chi-square test, $p = 0.0005$). The mRS at FU showed also a significant relationship with patient's age ($p = 0.005$), preoperative BNP ($p = 0.002$) and GCS at admission ($p = 0.04$). In the multivariate analysis, and after adjusting with mRS and GCS at admission, FD at discharge could be predicted through patient's age ($p < 0.01$), whereas FD at FU solely by the preoperative BNP serum level ($p < 0.01$).

Conclusion

The results of our study provide an important insight into prognostic factors after surgery of cSDH. Although advanced age predicted FD at discharge, it could not predict FD at FU. In contrast, elevated BNP serum levels at admission could predict FD at FD 3 to 6 months after surgery.

Chronische Subduralhämatome/*Chronic subdural haematomas*

V132

Evaluation eines Bewertungssystems zur Vorhersage von revisionsbedürftigen Rezidiven bei chronischen Subduralhämatomen nach Miniboehrlochtrepation

Evaluation of a grading system for prediction of chronic subdural haematoma recurrence requiring reoperation after twist-drill craniostomy

C. Wolfert, A. Von Seydlitz-Kurzbach, S. Hernández-Durán, V. Malinova, V. Rohde, C. Von der Brölie

Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Chronic subdural haematoma (cSDH) often causes mass effect and results in focal neurological deficits and / or reduced level of consciousness. Several techniques for cSDH evacuation have been described so far whereas twist-drill craniostomy (TDC) under local anesthesia represents the least invasive surgical approach. Drainage of the cSDH via TDC might be sufficient to interrupt the pathophysiological vicious circle of osmotic hematoma expansion but the rate of patients requiring reoperation (RrR) is high. This study aims to evaluate a score to predict reoperation after TDC.

Methods

We evaluated our patients who underwent TDC from 01/2014 to 09/2019 using the cSDH grading system from Stanic et al. Preoperative (>130ml: 1 point) and postoperative residual hematoma volume (>200ml: 2 points, 80 – 200ml: 1 point and <80ml: 0 points) were calculated in 0.6 mm axial CT scans. Radiographic appearance (isodense, hyperdense, laminar or separated subtypes [2 points], hypodense, gradation and trabecular subtypes [0 points]) was categorized. Recurrence of cSDH and (if required) further surgeries were documented. Receiver operative characteristic (ROC) curve evaluated the predictive value of the grading system.

Results

A total of 203 patients with mean age of 75 years (range 31-95) were included, 136 of which were male (67%). Single TDC was successful in 79 patients (38.9%), of which n=31 (15.3%) were categorized with 0 points, n=24 (11.8%) with 1 point, n=15 (7.4%) with 2 points, n=5 (2.5%) with 3 points, n=5 (2.5%) with 4 points, and n=0 (0%) with 5 points. RrR was observed in n=124 patients (61.1%). The applied grading system performed well in predicting the RrR risk in patients (AUC=.73). A total score >1 point exhibited a sensitivity of 78% and a specificity of 54% for identifying patients requiring more than a single TDC.

Conclusion

RrR rate in cSDH treated with TDC is high. However, there might be a subgroup of patients for whom TDC might be a suitable therapy option. Incorporation of objective tools such as the cSDH grading system leads to a recognition of individual factors and can allow a stratification of the risk of recurrent surgery in cSDH.

Chronische Subduralhämatome/*Chronic subdural haematomas*

V133

Entfernen der viszeralen Hämatommembran und präoperative Mittellinienverlagerung sind unabhängige Risikofaktoren für postoperative Krampfanfälle in Patienten mit chronischem Subduralhämatom
Visceral membranectomy and preoperative midline shift are independent predictors of postoperative seizures in patients with chronic subdural haematoma

L. Goertz¹, J. Speier¹, A. P. Schulte², P. Stavrinou¹, R. H. Goldbrunner¹, B. Krischek¹, M. Timmer¹

¹Universitätsklinikum Köln, Köln, Germany

²Sankt Franziskus-Hospital, Köln, Germany

Objective

Postoperative seizures represent a potential complication of surgical chronic subdural hematoma (cSDH) evacuation and may occur in 1 – 23% of cases. A risk factor analysis can help to identify patients that may benefit from anti-epileptic prophylaxis.

Methods

This is a retrospective, single-center analysis of consecutive patients with cSDH that underwent burr hole or open craniotomy within a 2-year period. We retrospectively collected patient characteristics, hematoma specifics and procedural aspects and evaluated their impact on postoperative seizures within a 14-day follow-up period by means of univariate and bivariate logistic regression analysis.

Results

The final population consisted of 101 patients with a mean age of 70.1 ± 32.1 years. The incidence of postoperative seizures was 13.9%. At discharge, the mean Markwalder Grading Scale score was higher in patients with seizures (1.1 ± 1.1) than in patients without seizures (0.5 ± 0.8 , $p=0.04$). In the univariate analysis, preoperative midline shift (8.3 mm vs. 4.5 mm, $p=0.045$), open craniotomy (85.7% vs. 55.2%, $p=0.031$), and visceral membranectomy (57.1% vs. 20.7%, $p=0.004$) were significantly associated with postoperative seizures. Binary logistic regression analysis confirmed preoperative midline shift (OR: 1.13, 95% CI: 1.01 – 1.26, $p=0.029$) and membranectomy (OR: 3.9, 95% CI: 1.0 – 15.0, $p=0.048$) as independent risk factors for seizures.

Conclusion

Since seizures can be associated with significant morbidity, patients with preoperative midline-shift may benefit from perioperative anti-epileptic prophylaxis. Furthermore, membranectomy may not be routinely necessary during surgery, as it may trigger seizures and it does not impact recurrence rates, as shown by previous studies.

Chronische Subduralhämatome/*Chronic subdural haematomas*

V134

Das modifizierte subdurale Hämatom im Elderly Score – Ergänzung eines neuen Modells zur Vorhersage von Mortalität bei geriatrischen Patienten mit chronischem Subduralhämatom

The modified subdural haematoma in the elderly score – improving a novel tool to predict mortality in elderly patients suffering from chronic subdural haematoma

A. Von Seydlitz-Kurzbach, C. Wolfert, V. Rohde, C. Von der Brelie, S. Hernández-Durán

Universitätsmedizin Göttingen, Klinik für Neurochirurgie, Göttingen, Germany

Objective

The Subdural Hematoma in the Elderly (SHE) score was published in April 2019 as a novel tool to predict mortality and outcome in elderly patients suffering from subdural hematomas resulting from minor or no trauma. However, the authors included both acute and chronic (CSDH) hematomas in their analysis, thus negating the underlying differences in the pathomechanisms mediating brain injury and clinical presentation between these entities. In this study, we attempted to validate the SHE in a cohort of only CSDH.

Methods

We applied the SHE in a retrospective cohort of elderly (>65 years) patients with CSDH admitted at our center from January 2015 to September 2019. Receiver operative characteristic (ROC) curves were then calculated for both 30-day mortality and outcome. Outcome was dichotomized as "good" for Glasgow Outcome Score (GOS) 4-5, and "poor" for GOS 1-3. Further variables were analyzed in our cohort as potential predictors of mortality, such as anticoagulant use, and hematoma appearance on imaging. Neurological status was further categorized with Markwalder grade. Statistically significant variables were then incorporated into a modified SHE (mSHE), which was then evaluated with ROC for 30-day mortality and outcome and compared to the SHE.

Results

A total of 171 patients were included. Mean age was 79 years (range: 65-95). Most patients were males (n=113, 66%), and used anticoagulants (n=104, 61%). Glasgow Coma Scale (GCS) was between 13-15 points in most patients (n=138, 81%), but patients had moderate to severe neurological deficits not captured by GCS (Markwalder ≥ 2 , n=111, 65%). An even distribution between trabecular and laminar hematomas was seen (n=99, 58%, and n=72, 42%, respectively), and mean hematoma volume was 61cc (range: 27-317). Mortality was low at n=7/171, 4%. SHE failed to predict mortality in our cohort (AUC=.56) but performed well for outcome prediction (AUC=.74). By adding the Markwalder grade into the SHE (mSHE), we were able to increase performance in mortality prediction (AUC=.67). Outcome prediction was similar for the mSHE (AUC=.75).

Conclusion

The SHE seems a reliable tool to predict outcome after CSDH in the elderly. However, incorporating a more detailed quantification of neurological deficits might increase its performance in mortality prediction.

Tiefenhirnstimulation I/Deep brain stimulation I

V135

Physiologische Exploration des periventriculären und periaquäduktalen Graus mittels intraoperativer Mikroelektrodenableitungen und postoperativer direktonaler Tiefenhirnstimulation *Physiological mapping of the human periventricular/periaqueductal gray matter using intraoperative microelectrode recordings and postoperative directional deep brain stimulation*

R. Van Paesschen¹, P. Van Loo¹, T. Van Havenbergh¹, C. Helmchen², D. Rasche³, V. M. Tronnier³, C. K. E. Moll⁴

¹GZA Ziekenhuizen, Campus Sint-Augustinus, Abteilung für Neurochirurgie, Antwerpen, Belgium

²Universitätsklinikum Schleswig-Holstein, Klinik für Neurologie, Lübeck, Germany

³Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Lübeck, Germany

⁴Universitätsklinikum Hamburg-Eppendorf, Institut für Neurophysiologie und Pathophysiologie, Hamburg, Germany

Objective

The periventricular and periaqueductal gray matter (PVG/PAG) is a common target in deep brain stimulation (DBS) surgery for intractable pain. Oculomotor side effects such as oscillopsia and gaze deviation are commonly reported in patients undergoing PVG/PAG-DBS. While the effects of electrical stimulation are relatively well described, the human midline mesodiencephalic transition zone is hitherto largely unexplored at a cellular level in man. Here, we describe both intraoperative and postoperative mapping results in the PVG/PAG region of a 51-year old patient suffering from intractable lower back and leg pain due to multiple failed back surgeries.

Methods

Microelectrode-recordings (MER) during awake stereotactic surgery provided unique close-up views of gaze-related neuronal activities. Directed electrical stimulation delivered through the implanted segmented DBS leads was then used during the postoperative phase to systematically explore stimulation-induced effects within the PVG/PAG region.

Results

Neuronal activity in the CM/Pf complex consisted of tonic regular single spike discharges intermingled with typical high-frequency burst discharges. At the ventral thalamic base, we noted the presence of neurons with tonic regular discharges at high frequency (70-100Hz). A decrease of background activity then indicated the transition to a fiber-rich area. On the right side, 4mm above the target level, the background became more active again. Here, we found several oculomotor responsive neurons over a course of 2mm on the central and posterolateral tracks, respectively. These neurons were silent at rest, and did not discharge upon upward or horizontal eye movements. All neurons became selectively active during downward movements of the eyes. During downward smooth pursuit, their discharge rate varied approximately with eye velocity. 3D-reconstruction revealed that the left lead tip was positioned within the PVG. The right lead tip, however, showed a depth deviation and was located slightly posterior within PAG.

Conclusion

Our case demonstrates that clinical assessment of ocular motility can be used intraoperatively to identify (pre-)motor centers for gaze in the human median rostral midbrain. Furthermore, the use of directional leads may prove especially helpful to further explore the intricate anatomical landscape of hitherto incompletely characterized brainstem DBS targets such as the PAG or the pedunculopontine nucleus.

Tiefenhirnstimulation I/Deep brain stimulation I

V136

Charakteristika des Beta-Bands in den lokalen Feldpotentialen des humanen *Nucleus subthalamicus* *Characteristics of the beta band of the local field potentials of the human subthalamic nucleus*

J. H. Mehrkens¹, F. Hell², T. Köglsperger², A. Plate², K. Bötzel²

¹Klinikum der Ludwig-Maximilians-Universität München, Klinik und Poliklinik für Neurochirurgie, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, Klinik und Poliklinik für Neurologie, München, Germany

Objective

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) in patients with Parkinson's disease allows for the recording of local field potentials (LFPs) in this part of the basal ganglia. Such recordings are of great interest since they may serve as possible biomarkers for the current "physiological status" of the patient and thus might be used for "sensing" and consecutive adaptive stimulation ("closed-loop DBS").

Methods

38 Parkinson-patients (mean age 60.1 years (range 47-71), 11 female/27 male, mean disease duration 11.6 years (range 7-20) having undergone STN-DBS were included. LFP-recordings were performed via externalized leads in all patients. Recordings were done with the patient in a recumbent position during rest (awake patient, eyes open), during right/ left hand opening and closing (frequency 2/s; 5 min.), during standing for 5 min, slow walking 30 m and fast walking 30 m. LFPs were amplified, recorded and digitally stored (resolution 0.1 μ V, sampling rate 2000 Hz, filter 0.1 Hz – 500 Hz). Raw data were high-pass filtered (3rd order Butterworth, 1 Hz) and resampled to a sampling frequency of 422 Hz. The fast Fourier algorithm of Malta and averaging the resulting spectra were used to compute the frequency spectrum of all data.

Results

Fifty-one of 76 (67.1%) recordings had one peak, eight (10.5%) recordings showed two peaks, and 17 (22.4%) recordings showed no peak. Movement of either hand did not reliably suppress beta peaks. Walking reduced the peaks in the high beta band (above 20.2 Hz) but not the peaks in the low beta band.

Conclusion

Beta-peaks can be detected in a high percentage of LFP-recordings using DBS-electrodes. Beta suppression caused by movement is dependent on the type of movement and the frequency of the peak. Further studies should consider the fact that the beta frequency band may host different physiological processes - that might be suitable biomarkers for "adaptive DBS".

Tiefenhirnstimulation I/Deep brain stimulation I

V137

Austausch von Standard-DBS Elektroden für ein direktionales System in Patienten mit fortgeschrittenem essentiellen Tremor – Ergebnisse der "RESCUED- Studie"

Replacing standard DBS with a directional lead system in patients with advanced essential tremor – results from the "RESCUED – trial"

M. T. Krüger^{1,2}, J. Avecillas-Chasin², C. R. Honey²

¹Kantonsspital Sankt Gallen, Neurochirurgie, St. Gallen, Switzerland

²University of British Columbia, Neurosurgery, Vancouver, Canada

Objective

Patients with advanced Essential Tremor (ET) treated with deep brain stimulation (DBS) of the ventral intermediate nucleus (VIM) can experience reduced tremor control with progression of their disease. Initially, tremor improvement can be obtained by increasing the stimulation. Eventually, this can cause side effects as the standard lead causes unwanted stimulation of adjacent regions (e.g. internal capsule). In this study, we replaced the standard leads with directional leads in a cohort of patients with advanced ET and insufficient tremor control. This prospective trial was designed to evaluate the clinical benefits and complications of directional leads in this cohort of patients.

Methods

Six patients with advanced ET and bilateral DBS with standard leads in the VIM were entered into the study. Patients must have initially experienced optimal tremor control but later developed tremor, which could only be controlled with concurrent unwanted side-effects. Leads must have been optimally placed (post-operative CT fusion). Patients then had their standard DBS system (sDBS, Medtronic) replaced with directional leads (dDBS, Boston Scientific). Tremor rating scale (TRS) and quality of life tests were performed before and after replacement surgery. The primary endpoint was the degree of tremor reduction with no side effect for the standard and directional lead systems. The secondary endpoints were improvements in quality of life measures e.g. QUEST.

Results

When comparing the amount of tremor (OFF-ON) with no side effects before (sDBS) and after replacement (dDBS), there is a statistically significant improvement (Wilcoxon Signed- Rank Test: $p < 0.05$) in favour of the dDBS system. The results of the QUEST (Quality of Life in Essential Tremor Questioner) and VHI (Voice Handicap Index) show an improvement in most patients (5/6). The amount of hours needed to program the directional leads, reflect a learning curve (from 28 hours for the first to four hours for the last patient). There were no complications from surgery.

Conclusion

Directional leads can significantly improve tremor without additional side effects in advanced ET patients with VIM DBS when compared to standard DBS leads. This can improve patients' quality of life related to their tremor and voice. Exchanging systems is a safe option for advanced ET patients. Furthermore our data supports the initial implantation of dDBS to improve patients' tremor without side-effects in less severely affected patients at an earlier stage.

Tiefenhirnstimulation I/Deep brain stimulation I

V138

Genauigkeit und Effizienz der 3D-Volumentomographie (XT) im Vergleich zur Computertomographie (CT) basierten Tiefenhirnstimulation (THS)

Accuracy and efficiency of 3D-fluoroscopy (XT) versus computed tomography (CT) based deep brain stimulation (DBS) surgery

M. Cooper¹, C. Restrepo¹, R. Hill¹, M. Hong¹, R. Greene¹, L. Weise^{1,2}

¹Dalhousie University, Neurosurgery, Halifax, Canada

²Johann Wolfgang Goethe-Universität Frankfurt am Main, Neurochirurgie, Frankfurt am Main, Germany

Objective

To compare stereotactic frame registration with computed tomography (CT) or 3D fluoroscopy (XT) for accuracy and precision of lead implantation, efficiency, and radiation dose delivered in frame-based deep brain stimulation (DBS) surgery.

Methods

A retrospective chart review was performed that included patients with movement disorders that underwent DBS surgery at our centre by the same surgeon between December 2016 and August 2019. Patients received frame registration with either CT or XT. The actual site of electrode placement on postoperative CT was compared to the planned lead trajectory on preoperative CT to determine mean absolute differences and Euclidean distance for precision and accuracy of implantation. Efficiency was measured as the time required to register the stereotactic frame (i.e. the time between the patient entering the OR and the initial skin incision). The radiation exposure from CT or XT was measured by the dose length product (DLP). These parameters were compared between CT and XT patient groups using a one-way ANOVA.

Results

Twenty-five patients in the CT group and 16 in the XT group underwent DBS surgery (Table 1). The mean absolute difference between patient groups did not differ significantly for the x ($p=0.331$), y ($p=0.951$) or z ($p=0.807$) coordinates (Table 2). The Euclidean distance (\pm standard error of the mean, or SEM) between the CT group (2.11 ± 0.25 mm) and XT group (2.17 ± 0.21 mm) was not significantly different ($p=0.874$). The mean radiation dose (\pm standard deviation, or SD) delivered by CT was 1269.3 ± 112.9 mGy*cm, which was significantly higher than XT (220.0 ± 0.1 mGy*cm) ($p<0.001$). The difference in frame registration time (\pm SD) between CT (107.8 ± 23.1 minutes) and XT (106.0 ± 18.2 minutes) did not reach statistical significance ($p=0.518$).

Conclusion

XT-based frame registration was shown to result in accurate lead implantation, which did not significantly differ from CT. XT was shown to result in significantly lower radiation exposure, which may improve both patient and provider safety. Surprisingly, registration time was not significantly different between patient groups, but this might be attributed to a learning curve effect as XT was only recently introduced at our centre for DBS. Future studies might further examine the difference in registration time between these patient groups and explore complications and clinical outcomes associated with XT-based registration.

Fig 1

Table 1 Comparison of demographic data and lead target between CT and XT patient groups

Characteristic	CT	XT
Total No. of Patients	25	16
Mean Age \pm SD	55.4 \pm 9.9	61.8 \pm 12.4
Sex: Male/Female	19/6	11/5
Diagnosis		
Parkinson's Disease	18	8
Dystonia	4	3
Tremor	3	5
Anesthesia		
Local	17	10
General	8	6
Total No. of Leads	45	31
Anatomical Target		
STN	30	13
VIM	6	12
GPi	9	6
Side		
Unilateral	5	1
Bilateral	20	15

Fig 2

Table 2 Mean absolute differences \pm SEM (mm) between final electrode location and planned trajectories at x, y, and z coordinates for either CT or XT-based frame registration

Coordinate	CT	XT	Significance (p-value)
x	1.10 \pm 0.19 mm	1.38 \pm 0.18 mm	0.331
y	0.86 \pm 0.19 mm	0.84 \pm 0.15 mm	0.951
z	1.14 \pm 0.20 mm	1.06 \pm 0.23 mm	0.807

Tiefenhirnstimulation I/Deep brain stimulation I

V139

Operative Lernkurve in der roboterassistierten, stereotaktischen Chirurgie *Surgeon's learning curve in stereotactic robot-assisted surgery*

K. Machetanz, F. Grimm, A. Gharabaghi, M. Tatagiba, G. Naros

Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

Objective

Frame-based stereotactic procedures are still the gold standard in neurosurgery, however there is an increasing interest in robot-assisted technologies. Introducing these increasingly complex technologies in the clinical setting raises the question about the time efficacy of the system (i.e. operative time) and the essential learning curve of the surgeon.

Methods

This retrospective study enrolled 23 patients (52.4+/-24.1 years, 11 female) who underwent a robotic-assisted procedure performed by the same surgeon within the first four months after installation of the robot. We evaluated the intraoperative preparation time for setting-up the system and the operation time itself (i.e. skin-to-skin).

Results

In the first four months, we performed 23 robotic-assisted surgeries (19 biopsies, 3 SEEG implantations and 1 endoscopic procedure). The mean intraoperative preparation time was 36.7+/-16.0 min strongly depending on the applied registration technique - i.e. skin fiducials (59.5+/-4.7 min, n = 4), bone fiducials (29.1+/-8.3 min, n = 14) or surface registration (40.0+/-19.5 min, n = 5). However, there was a significant reduction of the preparation time during that period to 21.2+/-3.4 min (for the last five surgeries). Mean operation time was 54.6+/-34.3 min (biopsies: 39.6+/-11.1 min, SEEG: 110.3+/-28.7 min, Endoscopy: 72 min). In contrast to the preparation time, there was no significant improvement of the operation time over time.

Conclusion

Introducing stereotactic robotic-assisted surgery in an established clinical setting necessitates initially a prolonged intraoperative preparation time. However, there is a steep learning curve within the first 20 cases. Thus, a stereotactic robot can be integrated in the daily routines in a decent period of time.

Tiefenhirnstimulation I/Deep brain stimulation I

V140

Outcome nach Thalamotomie mittels MR-gesteuertem fokussierten Ultraschall in der Behandlung des essentiellen Tremors – Ergebnisse aus einem neu initiierten MRgFUS-Behandlungszentrum
Outcome after thalamotomy for treatment of essential tremor using MR-guided focused ultrasound (MRgFUS) – results from a newly initiated MRgFUS treatment centre

V. Borger¹, V. Purrer², V. C. Keil³, C. Kindler², C. C. Pieper³, H. Vatter¹, U. Wüllner²

¹Universitätsklinikum Bonn, Klinik und Poliklinik für Neurochirurgie, Bonn, Germany

²Universitätsklinikum Bonn, Klinik und Poliklinik für Neurologie, Bonn, Germany

³Universitätsklinikum Bonn, Neuroradiologie, Bonn, Germany

Objective

Magnetic resonance-guided focused ultrasound (MRgFUS) offers an effective approach for treatment of drug-resistant essential tremor (ET) using incisionless thalamotomy. Being a recently clinically approved option to treat movement disorders, this technology is increasingly gaining interest. Dozens of specialized centers around the world offer MRgFUS thalamotomy for treatment of tremor symptoms in essential tremor (ET) and Parkinson's disease (PD). The authors report their experience in treating patients with ET using MRgFUS at a newly initiated treatment center.

Methods

From May 2018 to August 2019, from a total of 35 eligible patients 30 were treated with unilateral thalamotomy using MRgFUS. The effects on tremor were assessed using the Clinical Rating Scale for Tremor (CRST) at baseline, directly post-interventional (T1), at 1 month (T2), and at 6 months (T3). Furthermore, treatment associated side effects were analyzed at 1 month and 6 months follow-up (FU) visits.

Results

From 30 patients, 2 patients were excluded from the analysis (1 PD patient, 1 patient lost for FU). In the remaining 28 patients with ET, the mean age was 69±12.45 years (y), the mean duration of symptoms was 29±17.3 y. The mean total CRST score at baseline was 59.75±15.15. Compared to baseline, the mean total CRST score was significantly decreased at each FU ($p<0.0001$ at T1; $p<0.0001$ at T2; $p<0.001$ at T3). The most often occurring side effects were gait disturbances (36% at T1; 29% at T2; 30% at T3), followed by paresthesia (22% at T1; 14% at T2; 30% at T3). None of the side effects were disabling.

Conclusion

MRgFUS thalamotomy in treating ET is effective and safe. In regard to reduce the occurrence of side effects and to maximize the treatment effect, more effort should be made to optimize the lesioning due to individualization of targeting for each individual patient.

Selläre Prozesse/*Sellar lesions*

V141

4K-3D Mikrovideoskop (Orbeye) in der transspheoidalen Hypophysenchirurgie ***4K3-dimensional microvideoscope (Orbeye) system for transspheoidal pituitary surgery***

R. Rotermund, J. Regelsberger, K. Osterhage, J. Flitsch

Universitätsklinikum Hamburg-Eppendorf, Neurochirurgie, Hamburg, Germany

Objective

Video microscopy represents a paradigm shift in microsurgery procedures. Multiple reports of experiences with different exoscope solutions in the neurosurgical field are present. In these first reports, this new technology was found not to be applicable for transspheoidal pituitary surgery. As a specialized center for pituitary surgery with a high case load of more than 300 microscopic transspheoidally operated patients per year, we tested the 3D 4K Orbeye (Olympus) as an attempt to evaluate the system to a greater extend for transspheoidal pituitary surgery with taking a learning curve for this new way of performing surgery into account.

Methods

We report 67 clinical cases performed with the Orbeye (Olympus). The patients cohort is grouped into a first group with sporadic (7 patients, 06.02.-01.05.2019) and a second group with continuous use of the Orbeye (60 patients, 03.05-19.07.2019). An observational study with a questionnaire was conducted. The functionality of the Orbeye was evaluated based on the extend of the tumor resection. The surgeon's impression was documented as benefits and disadvantages of the system.

Results

The patients presented with a wide range of pathologies, containing a majority of cases within the groups of non-functional pituitary adenomas (n=22), STH-adenomas (n=19), ACTH-adenomas (n=9). The patients had diverse clinical history with 30 % of patient being previously treated. No complications based on the usage of the new 3D 4K exoscope occurred intra- or postoperatively. Therefore there was no need to switch back to microscope in any of the cases. The Surgeons rated the Orbeye beneficial in instrument size, positioning, surgeon's ergonomics, small learning curve, image resolution and high magnification possibility.

Conclusion

Video microscopy challenges the currently used microscopes for pituitary surgery. Due to its digital zoom-option as well the 3-D visualization and depth perception it seems an advancement in comparison to conventional microscopy. Regarding a comparison with endoscopy techniques, a comparative study is needed, however, the 3D 4K-Orbeye-exoscope combines benefits of both techniques.

Selläre Prozesse/*Sellar lesions*

V143

Benötigt man Gadolinium bei der Identifikation von Resttumor bei Hypophysenadenom OPs in einem intraoperativen MRT?

Identification of tumour residuals in pituitary adenoma surgery with intraoperative MRI – Do we need gadolinium?

C. Roder¹, B. Bender², G. Gohla², U. Ernemann², M. Tatagiba¹, J. Honegger¹

¹Universitätsklinikum Tübingen, Neurochirurgie, Tübingen, Germany

²Universitätsklinikum Tübingen, Neuroradiologie, Tübingen, Germany

Objective

To evaluate the diagnostic accuracy of high-resolution T2w intraoperative magnetic resonance imaging (iMRI) with 1.5T for detecting pituitary adenoma remnants compared to contrast enhanced T1-weighted images.

Methods

42 patients underwent iMRI-guided resection of large pituitary macroadenomas and fulfilled the inclusion criteria for this retrospective analysis. Intraoperative and postoperative imaging evaluation of tumor residuals and localization were assessed by two experienced neuroradiologists in a blinded fashion. The diagnostic accuracy of T2w and contrast enhanced T1w images were evaluated.

Results

The diagnostic accuracy for detecting tumor residuals of high-resolution T2w images showed highly significant association to contrast enhanced T1w images ($p < 0.0001$). Furthermore, identification rate of tumor remnants in different compartments, e.g. cavernous sinus, was comparable. In total, coronal T2w images provided a diagnostic sensitivity of 97.7 % and specificity of 100 % compared to the gold standard of contrast enhanced T1w images. The postoperatively expected extent of resection proved to be true in 97.6 % according to MRI 3 months after resection.

Conclusion

High-resolution T2w intraoperative MR images provide excellent diagnostic accuracy for detecting tumor remnants in macroadenoma surgery with highly significant association compared to T1w images with gadolinium. The routine-use and need of gadolinium in these patients should be questioned critically in each case in the future.

Selläre Prozesse/*Sellar lesions*

V144

SIADH als Folge endoskopischer transsphenoidaler Hypophysen-Eingriffe – eine retrospektive Analyse *SIADH following endoscopic transsphenoidal pituitary surgery – a retrospective analysis*

M. E. Weidemeier¹, A. Steveling², H. W. S. Schroeder¹

¹Universitätsmedizin Greifswald, Klinik und Poliklinik für Neurochirurgie, Greifswald, Germany

²Universitätsmedizin Greifswald, Klinik und Poliklinik für Innere Medizin A, Greifswald, Germany

Objective

Hyponatremia caused by a syndrome of inappropriate antidiuretic hormone secretion (SIADH) represents a possible postoperative complication in pituitary surgery. Complication rates found in the literature diverge between 2.5 % and 38 %. Here we present a retrospective analysis of postoperative occurrence of SIADH in a case series of endoscopic transsphenoidal pituitary surgery.

Methods

Between November 2007 and June 2019 we consecutively performed 206 endoscopic transsphenoidal pituitary operations that were included. Perioperatively we monitored electrolytes in both serum and urine along their osmolality in order to look for SIADH and other hyponatremic episodes. All cases were supervised by our endocrinology department.

Results

Eight of the 206 cases developed postoperatively a SIADH (3.9 %). In average onset of hyponatremia was at the sixth postoperative day ($6.0 \text{ d} \pm 1.3 \text{ d}$), endured four days ($4.0 \text{ d} \pm 1.4 \text{ d}$) during which medium sodium levels were at $128.2 \text{ mmol/l} (\pm 4 \text{ mmol/l})$. Along the hyponatremic episodes not diagnosed as SIADH there were three patients (1.5 %) with a cerebral salt wasting syndrome (CSW) and one case of Addison crisis (0.5 %). In our series neither age nor gender nor revision surgery nor any other factors were identified as risk factors for developing postoperative SIADH.

Conclusion

Our results are generally in line with current results in the literature, however our rate is located at the lower end of reported SIADH complication rates. Hyponatremic episodes are not uncommon and a potentially dangerous complication of transsphenoidal pituitary surgery. It is critical to identify and treat hyponatremia as soon as possible. Moreover it is crucial to distinguish between SIADH and CSW as their respective therapies are oppositional.

Selläre Prozesse/*Sellar lesions*

V145

Stellenwert der intraoperativen MRT zur Resektion hormonaktiver Hypophysentumoren – Ergebnisse einer konsekutiven retrospektiven Analyse von 114 Fällen

Value of intraoperative MRI in functional pituitary adenomas with active hormone secretion – observations from a consecutive retrospective single-centre cohort of 114 cases

M. Scherer¹, P. Zerweck¹, M. Bendszus², A. W. Unterberg¹, C. Beynon¹

¹Universitätsklinikum Heidelberg, Heidelberg, Germany

²Universitätsklinikum Heidelberg, Heidelberg, Germany

Objective

Functional pituitary adenomas (FPA) represent a special sub-entity among pituitary adenomas which come with characteristic challenges for imaging diagnostics, medical and surgical treatment. Transsphenoidal surgery (TSS) is an established treatment option for FPAs aiming at better hormone remission associated with complete resections. In this series we evaluated the role of intraoperative 1.5 tesla MRI for resection of FPAs emphasizing on intraoperative findings, the extent of resection and postoperative hormone function.

Methods

From 01/2010 to 12/2017 a total of 114 consecutive FPAs with TSS were retrospectively reviewed. All cases had excess hormone secretion on preoperative endocrinological evaluation. IMRI findings were analysed focussing on intraoperative decision making. Extent of resection was evaluated on postoperative MRI and compared to iMRI findings. Postoperative hormonal remission was evaluated according to consensus criteria. Variables of incomplete resections and persistent hormone excess was evaluated in binary regression analysis.

Results

We included 23 cases with hypercortisolism (20%), 56 with acromegaly (49%) and 35 with prolactinoma after failed medical therapy (31%). Preoperative MRI showed 81 macroadenomas (71%) with a median Knosp grade 1 (range 0-4) and involvement of optic chiasm in 41 cases (36%). After iMRI, re-inspection of the cavity helped to clear equivocal iMRI findings in 19 cases (17%). Additional tumor was removed in 22 (20%) leading to complete resections in all but 4 cases. Overall, complete resection was achieved in 82%. IMRI had no direct effect on surgical results in 2/3 of cases but exhibited excellent agreement with postoperative MRI. Hormonal remission was achieved in 59%. Supra- and parasellar invasion and preoperative visual impairment were significant predictors for incomplete resections. Risk for persistent hormone excess was increased 7-fold after incomplete resections.

Conclusion

While the strong impact of complete adenoma resections was corroborated particularly for treatment of excess hormone secretion in this series, we observed a manifold value for iMRI in resections of FPAs. It expectedly assisted to detect remnants in large and invasive tumors but also helped to rule out residual tumor by allowing for focused re-inspection of equivocal findings. High diagnostic quality might repeal the need for postoperative MRI which supports use of iMRI in FPA resections.

Selläre Prozesse/*Sellar lesions*

V146

Kultivierung von primären Chordomzellen und experimentelle Untersuchung der 5-ALA gestützten photodynamischen Therapie

Cultivation of primary chordoma cells and examination of 5-aminolevulinic acid based photodynamic therapy

H. Gull, C. Karadag, B. Senger, H. J. Steiger, D. Hänggi, J. F. Cornelius

Universitätsklinikum Düsseldorf, Neurochirurgie, Düsseldorf, Germany

Objective

Chordoma is a locally aggressive, osteodestructive and metastasizing tumor. Current adjuvant treatment is ineffective. New effective treatment modalities have to be explored. 5-ALA PDT has shown promise in *proof of principle*- experiments with immortalized human chordoma cell lines. The objective was to confirm these findings in primary cells and to report interim results.

Methods

Tissue samples from 2 different chordoma patients were harvested and processed for cultivation according to a lab internal adapted protocol. Then cells were incubated with different 5-ALA concentrations for 6h and afterwards exposed to PDT (diode laser for 625 seconds at $\lambda=635$ nm with 15,6 J/cm²). Negative control groups were also realized. Cell viability was assessed by WST-1 assay.

Results

Cultivation of primary chordoma cells was successful. The higher the number of passage, the shorter the doubling-time of the two primary chordoma cell cultures. Initially, doubling-time was 28 days. Cells from the fifth passage reached a doubling-time of about 10 days. Light-microscopy confirmed typical morphology for chordoma cells, so-called physaliphorous cells (Fig. 1 and 2). Tumor cells were significantly destroyed by 5-ALA PDT. Cell viability of primary cells, established from tissue samples of the first chordoma was significantly lower at higher 5-ALA concentrations (ANOVA; $p \leq 0.001$ for ≥ 30 $\mu\text{g/ml}$ ALA). Primary cells from tumor tissue of the second chordoma operation are currently in period of cultivation.

Conclusion

Two primary chordoma cell cultures based on intra-operatively resected tumor tissue could successfully be established. The presented *in vitro*-model allowed analysis of successful 5-ALA PDT in individual patient's tissue. Further, experiments with different parameters like co-drugs, different incubation time and laser parameters are planned. This research avenue harbors great potential for future adjuvant therapy of chordomas.

Fig 1

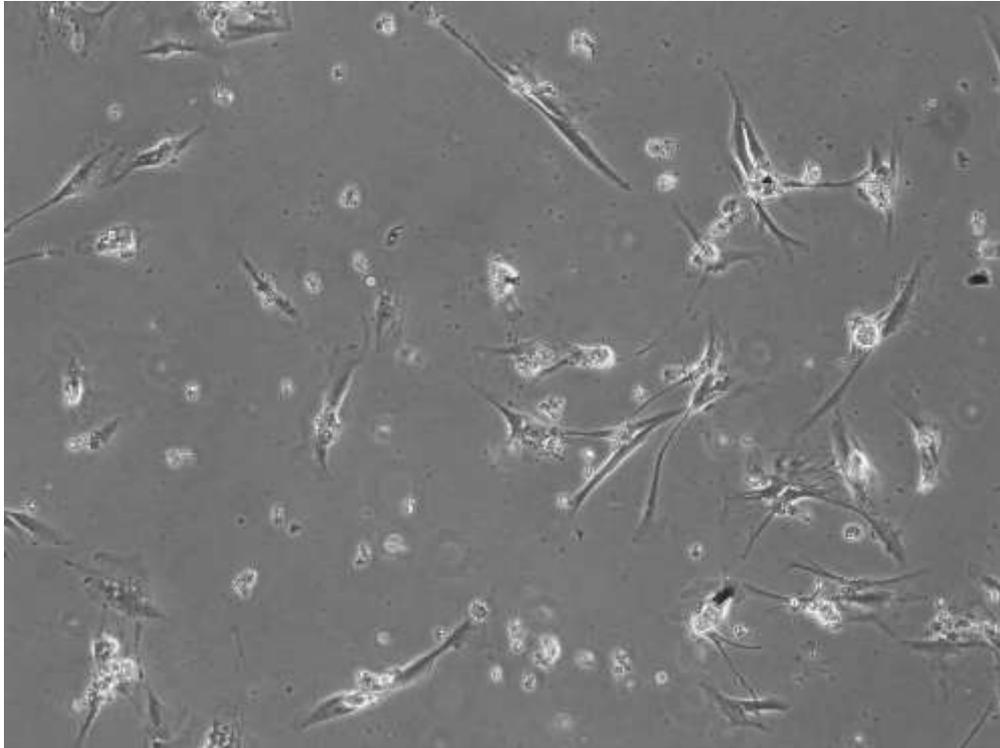
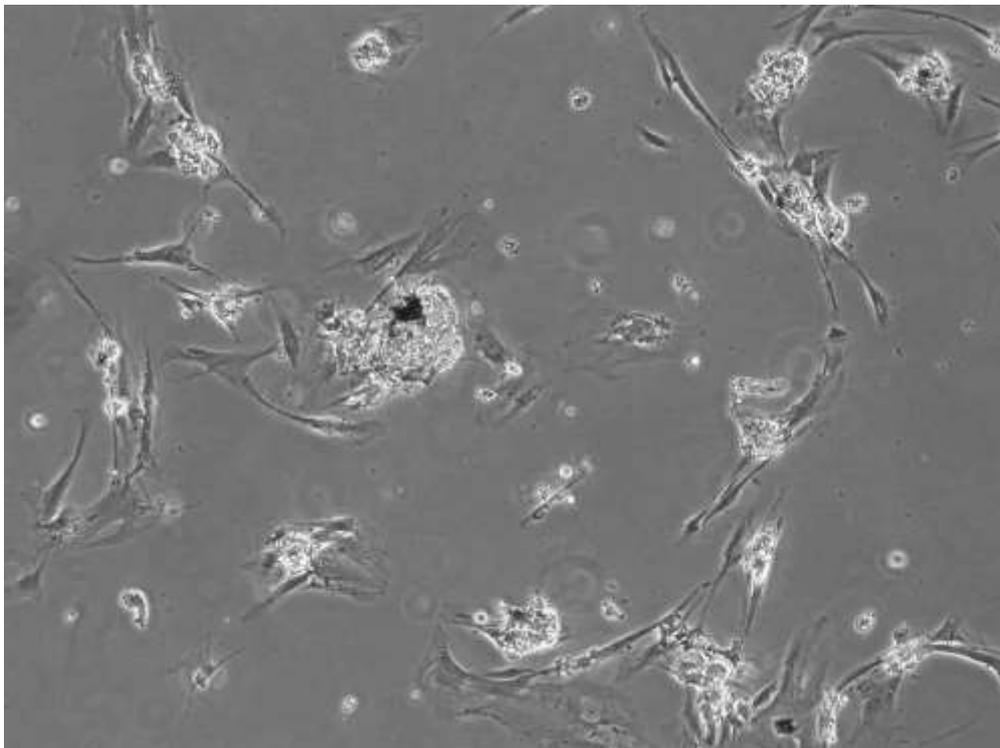


Fig 2



Pädiatrische Neurochirurgie I / Paediatric neurosurgery I

V147

Management der Chiari Malformation – individualisierte Therapie und Outcome *Management of Chiari malformation – individualised treatment and outcome*

M. Messing-Jünger, F. Knerlich-Lukoschus, A. Röhrig, S. T. Jünger

Asklepios Klinik Sankt Augustin, Neurochirurgie, Sankt Augustin, Germany

Objective

The contemporary concept of the so called Chiari malformation (CM) comprises different conditions in respect of the underlying pathology, also classified as CM0, CM1, CM1.5 and CM2. Specific treatment options should be offered according to the individual clinical condition. The presented clinical series reflects the variety of the clinical Chiari spectrum.

Methods

This is a retrospective study of a consecutive single unit (5 surgeons) series of patients who underwent foramen magnum decompression between 2010 and 2019 due to CM. Patients managed conservatively or with shunting procedure alone were excluded. Demographic data, diagnostic findings, relevant comorbidities, surgical treatment and outcome data are presented.

Results

A total of 96 patients have been operated. Mean age was 10 years (range 0.2 – 60 y; 4 < 1 y; 10 > 18 y). 50 patients were male, 46 female. 48(50%) presented with additional syringomyelia at time of surgery, 36(37.5%) with scoliosis. 11 patients required secondary surgeries (7 own / 4 external). The following CM subtypes have been treated: CM0(4), CM1(47), CM1.5(27) and CM2(18). Associated syrinx and scoliosis were most often seen in CM2 patients (67%, 83%). All CM0 patients underwent intradural management. In the CM1 group 25(53%) received bone only decompression (11[41%] in CM1.5), 23(49%) intradural inspection and dural augmentation (36[49%] in CM1.5), 14(30%) tonsillar shrinking (25[34%] in CM1.5) and additional instrumentation due to instability in 1(2%) patient (8[11%] in CM1.5). In the CM2 group, 6 bone only and 10 intradural procedures with dural augmentation and additional tonsillar shrinking in 2 have been performed. The overall complication rate after complete follow up is 8.3%, leading to secondary surgery in 2 (2.1%) cases (CSF collections). Resolution or improvement of symptoms could be observed in all patients, syringomyelia resolution in 11 out 32 patients (CM2 excluded). There was no statistical difference regarding CM type, treatment and outcome. Bone only decompression provides similar results in CM1, CM1.5 and CM2 compared to intradural procedures, but syrinx resolution takes a longer time.

Conclusion

Different CM subtypes require specific surgical treatment. Bone only decompression seems to have similar good results in respect of resolving symptoms and syringomyelia as well as preventing scoliosis progress compared to intradural techniques. No severe complications occurred. Secondary complication surgery became necessary in 2 patients only.

Pädiatrische Neurochirurgie I/Paediatric neurosurgery I

V148

Expressionsprofile proinflammatorischer Zytokine und Chemokine während des pränatalen Zeitverlaufes in einem spinalen Dysraphie-Modell in der Ratte

Expression profiles of cytokines and chemokines at different prenatal time-points in a rat model of open spinal dysraphism

G. Cohrs¹, A. K. Blumenröther¹, J. P. Sürrie¹, M. Synowitz¹, J. Held-Feindt¹, F. Knerlich-Lukoschus^{1,2}

¹Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Kiel, Germany

²Asklepios Klinik Sankt Augustin, Klinik für Kinderneurochirurgie, Sankt Augustin, Germany

Objective

Cellular and molecular mechanisms induced by the hypothesized "second hit", which underlies progressive functional decline of the myelomeningocele (mmc) placode, are not well understood. We previously identified key players of post-traumatic lesion cascades in human mmc tissues obtained during post-natal repair. We went back to bench and investigated these mediators in the prenatal course in standardized conditions of an mmc-animal model.

Methods

A retinoic acid mmc model was established using time-dated Sprague-Dawley rats, which were gavage-fed with all-trans retinoic acid (RA; 60 mg/kg) dissolved in olive oil at day E10. Controls received olive oil only. Fetuses were obtained at E16, E18, E22. Spinal cord tissues were screened by real-time RT-PCR for cytokines and chemokines, known to play a role in lesion cascades in the central nervous system. Proinflammatory cytokines which were found on elevated mRNA level like TNFalpha (TNFa), Interleukin-1beta (IL-1b), and their receptors were analysed further by immunohistochemistry (IHC) and double-immunofluorescence-labelling (DIF) with cellular markers. Representing neuro-restorative markers the ligand-receptor pair Erythropoietin (Epo) and EpoR were investigated. Fetal control sc tissue was obtained at the respective time points.

Results

IL-1b showed significant induction at E22, its IL1-RI was induced at E16 and E22, in IHC staining was confined to the matrix and marginal layer. Co-staining of IL-1b and Vimentin (VIM) suggests astroglial cells as a possible source of these mediators, whereas IL1-RI co-stained with VIM and Iba1, a marker for microglia. TNFa/-R showed significant induction at E22, DIF confirmed co-staining with Iba1 for the ligand-receptor pair. CXCL12 and CXCR4 showed elevated mRNA levels in controls and mmc, as these cytokines play a crucial role in developmental processes, mRNA levels drop throughout the prenatal time course as expected. The fractalkine CX3CL1 and its receptor CX3CR1 show significant elevation throughout the investigated time course, there is no significant induction compared to controls. Epo is induced significantly at E16, EpoR shows high levels at E22.

Conclusion

Pro-inflammatory cytokines like TNFa/-R, IL-1b/-RI exhibited a time-dependent prenatal expression in the retinoic induced mmc rat model. Epo/-R also exhibited different expression patterns compared to controls. These mediators provide potential trial targets in the development of adjuvant therapies.

Pädiatrische Neurochirurgie I/Paediatric neurosurgery I

V149

Modeling guides in der Kraniosynostosenchirurgie – "Cutting guides" wurden anhand von CT-Daten in den letzten Jahren in die Kraniosynostosen-Chirurgie eingeführt. Ziel der vorliegenden Studie ist es, die Genauigkeit und Praktikabilität von "modeling guides" durch 3D-Fotographie zu evaluieren.

Modelling guides for craniosynostosis surgery and follow-up by 3D photography – "Cutting guides" produced on CT-data have been introduced to craniosynostosis surgery in recent years. The aim of this study is to evaluate the accuracy and practicability of "modelling guides" through 3D photography.

J. C. Roldán¹, J. Gliemroth²

¹Katholisches Kinderkrankenhaus Wilhelmstift Hamburg, Plastische Kindergesichtschirurgie und Gesichtsfehlbildungschirurgie, Hamburg, Germany

²Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Lübeck, Germany

Objective

Despite efforts to avoid ionizing radiation, the so-called "cutting guides" for cranioplasty in craniosynostosis, based on CT data, have been propagated in recent years. The aim of the present study is to evaluate the feasibility and accuracy of the planning and implementation of "modeling guides" for cranioplasty in craniosynostosis surgery by using 3D photography.

Methods

Since 2014, 50 craniosynostosis operations have been performed. One week before surgery a 3D photography was taken (Canfield, New Jersey, USA). The patient photography was overlaid with normal heads at the same age in order to define ideal profile (sagittal plane) and width (axial plane). Standard osteotomies were performed. Osteosynthesis took place by resorbable plates (Sonic-Weld, KLS-Martin, Tuttlingen, Germany). 3-D images were taken 4 weeks, 2 and 6 months postoperatively, and then annually up to 5 years. The result was rated as: 1 very good; 2 good; 3 satisfactory; 4 bad.

Results

Six months after surgery the result was stable as anticipated by the modeling guides (scale 1-2). One year after surgery a slightly deterioration was observed (scale 2-3): Trigenocephaly (n=20): Narrowing of the fronto-basal angle. Outcome improved through vertical releasing osteotomies of the frontal segment (n=17). Scaphocephaly (n=17): Narrowing of the posterior cranial width. The elimination of plates for lateral stabilization (n=8) improved outcome. Plagiocephaly (n = 6): 90° transposition of the ipsilateral frontal bone (n=1) improve outcome (1). Lambdoid synostosis (n = 2): Bone flap transposition right-to-left (n = 1) improved result (1). Brachycephalus (n = 5): The result was good and remained constant.

Conclusion

The modeling guides created by 3D photography showed to be practicable, accurate, reproducible and cost effective. The long-term outcome does not correlate with the immediate result. Changes in skull shape correlates with the placement of releasing modeling osteotomies and the intrinsic expansion of brain lobes.

Pädiatrische Neurochirurgie I/*Paediatric neurosurgery I*

V150

Chirurgische Therapie und funktionelles Outcome bei symptomatischen temporalen Arachnoidalzysten *Surgical options and functional outcome in symptomatic temporal arachnoid cysts*

R. Ibel¹, A. Biczok², M. Kunz², M. Schuler-Ortholi¹, A. Peraud¹

¹Universitätsklinikum Ulm , Neurochirurgische Klinik, Sektion Pädiatrische Neurochirurgie, Ulm, Germany

²Ludwig-Maximilians-Universität München, Neurochirurgische Klinik und Poliklinik, München, Germany

Objective

Arachnoid cysts (ACs) are rare and the majority is discovered during childhood. The most common location is the middle cranial fossa. The clinical spectrum is diverse. So far there is no clear recommendation of whether and how symptomatic ACs should be treated surgically. The optimal surgical approach (microsurgical or endoscopic fenestration, cyst shunts) remains still controversial.

Methods

33 children (29 boys, 4 girls; mean age at the time of surgery 8.3 years), who were operated for a symptomatic temporal AC between 1995 and 2019 were retrospectively analysed. Chart review and postoperative quality of life assessment (SF-36, KINDL[®], GBI, GCBI) was performed. Cyst volume was measured with Horos[™] software pre- and postoperatively. Clinical outcome was graded into four subgroups (free of symptoms, improved, unchanged, worse). Written consent from the caregivers as well as an ethical approval was obtained.

Results

ACs were located on the right in 13, on the left in 18 and bilateral in 2 cases. There were 4 Galassi type I, 4 type II and 25 type III ACs. Mean follow-up time was 44.5 months (range 1-203 months). 8/33 became symptomatic with posttraumatic cyst rupture and bleeding. 20/33 complained of headaches, 9/33 presented with non-specific symptoms, 5/33 had epilepsy, 4/33 had macrocephaly, 4/33 had psychological problems and 3/33 had hydrocephalus. Preoperative cyst volume varied from 10 to 325.8 cm³ and postoperative (>6 months) from 2.4 to 201.1 cm³. Surgical management consisted in microsurgery in 25/33, endoscopic fenestration in 7/33 and shunt insertion in 1/33. Concerning the outcome, 24/33 (72.7%) patients were symptom-free at >6 months follow-up, 4/33 were clearly improved (12.1%), 5/33 (15.2%) were unchanged. Four patients required repeat surgery for insufficient cyst drainage, one after microsurgical fenestration, 2 after endoscopy and one after an internal shunt. Two subdural hygroma/hematoma required surgical intervention. Subdural effusions resolved completely without intervention in 14/33.

Conclusion

It can be challenging to select the right surgical candidate in temporal ACs, but the long-term outcome is favourable in most patients. Microsurgical fenestration seems to be more effective in cyst drainage than other surgical options.

Pädiatrische Neurochirurgie I / Paediatric neurosurgery I

V151

Ventriculomegalie bei Kindern – die nächtliche ICP-Dynamik identifiziert einen druckausgeglichenen, aber aktiven pädiatrischen Hydrozephalus

Ventriculomegaly in children – nocturnal ICP dynamics identify pressure compensated but active paediatric hydrocephalus

S. Fernandes Dias^{1,2}, E. Jehli³, K. Haas-Lude⁴, J. Zipfel², A. Bevo⁴, H. Okechi², M. U. Schuhmann²

¹Schulthess Klinik, Neurochirurgie, Zürich, Switzerland

²Universitätsklinikum Tübingen, Pädiatrische Neurochirurgie, Tübingen, Germany

³Universitätsspital Zürich, Neurochirurgie, Zürich, Switzerland

⁴Universitätsspital Zürich, Neurologie, Tübingen, Germany

Objective

Pediatric ventriculomegaly without obvious signs/symptoms of raised intracranial pressure (ICP), is often interpreted as either resulting from relative brain atrophy, shunt independency or "successful" ETV. We hypothesised, that the typical ICP "signature" found in symptomatic hydrocephalus (increased ICP dynamics and decreased compliance) can be present in oligosymptomatic ventriculomegalic children, indicating chronic, but still active hydrocephalus. We aimed to study ICP and derived parameters in those children and in case of active hydrocephalus suspicion whether shunt implantation improved symptoms and child's development.

Methods

37 children with ventriculomegaly and suspicion of increased ICP underwent computerised ICP overnight monitoring (ONM). ICP and calculated dependent variables were analyzed for nocturnal ICP dynamics: ICP peak, "wave" and baseline pressures, ICP "wave" and baseline amplitudes, magnitude of slow waves and RAP index. Depending on ONM's result, children were surgically treated or assigned to clinical observation. Measurements of ventricular width were performed at the time of ONM and last follow-up.

Results

The ONM recordings of 14 children (Group A) were considered normal with baseline ICP of 10.5 mmHg (95% CI 5.6, 15.3), ICP wave of 12.3 mmHg, RAP 0.44 and baseline AMP 1.13 mmHg. In the 23 children with pathologic measurements (Group B), all ICP values, AMP and slow wave were significantly higher. The RAP index did not varied significantly between both groups ($p=0.13$). Group A children had less nocturnal wave episodes compared to Group B ($p=0.001$). Group B children received treatment for hydrocephalus, with the frontal-occipital horn ratio being significantly lower after surgery ($p=0.007$). At follow up a positive neurological development was seen in 74% children of Group A and 96% of Group B.

Conclusion

Ventriculomegaly in absence of signs and symptoms of raised ICP was associated 62% of cases with significantly accelerated ICP dynamics and indices of low intracranial compliance, as typical in symptomatic children. After neurosurgical intervention, all but one child improved in development, as compared to 74% of those considered to have normal intracranial ICP dynamics. Asymptomatic ventriculomegaly in children needs further investigation and, if associated with abnormal ICP dynamics, should be treated in order to provide a normalized intracranial physiology as basis for best possible long-term outcome.

Pädiatrische Neurochirurgie I/*Paediatric neurosurgery I*

V152

Implementation und Lernkurve der neuroendoskopischen Lavage bei Neugeborenen *Implementation and learning curve of neuroendoscopic lavage in neonates*

T. Beez, C. Munoz-Bendix, H. J. Steiger, K. Beseoglu, D. Hänggi

Heinrich-Heine-Universität Düsseldorf, Klinik für Neurochirurgie, Düsseldorf, Germany

Objective

Treatment protocols for ventricular hemorrhage in neonates vary significantly between centers. Neuroendoscopic lavage (NL) has been demonstrated to be feasible, safe and effective in recent publications. We have thus adopted this technique and describe our initial experience and learning curve.

Methods

We retrospectively analyzed our initial case series of this new technique in neonatal neurosurgery with regard to learning curve.

Results

Five neonates born at a mean gestational age of 35 weeks (range 27-40 weeks) were analyzed. Four patients had symptomatic PHH with a mean preoperative frontal to occipital horn ratio of 0.58 (range 0.42-0.69). One term newborn presented with acute thalamic hemorrhage 20 days after birth. NL was performed at a mean of 20 days after birth (range 7-39 days). Pre-NL CSF protein was 317mg/dl (range 130-600mg/dl). NL of both lateral ventricles and third ventricle was performed via a unilateral approach and septostomy. NL was combined with Ommaya reservoir (N=2), Ommaya reservoir and ETV (N=1) and VPS (N=2). After initial treatment with NL and reservoir, a VPS was implanted after 20 and 26 days, respectively. NL reduced mean CSF protein to 60mg/dl (range 15-104mg/dl) and sonographic blood clot volume. In shunted infants (N=4), no VPS occlusion was observed within 30 days. No direct complications of NL occurred, but one CSF leak required revision.

Conclusion

NL reduces CSF protein and blood clot volume. No complications or early VPS failures were encountered in this small initial series, but certainly larger cohorts are required to assess the value of NL with regard to improving VPS outcome or even avoiding VPS in PHH. In our subjective learning curve, prior pediatric neuroendoscopic experience, interdisciplinary agreement on treatment, initial patient selection of term newborns and adherence to the published protocol allow safe implementation of this promising technique.

Vaskuläre Malformationen/*Vascular malformations*

V153

Verbesserung der Traktographie in Patienten mit Hirnstamm-Kavernomen durch Verzerrungs-Korrektur *Improving tractography in brainstem cavernoma patients by distortion correction*

S. Ille, M. Grziwotz, M. Wostrack, B. Meyer, S. Krieg

Technische Universität München, München, Germany

Objective

The resection of brainstem cerebral cavernous malformations (CCM) harbors the risk of damage to the corticospinal tract (CST). Hence, the visualization of the CST potentially supports the planning in patients who undergo resection. However, diffusion tensor imaging fiber tracking (DTI FT) at brainstem level suffers from distortion due to field inhomogeneity and eddy currents because of diffusion gradients within the brainstem but also bony structures. The study aims to detect differences of the CST tractography in brainstem CCM patients by cranial distortion correction (CDC), which applies a deformation algorithm to DTI sequences by semi-elastic fusion.

Methods

We included 25 patients (mean age 46 ± 18 years) who underwent resection of brainstem CCM. We performed anatomy-based CST tractography (mean minimal fractional anisotropy of 0.22 ± 0.04) before and after CDC using perioperative DTI sequences and the same region of interest for both methods.

Results

The application of CDC led to a more precise CST tractography regarding its true anatomical localization in all cases. As measured by the distances to the basilar artery and the clivus, the CST was located significantly more ventral by a mean of 1.5 ± 0.5 mm (6.1 ± 2.6 mm vs. 4.6 ± 2.1 mm, $p < .001$) and 1.7 ± 0.5 mm (8.9 ± 2.6 mm vs. 7.2 ± 2.1 mm, $p < .001$). Aberrant fibers could be reduced by CDC in 44% of patients. We could not detect surgery-related motor deficits after resection of distorted fibers.

Conclusion

The present results show that CDC improves tractography of the CST in brainstem CCM patients regarding its true anatomical localization. Artifacts of DTI sequences due to bony structures can be reduced by CDC, being clinically relevant for tractography at brainstem level.

Vaskuläre Malformationen/*Vascular malformations*

V154

Einfluss der zuführenden Arterien auf das Blutungsrisiko von zerebralen arteriovenösen Malformationen *Impact of feeding arteries on haemorrhage risk in brain arteriovenous malformations*

M. Eibach¹, S. Y. Won¹, J. Quick-Weller¹, J. Berkefeld², J. Konczalla¹, E. Herrmann³, V. Seifert¹, G. Marquardt¹, N. Dinc¹

¹Universitätsklinikum Frankfurt am Main, Neurochirurgie, Frankfurt am Main, Germany

²Universitätsklinikum Frankfurt am Main, Neuroradiologie, Frankfurt am Main, Germany

³Johann Wolfgang Goethe-Universität Frankfurt am Main, Biostatistik und mathematische Modellierung, Frankfurt am Main, Germany

Objective

Angioarchitectur and hemodynamic conditions play an important role in the hemorrhage risk in brain arteriovenous malformations. Knowledge of hemodynamics of blood flow is required for risk assessment and treatment options. The purpose of this study was to investigate whether the number or the origin of arterial feeders are risk factors for bleeding in AVMs.

Methods

We retrospectively examined all patients who were admitted to our hospital with a diagnosed brain AVM between December 2005 and February 2018.

Digital subtraction angiography was used to identify the number and origin of arterial feeders. We counted the number of the major brain arteries. Single Feeder was defined as one major artery feeding an AVM nidus. Furthermore, we evaluated the presence of aneurysms and the number of draining veins.

We dichotomized the patients according their hemorrhage status at the initial diagnosis and compare the different potential impact factors.

Results

We included a total of 180 patients in our study. Patients with ruptured AVM had significant more often a single arterial feeder (51.9 % vs. 34.3 %) and a single draining vein (54.3 % vs. 21.2 %) than patients with unruptured AVM on first diagnosis. In addition, a supply from cerebellar arteries (28.4 % vs 11.1 %) was significant more often identified in ruptured AVM than in unruptured AVM. The presence of aneurysms did not differ between ruptured and unruptured AVMs. In the multivariable analysis, single feeder (OR 2.17), single draining vein (OR 3.34) and a supply from cerebellar arteries (OR 2.97) were independent risk factors for hemorrhage in AVM.

Conclusion

Our results suggested that a single arterial feeder, cerebellar feeder and a single draining vein are independent risk factors for hemorrhage in brain AVMs. These variables should be considered in the decision process for treating or not treating unruptured AVMs.

Vaskuläre Malformationen/*Vascular malformations*

V157

Hirnstamm-Kavernome – Relevanz postoperativer neuropathischer Schmerzen

Brainstem cavernous malformation (CCM) – relevance of postoperative neuropathic pain sensations

A. Herten, D. V. Saban, S. Rauscher, R. Jabbarli, K. H. Wrede, U. Sure, P. Dammann

Universitätsklinikum Essen, Klinik für Neurochirurgie, Essen, Germany

Objective

To estimate postoperative neuropathic pain sensations in patients with surgically treated brainstem cavernous malformation (CCM).

Methods

87 cases of brainstem cavernoma who were treated surgically between 2008 and 2018 were observed for the occurrence of neuropathic pain. Relevance of CCM location, postoperative complications, duration of hospitalization and influence on functional outcome was evaluated. Descriptive statistical analysis was performed.

Results

19 patients suffered from neuropathic pain sensations like dysesthesia and paresthesia. Typically one limb or half of the body were involved. In our cohort, occurrence of neuropathic pain was not correlated with specific brainstem location (thalamus, mesencephalon, pons, medulla oblongata). Averaged extend of pain, measured by visual analog scale (VAS), was 4- 5 points and ranged from 2 to 7 points. Duration of hospitalization, financial effort and occurrence of other complications did not correlate with neuropathic pain sensations. Neuropathic pain tends to evoke a worse functional outcome. Furthermore, health related quality of life (HRQOL) is reduced compared to normal population control group, in particular, as expectable, in the subdomain of pain ($p < 0.05$).

Conclusion

Surgical therapy of a brainstem CCM can lead to HRQOL decreasing pain sensations. Pain fibers may be involved at multiple potential lesion sites along the nociceptive pathways. Patients have to be aware of this and postoperative specific treatment should be anticipated early.

Vaskuläre Malformationen/*Vascular malformations*

V158

Propranolol hemmt SDF-1 α /CXCR4 Achse – möglicher Therapie-Wirkmechanismus von zerebralen Kavernomen

Propranolol inhibits SDF-1 α /CXCR4 axis – a possible treatment mechanism of cerebral cavernous malformations

S. Kashefiolas¹, M. Leisegang², L. Imöhl¹, C. Senft¹, V. Seifert¹, J. Konczalla¹

¹Universitätsklinikum Frankfurt am Main, Neurochirurgie, Frankfurt am Main, Germany

²Johann Wolfgang Goethe-Universität Frankfurt am Main, Kardiovaskuläre Physiologie, Frankfurt am Main, Germany

Objective

Cerebral cavernous malformations (CCMs) are frequently diagnosed vascular malformations of the brain. Although most CCMs are asymptomatic, some can be responsible for intracerebral hemorrhage or seizures. Treatment with the β -blocker propranolol has been presumed to stabilize and eventually lead to CCM size regression in a limited number of published case series; however, the underlying mechanism and evidence for this effect remain unclear.

Methods

Single-center database containing data on patients harboring CCMs was retrospectively interrogated for a time period of 20 years. The database included information about hemorrhage and antihypertensive medication. Statistical analyses were performed, focusing on the risk of hemorrhage and the size of the lesion at presentation and during follow-up in patients on β -blocker medication versus those who were not. Furthermore, cavernoma tissue was cultured in a cell culture incubator after surgical resection for 72 hours. Experiments were performed in the presence of propranolol or solvent DMSO. The expression level of SDF-1, CXCR4, and dependent factors was measured by qRT-PCR. CXCR4 antagonist, AMD3100, was also used to detect its effects on cerebral vasculogenesis and SDF-1 expression.

Results

488 CCMs among 338 patients, 69 (20,4%) were under treatment with β -blocker. 26% CCMs presented with hemorrhage at diagnosis. Patients under β -blocker treatment had a lower risk of hemorrhage at the time of diagnosis in a univariate descriptive analysis ($p < 0,05$; OR2). Univariate descriptive and univariate Cox proportional-hazards regression analysis showed a decreased risk for follow-up hemorrhage under treatment with β -blocker medication ($p < 0,05$, HR3,5). Multivariate regression analysis including brainstem location, hemorrhage at diagnosis, age, and β -blocker treatment showed reduced risk for follow-up hemorrhage under β -blocker treatment ($p < 0,05$, HR1,36).

The expression of CXCR4 was suppressed by propranolol most likely through the Akt and MAPK pathways. The gene expression of vasculogenesis factors such as VEGF was decreased in with propranolol incubated CCM.

Conclusion

In this study, β -blocker medication seems to be associated with a decreased risk of CM-related hemorrhage and CM-growth at presentation or during follow-up.

Propranolol inhibits SDF1 α -induced vasculogenesis by suppressing the expression of CXCR4 most likely through the Akt and MAPK pathways. The SDF-1/CXCR4 axis plays an important role in the vasculogenesis in cerebral CM lesions.

Vaskuläre Malformationen/*Vascular malformations*

V159

Funktionelles Outcome nach chirurgischer Therapie spinaler duraler arteriovenöser Fisteln *Functional outcome in patients with dural arteriovenous fistulae after surgical treatment*

I. Hostettler, L. Hönikl, B. Meyer, M. Wostrack

Klinikum rechts der Isar München, Neurochirurgische Klinik und Poliklinik, München, Germany

Objective

Spinal dural arterio-venous fistulas (SDAVF) are rare vascular pathologies. The degree of symptom improvement after surgical treatment remains unclear. We evaluated surgically treated SDAVF patients for symptom improvement.

Methods

Retrospective inclusion of all patients treated surgically in our department for SDAVF consecutively between 2007 and 2019. We measured functional outcome using the McCormick Scale.

Results

We included a total of 27 patients. Mean age was 61.8years (standard deviation 8.4), 40.7% were female. The most frequent location was the thoracic spine in 15 (55.6%) followed by lumbar in 8 (29.6%), cervical in 3 (11.1%) and sacral spine in one patient (3.7%). The most common presenting symptom was progressive myelopathy in 24/27 patients (88.9%). Two patients (7.4%, both with foramen magnum SDAVF) presented with acute haemorrhage. Only in one patient was the SDAVF an incidental finding. In three patients (11.1%) SDAVF were embolised before surgery. In all patients the SDAVF was completely resected, however in 4 patients (14.8%) complete surgical resection required a second surgical interventions. Four patients (14.8%) deteriorated initially after surgery. On discharge, presenting symptoms had improved in 17 patients (63%), 9/27 patients (33.3%) had a McCormick score of 1. Follow-up was available in 19 patients (67.4%) with a median of 10.3 months (IQR 42.5, minimum 1.2, maximum 252). Seventeen patients (89.5%) continued to improve on follow-up. In total 22/27 patients (81.5%) improved.

Conclusion

Untreated SDAVF lead to progressive myelopathy which may result in considerable disability. Surgical disconnection and resection of the SDAVF provides a safe treatment option with relatively low perioperative morbidity and good chances for improvement or at least myelopathy progression prevention.

Neuromonitoring

V160

Detektion der zerebralen Hypoperfusion nach aneurysmatischer Subarachnoidalblutung mittels Ultraschallperfusionsbildgebung – eine prospektive Studie

Detection of cerebral hypoperfusion after aneurysmal subarachnoid haemorrhage by ultrasound perfusion imaging – a prospective trial

C. Fung¹, D. H. Heiland¹, R. Reitmeir², J. Eyding³, A. Raabe², J. Gralla⁴, W. Z'Graggen², J. Beck¹

¹Universitätsklinikum Freiburg, Neurochirurgie, Freiburg, Germany

²Universitätsspital Bern, Neurochirurgie, Bern, Switzerland

³Klinikum Dortmund, Neurologie, Dortmund, Germany

⁴Universitätsspital Bern, Institut für Diagnostische und Interventionelle Neuroradiologie, Bern, Switzerland

Objective

Cerebral vasospasm contributes to increased morbidity and mortality after aneurysmal subarachnoid hemorrhage (aSAH). Current methods for screening and detection of cerebral vasospasm have either a low sensitivity and specificity, are dependent on x-ray, are costly, and/or extremely time-consuming and laborious. Ultrasound perfusion imaging is a non-invasive tool that measure cerebral perfusion, is applicable bedside and at will repeatable. This prospective trial investigates ultrasound perfusion imaging (UPI) in aSAH patients to detect impaired perfusion in the setting of cerebral vasospasm.

Methods

High mechanical index contrast-enhanced ultrasound was prospectively used in 30 patients suffering of aSAH throughout multiple time points between day 3 and day 14 after ictus. Delayed ischemic neurologic deficit (DIND) were defined as new neurological deficit or drop in GCS by 2 points. Time-to-peak (TTP) intensity and mean transit time (MTT) of 4 regions of interest (ROIs) of the middle cerebral artery (MCA) territory per patient were quantified by UPI and midbrain perfusion records were used to normalize the MCA territory measurements. We analyzed absolute values and performed intra- and interhemispheric comparisons. The correlation between the least perfused regions (measured by UPI or CTP) and occurrence of DIND was investigated by non-parametric tests.

Results

18 patients had no DIND and 12 patients presented a DIND. The left-right difference of the minimal obtained perfusion predicts most likely a potential vasospasm. In DIND patients TTP values showed a significant increase after day 6 with a peak at day 8-10 compared to no-DIND patients. TTP values showed a significant difference between the DIND and no-DIND group ($p=0.005$).

Conclusion

UPI combines features of an optimal screening tool to be applied in the daily routine. It can detect cerebral hypoperfusion after aSAH.

Neuromonitoring

V162

Einfluss physiologischer Parameter auf Cortical Spreading Depolarization nach malignem Mediainfarkt *Impact of physiologic variables on cortical spreading depolarisation after malignant hemispheric stroke*

L. Schumm¹, J. P. Dreier², S. Major², C. Lemale², P. Martus^{2,3}, J. Woitzik¹

¹Carl von Ossietzky Universität Oldenburg, Universitätsklinik für Neurochirurgie, Oldenburg, Germany

²Charité – Universitätsmedizin Berlin, Klinik für Neurologie, Berlin, Germany

³Eberhard Karls Universität Tübingen, Institut für Klinische Epidemiologie und Angewandte Biometrie, Tübingen, Germany

Objective

Spreading Depolarization (SD) occurs frequently after malignant hemispheric stroke (MHS) and may promote lesion growth. In the experimental setting, several physiologic parameters were shown to influence SD and its features. In this study we analyzed the impact of temperature (T°), intracranial pressure (ICP), mean arterial blood pressure (MAP) and cerebral perfusion pressure (CPP) on the incidence and duration of SD in patients with MHS.

Methods

60 patients with MHS requiring hemicraniectomy were included in the clinical study. Electrocorticography (ECoG) of the periinfarct zone was performed with a linear subdural electrode strip (6 Pt/Ir contacts spaced at 10mm). Body temperature, MAP and ICP were monitored continuously. Mean values of 30 minute-periods before and after every SD were compared to the level of physiologic variable at the moment of SD in a linear mixed model with random intercept. The duration of each SD was correlated with the measurements of physiologic variable at this SD.

Results

During 7480h of ECoG, 1692 SD occurred with a total depression time of 821h and a mean number of 7.1±6.7 SD per patient per day. All the parameters of interest showed specific patterns around the incidence of an SD. Mean T° was increased during SD and dropped afterwards (p=.0002). ICP levels started rising shortly before SD, was highest during SD and fell again after (p<.00001). On the other hand, MAP was lower during SD than before and after the event (p=.002); the CPP pattern was accordingly (p=.002). There was no correlation between the depression duration and the four parameters of interest T° (p=.29), MAP (p=.66), ICP (p=.068), CCP (p=.40).

Conclusion

Compared to patients with traumatic brain injury (Hartings et al. 2009), differences in T°, MAP, ICP or CPP between time points with and without SD were smaller, but our data is a proof of principle of the experimental findings in humans. This finding might explain an important mechanism in the pathophysiology of SD and can be relevant for the prevention of secondary damage in the treatment of MHS patients.

Hartings JA et al. Spreading depolarizations and late secondary insults after traumatic brain injury. Journal of neurotrauma 2009; 26: 1857-1866.

Neuromonitoring

V163

Die automatisierte Infrarot-Pupillometrie (aiPM) als nicht-invasives Verfahren zur Vorhersage der Notwendigkeit einer permanenten Liquordrainage bei akutem Hydrozephalus
Automated infrared pupillometry (aiPM) as non-invasive tool to predict the need for permanent shunt diversion in acute hydrocephalus

J. Halfmann, T. P. Schmidt, H. R. Clusmann, W. Albanna, G. A. Schubert

Universitätsklinikum RWTH Aachen, Neurochirurgie, Aachen, Germany

Objective

Acute hydrocephalus is readily addressed by implantation of an external ventricle drain (EVD). To determine the need for permanent CSF diversion, probatory closure of the EVD is performed after the acute stage. Typically, the EVD is re-opened if clinical deterioration or progressive dilatation of the ventricles is observed, or removed if secondary deterioration is not observed. Automated infrared pupillometry (aiPM) has been shown to facilitate early detection of elevated ICP non-invasively. This technique may hold the potential to bypass the risk of exposing a patient to a potentially harmful secondary deterioration by timely prediction of hydrocephalic enlargement.

Methods

We prospectively enrolled 65 consecutive adult patients ($56,89 \pm 12,10$ yrs) with EVD due to acute hydrocephalus from May 2016 - October 2019. Patients were stratified into two groups based on whether weaning of EVD was successful or failed (groupS, groupF, resp.). Pupillometry data were collected before EVD closure until after eventual reopening or removal. The following parameters were recorded: Neurological Pupil index (NPi), pupil size (SIZE), minimum pupil diameter (MIN), decrease in pupil diameter after light stimulation (DIA), constriction velocity (CV), maximum constriction velocity (MCV), dilation velocity (DV) and latency (LAT).

Results

Weaning of EVD was successful in 44 cases (67.7%; groupS) and failed in the remaining third of all patients ($n=21$, 32.3%; groupF). Baseline parameters of aiPM were comparable in both groups before probatory closure of the EVD. Two days after closure, patients with eventual weaning failure showed significantly reduction of both constriction velocity (CV, MCV) and dilation velocity (DV) compared to groupS ($p < 0.05$, $p < 0.05$, $p < 0.05$). A trend towards an early, incipient reduction of constriction velocity was already observed 24hrs after closure ($p=0.164$, $p=0.114$). NPi, SIZE, MIN, DIA, LAT showed no differences. After reopening the EVD, all pupillometry parameters of the failure group recovered to comparable values.

Conclusion

During EVD weaning, aiPM detects specific fluctuations in pupillary function, suggesting progressive impairment of neuronal circuitry in patients requiring permanent CSF diversion. If these results are confirmed in an even larger cohort, this non-invasive monitoring technique may enable us to shorten the weaning process, thus avoiding prolonged probatory closure and provocation of significant clinical deterioration.

Neuromonitoring

V165

Der Einfluss der zerebralen Mikrodialyse im akuten neurointensivmedizinischen Setting – Realität oder Fiktion?

The impact of cerebral microdialysis in the acute neurosurgical intensive care setting – Fact or Fiction?

A. Hosmann¹, J. Herta¹, A. Reinprecht¹, W. Plöchl², A. Gruber³, K. Rössler¹

¹Medizinische Universität Innsbruck, Neurochirurgie, Wien, Austria

²Medizinische Universität Innsbruck, Anästhesie, Wien, Austria

³Kepler Universitätsklinikum, Neurochirurgie, Linz, Austria

Objective

Multimodality neuromonitoring is crucial in the management of critically ill neurosurgical patients under intensive care unit conditions. While brain tissue oxygen tension (pbrO₂) monitoring has already entered the clinical routine, this is not the case for cerebral microdialysis. However, many discrepancies between pbrO₂ and cerebral metabolism are observed in the clinical setting.

Methods

Multimodality neuromonitoring data were analyzed in 35 patients suffering severe subarachnoid hemorrhage. The impact on cerebral metabolism and tissue oxygenation of diagnostic and therapeutic interventions, such as intrahospital transports, oral nimodipine administration, and selective intra-arterial papaverine-hydrochloride infusion were systematically analyzed.

Results

During intrahospital transports significant increase of intracranial pressure occurred. Although pbrO₂ was not impaired, significant changes of cerebral glucose, lactate, and glycerol were evident.

Oral nimodipine administration induced significant decrease of cerebral perfusion pressure. In already compromised patients, nimodipine had detrimental effects on cerebral metabolism.

Endovascular rescue therapy for severe cerebral vasospasm, using intra-arterial papaverine-hydrochloride, showed only transient improvement of cerebral metabolism while pbrO₂ remained unchanged.

Conclusion

Cerebral microdialysis provides valuable information beyond pbrO₂ in the clinical setting and may therefore have a direct impact on our neurointensive care management. It allows to evaluate the individual effects of diagnostic and therapeutic interventions and personalize targeted therapy to optimize patients' outcome.

Neuromonitoring

V166

Invasives Hirndruckmonitoring nach dekompressiver Hemikraniektomie im malignen Hirninfarkt *Invasive monitoring of intracranial pressure after decompressive craniectomy in malignant stroke*

S. Hernández-Durán, L. Meinen, V. Rohde, C. Von der Bröle

Universitätsmedizin Göttingen, Klinik für Neurochirurgie, Göttingen, Germany

Objective

The role of intracranial pressure (ICP) monitoring has long been established in traumatic brain injury (TBI), where it aids clinicians in their therapeutic decision-making, including the indication for decompressive craniectomy (DHC). In malignant stroke (mStroke), there are no guidelines for ICP monitoring, even though this condition is associated with cerebral edema, ischemia and secondary injury. Furthermore, there are no thresholds of ICP to guide therapeutic decisions after DHC. In this study, we aimed to investigate the course of ICP values and how they correlated with mortality, attempting to establish thresholds to guide clinical decision-making.

Methods

We conducted a retrospective study of mStroke patients undergoing DHC at our center between 2011 and 2018. Postoperative ICP was analyzed hourly, recording minimum, mean and maximum values for each day and patient. Then, mean values were calculated for the entire cohort, based on the mean daily values for mean, minimum, and maximum ICP. Patients were categorized in two groups: deceased and survivor. These groups were then compared in their ICP course with an independent sample t-test.

Results

A total of 110 patients were included. Mean age was 60 years (range: 18-54). The majority were males (n=67, 60%), and presented between 6 to 12 hours after symptom begin (n=26, 23%). Mean Aspects Score was 2.7 (range: 0-10). Preoperative factors failed to be significantly associated with a higher postoperative ICP course. The same holds true for size of defect. A statistically significant difference was seen in mean and maximum ICP values between patients who passed and those who survived: Mean ICP was 7.4 mmHg in the survival group, and 9.3 mmHg in the mortality group ($p < 0.01$); Maximum ICP values were 13 mmHg and 17 mmHg ($p < 0.01$), respectively. Maximum ICP also exhibited a statistically significant correlation with mortality (Pearson's correlation coefficient = .225, $p = .018$).

Conclusion

Our study reveals a clear correlation between ICP and mortality. Interestingly, values associated with mortality were well below the commonly accepted 20 mmHg threshold referenced in the literature, thus raising the question of whether patients with mStroke undergoing DHC should receive more aggressive management at lower ICP thresholds to avoid further secondary injury due to generalized cerebral edema and resulting intracranial hypertension.

Neuromonitoring

V233

Auf der Suche nach dem optimalen Zeitpunkt der prophylaktischen Antikoagulation nach subarachnoidaler Blutung – Je eher, desto besser?

The best time for prophylactic anticoagulation after subarachnoid haemorrhage – The earlier, the better?

A. Hantsche, F. Wilhelmy, D. Lindner, J. Meixensberger

Universitätsklinikum Leipzig, Klinik und Poliklinik für Neurochirurgie, Leipzig, Germany

Objective

In neurosurgery generally, and especially regarding subarachnoid hemorrhage (SAH) - being a severe and complex pathology with dreaded both ischemic and hemorrhagic complications - the optimal prophylactic heparin regimen is still controversial. The goal of this study was to analyse the impact of the timepoint of heparin initiation (ToH) on the incidence of ischemic and haemorrhagic events after SAH.

Methods

Patients who received acute treatment for non-traumatic SAH between 2011 and 2018 were considered for this retrospective study. 370 patients were included. The influence of the ToH on the incidence of ischemic and haemorrhagic events and changes in outcome scores was assessed. Therefore, the period between admission or, if possible, securing the source of bleeding (SOB) and ToH in hours was calculated. Statistical analysis was performed using Mann-Whitney U-Test, Chi-square test, Fisher's exact test and univariate binomial logistic regression. P-values lower than 0.05 were considered statistically significant.

Results

The incidence of extracranial ischemia was 4.6%, thromboembolic intracranial ischemia 12.2% and intracranial re-bleeding 14.6%. The ToH as a continuous parameter significantly affects the incidence of extracranial ischemia ($p=0.009$), but does not have an impact on intracranial ischemia or rebleeding. Patients anticoagulated within 48 hours have a significantly lower incidence of extracranial ischemia than those with later ToH ($p=0.020$). Yet, the outcome at discharge did not diverge. When starting heparin later than 72h after admission or securing the SOB, extracranial ischemia occurs significantly more often ($p=0.037$), along with a significantly worse outcome at discharge (modified Rankin Scale (mRS) $p=0.031$, Glasgow Outcome Scale (GOS) $p=0.026$) and after 12 months (mRS $p=0.014$, GOS $p=0.019$), but without differences in mortality or readmission rates. No significant differences in the occurrence of initial World Federation of Neurosurgical Societies (WFNS) Scores above 3 could be detected between the time windows.

Conclusion

While later initiation of heparin is associated with higher incidence of extracranial ischemia, it does not influence the incidence of intracranial ischemia or intracranial re-bleeding. All patients suffering from SAH can therefore be administered heparin within 24 hours after admission or securing of SOB, respectively, as prophylactic doses do not promote re-bleeding.

Spinale Frakturen und zervikale Myelopathie/*Spine fractures and cervical myelopathy*

V167

Bilaterale Dekompression des Spinalkanals über einen unilateralen Zugang als alternative Laminektomie bei der degenerativen zervikalen Myelopathie

Bilateral posterior spinal canal decompression via a unilateral approach as an alternative to laminectomy in cervical spondylotic myelopathy

S. Siller, L. Pannenbaecker, J. Tonn, S. Zausinger

Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik, München, Germany

Objective

Laminectomy and laminoplasty are common methods for posterior decompression of the spinal cord in patients with cervical spondylotic myelopathy (CSM), but imply potential disadvantages (e.g. bilateral paraspinal muscle atrophy as a risk factor for instability or chronic pain). We evaluated if an unilateral posterior approach followed by bilateral decompression of the spinal canal could be a less invasive alternative.

Methods

All patients undergoing posterior decompression due to CSM between 2012 and 2018 in our university neurosurgical clinic were included and divided into two groups by surgical procedure: unilateral approach via laminotomy/hemilaminectomy combined with an "undercutting procedure" (group I) and laminectomy/laminoplasty (group II). We investigated the patients' characteristics, imaging and surgical parameters as well as outcomes and quality-of-life (QOL) after long-term follow-up (ltFU).

Results

From altogether 616 CSM patients with decompressive surgery, 96 patients underwent posterior procedures, accounting within 7yrs for 23% of patients in this population. Mean age was 72.7yrs, with a predominance of the female sex (m:f=1:1.3). The most frequent symptoms were ataxia (74%) and sensory changes (57%) with a mean duration of 14.7mos. The most often location of stenosis was C3-5 (81%) with 1-level stenosis in 85% and 2-level stenosis in 9%, 3- or more level stenosis in 6% of the cases. None of the patients showed signs of spinal instability or required secondary stabilization. 45 patients with lateralized cord compression underwent an unilateral approach with bilateral decompression and 51 patients with circular pathology underwent laminectomy/laminoplasty (both groups: median Naganawa grade 3, i.e. severe cord impingement/deformity). There were no sign. differences of patients' characteristics, intraop. blood loss, operation time and length of in-patient stay between both groups. Independend from the mode of surgical decompression, the spinal canal was sign. ($p<0.001$) widened (both groups: median postop. Naganawa grade 0, i.e. no stenosis) and both pain ($p=0.026$), myelopathic symptoms (mJOA-Score: $p=0.003$) and QOL (SF-36-PCS/-MCS: $p=0.03/p=0.046$) were sign. improved at ltFU (mean 28.3mos).

Conclusion

For posterior decompression of CSM, unilateral approach followed by bilateral decompression of the spinal canal via "undercutting" procedure could be an equally effective alternative to laminectomy in case of lateralized compression.

Spinale Frakturen und zervikale Myelopathie/*Spine fractures and cervical myelopathy*

V168

Störung der Blut-Rückenmark-Schranke bei Patienten mit degenerativer zervikaler Myelopathie – Potential zur Wiederherstellung? *Blood spinal cord barrier disruption in patients with degenerative cervical myelopathy – potential to restore?*

C. Blume¹, L. O. Brandenburg², V. Mainz³, J. Kalder^{2,4}, M. Müller⁵, H. R. Clusmann⁶, C. A. Mueller⁶

¹Rheinisch-Westfälische Technische Hochschule Aachen, Neurochirurgie, Aachen, Germany

²Rheinisch-Westfälische Technische Hochschule Aachen, Institut für Anatomie und Zellbiologie, Aachen, Germany

³Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Psychiatrie, Aachen, Germany

⁴Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Gefäßchirurgie, Aachen, Germany

⁵Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neuroradiologie, Aachen, Germany

⁶Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neurochirurgie, Aachen, Germany

Objective

Blood spinal cord barrier (BSCB) disruption plays an elementary role in acute and neurodegenerative diseases of the spinal cord (SC). This study was set out to detect BSCB disruption in patients with degenerative cervical myelopathy (DCM) and possible recovery after surgical decompression of the cervical SC.

Methods

The study was prospectively enrolled with 58 DCM patients (25 female; 33 male; mean age 62.0 ± 12.0 years) of which 38 were included. As neurological healthy controls, 49 (17 female; 32 male; mean age 62.3 ± 14.4 years) patients with thoracic abdominal aortic aneurysm (TAAA) were recruited of which 38 were included.

Preoperatively, CSF and blood serum samples were taken. All participants underwent neurological examination including mJOA and NDI. In eight DCM patients, samples could be collected three months postoperatively. To assess the status of the BSCB we used the Reiber diagnostic, measuring Albumin, IgG, IgA and IgM (all mg/dl). Quotients (CSF/serum) were calculated ($n \times 10^{-3}$) for all parameters (QIgG, QIgA, QIgM and QAlb). The individual age-related reference range of QAlb for patients and controls were calculated: $QAlb = (4 + \text{age}/15) \times 10^{-3}$

Results

Clinical status differed significantly between patients and controls (mJOA: DCM 10.4±3.2, TAAA 17.4±1.2, $p < .001$; NDI: DCM 42.3±19.4, TAAA 4.6±7.7, $p < .001$). In the DCM group 32 patients showed a BSCB disruption. In the control group none of the patients had a BSCB disruption. QAlb as expression of BSCB impairment significantly differed between groups (QAlb: DCM: 12.6±8.2; TAAA: 5.1±1.8, $p < .001$). Intrathecal immunoglobulin concentrations significantly differed between groups (QIgG DCM 5.8±3.9, TAAA 2.5±0.9, $p < .001$; QIgA DCM 3.4±2.4, TAAA 1.5±0.8, $p < .001$). Three months after decompressive surgery eight DCM patients agreed to be lumbar punctured again. Postoperatively, results reveal a reduction of QAlb in all patients (QAlb DCMpre 12.6±1.3, DCMpost 7.0±1.0, $p < .001$). In three patients BSCB disruption was completely restored.

Conclusion

DCM patients present with BSCB disruption. Higher concentrations of intrathecal immunoglobulin as an expression of pathological diffusion were detected. Postoperatively, BSCB seems to restore after decompressive surgery. These results indicate BSCB disruption to be a pathomechanism in DCM.

Spinale Frakturen und zervikale Myelopathie/*Spine fractures and cervical myelopathy*

V169

Degenerative zervikale Myelopathie – quantitative Analyse von MR-Spektroskopien mittels Segmentation in grauer und weißer Substanz im primären Motorkortex um anhaltende Pathologien zu evaluieren
Degenerative cervical myelopathy – quantitative analysis of MR spectroscopy via segmentation of grey and white matter in the primary motor cortex to evaluate on-going pathomechanisms

C. Blume¹, H. R. Clusmann¹, V. Mainz², H. Ridwan³, K. Jütten¹, C. A. Mueller¹

¹Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neurochirurgie, Aachen, Germany

²Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Psychiatrie, Aachen, Germany

³Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neuroradiologie, Aachen, Germany

Objective

The exact pathophysiological mechanisms in the primary motor cortex (PMC) of patients with degenerative cervical myelopathy (DCM) are still unclear. The aim of the present study was to detect pre- and postoperative alterations of crucial neuro-metabolites in the PMC of patients with DCM using MR spectroscopy (MRS). Specifically, and to establish a precise method of measurement, alterations were inspected in grey (GM) and white matter (WM). Respectively, while excluding/controlling for cerebral spinal fluid (CSF) for partial volume effects.

Methods

MR spectroscopy was performed in 38 DCM patients (mean age 61.3±11.4; male n=24 and female n=14) with indication for surgical decompression before and, additionally, in 20 patients six months after surgery. 20 healthy and age matched volunteers served as control group (CG) (mean Age 63.7±6.3; male n=11 and female n=9). The neurological status and clinical scores (mJOA, NDI) of patients and volunteers were collected. MRI was performed at a 3T scanner with following sequences for the brain: 3D-T1, fMRI for finger tap paradigm for spectroscopy voxel positioning at the PMC. MR spectroscopy assessing: Creatinine (Cr), N-acetyl-aspartam (NAA), Choline (Cho), and Inositol (Ins). Spectroscopy voxel was classified into grey matter (GM), white matter (WM) and cerebrospinal fluid (CSF) using Matlab and SPM12. Metabolite concentrations were corrected for CSF-partial volume effects and additionally analysed accounting for GM- respectively WM-fraction.

Results

DCM and controls differed significantly concerning the clinical status (mean mJOA: DCM 11.2±3.2; CG 18±0, $p<.001$; NDI: DCM 40.7±23; CG 4±6.5, $p<.001$). Measurements corrected for CSF revealed significant concentrations of NAA between patients and CG (mean NAA DCM: 120.0±23.2; CG 135.7±16.5, $p=.012$). In the analyses of pre- and postoperative patients, metabolites presented significant differences 6 months postop. especially in the GM of the PMC (mean Cr: preop. 203.3±75 vs. Postop. 166.8±52.4, $p<.05$. mean Ins: preop. 141.1±62.8 vs. Postop 114.7±39.9, $p<.05$. mean Cho: preop. 113.4±43.2 vs. Postop. 97.6±31.6, $p<.05$).

Conclusion

Decreased NAA in the primary motor cortex presents an impairment of neuronal function, mitochondrial dysfunction and neuronal density in DCM patients. Postoperatively, metabolites for reactive gliosis/neuroinflammation (Ins) are decreased. Reduced cellular turnover (Cho) and metabolic activity (Cr) seems to be an on-going pathomechanism in the primary cortex even after decompressive surgery.

Spinale Frakturen und zervikale Myelopathie/*Spine fractures and cervical myelopathy*

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Die Untersuchung der zerebralen Reorganisation bei degenerativer zervikaler Myelopathie – eine prospektive, multizentrische Studie
Investigating cerebral reorganisation in degenerative cervical myelopathy – a prospective, multi-centre trial

A. Zdunczyk¹, L. Kawelke¹, S. Ille², S. Krieg², C. Weiß Lucas³, T. Picht¹, P. Vajkoczy¹

¹Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

²Technische Universität München, Klinik für Neurochirurgie, München, Germany

³Universitätsklinikum Köln, Klinik für Neurochirurgie, Köln, Germany

Objective

The concept of "Cortico-spinal Reserve in patients suffering from degenerative cervical Myelopathy" (CRMe) has been recently introduced. In patients suffering from mild symptoms (JOA>12) and thus preserved reserve an enlarged motor area due to a higher recruitment of supplementary motor areas (M2) was observed. In contrast, severely symptomatic patients (JOA≤12) with an exhausted reserve presented with a restricted motor area, reduced recruitment curve and increased inhibition. The current prospective multicentre trial has been designed to validate the new pathophysiological concept.

Methods

In our on-going trial, we have enrolled 120 patients with degenerative cervical myelopathy (DCM) from 4 spine centres in Germany and Switzerland. The study was sponsored by a DWG research grant. On the basis of the initial Japanese Orthopaedic Association (JOA) Score three patient groups were established (JOA≤12, 13-15, 15-17). Corticospinal excitability was determined by navigated transcranial magnetic stimulation (nTMS) with the following parameters: Resting motor threshold (RMT), Recruitment curve (RC), Cortical silent period (CSP) and Motor area.

Results

In patients with moderate symptoms (JOA 12-15) we encountered a compensatory increase of motor cortex activation (motor area: $p<0.05$; mean \pm SD JOA 12-15: $308,5 \pm 213,3$ vs. JOA ≤ 12 : $225,7 \pm 159,5$) and maintained corticospinal excitability (RC slope $p=0.4$; JOA 12-15: $10,6 \pm 6$ vs. JOA 15-17: $11,1 \pm 5,2$). In contrast patients with severe symptoms (JOA ≤ 12) presented a reduced excitability of cortico-cortical axons reflected by an elevated RMT ($p<0.05$; JOA ≤ 12 : $43,8 \pm 11,4$ vs. JOA 15-17: $39,2 \pm 8,4$) and reduced corticospinal excitability expressed by a lower RC slope ($p<0.05$; JOA ≤ 12 : $8,4 \pm 4,8$ vs. JOA 15-17: $11,1 \pm 5,2$). The diminished cortical motor area ($p<0.05$, see above) further revealed a functional restriction on the cortical level in this group.

Conclusion

In summary our prospective multicentre trial has confirmed our concept for functional reorganization in patients suffering from DCM i.e. the "corticospinal reserve capacity". It became apparent that the individual pattern of compensation is a sensitive marker to objectify the state of the disease and may indicate imminent non-reversible clinical deterioration. This innovative approach to describe the pathomechanisms in DCM might revise current concepts of clinical diagnostics and might have an impact on future treatment strategies.

Spinale Frakturen und zervikale Myelopathie/*Spine fractures and cervical myelopathy*

V172

Entwicklung eines ovinen *in vitro* Wirbelkörper-Osteoporosemodells zur Untersuchung eines neuen bioresorbierbaren und osteoinduktiven Knochenzementes zur Versorgung osteoporotischer Wirbelkörperfrakturen

Development of a novel in vitro model of osteoporotic bone to examine a new biodegradable and osteoinductive bone cement for the management of osteoporotic vertebral fractures

H. Krenzlin¹, A. Foelger¹, V. Mailänder², C. Blase³, F. Ringel¹, N. Keric¹

¹Universitätsmedizin Mainz, Neurochirurgische Klinik, Mainz, Germany

²Max-Planck-Institut für Polymerforschung, Mainz, Germany

³Frankfurt University of Applied Sciences, Personalised Biomedical Engineering Lab, Frankfurt am Main, Germany

Objective

Osteoporosis is the most common age-related progressive skeletal disease characterized by bone loss and concomitant tendency for osteoporotic vertebral fractures (OVF). The management of OVF often necessitates fusion surgery, with high rates of implant failure due to the brittle bone substance. *In vitro* models of osteoporosis to test implant pull out strength are scarce. We present a novel ovine model of osteoporotic bone to test a new composite osteoinductive and biodegradable bone cement to boost the anti-osteoporotic therapy and improve long term implant integrity.

Methods

12 sheep vertebrae were perfused with 25% TBD-1 decalcifier solution using a double syringe pump set-up for 24h. Bone density was measured prior and after decalcification using dual-energy X-ray absorptiometry (DEXA). Osteoinductive synthetic collagen I mimetic peptide (P15) was mixed with biodegradable calcium phosphate cement (CaP). Pedicle screws were introduced into one pedicle of each vertebra and augmented with CaP/P15. Standard polymethylmethacrylate (PMMA) cement and non-augmented screws served as control. Linear pullout testing was performed. Osteoblastic transformation of human mesenchymal stem cells (MES) was verified via osteoblast-related gene expressions of bone-specific alkaline phosphatase2 (ALP2) and osteocalcin using Immunofluorescence and RT-PCR.

Results

Bone marrow density (BMD) prior to decalcification was 0.72 ± 0.02 g/cm² prior and 0.53 ± 0.04 g/cm² after decalcification. BMD was decreased by $28.75 \pm 2.6\%$. mRNA expression of ALP2 increased $32.76 \pm 0.21\%$, while osteocalcin was increased by $16.15 \pm 0.72\%$ after co-culture of MES with CaP/P15. Immunofluorescent staining was increased in a similar manner. Biomechanical testing showed improved pullout loads of CaP/P15 augmented screws compared to controls in decalcified bone. Difference of pullout loads between pre- and post-demineralizing process were also statistically significant ($p < 0.001$).

Conclusion

The CaP/P15 composite cement is capable of inducing osteoblastic differentiation in human MES *in vitro*. The ovine decalcification model provides a similar loss of bone marrow density as expected from osteoporotic vertebrae *in vivo* and is capable of mimicking the decreased pull out loads of pedicle screws *in vitro*. Pull out loads of CaP/P15 augmented pedicle screws are superior to controls in our model.

Spinale Frakturen und zervikale Myelopathie/*Spine fractures and cervical myelopathy*

V173

Klinische Ergebnisse nach konservativer oder operativer Behandlung osteoporotischer thorakolumbaler Frakturen – erste Daten aus der prospektiven, multizentrischen Studie zur Evaluierung von OF-Klassifikation, OF-Score und Therapieempfehlungen für osteoporotische Wirbelfrakturen (EOFTT)
Clinical treatment outcomes and complications of osteoporotic thoracolumbar fractures after conservative or surgical treatment – initial data from the prospective, multi-centre study evaluating the OF classification, OF-score and therapy recommendations for osteoporotic vertebral fractures (EOFTT)

B. Ullrich¹, S. Katscher², P. Schenk^{2,3}, K. Schnake^{2,3,4}, U. Spiegel^{2,3,4,5}, V. Zimmermann^{2,3,4,5,6}, M. Perl^{2,3,4,5,6,7}, M. Scherer^{2,3,4,5,6,7,8}, N. Isik¹, D. G. F. Sektion Wirbelsäule^{2,3,4,5,6,7,8,9}

¹Berufsgenossenschaftliche Kliniken Bergmannstrost, Unfall- und Wiederherstellungschirurgie, Halle/Saale, Germany

²Sanan Kliniken Borna, Klinik für Unfallchirurgie und Orthopädie, Borna, Germany

³Berufsgenossenschaftliches Klinikum Bergmannstrost Halle, Stabstelle Wissenschaft, Forschung und Lehre, Halle/Saale, Germany

⁴Schön Klinik Nürnberg Fürth, Zentrum für Wirbelsäulen- und Skoliosetherapie, Fürth, Germany

⁵Universitätsklinikum Leipzig, Klinik und Poliklinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Leipzig, Germany

⁶Klinikum Traunstein, Klinik für Unfallchirurgie und Orthopädische Chirurgie, Traunstein, Germany

⁷Universitätsklinikum Erlangen, Unfallchirurgische Klinik- Orthopädische Chirurgie, Erlangen, Germany

⁸Helios Amper-Klinikum Dachau, Klinik für Unfallchirurgie und Orthopädie, Dachau, Germany

⁹Deutsche Gesellschaft für Orthopädie und Unfallchirurgie (DGOU), Sektion Wirbelsäule, Berlin, Germany

Objective

Osteoporotic fractures of the spine are a rising health issue. The research group 'Osteoporotic fractures' of the spine section of the German Society for Orthopaedics and Trauma (AG-OF) has initiated a prospective, multicentre study evaluating the OF classification, OF-score and therapy recommendation for osteoporotic vertebral fractures (EOFTT).

The OF-score takes account of fracture classification, bone density, sintering dynamics, pain, neurology, mobilization and health status and separates between recommendation on surgical or conservative therapy. This sub-study examines the therapy and its influence on the score and the complication rate.

Methods

Complications that required revision were gathered as well as the OF-score at following date set: day of treatment decision (dtd), discharge and 6 week follow up (FU). A change in the score was evaluated by repeated measures of ANOVA at 3 points in time. To examine the effects of the therapy (surgical/conservative) on the score, repetitive measurements via ANCOVA were carried out. At the same time the scores were taken into consideration as a baseline (covariant) at the time of treatment decision.

Results

101 surgically and 73 conservatively treated patients (39♂, 135♀), with a mean age of 73±9 years (50-94) could be acquired from the data. Fig.1 illustrates the distribution of the OF-score at dtd. Fig 2 shows the distribution at discharge. ANOVA shows a reduction of the OF-score ($p<0.001$). ANCOVA shows a sig. influence of baseline ($p<0.001$) and therapy ($p=0.031$).

Surgically treated patients have a sig. greater reduction of the OF-score than conservatively treated patients. 4 patients had complications that required revision at the time of discharge. At the time of FU 2 of 38 OF 4 (5%) patients showed complications that required revision (implant-assoc.). Moreover, 4 of 73 FU patients (5%) had to switch from conservative to surgical treatment.

Conclusion

With an improved score over time, surgically treated patients appear to benefit from a reduction in the OF-score. Therefore, the application of the OF-score seems to be prognostically beneficial. In terms of complications that required revision, attention must be given to the OF classifications 4 and 5, even if the overall complication rate is like in bone healthy patients.

Fig 1

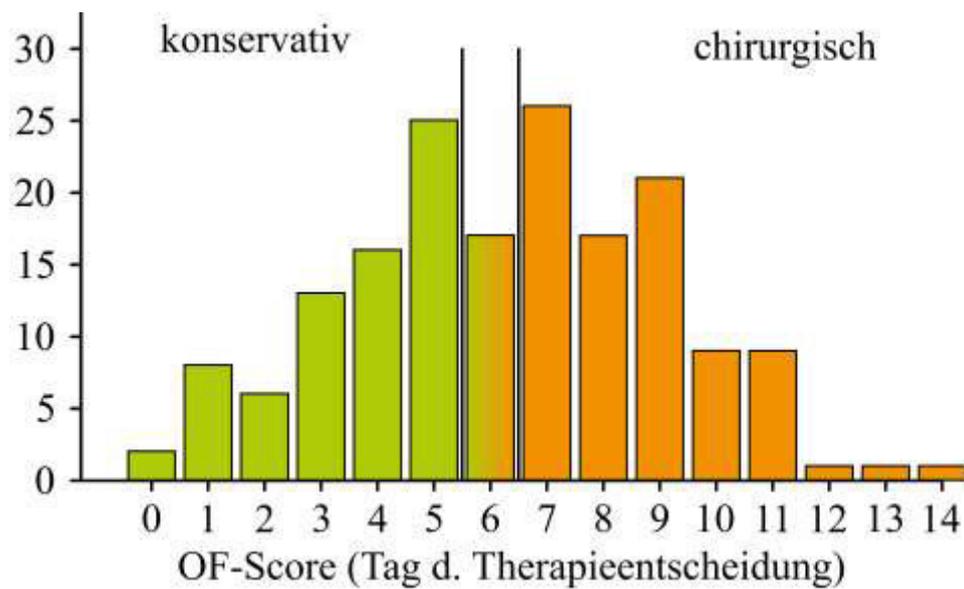
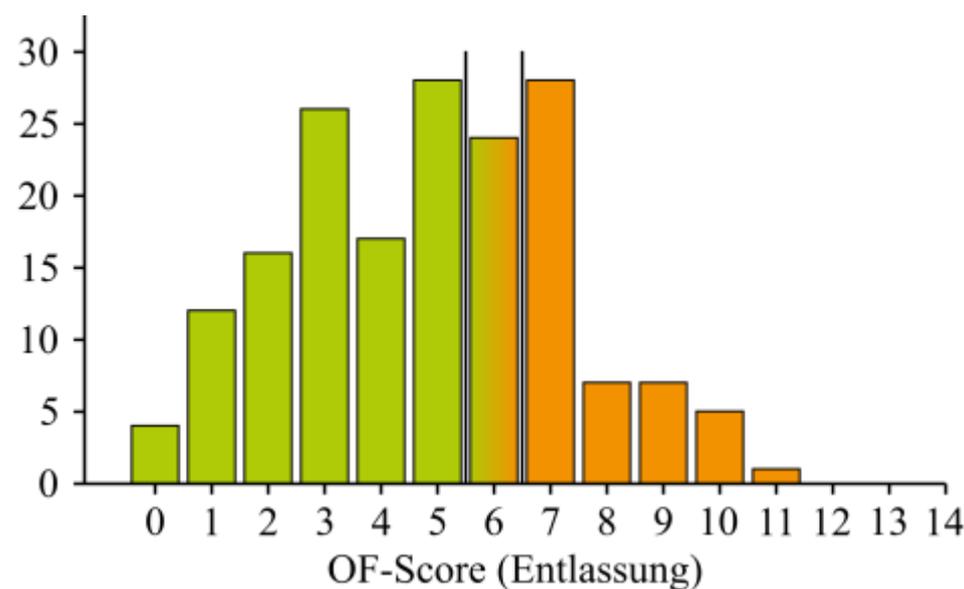


Fig 2



Tiefenhirnstimulation II/*Deep brain stimulation II*

V174

Leukenzephalopathie bei Patienten mit Morbus Parkinson und Tiefenhirnstimulation – Ein höheres Risikoprofil?

Leucoencephalopathy in patients with Parkinson's disease and deep brain stimulation – A higher risk profile?

P. Jarski, T. Gasimov, D. Mielke, V. Rohde, V. Malinova

Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Leucoencephalopathy (LE) is often detected on magnetic resonance imaging (MRI) in elderly patients. White matter lesions may interfere with the lead trajectories for deep brain stimulation (DBS) in patients with Parkinson's Disease (PD) with the result of less possible trajectories for microelectrode recording (MER). Furthermore, LE is deemed to be possibly associated with higher complication rate after DBS-surgery. In this study we assessed the incidence of LE in PD-patients and evaluated a possible correlation with complications after DBS-surgery and with MER.

Methods

We performed a retrospective analysis of PD-patients, who underwent DBS-surgery. The presence of LE was evaluated on the pre-operative MRI and was quantified using the modified Fazekas scale. Postoperative complications such as bleeding and infections were documented from the medical records. The number of used trajectories and the length of subthalamic nucleus (STN) signal were documented. DBS-efficacy was calculated using the side specific motor symptom ratio (UPDRS-3, Unified Parkinson Disease Rating Scale, recorded for motor symptoms only on each side separately; stimulation ON medication OFF postoperative divided by medication OFF preoperatively) at one-year follow-up.

Results

A total of 141 patients were included. The mean age was 61.0 years (range 42-81). The incidence of LE was 37.59% (Fazekas 1 in 69.8%, 2 in 22.6%, and 3 in 7.5%). Periventricular lesions (PVL) were found in 51.78% (73/141) and deep lesions (DL) in 59.6% (84/141). Postoperative complications occurred in 12% (17/141), one patient had superficial peri-lead hemorrhage and the rest 16 patients had an infection. We found a statistically significant correlation of complications with PVL ($r=0.17$, $p=0.03$), but not with DL. There was a significant correlation of the LE with the length of STN-signal ($r=0.18$, $p=0.02$). We found no correlation of LE with the number of trajectories or with the side specific motor symptom ratio.

Conclusion

We confirmed a high incidence of LE in PD-patients, which correlated with the length of STN-signal, but did not result in less DBS-efficacy. PVL correlated significantly with the complication rate. Considering the low incidence of postoperative bleeding and the high incidence of PVL and DL, white matter lesions seem not to be a risk factor for postoperative bleeding after DBS-surgery.

Tiefenhirnstimulation II/*Deep brain stimulation II*

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Physiologische Kartierung der subthalamischen Region von in Allgemeinanästhesie operierten Parkinson-Patienten – I. Mikroelektrodenableitungen

Physiological mapping during asleep procedures in patients with Parkinson's disease – I. intraoperative microelectrode recordings

M. Schaper¹, A. Gulberti², W. Hamel¹, M. Pötter-Nerger³, J. Köppen¹, U. Hidding³, C. Buhmann³, S. Zittel³, C. U. Choe³, A. K. Engel², C. Gerloff³, C. Zöllner⁴, M. Westphal¹, C. K. E. Moll²

¹Universitätsklinikum Hamburg-Eppendorf, Klinik für Neurochirurgie, Hamburg, Germany

²Universitätsklinikum Hamburg-Eppendorf, Institut für Neurophysiologie und Pathophysiologie, Hamburg, Germany

³Universitätsklinikum Hamburg-Eppendorf, Klinik für Neurologie, Hamburg, Germany

⁴Universitätsklinikum Hamburg-Eppendorf, Klinik und Poliklinik für Anästhesiologie, Hamburg, Germany

Objective

To compare microelectrode recordings (MER) within the subthalamic region of awake patients with Parkinson's disease (PD) to electrophysiological mapping results obtained during bilateral deep brain stimulation (DBS) surgery of the subthalamic nucleus (STN) under general anesthesia (GA)

Methods

We retrospectively reviewed and analyzed intraoperative MER from 51 consecutive PD patients (20F, 31M; age 61±10y; disease duration 12±4y) undergoing STN-DBS surgery under GA with propofol and remifentanyl at our institution between 2015 and 2018. Data were compared to MER results from 51 consecutive PD patients (15F, 36M; age 62±7y; disease duration 11±4y) undergoing MER-guided STN-DBS surgery in the awake state.

Results

Both the dorsal and ventral STN boundaries could reliably be identified by a combination of single cell spiking properties and background changes under both anesthesia conditions. Crisp background changes at penetration of the fiber capsule alleviated mapping of the dorsal STN circumference during awake surgeries and lighter levels of GA, respectively. In contrast, the dorsal entry of the STN consistently appeared slightly deeper (~0.5mm) under GA, reflecting decreased activity levels of STN neurons. Deeper levels of anesthesia were generally associated with decreased discharge rates and increased burstiness of STN neurons, respectively. Despite these differences, the average hit rate was not significantly different between the two groups. Irrespective of anesthesia condition, we successfully confirmed the STN electrophysiologically in 80-90% of the trajectories. Furthermore, average recording length through the STN was ~5mm and did not differ between conditions. However, as expected, prevalence of oscillatory single cell activities at tremor (3-8Hz) and beta (12-35Hz) frequencies was significantly higher in awake patients compared to GA. Likewise, further physiological mapping could not be performed (e.g. somatotopic assessment of movement-related responses) or was unsuccessful (assessment of kinesthetic responses) during GA. Total recording duration was only slightly (~8min.) longer under GA.

Conclusion

General anesthesia with propofol and remifentanyl has strong effects on neuronal activity in the parkinsonian STN. Nevertheless, MER-guided mapping of the subthalamic region can safely and reliably be performed under GA with high precision. We conclude that MER are a helpful tool for STN-DBS procedures performed under GA.

Tiefenhirnstimulation II/*Deep brain stimulation II*

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Physiologische Kartierung der subthalamischen Region von in Allgemeinanästhesie operierten Parkinson-Patienten – II. intraoperative Teststimulation

Physiological mapping during asleep procedures in patients with Parkinson's disease – II. intraoperative test-stimulation

M. Schaper¹, A. Gulberti^{2,3}, J. Köppen¹, U. Hidding³, C. Buhmann³, S. Zittel³, C. U. Choe³, C. Zöllner⁴, A. K. Engel², M. Westphal¹, C. Gerloff³, M. Pötter-Nerger³, W. Hamel¹, C. K. E. Moll²

¹Universitätsklinikum Hamburg-Eppendorf, Klinik für Neurochirurgie, Hamburg, Germany

²Universitätsklinikum Hamburg-Eppendorf, Institut für Neurophysiologie und Pathophysiologie, Hamburg, Germany

³Universitätsklinikum Hamburg-Eppendorf, Klinik für Neurologie, Hamburg, Germany

⁴Universitätsklinikum Hamburg-Eppendorf, Klinik und Poliklinik für Anästhesiologie, Hamburg, Germany

Objective

To compare capsular side effect (SE) profiles and thresholds of intraoperative test stimulation obtained within the subthalamic region of awake Parkinson's disease (PD) patients undergoing bilateral deep brain stimulation (DBS) surgery of the subthalamic nucleus (STN) with those obtained under general anesthesia (GA).

Methods

We retrospectively reviewed and analyzed intraoperative test stimulation protocols from 51 consecutive PD patients undergoing STN-DBS surgery under GA with propofol and remifentanyl at our institution between 2015 and 2018. Data was compared to stimulation results obtained in 51 consecutive PD patients undergoing STN-DBS surgery under local anesthesia (LA). We employed bipolar DBS at the dorsal STN border with high-frequency (130Hz) trains of monophasic impulses. Pulse width was set to 60 μ s (LA) and 100 μ s (GA), respectively. Spread of the electrical field to neighbouring cortico-spinal and cortico-bulbar motor fibers was assessed both clinically and with electromyography (EMG). To this end, surface polymyography was routinely performed in every case.

Results

Irrespective of anesthesia condition, capsular SE were successfully elicited intraoperatively in all patients. Both under LA and GA, lateral trajectories had significantly lower SE thresholds (LA, 3.4 \pm 1.2mA/GA, 3.0 \pm 1.0mA) compared to central (LA, 4.3 \pm 1.3mA/GA, 4.1 \pm 0.9mA) and anterior (LA, 5.2 \pm 1.6mA/GA, 4.7 \pm 1.2mA) tracks, as judged clinically (p <0.01). Notably, capsular thresholds did not differ between anesthesia conditions, when adjusting for total electrical energy delivered (p >0.05). Stimulation-induced tetanic muscle contractions (TMC) predominantly affected face and arm muscles. TMC thresholds for face and arm were not significantly different (p >0.05). Transient paresthesia—consistently reported by awake patients ~0.5mA below TMC threshold—and stimulation-induced dysarthria could not be assessed during GA. It is of note that the earliest signs of capsular spread under GA (activation of single muscle fibers) were visible in the EMG long before TMC was apparent upon visual inspection (EMG threshold, 3.5 \pm 0.9mA/visual threshold, 4.6 \pm 0.7mA; p <0.0001).

Conclusion

We conclude that, regardless of the anesthetic regimen and despite obvious limitations, intraoperative test stimulation—especially in conjunction with polymyography—provides a detailed account of capsular spread during STN-DBS surgery and may be key to a successful surgical outcome.

Tiefenhirnstimulation II/*Deep brain stimulation II*

V177

Implantation direktonaler DBS-Elektroden in Narkose bei Parkinson-Patienten – Wie groß darf die Abweichung von der optimalen Position sein?

Implantation of directional deep brain stimulation electrodes under general anesthesia in Parkinson's disease patients – How much lead deviation from the optimal position can be revised?

V. Malinova¹, N. Nerntengian¹, C. Dragaescu², F. Sixel-Döring², C. Trenkwalder^{1,2}, V. Rohde¹, D. Mielke¹

¹Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

²Paracelsus-Elena-Klinik Kassel, Neurologie, Kassel, Germany

Objective

Deep brain stimulation (DBS) is an established treatment option in patients with Parkinson's Disease (PD). Directional DBS (dDBS) represents one of the recent advances in DBS-surgery. Since its introduction, the number of DBS-surgeries under general anesthesia is rising, which might bear a higher risk for suboptimal lead position compared to awake surgery. We evaluated the correlation of lead position with the postoperative stimulation effect in PD-patients with implanted dDBS-system under general anesthesia.

Methods

We performed a retrospective analysis of patients with dDBS-system (Vercise, Boston Scientific) implantation under general anesthesia at our department between 2017 and 2019. The lead position in relation to the subthalamic nucleus (STN) was evaluated after fusion of the postoperative CT dataset with the preoperative MRI dataset and after anatomical mapping and autosegmentation of the STN by means of the stereotactic planning software Elements Brainlab. The lead position was classified as optimal (dorsolateral part of STN), marginal lateral, marginal medial, marginal anterior and marginal posterior or outside of the STN, respectively. The stimulation effect was calculated as the ratio of motor UPDRS-III pre- and postoperatively.

Results

A total of 29 patients with 58 implanted leads were included. The mean age was 68.8 (range 43-71) years. The lead positions were as followed: optimal in 29.3% (17/58), marginal lateral in 19.1% (11/58), marginal medial in 34.5% (20/58), marginal dorsal in 1.7% (1/58) and none of the leads had a marginal anterior position. A position outside of the STN was detected in 15.5% (9/58) with a mean distance to the STN of 1.5 mm (range 0.6 -3.6 mm). The mean UPDRS-III ratio was 2.5 (range 0.9-4,6). In patients with an optimal lead position, the UPDRS-III ratio was 3.1 compared to 2.7 in patients with a lead position outside of the STN, which was not statistically significant. In one patient with a marginal medial lead position no satisfactory stimulation was achieved.

Conclusion

dDBS seem to compensate a suboptimal lead position in most of the cases. Even in cases with a lead position outside of the STN, no significant differences in stimulation effects compared to the cases with an optimal lead position. Nevertheless, in exceptional cases a suboptimal lead position might result in an unsatisfactory stimulation, which should be avoided by increasing the accuracy of lead positioning.

Tiefenhirnstimulation II/*Deep brain stimulation II*

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Über die Konnektivität von Nebenwirkungen-induzierenden Kontakten im Rahmen der Tiefenhirnstimulation bei Morbus Parkinson

Connectivity of side-effect inducing contacts in deep brain stimulation for Parkinson's disease

J. Schlaier¹, Q. Strotzer¹, J. Anthofer¹, R. Faltermeier¹, N. O. Schmidt¹, A. Beer²

¹Universitätsklinikum Regensburg, Klinik und Poliklinik für Neurochirurgie, Regensburg, Germany

²Universität Regensburg, Experimentelle Psychologie, Regensburg, Germany

Objective

The aim of our study was to investigate which subcortical fiber tracts and cortical areas are involved in the occurrence of side-effects in deep brain stimulation for Parkinson's disease.

Methods

21 patients with Parkinson's disease and bilaterally implanted electrodes in the subthalamic nucleus were investigated. Diffusion weighted images (DWI) with 64 gradient directions were included in the routine preoperative imaging procedure for deep brain stimulation. Post-operative CT scans were fused to the DWI data set and the position of the individual contacts of the electrodes were determined. Probabilistic fiber-tracking was performed with seed regions based on each individual contact of the electrodes and the resulting anatomical fiber tracts and cortical areas were determined. We compared the connectivity pattern of contacts, which induced side effects with the connectivity pattern of contacts that did not.

Results

Electrode-contacts that provoked motoric side-effects were significantly more often connected with the primary motor cortex than contacts without this effect. However, they were not connected more frequently with fibers of the pyramidal tract than contacts without motoric side effects. Although paresthesia provoking contacts had a positive contingency with the superior parietal lobe, they were not significantly more often connected to the medial lemniscus than non-provoking contacts (82.4% of provoking and 77.8% of non-provoking contacts; $p=0.502$). Oculomotor side effects were positively associated with connections to the inferior frontal gyrus and the lateral part of the anterior limb of the capsula interna. A positive contingency for hyperkinesia existed with the supplementary motor area.

Conclusion

Contacts that evoked side effects were connected to the expected cortical areas but less so to their adjacent subcortical fiber tracts. Categorization of subcortical fiber tracts seems to be error-prone.

Tiefenhirnstimulation II/*Deep brain stimulation II*

V179

Direktionale versus omnidirektionale Tiefenhirnstimulation beim M.Parkinson – 12-Monatsergebnisse einer prospektiven, verblindeten, Cross-over-Multicenter Studie

Directional versus omnidirectional deep brain stimulation for Parkinson's disease – 12-month results of a multi-centre, prospective, blinded, crossover study

J. Vesper¹, P. J. Slotty¹, S. J. Groiss², A. Schnitzler²

¹Heinrich-Heine-Universität Düsseldorf, Sektion Stereotaktische und Funktionelle Neurochirurgie, Düsseldorf, Germany

²Heinrich-Heine-Universität Düsseldorf, Zentrum für Bewegungsstörung und Neuromodulation, Düsseldorf, Germany

Objective

Deep Brain Stimulation (DBS) has been delivered through circumferential electrodes for over a quarter century to treat symptoms of levodopa-responsive Parkinson's disease. Recently introduced directional leads for DBS have the two middle rings divided into three segments, which allows for axially asymmetric stimulation. The Infinity DBS system (Abbott) delivers conventional omnidirectional stimulation to all three segments of the ring, or directional stimulation to only one or two segments. PROGRESS is the first large, prospective, multi-center study conducted to evaluate safety and clinical performance of directional DBS.

Methods

Directional and omnidirectional stimulation were compared in 66 subjects receiving DBS in the subthalamic nucleus for Parkinson's disease. Subjects were programmed with omnidirectional stimulation for 3 months, followed by directional for 3 months and blinded to stimulation type for the first 6 months. The primary endpoint was the difference in therapeutic window (TW) for directional vs. omnidirectional stimulation assessed at the 3-month follow-up visit. Subjects were blinded to stimulation type for the first 6 months, and a blinded assessment was made for therapeutic window. Additional endpoints included blinded UPDRS part III motor examination scores, UPDRS part II for activity of daily living, PDQ-39 for quality of life, safety, subject and clinician stimulation preference and subject and programmer satisfaction with product usability.

Results

There was a wider TW for directional stimulation in 59 of 66 subjects (89.4%), meeting the endpoints for both non-inferiority and superiority. Single-segment activation produced wider TW than omnidirectional stimulation in 56 of 66 subjects (84.8%). Directional stimulation was able to produce a 35% wider TW, and therapeutic current strength was 30% lower using the optimal directional configuration. When asked for their preferred period, more than 2 times as many subjects and 4 times as many clinicians chose the period using directional stimulation.

Conclusion

PROGRESS met its superiority endpoint, with 89.4% of subjects having a wider TW using directional DBS stimulation. This international prospective blinded crossover study is the largest clinical evaluation of directional DBS to date.

Tiefenhirnstimulation II/Deep brain stimulation II

V180

Gangstörungen bei Morbus Parkinson nach Stimulation des Nucleus subthalamicus – eine Bildanalyse

Gait alterations in Parkinson's disease after subthalamic neurostimulation – an imaging study

A. Großmann¹, R. Nickl², J. Roothans¹, F. Lange¹, J. Volkmann¹, M. Reich¹

¹Universitätsklinikum Würzburg, Neurologische Klinik und Poliklinik, Würzburg, Germany

²Universitätsklinikum Würzburg, Neurochirurgische Klinik und Poliklinik, Würzburg, Germany

Objective

Deep brain stimulation of the subthalamic nucleus (STN-DBS) is an established therapy for Parkinson's Disease. Unfortunately, individual outcomes vary and often residual gait disturbances ameliorated mobility. The exact lead localisation and stimulation parameters may be responsible for this aspect. So far, no study has been able to identify an "optimal efficacy volume" in respect of mobility and gait for DBS within the STN. We investigated Volumes of Tissue activated (VTA) in subjects with Parkinson's Disease undergoing STN-DBS. We aimed to distinguish anatomic areas that, affected by DBS, have a positive effect on gait.

Methods

86 subjects with idiopathic Parkinson's Disease (Hoehn & Yahr 2.90.7, UPDRS III 48.712.3, disease duration 16.04.8 years) undergoing bilateral STN-DBS were stratified for motor improvement. To take a closer look at gait disturbances, we divided our subjects into groups according to their change in gait items of UPDRS III. To correlate the clinical outcome with the exact anatomical location of stimulation, we simulated VTAs in subject's related MRI space and associated them with gait alterations. All patient images were registered to a common MNI-space. Only voxels that were overlapped by ≥ 6 VTAs were visualized to define a volume, where DBS has a positive effect on gait disturbances (= "sweetspot").

Results

Our cohort shows motor improvement of 51.13% by stimulation alone (reduction of 24.913.2 points in UPDRS III). 24 subjects experienced a complete remission of gait problems by STN-DBS, meanwhile 9 subjects show de-novo gait disturbances. We observed no differences in stimulation parameters and global parkinsonism. Interestingly, the anatomic area of stimulation allows a clear separation of the groups. For individuals with an improvement of gait by DBS, the most commonly stimulated area was located more dorsal and antero-medial than the spot stimulated in individuals with a worsening of gait problems. Stereotactic coordinates for the centre of mass in improvement on gait were L=13.1, A=2.5, I=3.0 and coordinates for aggravation of gait problems were L=14.2, A=1.2, I=3.2.

Conclusion

We were able to show that the exact anatomical localisation of stimulation is correlated with gait alterations. The most beneficial spot to stimulate is located more dorsal and antero-medial, within the transition zone of the sensory-motor part of the STN and bordering white matter. In the future, these results could improve re-programming attempts in STN-DBS with gait problems.

Gliome experimentell II/*Gliomas experimental II*

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Inhibierung von PI3K, jedoch nicht der MEK/ERK Pathway sensitivieren humane Gliome bezüglich alkylirender Therapeutika

Inhibition of the PI3K but not the MEK/ERK pathway sensitises human glioma cells to alkylating drugs

M. Timmer¹, B. Haas², V. Klinger^{2,3}, C. Keksel^{2,4}, D. Kiefer^{2,4}, J. Caspers^{2,5}, J. Walther^{2,3}, M. Wos-Maganga M², S. Weickhardt², R. Frötschl², N. Eckstein⁴

¹Universitätsklinikum Köln, Klinik für Neurochirurgie, Köln, Germany

²Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), Bonn, Germany

³Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), Bonn, Germany

⁴Hochschule Kaiserslautern, Kaiserslautern, Germany

⁵Technische Hochschule Köln, Leverkusen, Germany

Objective

Intrinsic chemoresistance of glioblastoma (GBM) is frequently owed to activation of the PI3K and MEK/ERK pathways. These signaling cascades are tightly interconnected, however, the quantitative contribution of both to intrinsic resistance is still not clear. Here, we aimed at determining the activation status of these pathways in human GBM biopsies and cells and investigating the quantitative impact of both pathways to chemoresistance.

Methods

Receptor tyrosine kinase (RTK) pathways in temozolomide (TMZ) treatment naive or TMZ resistant human GBM biopsies and GBM cells were investigated by proteome profiling and immunoblotting of a subset of proteins. Resistance to drugs and RTK pathway inhibitors was assessed by MTT assays. Apoptotic rates were determined by Annexin V staining and DNA damage with comet assays and immunoblotting.

Results

We observed substantial activation of the PI3K and MEK/ERK pathways in both groups. However, AKT and CREB phosphorylation was reduced in biopsies of resistant tumors while ERK phosphorylation remained unchanged. Subsequent proteome profiling revealed that multiple RTKs and downstream targets are also activated in three GBM cell lines. We then systematically describe a mechanism of resistance of GBM cell lines and human primary GBM cells to the alkylating drugs TMZ and cisplatin. No specific inhibitor of the upstream RTKs sensitized cells to drug treatment. In contrast, we were able to restore sensitivity to TMZ and cisplatin by inhibiting PI3K in all cell lines and in human primary GBM cells. Interestingly, an opposite effect was observed when we inhibited the MEK/ERK signaling cascade with two different inhibitors.

Conclusion

Temozolomide treatment naive and TMZ resistant GBM biopsies show a distinct activation pattern of the MEK/ERK and PI3K signaling cascades indicating a role of these pathways in resistance development. Both pathways are also activated in GBM cell lines, however, only the PI3K pathway seems to play a crucial role in resistance to alkylating agents and might serve as drug target for chemosensitization.

Gliome experimentell II/*Gliomas experimental II*

V182

Der Effekt von kombinierter Behandlung mit 5-Aminolevulinsäure und Röntgenbestrahlung auf Proliferation und Migration von humanen U-87 Glioblastom Zelllinien

The effect of combined treatment with 5-aminolevulinic acid and X-Ray irradiation on proliferation and migration of human U-87 glioblastoma cell line

M. Khaleghi Ghadiri¹, M. Jalili-Nik^{2,3}, A. Maghrouni¹, F. Abbasinezhad Moud¹, B. Al Barim¹, A. Gorji², W. Stummer²

¹Westfälische Wilhelms-Universität Münster, Neurochirurgie, Münster, Germany

²Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

³Ferdowsi University of Mashhad, Neuroscience, Mashhad, Iran

Objective

5-Aminolevulinic acid (5-ALA)-induced fluorescence guidance for surgical treatment has been shown to improve overall survival in patients with glioblastoma (GBM). The aim of this study was to investigate the potential cytotoxic effects of combined treatment with 5-ALA and X-ray irradiation on the viability and migration of human U87 GBM cells.

Methods

The U87 human GBM cells were treated with various concentrations of 5-ALA (100 and 300 µg/ml) with and without X-ray irradiation (2-14 Gy) and the cell viability and migration was assessed after 10 days.

Results

Combined treatment with 5-ALA and X-ray irradiation at a dose rate of 2 Gy did not affect the viability of human U87 GBM cells. However, higher dosages of X-ray irradiation (4-8 Gy) in combination with 5-ALA at a concentration of 300 µg/ml significantly decreased the viability of human U87 GBM cells. 5-ALA at both concentrations of 100 and 300 µg/ml significantly and dose-dependently reduced the cell viability of human U87 GBM cells exposed to X-ray irradiation at a dose rate of 14 Gy compared to the control groups. Application of 5-ALA alone significantly reduced the cell viability at both concentrations compared to non-treated controls. Administration of 5-ALA in combination of X-ray irradiation significantly increased the amount of apoptotic cells and SUB-G1 cell-cycle arrest compared to the control groups. Furthermore, co-administration of 5-ALA and X-ray irradiation significantly inhibited the migration ability of human U87 GBM cells.

Conclusion

Our results suggest that treatment with 5-ALA efficiently sensitized human U-87 glioblastoma cells to X-ray irradiation.

Gliome experimentell II/*Gliomas experimental II*

V183

Der PLEKHG5/RAB26-Signalweg reguliert die Expression des Chemotherapie-Resistenzgens MGMT im humanen Glioblastom

PLEKHG5/RAB26 signalling regulates expression of the chemotherapy resistance gene MGMT in human glioblastoma

K. E. Witte¹, C. Slotta¹, A. Kitke¹, J. F. W. Greiner¹, R. Coras², F. Mertzlufft³, M. Simon⁴, B. Kaltschmidt¹, C. Kaltschmidt¹

¹Universität Bielefeld, Abteilung Zellbiologie, Bielefeld, Germany

²Universitätsklinikum Erlangen, Abteilung für Neuropathologie, Erlangen, Germany

³Evangelisches Krankenhaus der Stiftung Bethel, Wissenschaftlicher Direktor, Bielefeld, Germany

⁴Evangelisches Krankenhaus der Stiftung Bethel, Abteilung für Neurochirurgie, Bielefeld, Germany

Objective

Pleckstrin homology containing family member 5 (PLEKHG5) is an exchange factor for the RAS-related protein RAB26 and was described as a target of the tumor necrosis factor α (TNF α)-protective pathway. PLEKHG5-signaling might play a key role in cancer through NF- κ B activation and TNF α has been implicated in cancer chemoresistance. Expression of the DNA repair gene O-6-methylguanine-DNA methyltransferase (MGMT) by glioblastoma stem cells (GSCs) likely underlies chemoresistance of glioblastoma multiforme (GBM). Here we investigate a potential regulatory interplay between TNF α , PLEKHG5, RAB26 and MGMT in GBM and GSCs.

Methods

The CRISPR/Cas9-system and lentiviral transduction were used for gene knockout and gene transfer in human U251-MG cells. Cellular morphology was investigated using phalloidin/rhodamine staining of the cytoskeleton and digital fluorescence-based image analysis. GSCs were isolated from primary GBM tissues (n = 4) in the presence of EGF and bFGF-2 for selection of potential GSCs after enzymatic digestion of the primary GBM tissue. GSCs were positive for the stem cell markers nestin, CD133 and CD44 on protein level. The corresponding tumor tissues, isolated GSCs, U251-MG wildtype- and the U251-MG *PLEKHG5*^{-/-} cells were investigated for MGMT, PLEKHG5 and RAB26 proteins using immunohisto- and immunocytochemistry. TNF α -induced cell death was analyzed in U251-MG *PLEKHG5*^{+/+} and *PLEKHG5*^{-/-} cells employing a cellular apoptosis assay.

Results

We generated homozygous *PLEKHG5* U251-MG knockout cells validated on the genomic DNA level and by negative *PLEKHG5* immunocytochemistry. *PLEKHG5*, RAB26 and MGMT protein expression was detected in human glioma tissue and primary GCSs. In comparison with the wildtype, U251-MG *PLEKHG5*^{-/-} cells showed a significantly compressed cell shape and decreased size (mean cell size, 2D fluorescence microscopy: $3285 \pm 161 \mu\text{m}^2$ vs. $804 \pm 67 \mu\text{m}^2$, $p < 0.001$). Expression of a constitutively active RAB26 variant led to a phenotypic rescue of the *PLEKHG5* knockout and to specific overexpression of MGMT. TNF α mediated cell death was significantly increased in *PLEKHG5*^{-/-} cells compared to *PLEKHG5*^{+/+} cells (30 min TNF exposure: $60.9 \pm 4.6 \%$ vs. $35.0 \pm 3.9 \%$ and 90 min: $88.1 \pm 7.6 \%$ vs. $54.6 \pm 5.1 \%$, $p < 0.05$).

Conclusion

Our results suggest MGMT as a novel target of *PLEKHG5*/*RAB26* signaling and thus provide additional insights into the regulation of chemotherapy resistance in GBM.

Gliome experimentell II/*Gliomas experimental II*

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Exploration der autokrinen Funktion von mGluR3 Rezeptoren zur Sensitivierung gegen Temodal-Therapie *Exploiting autocrine glutamate signalling via mGluR3 for temozolomide sensitisation*

J. P. Maier, K. Joseph, S. P. Behringer, V. M. Ravi, N. Neidert, J. Beck, O. Schnell, D. H. Heiland

Universitätsklinikum Freiburg, Klinik für Neurochirurgie, Freiburg, Germany

Objective

Invariably, malignant glioma develops resistance against temozolomide (TMZ) chemotherapy during the course of the disease through clonal selection of resistant cells. Autocrine glutamate signalling via metabotropic glutamate receptors (mGluR) was reported to sustain malignant hallmarks, however the extent to which chemoresistance is supported by glutamate signalling remained unknown. Here we aimed to evaluate the potential of mGluR3 blockade therapy as a potential add-on to TMZ in patients suffering from primary glioblastoma.

Methods

Three different primary GBM cell lines were analysed by IncuCyte® Live-Cell Analysis in order to monitor cellular response in the presence of TMZ, LY341495 or the combination of both drugs. Treatment response was validated in vitro and a human neocortical slice model. Visual assessment of cell viability & apoptosis was performed using a polarity sensitive kinetic apoptosis assay under live-imaging conditions. Cell viability assay and BrdU proliferation assay with TMZ, LY341495 and an alternative mGluR3 inhibitor, β -NAAG were carried out for further validation. Gene expression analysis was performed to investigate down-stream transcription effects.

Results

In two of our three cell lines TMZ resistant clones remained after 48 hours TMZ treatment which were lost by mGluR inhibition (LY34149) in the in-vitro and neocortical slice model. We showed that autocrine release of glutamate was increased under hypoxic conditions but inhibition of mGluR reduces the hypoxic resistance. Single cell profiling revealed a heterogeneous distribution of mGluR associated with stem-cell markers. Further characterizing the mGluR family we found that TMZ-resistance is mediated by mGluR3 signalling and downstream upregulation of NFkB signalling.

Conclusion

Autocrine glutamate signalling via mGluR3 is crucial for tumour cell metabolism and affects chemotherapeutic efficacy by altered intracellular signalling. In particular, the specific inhibition of mGluR3 with a selective antagonist like LY341495 could sensitize primary glioblastoma tumour cells for TMZ-induced cytotoxicity – which may constitute a promising new therapeutic strategy in the field of translational glioblastoma research.

Gliome experimentell II/*Gliomas experimental II*

V185

Der TERT Promoter Mutationsstatus definiert Subgruppen diffuser IDH-Wildtyp Gliome *TERT promoter mutational status defines distinct subgroups in diffuse IDH wildtype gliomas*

J. Weller¹, S. Kreth², A. Biczok¹, S. Lietke¹, J. Tonn¹, F. W. Kreth¹, U. Schüller³

¹Klinikum der Ludwig-Maximilians-Universität München, Klinik für Neurochirurgie, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, Klinik für Anästhesiologie, München, Germany

³Universitätsklinikum Hamburg-Eppendorf, Institut für Neuropathologie, Hamburg, Germany

Objective

IDH wildtype (wt) WHO grade II-IV gliomas are widely assumed to be associated with poor outcome, although IDH wt status does not warrant poor prognosis in all glial tumours. Further molecular stratification of IDH wt gliomas according to TERT promoter mutational status, EGFR amplification and chromosome 7/10 status has been proposed, since these alterations predict unfavourable clinical course. On the other hand, distinct subgroups of diffuse IDH wt gliomas lacking these molecular alterations, e.g. TERT promoter wildtype (TERT p-wt) diffuse gliomas, seem to behave less aggressively. Here, we investigated IDH wt gliomas WHO grade II and III with respect to their TERT promoter mutational status.

Methods

In total, 126 IDH wt gliomas WHO grade II and III were included. Two neuropathologists, both blinded for molecular and clinical characteristics, reviewed the tissue samples independently. TERT promoter mutational status (C250T/C228T) was analyzed by Sanger sequencing. IDH1/IDH2 mutational status was assessed through pyrosequencing. Progression-free survival (PFS), time to malignization (TTM) and overall survival (OS) were estimated with the Kaplan Meier method. Prognostic factors were obtained through proportional hazard models.

Results

TERT promoter mutation (p-mut) was seen in 38/68 (52.9%) grade II and 38/58 (65.5%) grade III IDH wt gliomas. In IDH wt WHO grade II gliomas, favourable OS was seen in the subpopulation with IDH wt/TERT p-wt status (median OS TERT wt vs. TERT p-mut: 115.0 vs 33.0 months; $p < 0.001$). Additionally, time to malignization (TTM) was longer in this subgroup (median TTM 112.0 vs 16.0 months; $p < 0.001$) and patients were younger at time of diagnosis (median age TERT wt vs. TERT p-mut 40.4 vs 64.4 years; $p < 0.001$).

Conclusion

In WHO grade II gliomas, the prognostic impact of IDH wt status depends on TERT promoter mutational status. IDH wt TERT p-wt WHO grade II gliomas show a favourable clinical course, are characterized by a younger patient age at time of diagnosis and display a longer TTM when compared to IDH wt TERT p-mut gliomas. Nonetheless, these tumours possess the potential to undergo malignant transformation and thus should not be considered as pilocytic-astrocytoma like gliomas in the context of clinical management.

Gliome experimentell II/*Gliomas experimental II*

V186

Prädiktion der IDH-Mutation in Gliomen – ein multimodales diagnostisches Konzept *IDH mutation prediction in glioma – a multimodal diagnostic approach*

T. Juratli¹, A. Zolal¹, S. Stasik², G. Eisenhofer³, J. Linn⁴, G. Schackert¹, C. Thiede², A. Werner⁴, D. Krex¹

¹Universitätsklinikum Carl Gustav Carus Dresden, Klinik für Neurochirurgie, Dresden, Germany

²Universitätsklinikum Carl Gustav Carus Dresden, Medizinische Klinik I, Dresden, Germany

³Universitätsklinikum Carl Gustav Carus Dresden, Institut für Klinische Chemie und Laboratoriumsmedizin, Labor Klinische Neurochemie, Dresden, Germany

⁴Universitätsklinikum Carl Gustav Carus Dresden, Institut und Poliklinik für Diagnostische und Interventionelle Neuroradiologie, Dresden, Germany

Objective

Non-invasive and accurate diagnostic techniques to detect isocitrate dehydrogenase (IDH) mutant glioma may have great potential in routine clinical practice. With this in mind, we performed a multimodal diagnostic approach to predict the *IDH* mutation status in newly diagnosed gliomas using: 2-Hydroxyglutarate (2HG) single-voxel spectroscopy (SVS), *IDH*-mutant cell-free tumor-derived DNA (tDNA) in the CSF, in addition to 2HG (D- and L- forms) concentration measurement in the CSF.

Methods

2HG MR spectroscopy was obtained in 18 patients with a newly diagnosed *IDH*-mutant glioma. The *IDH1/2* mutation status was determined using next-generation sequencing in the glioma tissue and in the CSF-tDNA (n=55). In addition, in a subset of patients (n=15), 2HG concentrations were measured in the CSF using liquid chromatography-tandem mass spectrometry (LCMS). Ratios of D-and L-2HG were used to evaluate differences in 2HG accumulation in tumors.

Results

IDH mutations were correctly predicted using the 2HG spectroscopy with 93.3% sensitivity (17/18, 95% CI, 85.3-100%) and 100% specificity (18/18, 95% CI, 88.6-100%). The *IDH* mutation in the CSF-tDNA was successfully detected with 100% specificity (95% CI, 87.6-100%) and 73.3% sensitivity (95% CI, 65.6-88.3%). The range of the *IDH* mutation variant allele frequency (VAF) in the CSF-tDNA was 1.53- 47.9%. 2HG detection in the CSF revealed higher sensitivity (100%) and specificity (100%) in a small subset of patients (n = 7). The D-2HG/L-2HG ratios in *IDH*-mutant cases varied between 1.2 – 13.8, compared with 0.1 – 0.5 in *IDH* wild-type gliomas.

Conclusion

Our findings suggest that 2HG spectroscopy and 2HG detection in the CSF are two reliable methods in *IDH* mutation prediction in gliomas. On the other hand, the sensitivity of genomic *IDH* mutation detection in the CSF-tDNA was lower when compared with 2HG detection. Further studies are needed to complement the findings of our exploratory analysis.

Gliome experimentell II/*Gliomas experimental II*

V187

Fibertracking von DCS positiven Sprachpunkten während Wachkraniotomien macht fehlerqualitätsabhängige Konnektivitätsmuster deutlich

Fibre tracking from DCS positive language spots during awake surgeries reveals error-dependent connectivity patterns

K. Faust, I. Bährend, P. Vajkoczy, M. Münch, S. König, G. Bohner

Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

Objective

Little is known about the functional neuroanatomy of language. Currently, a hodotopic concept of language is propagated that draws the focus to subcortical fiber connections. 5 relevant fiber tracts have been assigned to the processing of language: the Superior Longitudinal Fasciculus/ Arcuate Fasciculus (AF), the Inferior Longitudinal Fasciculus (ILF), the Inferior Fronto-Occipital Fasciculus (IFOF), the Frontal Aslant Tract (FAT) and the Uncinate Fasciculus (UC). Cortical and subcortical mapping is used as the gold standard to define functional resection boundaries in language eloquent areas. Our aim was to investigate the functional connectivity of language positive spots during awake surgeries.

Methods

13 patients with brain tumors in speech-related areas were evaluated with direct cortical stimulation (DCS, 50Hz, 6-8 mA, 200µs pulse width) and subcortical stimulation during awake surgeries, employing a picture-naming task. Preoperatively, they all received an MRI with MP-RAGE and DTI sequences. Positive and negative stimulation spots within the craniotomy were documented in the same MRI data set with respect to the linguistic quality of the error. The spots were converted into tract seeding points for DTI fibertracking, using a fractional anisotropy of 80% of the respective threshold value. Emerging fibers were analyzed with respect to their integration into well-established language tracts

Results

Altogether, 61 cortical and 15 subcortical language positive spots were documented. 32 integrated into FA, 21 to IFOF, 6 to FAT, 6 into association fibers, 9 into commissural fibers, 2 to the parasagittal parietal cortical region. The majority (62%) of cortical spots connecting into AF originated in the pars opercularis of the frontal operculum. All speech errors within the supramarginal gyrus connected into AF. The majority (87%) of spots connecting to IFOF originated in the dorsal part of the superior and middle temporal gyrus. All speech errors within the pars triangularis of the frontal operculum integrated into FAT. No cortical speech eloquent spots integrated into UF or ILF.

The main speech error integrating into FA was anomia. The main speech error integrating into IFOF was semantic. 100% of speech errors integrating into FAT were semantic.

Conclusion

Fibertracking from speech eloquent areas may help allocate subfunctions to the fiber tracts that implement speech in the human brain, and may thus contribute to solving the cortico-subcortical connectivity patterns of language.

Pädiatrische Neurochirurgie II/*Paediatric neurosurgery II*

V188

Verletzungen der Halswirbelsäule im Kindesalter – Ergebnisse einer Multicenterstudie an 367 Kindern *Childhood cervical spine injuries – results of a multi-centre study in 367 children*

H. Meinig¹, M. Ruf¹, T. Pitzen¹, S. Matschke², A. Disch³, J. S. Jarvers⁴, C. Herren⁵, T. Weiß⁶, H. Rüter⁷, T. Welk⁸, C. Heyde⁴

¹SRH Klinikum Karlsbad-Langensteinbach, Zentrum für Wirbelsäulen Chirurgie, Orthopädie und Traumatologie (ZWOT), Karlsbad, Germany

²ATOS Klinik, Praxis für Wirbelsäulen Chirurgie, Heidelberg, Germany

³Universitätsklinikum Carl Gustav Carus Dresden, Centrum für Orthopädie und Unfallchirurgie, Dresden, Germany

⁴Universitätsklinikum Leipzig, Klinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Leipzig, Germany

⁵Universitätsklinik RWTH Aachen, Klinik für Unfall- und Wiederherstellungschirurgie, Aachen, Germany

⁶Berufsgenossenschaftliches Universitätsklinikum Bergmannsheil, Wirbelsäulen Chirurgie, Murnau, Germany

⁷Universitätsmedizin Göttingen, Zentrum für Unfallchirurgie, Orthopädie und Plastische Chirurgie, Göttingen, Germany

⁸SRH Klinikum Karlsbad-Langensteinbach, Zentrum für Wirbelsäulen Chirurgie, Orthopädie und Traumatologie (ZWOT), Karlsbad, Germany

Objective

Serious injuries of the children's spine are rare. Recommendations or even guidelines for the diagnosis and treatment of such injuries are rare, and a comparison with injuries in adults is often not useful.

Our main questions were:

1. The accident mechanism
2. The level of injury
3. Trends in the treatment of child spinal injuries

Methods

The data were collected retrospectively in 5 spinal centres from 01/1010 to 12/2016. Data from inpatient children up to and including the age of 16 were collected using specific ICD codes. A descriptive analysis examined the accident mechanism, injury level, differences between girls and boys, surgical and conservative therapy, age differences and accompanying injuries.

Results

367 children (♀171 : 196♂) with an average age of 12.39 (+/- 3.5) were included. The most common accident mechanism was a fall of less than 3m, traffic accidents and winter sports accidents. 214 cervical, 93 thoracic and 60 lumbar injuries were documented, with younger children suffering more cervical injuries. The vast majority of the children affected (n=351) had no pre-existing conditions, 11 children did not have pre-existing conditions in the spine, 5 children had spinal problems. Accompanying injuries did not occur in 265 cases. A positive correlation could be found for the sex (boys), the injury level (cervical) and for the occurrence of accompanying injuries. 274 children were conservatively cared for and 93 children were provided with surgical care.

Conclusion

Spinal injuries in childhood are rare and should be treated in specialized spinal centres. 25% of the children admitted had to have surgery. In most cases (72%) isolated injuries occurred. In the younger children, cervical injuries dominate.

Pädiatrische Neurochirurgie II/*Paediatric neurosurgery II*

V189

Traumamechanismen und Verletzungsschwere von pädiatrischen Patienten mit stationärer/intensivmedizinischer Behandlung nach Schädel-Hirn-Trauma – Daten der CENTER-TBI Studie
Mechanisms and severity of traumatic brain injury in paediatric patients admitted to the ward or intensive care unit – data from the CENTER-TBI study

A. Younsi, L. Riemann, A. El Damaty, K. Zweckberger, A. W. Unterberg

Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

Objective

Traumatic brain injury (TBI) is the leading cause of death and disability in children. It includes a range of different pathologies that differ considerably from adult TBI in regard to pathophysiology, injury patterns, and clinical management. Analyzing and understanding injury patterns of pediatric TBI is essential to finding and establishing new preventive efforts and public campaigns as well as to improve clinical management.

Methods

The multi-center prospectively collected Collaborative European Neurotrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) core and registry databases were screened and patients were included when younger than 18 years at enrollment and admitted to the regular ward (admission stratum) or intensive care unit (ICU stratum) following TBI. Patient demographics, injury mechanisms, clinical findings, brain CT imaging details, and outcome (GOSE at 6-months follow-up) were retrieved from the core database and analyzed. Injury characteristics were compared between patients admitted to the regular ward and ICU. Results from the core study were compared to the registry dataset which includes larger patient numbers but no follow-up data.

Results

227 patients in the core dataset and 687 patients in the registry dataset were included in this study. In the core dataset, road-traffic incidents were the most common cause of injury overall and in the ICU stratum, while incidental falls were most common in the admission stratum. Brain injury was considered serious to severe in the majority of patients and concurrent injuries in other body parts were very common. Intracranial pathologies were detected in 60% of initial brain CTs. Intra- and extracranial surgical interventions were performed in one fifth of patients. The overall mortality rate was 3% and the rate of unfavorable outcome 10%, with those numbers being considerably higher in the subgroup of ICU patients. Injury characteristics from the core study could be confirmed in the registry dataset.

Conclusion

Our study displays the most common injury mechanisms and characteristics of pediatric TBI in Europe. Road-traffic incidents were especially common in ICU patients and patients with severe TBI, indicating that preventive efforts such as advertising the use of safety helmets could be effective in decreasing the incidence of this serious condition in children.

Pädiatrische Neurochirurgie II/*Paediatric neurosurgery II*

V190

Vorhersage von postkommotionellen Symptomen bei Kindern und Jugendlichen mit Schädel-Hirn-Trauma – eine Analyse der CENTER-TBI Studie

Prediction of post-concussive symptoms in children and adolescents with traumatic brain injury – a CENTER-TBI study analysis

A. Younsi¹, L. Riemann¹, D. Voormolen^{1,2}, K. Zweckberger¹, A. W. Unterberg¹

¹Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

²Erasmus University Medical Center Rotterdam, Department of Public Health, Rotterdam, Netherlands

Objective

Post-concussive symptoms are frequent in patients with traumatic brain injury (TBI). While various efforts have been made to develop clinical prediction models for post-concussive syndrome (PCS) in adult TBI, data on this condition in children or adolescents is scarce. We, therefore, aimed to develop a set of clinical predictors that would allow identifying pediatric or adolescent TBI patients with a high risk for PCS.

Methods

The multicenter prospective CENTER-TBI database was screened and only patients < 25 years with available Rivermead Post-Concussion Questionnaire (RPQ) at 6-months were included. PCS was dichotomized and defined as having at least three of the sixteen symptoms included in the RPQ. Potential predictors were selected based on existing literature and regression analysis with the least absolute shrinkage and selection operator (LASSO) method was performed to select a multivariate model with the most important determinants predicting PCS. Model performance was assessed using bootstrap validation.

Results

424 eligible young TBI patients were identified (median age 19 (IQR 16-22) years, 70% males). Age, gender, history of psychiatric illness, GCS score at admission, abnormality on CT imaging, post-traumatic amnesia, loss of consciousness, and ICU admission were found to be the strongest predictors for PCS after LASSO model selection. This model displayed reasonable discrimination (area under the receiver operating curve of 0.70) but explained only 16% of the variance in outcome after bootstrap validation.

Conclusion

A set of 8 clinical factors easily obtainable in the emergency room is predictive for PCS in children and adolescents. Using these predictors might help to identify young patients that would benefit from early follow-up appointments with e.g. neurocognitive testing. However, these factors only explain a small part of the variation in outcome after TBI and additional variables such as biomarkers might be needed to improve outcome prediction.

Pädiatrische Neurochirurgie II/*Paediatric neurosurgery II*

V191

Dekompressionskraniektomien bei raumfordernden ischämischen Hirninfarkten im Kindesalter – eine evidenzbasierte Perspektive

Decompressive craniectomy for malignant ischemic stroke in children – an evidence-based approach

T. Beez, C. Munoz-Bendix, H. J. Steiger, K. Beseoglu, D. Hänggi

Heinrich-Heine-Universität Düsseldorf, Klinik für Neurochirurgie, Düsseldorf, Germany

Objective

Ischemic stroke occurs in only 1.2 to 3.6 children per 100,000 per year, and less than 2% of cases account for space-occupying or malignant ischemic strokes. Here we review the current evidence for decompressive craniectomy (DC) in children with supra- and infratentorial ischemic stroke.

Methods

A systematic search of the PubMed database was performed for "decompressive craniectomy", with a filter for "Child: birth to 18 years". Relevant articles on ischemic stroke were identified manually. Methodology followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.

Results

We identified 14 articles on DC for supratentorial ischemic stroke, reporting data on 28 children (27 MCA territory, 1 PCA territory) with a mean age of 7.5 years (range 6 months to 16 years). In 57% (N = 16) mydriasis occurred before DC, which was performed with a mean latency of 37 hours (range 2 to 291 hours) after stroke onset. 96% (N = 27) reached good outcome (i.e. mRS 1-3 or GOS 4-5). DC for infratentorial ischemic stroke was reported in 3 articles with data on 5 children with a mean age of 6.5 years (range 5 months to 11 years). DC was performed within 72 hours and reported outcome was good in all cases. No study exceeded evidence level 4 (i.e. case series), according to the definition of the Oxford Centre of Evidence-based Medicine.

Conclusion

In the absence of high-level evidence, most authors adduce findings from studies in adults as reference for treatment decisions in children. However, when reviewing the reported cases it seems that DC for supratentorial stroke is performed rather late, as a high proportion of children had preoperative mydriasis indicating herniation. Nevertheless the outcome appears to be much better than in adults, which could either be attributed to brain plasticity and higher potential of recovery in childhood or be explained by reporting bias.

Pädiatrische Neurochirurgie II/*Paediatric neurosurgery II*

V192

Thrombozytopenie – ein Indikator zur Vermeidung eines posthämorrhagischen Hydrocephalus nach intraventrikulärer Blutung in Neugeborenen?

Thrombocytopenia – an indicator for escaping post-haemorrhagic hydrocephalus after intraventricular haemorrhage in neonates?

A. El Damaty, L. Giannone, A. W. Unterberg, H. Bächli

Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

Objective

Posthemorrhagic hydrocephalus (PHH) is a rare but serious complication among premature babies in the neonatal intensive care unit, with consequences including mortality and severe neurodevelopmental disabilities. The causes of PHH are still not entirely understood, and its prevention and treatment are controversial. We tried to analyse the risk factors for such complication in our cohort.

Methods

We reviewed our neonatology data bank and included all patients who were born in the period from 1999 - 2014 with a gestational age below 28 weeks and suffered from an intraventricular hemorrhage of any degree. The following data were collected: date of birth, gestational age, gender, birth weight, type of birth, IVH degree (I-IV), comorbidities, therapy measures, complications, period from first diagnosis PHH to implantation of a VP shunt, protein content of cerebrospinal fluid content before shunt implantation, clinical follow-up. All patients with a follow-up period of less than one year were excluded from the study.

Results

We identified 180 patients, the cohort was divided into two subgroups, "B1" with 37 cases (patients with IVH and development of a PHH requiring therapy) and "B2" with 143 cases (patients with IVH, but without development of PHH). In group B1, the average gestational age was 25 weeks + 3 days of gestation. 11% of patients had an IVH grade I, 19% IVH grade II and 70% an IVH III. or IV. degrees. 19 patients were treated with a Rickham reservoir or EVD. A total of 19 shunts were implanted, with 11 revisions (58%). Unfortunately, 10 patients (27%) die, only 1 patient in this group from thrombocytopenia. In subgroup B2, the average age was also 25 weeks + 3 days of gestation. The majority of patients showed 51% IVH grade I, whereas severe IVH grade III was only present in 22%. 25.9% suffered from thrombocytopenia. The IVH grade showed strong significance (p-value: 0.0005). We found thrombocytopenia significantly higher in patients who did not develop PHH. (p-value: 0.002)

Conclusion

According to our results, thrombocytopenia could play a decisive role in avoiding development of PHH as a sequel of IVH. We recommend a randomized controlled trial to assess efficacy of antiplatelet drugs in avoiding PHH in this vulnerable group.

Pädiatrische Neurochirurgie II/*Paediatric neurosurgery II*

V193

Endoskopische Drittventrikulostomie in Kindern unter 2 Jahren

ETV in infancy and childhood below 2 years of age

A. El Damaty¹, S. Marx², G. Cohrs³, E. EL Refaee^{2,4}, J. Baldauf², S. Fleck², H. Bächli¹, A. Zohdi⁴, M. Synowitz³,
A. W. Unterberg¹, H. W. S. Schroeder²

¹Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

²Universitätsmedizin Greifswald, Klinik für Neurochirurgie, Greifswald, Germany

³Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Kiel, Germany

⁴Cairo University, Department of Neurosurgery, Kairo, Egypt

Objective

Endoscopic third ventriculostomy (ETV) has become the method of choice in the treatment of obstructive hydrocephalus. Age and etiology could determine success rates of ETV. The outcome is worse in children <2 years of age, and controversies still exist whether ETV is superior to shunt placement in this age group. We retrospectively analyzed the data of 70 patients <24 months of age from 4 different university centers treated with ETV and assessed its feasibility as a treatment for hydrocephalus.

Methods

We included all children <2 years of age who received ETV as a treatment for obstructive hydrocephalus regardless of the etiology within the time period from December 1994 till December 2018. Cases were collected from 4 surgical centers. We classified the patients according to age and etiology; 3 age groups: <3, 4-12 and 13-24 months. Etiologically there were 6 groups; idiopathic aqueductal stenosis, post-hemorrhagic hydrocephalus (PHH), tumor-related hydrocephalus, fourth ventricle outflow obstruction, with Chiari malformation type II and following CSF infection.

Results

We collected 70 patients. ETV was successful in 41.4% (29/70). ETV was successful in tumor-related hydrocephalus in 62.5% (5/8), fourth ventricle outlet obstruction in 60% (3/5), aqueductal stenosis in 44% (11/25), PHH in 40.9% (9/22), Chiari Type II in 16.7% (1/6) and none with post-infection hydrocephalus (0/4). According to age groups, the first age group (below 3 months age) showed success rate 33.3%, second age group (4-12 months) with 46.4% and third age group (13-24 months) with 46.6%.

Conclusion

Factors suggesting a high possibility of failure were age <3 months and etiology such as Chiari malformation type II or following CSF infection. ETV is the method of choice in patients with obstructive hydrocephalus. Altered CSF dynamics in patients with PHH and under-developed arachnoid villi may play a role in ETV failure. We still recommend ETV to be the first line of treatment even in children <3 months of age depending on the etiology.

Pädiatrische Neurochirurgie II/*Paediatric neurosurgery II*

V194

Pilotstudie zur Evaluation der Ängste und Bedürfnisse von Eltern mit Shunt versorgten Kindern *Evaluating concerns and needs of parents caring for children with shunt-treated hydrocephalus – an institutional pilot study*

F. Knerlich-Lukoschus¹, G. Cohrs², M. Mehdorn³, S. Goebel⁴

¹Asklepios Klinik Sankt Augustin, Kinderneurochirurgie, Sankt Augustin, Germany

²Universitätsklinikum Schleswig-Holstein, Neurochirurgie, Kiel, Germany

³Mehdorn Konsilium, Kiel, Germany

⁴Christian-Albrechts-Universität zu Kiel, Abteilung für Klinische Psychologie und Psychotherapie, Kiel, Germany

Objective

A child's serious chronic illness like shunt-dependent hydrocephalus passes a large burden to the affected parents and care givers. Understanding their concerns and needs regarding communication, information, and support potentially improves treatment success and outcome of the shunt-treated children and lessens the psycho-social burden of their families. To address this question, we performed an institutional pilot-study in an outpatient neurosurgical service setting.

Methods

Different questionnaires addressing various aspects of patients/parents/physician communication, need of support, psychological aspects etc. were sent to parents whose child was currently followed-up in our outpatients service (9/2012 – 9/2013 n = 72). Questionnaires included among others the Hydrocephalus Concerns Questionnaire (HCQ), the Distress Thermometer (DT), the GAD-7 and the PHQ-9. Twenty parents agreed to additionally participate in a comprehensive assessment including the assessment of communication preferences (adapted version of the Measure of Patients' Preferences MPP), of need-for-information (self-developed structured questionnaire), and of supportive care needs (adapted version of the Supportive Care Needs Survey, SCNS-34). Data on parents' sociodemographic background was collected. The medical history of affected children was evaluated retrospectively.

Results

47% of the contacted parents returned completed forms that were valid for evaluation. 21% returned incomplete or blank forms. Children's age of included parents was 3-21 years. 57 % of parents described high psychosocial distress (scored ≥ 5 in the DT). All parents described a variety of concerns regarding the medical and psychosocial well-being of their child. In this neurosurgical setting, parents' main concerns were focused on medical treatment (e. g., re-operation, shunt complications). Parents' needs for information and emotional support were high and independent of objective data. However, more distressed parents expressed higher communication, information and support needs.

Conclusion

This pilot study demonstrated that parents of shunt-treated children bear a significant socio-psychological burden that should be considered in the treatment of this group of children. Further, physicians should be aware of the specific psychological problems of the affected parents and care givers and offer respective professional support.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P114

Entwicklung einer p53-"Replacement"-Therapie für Gliome *Development of a p53-replacement therapy for gliomas*

W. Jügel¹, F. Broghammer¹, S. Michen¹, A. Temme^{1,2,3}, G. Schackert^{1,2,3}

¹Universitätsklinikum Carl Gustav Carus Dresden, Sektion Experimentelle Neurochirurgie und Tumorimmunologie, Dresden, Germany

²Deutsches Konsortium für Translationale Krebsforschung (DKTK), Dresden, Germany

³Deutsches Krebsforschungszentrum (DKFZ), Heidelberg, Germany

Objective

Hot spot mutations and deletions of the tumor suppressor p53 are detected in 35% of IDH1 wildtype and in more than 65% of IDH1-mutant glioblastoma (GBM). Accelerated degradation of TP53, leading to loss of function is also considered to be caused by deletion or mutation of PTEN and LOH on chromosome 10q in IDH1, respectively. Due to TP53 deficiency, tumor malignancy gradually increases and resistance to radio and chemotherapy increases. We sought to develop an experimental p53-replacement therapy using a retroviral system and a sleeping beauty transposase system, respectively, for gene therapy of GBMs.

Methods

A codon-optimized p53 coding sequence was chemically synthesized and ligated into pHATrick-puro lentiviral vector or ligated into a transposon minicircle-DNA plasmid. Viral transduction or (poly)ethylenimine-mediated simultaneous transfection of SB100X sleeping beauty and transposon minicircle DNA were utilized for p53 replacement. HCT116 p53^{-/-} and HT1080 cells with knockdown of p53 were employed to analyze stable p53 transgene expression following genetic transfer of p53 using PCR and were used to verify a functional p53 response upon DNA damage. Transgenic expression and TP53-mediated damage response was confirmed using indirect immunofluorescence analysis of phospho-gammaH2AX in Zeozin-treated cells and was further investigated using Western blot analyses for TP53 and p21waf/cip. Long term effects of p53-replacement were investigated in clonogenic survival assays of HCT116 p53^{-/-}, HT1080 cells and primary cell cultures from GBM samples.

Results

Retroviral and sleeping beauty-mediated p53 gene transfer lead to expression of a fully functional transgenic TP53 tumor suppressor gene as validated by PCR analysis and a Zeozin-induced DNA-damage response. Experimental replacement of p53 in HCT116 p53^{-/-}, HT1080 cells and primary cell cultures from GBM samples caused up to 90% decrease in clonogenic survival of HCT116 p53^{-/-}, HT1080 cells and primary cell cultures from GBM samples when compared to mock-treated controls.

Conclusion

We successfully developed a p53-replacement for treatment of glioblastoma. In particular, in our in vitro experiments retroviral transduction was superior when compared to transfection of SB100X and p53-minicircle transposon DNAs. Further work for effective non-viral delivery of the sleeping beauty and p53-transposon, in particular in using nanoparticle delivery systems are mandatory for a future clinical use.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P115

Etablierung eines "Feederzell"-basierten *ex vivo*-Expansionsprotokolls zur Herstellung von GBM-reaktiven, NKG2C-positiven NK-Zellsubpopulationen

A novel ex vivo expansion protocol using feeder cells for efficient production of GBM-reactive NKG2C-positive NK cell subsets

A. Becker¹, S. Murad¹, S. Michen¹, G. Schackert^{1,2,3,4}, A. Temme^{1,2,3,4}

¹Universitätsklinikum Carl Gustav Carus Dresden, Sektion Experimentelle Neurochirurgie/Tumorimmunologie, Dresden, Germany

²Deutsches Konsortium für Translationale Krebsforschung (DKTK), Dresden, Germany

³Deutsches Krebsforschungszentrum (DKFZ), Heidelberg, Germany

⁴Nationales Centrum für Tumorerkrankungen (NCT), Dresden, Germany

Objective

Natural Killer (NK) cells have proven to be a promising candidate for the immunotherapy of tumours. As NK cells have a different cytokine-production profile compared to T cells, they do not bear the risk of inducing cytokine linked adverse side effects. Glioblastomas express elevated levels of HLA-E which is recognized by the inhibiting NKG2A receptor, blocking the natural cytotoxicity of NK cells. HLA-E is also recognized by the activating NKG2C receptor, albeit with a lower affinity. NKG2C+ NK cells therefore represent a potential candidate for the immunotherapy of GBM. In HCMV seropositive donors, the number of NKG2C+ NK cells is elevated. Nevertheless, the numbers are still too low for a therapeutic setup. Hence, an efficient and selective expansion method is needed. To this end, we want to validate feeder cell lines with expression of an artificial β -2-microglobulin-HLA-E trimer for the selective expansion of the NKG2C+ subset from peripheral blood of HCMV seropositive donors. In this project, we aim to (I) establish a selective *ex vivo* expansion protocol for NKG2C+ NK cells and (II) to prove their cytotoxic activity.

Methods

Primary NK cells from buffy coats of healthy donors were expanded for 14 days *ex vivo* using the newly developed feeder cell lines. NK cells were characterized concerning their expression of various activating and inhibitory surface receptors in addition to maturation and exhaustion markers. The characterization was performed by flow cytometry analysis. The cytotoxicity of the expanded NKG2C+ NK cells was analysed using chrome release assays and cytokine ELISA.

Results

The selective expansion of NKG2C+ NK cells using the modified feeder cell lines resulted in a NK cell product containing up to 95% single NKG2C+ NK cells. It was noted that such cells developed from CD56bright NK cells and developed through NKG2A+/NKG2C- early and NKG2A+/NKG2C+ intermediate states. A median expansion factor for single NKG2C+ NK cells of 104 respectively 115 could be achieved. Expanded NK cells were found to be mature and active with an increased expression of activating and inhibitory receptors, while maintaining their cytotoxicity.

Conclusion

Our results demonstrated an efficient *ex vivo* expansion of primary human NK cells, with a selective expansion of NKG2C+ NK cells. Expanded NK cells maintained their cytotoxicity. For further studies the *ex vivo* expansion must be adapted to reach clinically relevant numbers for immunotherapy of glioblastoma.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P116

Risiko-Nutzen-Analyse der mikrochirurgischen Resektion bei älteren Glioblastom-Patienten – eine retrospektive, multizentrische Studie

Risks and benefits of microsurgical resection of glioblastoma in older adults – a retrospective multi-centre study

C. Schwartz¹, B. Ladisich¹, A. Romagna¹, P. Geiger¹, J. Rechberger¹, H. Stefanits², G. Zimmermann³, G. Fastner⁴, L. Weiss⁵, P. A. Winkler¹, N. Thon⁶

¹Universitätsklinikum Salzburg, Universitätsklinik für Neurochirurgie, Salzburg, Austria

²Kepler Universitätsklinikum, Neurochirurgie, Linz, Austria

³Universitätsklinikum Salzburg, Neurologie, Salzburg, Austria

⁴Universitätsmedizin Salzburg, Radiotherapie und Radio-Onkologie, Salzburg, Austria

⁵Universitätsklinikum Salzburg, Universitätsklinik für Innere Medizin III, Salzburg, Austria

⁶Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgie, München, Germany

Objective

To assess the prognostic profile, clinical outcome, treatment-associated morbidity, and treatment burden of elderly patients with glioblastoma (GBM) undergoing microsurgical tumor resection as part of contemporary treatment algorithms.

Methods

We retrospectively identified patients with GBM ≥ 65 years of age who were treated by resection at 2 neuro-oncology centers. Survival was assessed by Kaplan-Meier analyses; log-rank tests identified prognostic factors.

Results

The study population included 160 patients (mean age, 73.1 \pm 5.1 years), and the median contrast-enhancing tumor volume was 31.0 cm³. Biomarker analyses revealed O(6)-methylguanine-DNA methyltransferase-promoter methylation in 62.7% and wild-type isocitrate dehydrogenase in 97.5% of tumors. The median extent of resection (EOR) was 92.3%, surgical complications were noted in 10.0% of patients, and the median postoperative hospitalization period was 8 days. Most patients (60.0%) received adjuvant radio-/chemotherapy. The overall treatment-associated morbidity was 30.6%. The median progression-free and overall survival were 5.4 months (95% confidence interval [CI], 4.6-6.4 months) and 10.0 months (95% CI, 7.9-11.7 months). The strongest predictors for favorable outcome were patient age ≤ 73.0 years ($P=0.0083$), preoperative Karnofsky Performance Status Scale score ≥ 80 ($P=0.0179$), postoperative modified Rankin Scale score ≤ 1 ($P<0.0001$), adjuvant treatment ($P<0.0001$), and no treatment-associated morbidity ($P=0.0478$). Increased EOR did not correlate with survival ($P=0.5046$), but correlated significantly with treatment-associated morbidity ($P=0.0031$).

Conclusion

Clinical outcome for elderly patients with GBM remains limited. Nonetheless, the observed treatment-associated morbidity and treatment burden were moderate in the patients, and patient age and performance status remained the strongest predictors for survival. The risks and benefits of tumor resection in the age of biomarker-adjusted treatment concepts require further prospective evaluation.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P117

Die Rolle des Calpain/Calpastatin Systems bei der Chemotherapie-Resistenz von Glioblastomen *The role of the calpain/calpastatin system in chemoresistance of glioblastoma*

J. Bartsch¹, M. Stillger², O. Schilling², C. Nimsky¹

¹Philipps-Universität Marburg, Klinik für Neurochirurgie, Marburg, Germany

²Albert-Ludwigs-Universität Freiburg, Klinische Pathologie, Freiburg, Germany

Objective

Calcium-dependent proteases (calpains) are involved in GBM cell infiltration and in therapy resistance. Calpains are cysteine proteases, naturally inhibited by Calpastatins, are highly expressed in tumor cells, and could serve as potential therapeutic targets in malignancies. Our study aims to target the calpain/Calpastatin system for therapeutic purposes in GBM.

Methods

Calpain expression profiles between first manifested and patient-matched recurrent GBM (n=20 patients) were correlated to patient outcome. The role of calpains in several GBM cell lines and in patient derived primary GBM cells was investigated and the activity of calpains was determined by fluorescence analysis in correlation to expression levels of calpastatin. To inhibit calpains, cells were treated with 50 µM PD 150606, a specific calpain inhibitor, either alone or in combination with Temozolomide (TMZ). Using shRNAs, calpain/calpastatin was knocked down in GBM cell lines to investigate its role in TMZ therapy.

Results

Calpains are over-expressed in recurrent GBM tissue compared to patient matched primary GBM tissue (11/19 for Calpain 1; 16/19 for Calpain 2). Calpain activities were analyzed in GBM cell lines and in patient derived GBM cells under TMZ therapy conditions and inhibited Calpains by treatment with 50 µM PD 150606. An additive effect of co-treatment with PD150606/TMZ was observed. Only those cells were sensitized to TMZ treatment that exerted cellular calpain activity, suggesting that calpain activity is part of the intrinsic TMZ resistance of GBM cells. Sensitization of Calpain inhibitor treated cells to TMZ was concomitant with enhanced apoptosis, as revealed by increased Caspase-3 activity in responding GBM cells. Moreover, knockdown of calpain 1 or 2 in U251N cells led to an increased Caspase-3 activity under TMZ treatment. A172 cells treated with TMZ showed an increased level of dead cells when calpain 2 was knocked down. Knockdown of calpastatin, the endogenous calpain inhibitor, reversed that effect.

Conclusion

To optimize GBM therapy, several molecular mechanisms of radio- and chemotherapy resistance have to be overcome. Here we show that inhibition of Calpains facilitates TMZ induced apoptosis of GBM cells, suggesting that a co-treatment with TMZ and Calpain inhibitor in GBMs could provide a better outcome than the standard TMZ chemotherapy.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P118

Die Inhibition des Discoidin-Rezeptors DDR1 verbessert die Effektivität der adjuvanten Therapie in Glioblastomen

Inhibition of the discoidin receptor 1 DDR1 improves efficacy of adjuvant therapy in glioblastoma

A. Vehlow¹, E. Klapproth¹, R. Hannen², A. Temme³, C. Nimsky⁴, N. Cordes¹, J. Bartsch²

¹Technische Universität Dresden, Onkologie, Dresden, Germany

²Philipps-Universität Marburg, Neurochirurgie, Marburg, Germany

³Technische Universität Dresden, Klinik für Neurochirurgie, Dresden, Germany

⁴Philipps-Universität Marburg, Klinik für Neurochirurgie, Marburg, Germany

Objective

A major obstacle to adjuvant GBM therapy using radiotherapy and temozolomide (TMZ) is the formation of drug- and radiation-resistant GBM stem cells (GSCs). Interestingly, GSCs utilize collagen signalling to regulate TMZ resistance. In order to understand this process in detail, a study was initiated to reveal the mechanisms of radiochemoresistance based on signalling by the Discoidin Domain Receptor (DDR1), a receptor tyrosine kinase that is activated by tumor cell derived collagen.

Methods

Expression of DDR1 in GSCs was evaluated in GBM patients by immunostaining using antibodies against DDR1 and the stem cell markers nestin, Sox2, and Musashi. Spheres derived from GSCs were irradiated (0-6 Gy) and TMZ (0.2-10 mM) treated ± DDR inhibitor (DDR1i). Furthermore, GSCs were implanted in nude mice and tumors were co-treated with TMZ±DDR1i. The interaction of DDR1 with intracellular signalling pathways was analyzed by co-immunoprecipitation in U343MG cells.

Results

We demonstrated that DDR1 is highly enriched in GSCs with expression levels negatively correlated to patient survival (n=20, significance p=0.08). The inhibition of DDR1 in combination with radiochemotherapy using TMZ in GSCs enhances sensitivity and prolongs survival of mice better than conventional therapy. Mechanically, we demonstrated that DDR1 forms an intracellular complex with the proteins 14-3-3 and Beclin1 to keep PI3K/AKT/mTOR signalling activated thereby triggering cell proliferation and survival. In contrast, the inhibition of DDR1 prevents 14-3-3 and Beclin-1 from binding to DDR1 and leads to alternative complexes of Beclin-1 with Vps 34 and Atg 14 to initiate autophagy that results in sensitization of GSCs to radiochemotherapy.

Conclusion

Here we unraveled a novel mechanism of radiochemoresistance. GBM stem cells utilise tumor-derived collagen as an extracellular trigger to suppress cytotoxic signals by DDR1 receptor signalling. In conclusion, these findings provide a rationale for improving radiochemotherapy in GBM patients by combinatorial therapies involving the inhibition of DDR1.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P119

NKG2C-positive NK-Zellen aus Patientenblut für die Immuntherapie von HLA-E-positiven Gliomen NKG2C-positive NK cells from patient blood for immunotherapy of HLA-E-positive glioma

S. Michen¹, S. Murad¹, M. Füssel², G. Schackert^{3,4}, A. Temme^{1,4}

¹Universitätsklinikum Carl Gustav Carus Dresden, Experimentelle Neurochirurgie/Tumorimmunologie, Dresden, Germany

²DKMS Life Science Lab GmbH, Dresden, Germany

³Universitätsklinikum Carl Gustav Carus Dresden, Dresden, Germany

⁴Deutsches Konsortium für Translationale Krebsforschung (DKTK), Dresden, Germany

Objective

Natural killer (NK) cells hold potential as promising effector cells in immunotherapy of human malignancies. This study focuses on NKG2C⁺ NK cells, a small NK cell subpopulation in the blood of human cytomegalovirus (HCMV) seropositive patients. These NK cells are able to recognize the HLA-G signal peptide or peptides of HCMV presented by HLA-E molecules on the surface of glioblastoma cells via their activating NKG2C receptor. Consequently, NKG2C⁺ NK cells have a higher intrinsic capability to specifically kill glioblastoma cells. In our study we investigated, whether *ex vivo* expanded NKG2C⁺ NK cells from HCMV seropositive GBM patients have an anti-tumour effect against autologous and allogenic HLA-E⁺ glioblastoma cells.

Methods

NK cells were isolated from blood of HCMV seropositive GBM patients and NKG2C⁺ NK cells were specifically expanded for two weeks via novel HLA-E⁺ feeder cell lines. Furthermore NK cells were analysed in respect to expression of inhibitory receptors, activation and exhaustion markers before and after expansion. In parallel GBM tumour tissue of the patients was cultivated and analysed in respect of GBM-associated immune cell populations by flow cytometry. Afterwards cytotoxicity of *ex vivo* expanded NKG2C⁺ NK cells was investigated by chromium release assays using autologous and allogenic primary glioblastoma cells.

Results

Co-cultivation of isolated primary NK cells with HLA-E⁺ feeder cells for 14 days resulted in percentage of more than 85% NKG2C⁺ NK cells. These expanded NKG2C⁺ NK cells displayed a slight increase of KIRs and an induced expression of high affinity IL-2 receptor (>70%). Of note, PD-1 levels were not affected. Parallel cultivated GBM tumour tissue of the patients displayed an infiltration of T lymphocytes (median of 4%), but no B and NK cells. In subsequent experiments expanded NKG2C⁺ NK cells showed cytotoxicity against HLA-E⁺ primary glioblastoma cells irrespective of KIR:KIR-ligand settings.

Conclusion

Our results demonstrate a novel highly efficient *ex vivo* expansion method to gain NKG2C⁺ NK cells from blood of HCMV seropositive GBM patients. This is a first step in the development of an adoptive cellular immunotherapy using NKG2C⁺ NK cells for treatment of GBM.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P120

Die Expression von ALDH1A3 bei Glioblastomen ist assoziiert mit dem Gesamtüberleben und dem Tumorödem

The expression of ALDH1A3 in glioblastomas and its association with tumour oedema and overall survival

C. Gan, D. Pierscianek, N. E. Hindy, Y. Ahmadipour, U. Sure, Y. Zhu

Universitätsklinikum Essen, Neurochirurgie, Essen, Germany

Objective

ALDH1A3 is an enzyme and a member of the aldehyde dehydrogenases (ALDHs) superfamily. Recently it emerges as cancer stem-cell marker in neoplasms including glioblastoma (GBM). However, the comprehensive information of ALDH1A3 in human GBM is still not fully known. The present study attempted to investigate the expression manner of ALDH1A3 in human GBM tissues and its association with clinical parameters.

Methods

Thirty tissue samples of primary GBM and 9 controls were enrolled in this study. The level of ALDH1A3 mRNA and protein was detected by real-time RT-PCR and Western blot, respectively. The regional and cellular expression of ALDH1A3 was evaluated respectively by immunohistochemistry (IHC) and by double immunofluorescence (IF) staining. The association of ALDH1A3 expression with multiple clinical parameters was analyzed.

Results

The mRNA level of ALDH1A3 was significantly lower in GBM compared with the controls ($p < 0.05$), which is in accordance with the result from the TCGA database. Interestingly, subgroup analysis showed 2.5-fold higher ALDH1A3 mRNA in GBMs with infiltration of the subventricular zone (SVZ) than that without SVZ-involvement. IHC classified two groups of GBM expressing low/negative and high ALDH1A3, which was confirmed by Western blot. The higher expression of ALDH1A3 was accompanied by an activation of Akt but reversely associated with PTEN expression. The immunoreactivity of ALDH1A3 was detected mostly in the infiltrative area and occasionally in the tumor center. Double IF staining indicated the co-expression of ALDH1A3 with GFAP in glia-shaped cells as well as in some tumor cells; but the immunoreactivity of ALDH1A3 does not overlap with vWF, CD68, CD133, and PCNA. Further analysis demonstrated a positive association of ALDH1A3 protein expression with the tumor edema grade ($p = 0.0193$) and with overall survival of patients ($p = 0.009$).

Conclusion

The protein expression of ALDH1A3 is associated with the overall survival of GBM, suggesting ALDH1A3 as a possible predictive marker and a potential therapeutic target for GBM. In this regard, a personalized strategy should be considered due to the heterogeneous manner of ALDH1A3 expression in a subgroup of GBM patients.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P122

Einfluss einer intrazellulären Infektion mit *Staphylococcus aureus* auf das Wachstum und die Zytokinsekretion von humanen Glioblastomzellen und Astrozyten

Influence of an intracellular infection with Staphylococcus aureus on growth and cytokine secretion of glioblastoma cells and human astrocytes

S. Grube¹, C. Lemke¹, L. Tuscherr², C. Ewald³, B. Löffler², R. Kalff¹, J. Walter^{1,4}

¹Universitätsklinikum Jena, Klinik und Poliklinik für Neurochirurgie, Jena, Germany

²Universitätsklinikum Jena, Institut für Medizinische Mikrobiologie, Jena, Germany

³Medizinische Hochschule Brandenburg - Theodor Fontane, Klinik für Neurochirurgie, Brandenburg an der Havel, Germany

⁴Klinikum Saarbrücken, Klinik für Neurochirurgie, Saarbrücken, Germany

Objective

A relationship between postoperative infections and a prolonged survival in glioblastoma patients still remains controversial. The pathogens most frequently detected in this context are *Staphylococcus* species. Although the interaction of *S. aureus* with different human cell types was investigated before, no data about infection of glioblastoma cells and astrocytes is known. The main objective of this study was to investigate the course of *S. aureus* infection of glioblastoma cells (GBM) and human brain astrocytes (HBA). Therefore, we established an in vitro infection model.

Methods

Four different GBM cell cultures and one HBA cell culture were infected with two wild-type strains of *S. aureus* (6850, LS1) with a MOI of 10. After 90 min the percentage of ingested bacteria was determined. In a persistence assay, the survival of intracellular bacteria was investigated after 2, 4, and 7 days post infection. At the same time points cell death of the human cells was examined. Changes in secretion of IL-6 and IL-8 were measured by ELISA.

Results

S. aureus was able to infect GBM as well as HBA cells. The cells ingested between 0.1% and 4.7% of the bacteria. After ingestion the bacteria induced cell death in about 28.5% of the host cells. The remaining human cells eliminated the bacteria very quickly; and the human cells recovered. In addition, the intracellular bacteria presented a high population of small colony variants (SCVs) which are associated with host immune response evasion. On day 4, 13.2% (6850) and 1.7% (LS1) of the intracellular bacteria were left in the GBM cells, of which 10.3% and 31.3% were SCVs. In the HBA cells 0.6% (6850) and 4.7% (LS1) bacteria were left, with 10.1% and 15.3% SCVs. The differences in the elimination of the bacteria between GBM cells and HBA and the phenotype switch during the course of infection were statistically significant for both *S. aureus* strains. The infected GBM cells and HBA became activated and secreted cytokines. There was a significant increase in secretion of IL-6 (6850: 109fold, LS1: 1001fold) and IL-8 (6850: 339fold, LS1: 488fold) 24h after infection, compared with the uninfected cells

Conclusion

Our data show for the first time, that *S. aureus* is able to infect glioblastoma cells as well as astrocytes cells. Moreover, the GBM cells were more susceptible to bacterial infection than the HBA cells. The inducible secretion of proinflammatory cytokines may lead to an enhanced antitumor immunity in GBM.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P123

Meclofenamate als potenter pharmakologischer Gap junction Inhibitor sensitiviert Glioblastomzellen für einen durch Lomustin vermittelten Zelltod

Drug repurposing of meclofenamate as a potent gap junction inhibitor sensitizes primary glioblastoma cells for lomustine

M. Schneider¹, A. L. Potthoff¹, K. Joseph^{2,3,4}, B. O. Evert⁵, E. Güresir¹, P. Schuss¹, A. Dolf⁶, M. A. Westhoff⁷, A. Waha⁸, O. Schnell^{2,3,4}, H. Vatter¹, D. H. Heiland^{2,3,4}, U. Herrlinger⁹

¹Rheinische Friedrich-Wilhelms-Universität Bonn, Abteilung für Neurochirurgie, Bonn, Germany

²Albert-Ludwigs-Universität Freiburg, Forschungsgruppe Translationale Neuroonkologie, Freiburg, Germany

³Albert-Ludwigs-Universität Freiburg, Medizinische Fakultät, Freiburg, Germany

⁴Albert-Ludwigs-Universität Freiburg, Abteilung für Neurochirurgie, Freiburg, Germany

⁵Rheinische Friedrich-Wilhelms-Universität Bonn, Abteilung für Neurologie, Bonn, Germany

⁶Rheinische Friedrich-Wilhelms-Universität Bonn, Institut für Experimentelle Immunologie, Bonn, Germany

⁷Universitätsklinikum Ulm, Abteilung für Pädiatrie und Jugendmedizin, Ulm, Germany

⁸Rheinische Friedrich-Wilhelms-Universität Bonn, Abteilung für Neuropathologie, Bonn, Germany

⁹Rheinische Friedrich-Wilhelms-Universität Bonn, Abteilung für Klinische Neuroonkologie, Bonn, Germany

Objective

Since inhibition of a syncytial intercellular communication via gap junctions has been shown to sensitize glioblastoma cells to temozolomide-mediated antitumoral effects, the idea of gap junction-targeted therapies has been proposed as a promising novel therapeutic strategy within translational glioblastoma research. However, the impact of gap junction inhibition in the context of lomustine therapy that has recently been shown to markedly improve survival of glioblastoma patients in combination treatment with temozolomide, has not been examined, so far. By repurposing of meclofenamate (MFA) - a clinically approved nonsteroidal anti-inflammatory drug - as a potent gap junction inhibitor, the present study aimed at investigating the effects of a gap junction-targeted therapy on primary human glioblastoma cells in the context of lomustine administration.

Methods

In order to quantify the extent of gap junction inhibition, Realtime-Imaging fluorescence-guided measurements of calcein cell-to-cell cytoplasm transfer were performed. We used RNA-sequencing and proteome profiling to study the downstream signalling due to meclofenamate treatment. DNA-fragmentation served as readout for cell death and was assessed by flow cytometric analysis of propidium iodide-stained nuclei.

Results

We observed a significant reduction of calcein cytoplasm transfer in MFA-treated cells as well as reduction of cell-cell connection based on 3D-confocal reconstruction. RNA-sequencing revealed an increased stress-induced gene expression pattern in samples with pharmacological inhibition of gap junctions and CCNU therapy. The CX-43 inhibition profoundly increased the percentage of lomustine-mediated cell death. Gap junction inhibition was associated with elevated activity of the JNK signalling pathway.

Conclusion

This study is the first to show that inhibition of intercellular communication via gap junctions profoundly sensitizes primary glioblastoma cells to lomustine-mediated cell death therefore constituting a promising new therapy strategy for patients suffering from this disastrous and currently incurable cancer. With regard to MFA



as a clinically-approved drug, MFA might harbour the potential of bridging the idea of gap junction-targeted therapeutic approaches into an instant subsequent clinical implementation.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P124

Hohe Interobserver-Übereinstimmung in der semiquantitativen Klassifikation der 5-ALA Fluoreszenzlevel in neu-diagnostizierten Glioblastomen

High interobserver agreement in the semiquantitative classification of 5-ALA fluorescence levels in newly diagnosed glioblastomas

M. Mischkulnig¹, B. Kiesel¹, M. Borkovec², L. Wadiura¹, D. Benner¹, A. Hosmann¹, S. Hervey-Jumper³, E. Knosp¹, K. Rössler¹, M. S. Berger³, G. Widhalm¹

¹Medizinische Universität Innsbruck, Abteilung für Neurochirurgie, Wien, Austria

²Ludwig-Maximilians-Universität München, Abteilung für Statistik, München, Germany

³University of California San Francisco, Department of Neurological Surgery, San Francisco, CA, United States

Objective

Fluorescence-guided resection of glioblastomas (GBM) using 5-aminolevulinic acid (5-ALA) improves intraoperative tumor visualization and is thus widely used nowadays. During resection, different fluorescence levels can usually be distinguished within the same tumor. Recently, we demonstrated that strong, vague, and no fluorescence correspond to distinct histopathological characteristics in newly diagnosed GBM. However, the semiquantitative fluorescence classification by the neurosurgeon is subjective and currently no comprehensive data on interobserver variability is available. The aim of this study was thus to investigate the interobserver variability in the classification of 5-ALA fluorescence levels in newly diagnosed GBM in a large cohort.

Methods

A questionnaire investigating the interobserver variability in 5-ALA fluorescence quantification was performed at a nation-wide neurosurgical oncology meeting. The participants involved in the neurosurgical/neurooncological field were asked to categorize 30 cases of 5-ALA fluorescence images derived from GBM resection according to the widely used three-tier fluorescence classification scheme (negative, vague or strong fluorescence). Additionally, participants were asked for information on their medical background such as specialty, level of training and experience with fluorescence-guided procedures. Interobserver agreement was defined as the calculated mean kappa values for each observer.

Results

A total of 36 questionnaires were included in the final analysis. The mean average kappa value in fluorescence classification within the entire cohort was 0.71±0.12 and 29 (81%) participants had a substantial or almost perfect interobserver agreement (kappa values 0.6-1.0). Interobserver agreement was significantly higher in neurosurgeons (mean kappa: 0.83) as compared to non-neurosurgeons involved in the neurooncological field (mean kappa: 0.52; $p<0.001$). Furthermore, interobserver agreement was significantly higher in participants who had experience with at least 25 5-ALA fluorescence-guided surgeries (mean kappa: 0.87) compared to less experienced colleagues (mean kappa: 0.82; $p=0.039$).

Conclusion

Our study found a high interobserver agreement in the semiquantitative classification of different 5-ALA fluorescence levels in newly diagnosed GBM. Interobserver agreement increases significantly in more experienced participants and therefore a high level of experience is crucial for reliable intraoperative fluorescence classification.

Neuroonkologie – Gliome I/Neurooncology – Gliomas I

P125

MicroRNAs als Therapeutika zur Verbesserung des Ansprechens von Glioblastomen auf Immuntherapie *MicroRNAs as potential "tissue sensitizers" for the augmentation of glioblastoma immunotherapy*

F. Erhart¹, A. Lang¹, M. Hackl², B. Kiesel¹, M. Mischkulnig¹, P. A. Mercea¹, S. Spiegl-Kreinecker³, D. Lötsch-Gojo⁴, A. Woehrer⁵, C. Marosi⁶, K. Rössler¹, W. Berger⁴, G. Widhalm¹

¹Medizinische Universität Innsbruck, Universitätsklinik für Neurochirurgie, Wien, Austria

²TAmiRNA GmbH, Wien, Austria

³Johannes Kepler Universität Linz, Universitätsklinik für Neurochirurgie, Linz, Austria

⁴Medizinische Universität Innsbruck, Institut für Krebsforschung, Wien, Austria

⁵Medizinische Universität Innsbruck, Klinisches Institut für Neurologie, Wien, Austria

⁶Medizinische Universität Innsbruck, Klinische Abteilung für Onkologie, Wien, Austria

Objective

Glioblastoma is the most frequent and most aggressive malignant brain tumor. Immunotherapies have so far not lived up to their promise. This is also true for a dendritic cell vaccination that was tested recently in a pan-Austrian phase II clinical trial. It failed to prolong survival. To better understand the reasons for treatment resistance and to explore novel therapeutic modalities, glioblastoma tissue from trial patients underwent a number of molecular and cellular analyses. In molecular biology, microRNAs (miRNAs) are increasingly recognized as potential master regulators of tissue phenotypes since one miRNA can regulate hundreds of messenger RNAs (mRNAs). was therefore also A microRNA sequencing approach was therefore also among the tissue investigation methods It led to the identification of miRNAs that seem to be survival-associated. The goal is now to develop these miRNAs towards a therapeutic usage in the context of immunotherapies.

Methods

In a first exploratory phase, glioblastoma tissue from 16 trial patients underwent miRNA sequencing. Then, in a validation phase, tissue from 38 trial patients underwent qRT-PCR, where miRNAs found in the exploratory phase were confirmed. In the current subsequent experiments, identified miRNAs are being characterized further. On the one hand, histopathology analyses (via in-situ hybridization) are being done to elucidate the cell type and the (sub)cellular location of the identified miRNAs. On the other hand, cell culture experiments are being carried out where miRNAs are artificially introduced into glioblastoma cells and the effects on gene expression, phenotype and function are evaluated.

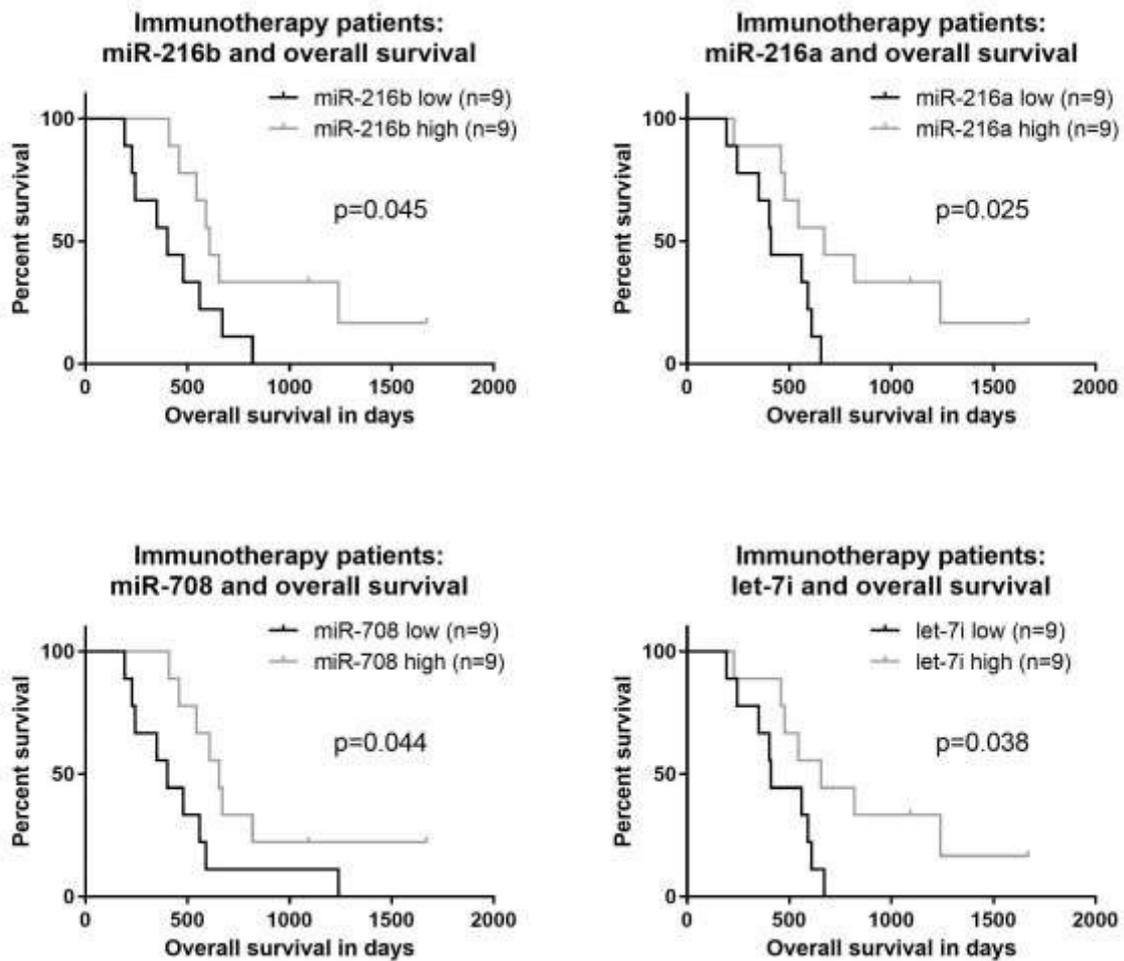
Results

MiRNAs that were found to be apparently survival-associated included miR-216b, miR-216a, miR-708 and hsa-let-7i. They were more abundant in patients that survived relatively long under immunotherapy and could significantly separate Kaplan-Meier curves.

Conclusion

MiRNAs seem to be relevant players in glioblastoma immunotherapy research. In the future, they might serve as therapeutic "tissue sensitizers" to make glioblastoma more susceptible to immunotherapies. Further preclinical and clinical work will be necessary to achieve that goal.

Fig 1



Neuroonkologie – Gliome I/*Neurooncology – Gliomas I*

P221

ALDH1A1 ist ein Marker für erworbene Chemoresistenz im Glioblastomrezidiv

ALDH1A1 is a marker for acquired drug resistance in recurrent glioblastoma

L. Rauschenbach^{1,2}, S. Kebir^{3,1}, V. Ullrich¹, C. Dobersalske¹, A. Till⁴, D. Trageser⁴, J. Siveke⁵, A. Rösch⁶, H. Fröhlich⁷, T. Pietsch⁸, G. Reifenberger⁹, M. Simon¹⁰, U. Sure², M. Glas^{3,1}, B. Scheffler¹

¹Deutsches Krebsforschungszentrum (DKFZ), DKTK Partnerstandort, Essen, Germany

²Universitätsklinikum Essen, Klinik für Neurochirurgie, Essen, Germany

³Universitätsklinikum Essen, Klinik für Neurologie, Abteilung für Klinische Neuroonkologie, Essen, Germany

⁴Universitätsklinikum Bonn, Institut für Rekonstruktive Neurobiologie, Bonn, Germany

⁵Deutsches Krebsforschungszentrum (DKFZ), DKTK Partnerstandort, Essen, Germany

⁶Universitätsklinikum Essen, Klinik für Dermatologie, Essen, Germany

⁷Rheinische Friedrich-Wilhelms-Universität Bonn, b-it, Bonn, Germany

⁸Universitätsklinikum Bonn, Institut für Neuropathologie, Bonn, Germany

⁹Universitätsklinikum Düsseldorf, Institut für Neuropathologie, Düsseldorf, Germany

¹⁰Universitätsklinikum Bonn, Klinik für Neurochirurgie, Bonn, Germany

Objective

Treatment of glioblastoma (GBM) is limited and fatal relapse occurs almost universally, even in patients that initially benefit from tissue resection, irradiation and chemotherapy with temozolomide. To abolish acquired resistance to temozolomide in recurrent GBM, driving mechanisms need to be identified and targeted.

Methods

We investigated paired samples of primary and recurrent GBM disease and performed in situ, in vitro and in vivo studies on tissue specimen and tissue-derived cell cultures. Treatment approaches were additionally evaluated in an orthotopic xenograft model.

Results

A subset of tumor cells in recurrent GBM exhibits temozolomide-resistance and paired sample analysis revealed elevated levels of phosphorylated AKT in this cell population. In consequence, inhibition of the AKT pathway reversed drug resistance and increased survival in xenograft models. ALDH1A1 is a marker for temozolomide-resistant tumor subclones and combinatorial treatment with temozolomide and an AKT-inhibitor suggested significantly increased survival by decreasing the ALDH1A1-expressing tumor cell population.

Conclusion

ALDH1A1-expressing tumor cells can be targeted in vivo to overcome temozolomide resistance in recurrent GBM.

Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P126

Definierte Glukosespiegel stimulieren die metabolische und ontogenetische Reprogrammierung in menschlichen Meningeomzellen

Defined glucose levels stimulate metabolic and ontogenic reprogramming in human meningioma cells

S. Huppertz, D. Freitag, U. Tiller, S. Grube, R. Kalff, J. Walter

Universitätsklinikum Jena, Neurochirurgie, Jena, Germany

Objective

Cancer cells modulate their metabolism to enhance their own survival, proliferation, growth and long-term maintenance. Even in the presence of oxygen, they alter their metabolism by switching from mitochondrial respiration to anaerobic glycolysis, concomitantly increasing their glucose uptake and the fermentation of glucose to lactate. This phenomenon was first characterized by Otto Warburg in 1924 and is commonly referred to as the "Warburg effect". The extent to which this effect plays a role in the glucose metabolism and genesis of meningiomas has not been extensively investigated.

Methods

The commercially available meningioma cell line Ben Men-1 was cultured for 24h and exposed to 14 different glucose concentrations, ranging from 0 to 100 mM. Subsequently the metabolic activity and the proliferation rate were measured using MTT assays and BrdU ELISA respectively. In order to identify the glucose concentration yielding maximal proliferative and glycolytic activity, we performed a peak fitting analysis. We determined five glucose concentrations that promote maximal, minimal and optimal glycolytic activity. These five conditions were further used for immunocytochemical analysis and the cells were cultured for five passages. Doubling times, morphological changes and marker expression levels (EMA, vimentin, GLUT1, GLUT3, p-mTOR, HIF1a, NANOG, SOX2 and OCT4) were determined by immunocytochemistry.

Results

The meningioma cells' proliferative state was assessed under glucose concentrations of 0, 15, 40, 65 and 100 mM. During long-term cultivation (>four passages), cell proliferation was increased in 15 to 65 mM glucose-containing medium, in comparison to 0 to 100 mM. In the 65 mM glucose condition, the cells displayed the highest doubling time. Interestingly, cellular staining revealed significantly reduced vimentin and EMA levels in the 65 mM glucose condition. In addition, we found increased levels for p-mTOR and GLUT3 as well as high expressions of NANOG, SOX2 and OCT4 at 65 mM glucose.

Conclusion

Increasing the levels of glucose positively impacts the meningioma cells' proliferation up to a concentration of 65 mM. At this level we found an increasing expression of stem cell markers. The increased expression levels of GLUT3 and p-mTOR suggest a possible metabolic reprogramming and the expression of NANOG, SOX2 and OCT4 an ontogenic reprogramming in this context.

Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P127

TERT-Genalteration identifizieren eine Subgruppe aggressiver Meningeome *TERT alterations identify a subset of aggressive meningiomas*

T. Juratli^{1,2}, I. Prilop^{1,3}, G. M. Shankar², S. Tummala², G. Schackert¹, D. Cahill², P. Brastianos⁴

¹Universitätsklinikum Carl Gustav Carus Dresden, Neurochirurgie, Dresden, Germany

²Massachusetts General Hospital, Department of Neurosurgery, Boston, MA, United States

³Universitätsklinikum Carl Gustav Carus Dresden, Neurochirurgie, Dresden, Germany

⁴Massachusetts General Hospital, Division of Neuro-Oncology, Department of Neurology, Boston, MA, United States

Objective

Although a significant proportion of aggressive meningiomas acquire *TERT* promoter (*TERTp*) mutations which drive *TERT* overexpression during progression, alternative mechanisms of telomere maintenance in meningioma are broadly unknown. *TERT* activating rearrangements are common in some aggressive cancers and associated with poor outcome. We sought to assess *TERT* rearrangements in a large cohort of patients with progressive meningiomas.

Methods

We determined the frequency of *TERT* mRNA overexpression in 126 temporally- and regionally-distinct specimens from 55 WHO grades II/III meningioma patients using reverse-transcriptase PCR. Subsequently, RNA sequencing was performed in samples with *TERT* overexpression to detect rearrangements. Additionally, the *TERTp* region was sequenced in all patients to assess hotspot mutations.

Results

We identified 9 samples from 3 patients (5.4%) with highly amplified *TERT* mRNA expression. RNA sequencing of these samples revealed a novel fusion *RETREG1-TERT* that was present in 2 patients, in addition to a previously-reported *LPCAT1-TERT* fusion in a third case. One of the 3 patients had received a course of radiotherapy prior to the emergence of detectable mRNA fusion. In all cases the *TERT* rearrangements began in either exon 2 or 3, upstream of the reverse transcriptase domain that begins in exon 4, consistent with a proposed activating mechanism-of-action. In total, 10 patients (18%) harbored *TERT* alterations in our cohort: 3 *TERT* rearrangements and 7 *TERTp* mutations. Importantly, patients whose meningiomas harbored *TERT* alterations had a significantly worse overall survival (5.1 years, 95% CI 3.1 – 7.2) compared to *TERT* wild-type patients (18.5 years, 95% CI 14.6 – 22.4, $p < 0.001$).

Conclusion

We discovered *TERT* rearrangements in a subset of aggressive meningiomas, including a novel *RETREG1-TERT* rearrangement. Two distinct mechanisms for *TERT* activation, *TERT* rearrangements and *TERTp* mutations were associated with a particularly poor outcome, suggesting a central role of telomere lengthening in the pathogenesis of aggressive meningioma. Detection of *TERT* alterations offers a basis for a more precise identification of patients at-risk for developing early progression of meningioma.

Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P128

Zielgerichtete Therapie der papillären Kraniopharyngeome mit einer BRAF V600E Mutation *Targeted treatment of papillary craniopharyngiomas harbouring BRAF V600E mutations*

T. Juratli^{1,2}, P. Jones², N. Wang³, F. Barker², Y. Odia⁴, E. Rostami⁵, D. Cahill², S. Santagata⁶, P. Brastianos³

¹Universitätsklinikum Carl Gustav Carus Dresden, Klinik für Neurochirurgie, Dresden, Germany

²Massachusetts General Hospital, Department of Neurosurgery, Boston, MA, United States

³Massachusetts General Hospital, Division of Neuro-Oncology, Department of Neurology, Boston, MA, United States

⁴Baptist Health South Florida, Miami Cancer Institute, Miami, FL, United States

⁵Uppsala University, Medical Clinic IV Endocrinology, Uppsala, Sweden

⁶Brigham and Women's Hospital, Department of Pathology, Boston, MA, United States

Objective

Craniopharyngiomas are surgically challenging brain tumors. After the operation, the quality of life is often significantly impaired due to neurological and endocrinological complications. Currently, FDA approved systemic treatments are not available for patients in whom craniopharyngiomas recur after surgery and radiation. Papillary craniopharyngiomas (PCP) are characterized by the presence of BRAFV600E mutations. To date, five case reports have been published on the treatment of BRAFV600E mutant papillary craniopharyngiomas with BRAF and/or MEK inhibitors.

Methods

In this study, authors from all previously published reports share their collective experience, provide updated follow-up on their patients, and thus generate an overview of all currently available information on targeted therapy in patients with BRAFV600E mutant PCP. We have also included information on an additional patient with a papillary craniopharyngioma recently treated with BRAF and MEK inhibitors after tumor biopsy alone, in the absence of recurrence, highlighting the potential for a neo-adjuvant therapeutic approach.

Results

All six cases in our series (100%) showed dramatic responses to targeted treatment with BRAF (and MEK) inhibitors. Altogether, our cases are highly promising and informative for patient treatment, although uncertainty remains with regards to the optimal timing, the specific agents (single agent or dual therapy) to be used and the duration of treatment. The ongoing multicenter phase II Alliance A071601 trial (NCT03224767) of vemurafenib and cobimetinib for patients with biopsy-proven residual or recurrent papillary craniopharyngiomas should provide additional information to help guide patient management.

Conclusion

PCPs are characterized by the presence of BRAFV600E mutations, which are emerging as a useful guide for diagnosis and treatment decision-making. The ongoing multicenter phase 2 Alliance A071601 trial is evaluating the efficacy of BRAF and MEK inhibitors for patients with PCP.

Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P129

Vergleich direkter Nervenstimulation und kortikobulbärer motorisch-evozierter Potentiale hinsichtlich ihres prädikativen Werts für Fazialispareesen nach Vestibularisschwannom-Operationen
Comparing direct nerve stimulation and corticobulbar MEPs in their diagnostic power to predict facial nerve palsy in vestibular schwannoma surgery

T. Greve¹, L. Wang², J. Tonn¹, C. Schichor¹, A. Szelényi¹

¹Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik und Poliklinik, München, Germany

²Beijing Tiantan Hospital, Abteilung für Neurochirurgie, Peking, China

Objective

We compared two IONM modalities for the precise prediction of facial nerve outcome in vestibular schwannoma surgery (VS): direct nerve stimulation (DNS) and facial muscle corticobulbar motor evoked potentials (FMcoMEP).

Methods

Data of 30 patients (45 ± 13.6 years, 14 f) were retrospectively analyzed. Monitored muscles were orbicularis oculi, orbicularis oris and mentalis. For DNS of the facial nerve, the proximal-to-distal amplitude ratio at the end of tumor resection was calculated (DNS_pdAMP). FMcoMEPs were elicited with close-to-threshold stimulation parameters and stimulation intensity was adjusted if amplitudes decreased. The baseline-to-final stimulation intensity increase (MEP_bfSI_inc) was calculated. To assess the predictive power of DNS_pdAMP and MEP_bfSI_inc, facial nerve function (FaF) on day 1 (D1) and day 7 (D7) was dichotomized between marked deterioration with impaired eye closure (HB increase ≥ 1 and absolute HB score ≥ 4) and mild deterioration without impaired eye closure (HB increase ≤ 2 and absolute HB score ≤ 3).

Results

On D1, ROC analysis revealed the highest area under the curve (AUC) for MEP_bfSI_inc, followed by DNS_pdAMP. On D7, DNS_pdAMP showed the highest AUC, followed by MEP_bfSI_inc. At 3M, MEP_bfSI_inc showed a much higher AUC than DNS_pdAMP. Using the Youden's index, optimal cutoff values for DNS_pdAMP and MEP_bfSI_inc were determined for D1, D7 and 3M. With these improved cutoffs, the false-negative rate was equal for D1 and D7 but 50% higher at 3M for DNS_pdAMP (Figure 1).

Conclusion

Ratios in DNS_pdAMP > 0.3 resp. of MEP_bfMT_inc $> 20\%$ reliably predict short term facial paresis. On a long-term basis, only FMcoMEPs seem to provide acceptable predictive value. DNS stimulation induces synchronized activation of fast conducting larger axons, which might result in overestimating axonal conductivity. On the contrary, near threshold TES only partially activates all axons within a nerve. This might result in underestimating peripheral axonal conductivity. This explains the lower predictive value for DNS at 3M. MEPs can be performed throughout the tumor removal, whereas DNS can only be intermittently performed.

Figure 1 Overview about warning criteria and their predictive power.

Fig 1

	AUC	OPTIMAL CUTOFF	SENSITIVITY	SPECIFICITY	FALSE-NEGATIVE RATE
D1					
DNS_pdAMP	0.84	0.33	86%	78%	17%
MEP_bfSI_inc	0.90	28%	86%	87%	17%
D7					
DNS_pdAMP	0.83	0.31	83%	79%	20%
MEP_bfSI_inc	0.79	19%	83%	71%	20%
3M					
DNS_pdAMP	0.38	0.2	50%	88%	50%
MEP_bfSI_inc	0.91	41%	100%	86%	0%

Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P130

Ein orthotopes Xenograft-Mausmodell für benigne humane Meningeome *An orthotopic xenograft mouse model for benign human meningiomas*

D. Freitag¹, K. H. Herrmann², J. R. Reichenbach², C. Ewald³, R. Kalff¹, J. Walter^{1,4}

¹Universitätsklinikum Jena, Klinik für Neurochirurgie, Jena, Germany

²Universitätsklinikum Jena, Institut für Diagnostische und Interventionelle Radiologie, Jena, Germany

³Städtisches Klinikum Brandenburg, Klinik für Neurochirurgie, Brandenburg an der Havel, Germany

⁴Klinikum Saarbrücken, Klinik für Neurochirurgie, Saarbrücken, Germany

Objective

Low-grade meningiomas are mainly characterized by their benign biological behavior, slow growth and low metabolic rates. Since the usual properties of malignant tumors, such as uncontrolled growth, tendency to migrate or infiltration, are therefore not usable, research on this tumor entity is particularly difficult. A reliable *in vivo* model close to the patient is still missing. The aim of this study was to develop a functioning orthotopic xenograft model for human WHO¹ meningiomas.

Methods

Fifteen 10-12 weeks old female NOD.SCID mice were subdurally injected with a suspension of 1x10⁶ cells. Cells of various differentiation levels were: (1) primary meningioma cells (PMCs) (differentiated, p1), (2) PMCs and 30% freshly isolated meningioma stem cells (MSCs) and (3) PMCs and 70% MSCs. Throughout the experiment, the animals were examined for general condition, weight and abnormalities. 2, 12 and 24 weeks follow-up controls were performed using 9.7T small MRI. The used MRI sequences were a T2-weighted spinecho, a T1-weighted 3D FLASH sequence both native and post contrast agent (100µl Gadovist, diluted 1:10). Since meningiomas often consist of very hard, dura-mater like tissue we used an additional T1-weighted UTE sequence post contrast to ensure that short T2 tissue will be visible. Based on the image data, the volumes of the contrast-enriching areas were calculated. After 24 weeks, the tissue was prepared and analyzed.

Results

The imaging showed that in the T1-weighted sequences after contrast agent (CA) administration in group 1 only very small or no CA-accumulating areas could be detected. We detected an increasing CA-enriching signal only in 1 animal of group 1. In contrast, both group 2 showed a strong tendency (p=0.051) and group 3 even a significant (p=0.024) volume increase of the CA-enriching areas after 24 weeks. The analysis of mortality rates showed a high mortality in group 3.

Conclusion

On the basis of the data, it can be clearly stated that it is possible to induce a meningioma in mice, with the help of meningioma stem cells. Thus, we were able to develop an orthotopic xenograft model for benign human meningiomas, which is now available for further applications.

Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P131

Immunmodulatorische Effekte von Bestrahlung in der Meningeomentstehung *Immunomodulatory effects of irradiation in the genesis of meningioma*

M. Walter-Diessars¹, D. Freitag¹, W. Dammermann², L. Hain¹, N. Abbasi-Senger³, T. Wiezorek³, A. Wittig³, R. Kalff¹, J. Walter^{4,1}

¹Universitätsklinikum Jena, Klinik für Neurochirurgie, Jena, Germany

²Medizinische Hochschule Brandenburg - Theodor Fontane, Innere Medizin II, Brandenburg an der Havel, Germany

³Universitätsklinikum Jena, Klinik für Strahlentherapie und Radioonkologie, Jena, Germany

⁴Klinikum Saarbrücken, Klinik für Neurochirurgie, Saarbrücken, Germany

Objective

Ionizing radiation is an established risk factor for meningioma formation. However, the underlying mechanisms are largely unknown. It is discussed whether radiation triggers mutations or immunomodulatory processes, might lead to dedifferentiation of somatic cells and ultimately to the development of tumor stem cells. The aim of this study was to investigate the short-term effects of ionizing radiation on immunomodulatory processes in non-pathological dura mater cells (DMCs), which are known as the origin of meningioma development.

Methods

Three DMC cultures were cultivated under standard conditions. The confluent monolayers were exposed to a single dose of photon irradiation (1, 2, 4, 8, 12, 16, 20 Gy). 24h and 7, 14, 21 and 28 days after treatment, cells were passed and analyzed. Analyses were performed in respect to morphology (cell shape, generation times, etc.), molecular biology (qPCR), immunocytochemistry (ICC) and immunological aspects (ELISA) of tumor genesis.

Results

In the 1Gy and 8Gy radiation group (G) DMC morphology showed significant differences especially regarding the confluence and spherogenesis compared to the untreated group. Further correlations were found between the IL6 and IL8 levels in the 1GyG compared to the untreated group. We revealed 25% of NANOG positive tumor-like structures in the 1GyG versus 3% in the 8GyG by immunocytochemistry. A significantly higher NANOG gene expression was found in 1GyG on day 14 (first occurrence of spheroids) compared to 8GyG. Additionally, a tendency for CD126 expression in 1GyG compared to 8GyG could be found.

Conclusion

Based on the presented data, we concluded a correlation between the secretion of IL6 and IL8 and the formation of stem cell specific spheroids. Thus, the formation of a tumor stem cell-like phenotype seems to be possible as a short-term effect of radiation-induced cytokine secretion in the low-dose group.

Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P132

Die Anwendung der Pupillometry ermöglicht eine Evaluation der Chiasma opticum-Dekompression nach transssphenoidaler Resektion von Hypophysentumoren

Automated pupillometry indicates decompression of the optic chiasm following transsphenoidal resection of pituitary tumours

C. Beynon¹, M. Nofal¹, J. Jesser², P. Dao Trong¹, K. Zweckberger¹, E. Santos¹, A. W. Unterberg¹

¹Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

²Universitätsklinikum Heidelberg, Neuroradiologische Klinik, Heidelberg, Germany

Objective

Pituitary tumours may lead to compression of the optic chiasm and visual impairment in patients. Therefore, decompression of the optic chiasm is a major goal of surgical treatment. Automated pupillometry has been used in various clinical settings for assessing the optic system. The aim of the present study was to evaluate its potential to improve diagnostic modalities in patients undergoing transsphenoidal resection of pituitary tumours.

Methods

The automated pupillometer NPi-200® (Neurooptics, CA, USA) was used in patients treated at our institution for transsphenoidal resection of a pituitary tumour. The neurological pupil index (NPi) was assessed before and within 24 hours after surgery. Patients were divided into two groups depending on pupillometry findings prior to surgery (Group A: NPi < 4.0; Group B: NPi > 4.0). Clinical findings of visual impairment and optic chiasm compression on imaging studies were analysed. The impact of transsphenoidal tumour resection on NPi values was analysed and compared between both groups.

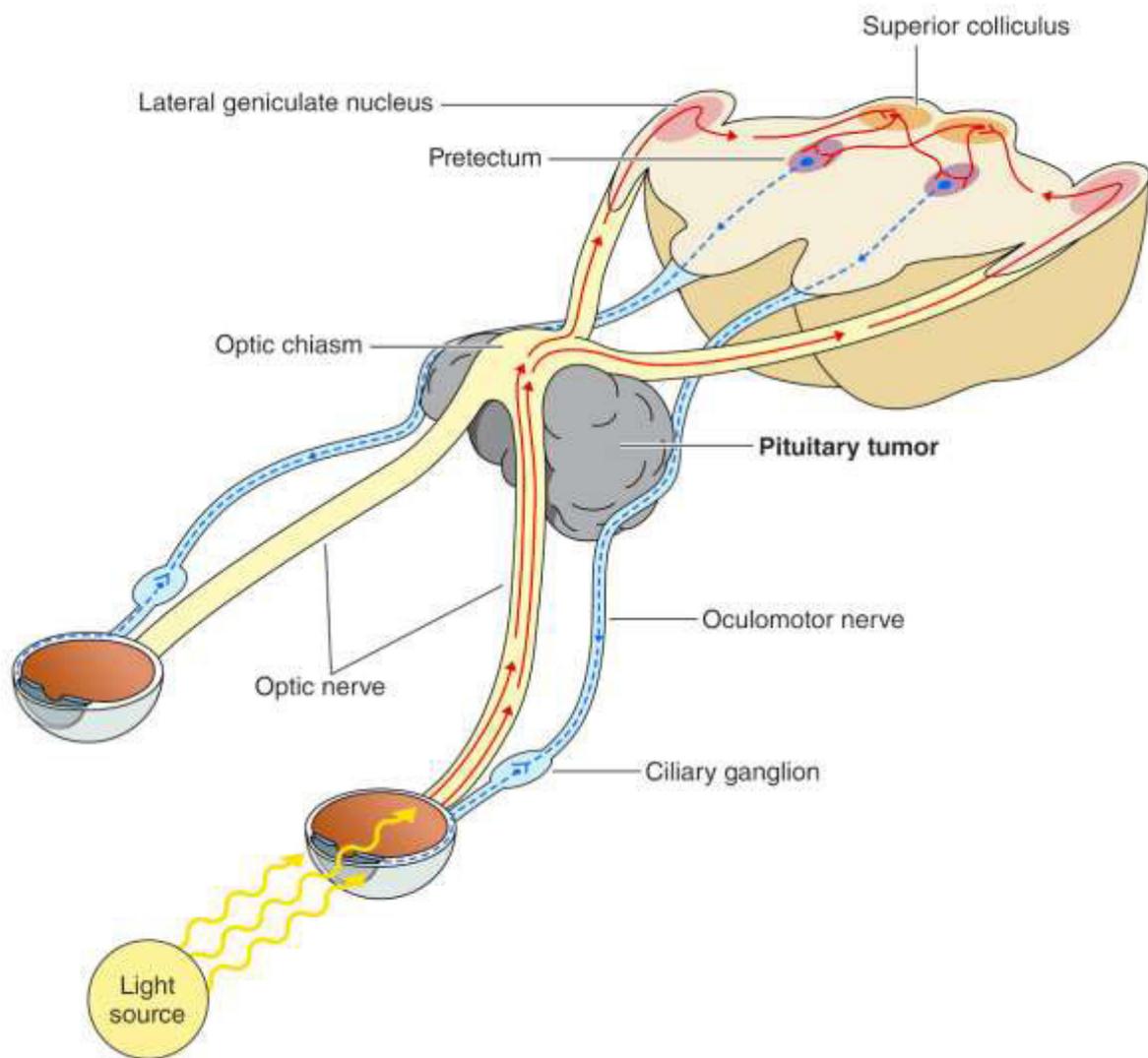
Results

A total of 32 patients were included in this study. NPi values below 4.0 were observed in 7 patients (Group A) and of these, 7 (100%) suffered from visual impairment and compression of the optic chiasm. Only 47% patients of group B (n=25) had impaired vision and/or compression of the optic chiasm. During transsphenoidal tumour resection, intraoperative magnetic resonance imaging revealed decompression of the optic chiasm in all patients. NPi values of patients from group A improved significantly from a mean of 3.6±0.4 (before surgery) to 4.2±0.4 (after surgery; p=0.0002). In contrast, NPi values did not change significantly after surgery in patients from group B (before surgery: 4.5±0.2; after surgery: 4.5±0.3; p=0.07). The sensitivity of NPi

Conclusion

The use of automated pupillometry may detect optic chiasm compression in patients with pituitary tumours and moreover, postoperative improvement of initial NPi values < 4.0 indicates sufficient decompression of the optic chiasm following transsphenoidal tumour resection. Further studies are needed to evaluate the potential of this technique to gain valuable information in the surgical treatment of pituitary tumours.

Fig 1



Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P133

Medulloblastome im Erwachsenenalter – ein unterschiedliches epigenetisches Profil legt eine modifizierte Behandlung nahe

Medulloblastoma in adults – a different epigenetic profile implies a modification in treatment

F. S. Fritzsche¹, F. L. Ricklefs¹, U. Schüller², G. Kammler¹, M. Westphal¹, L. Dührsen¹

¹Universitätsklinikum Hamburg-Eppendorf, Neurochirurgie, Hamburg, Germany

²Universitätsklinikum Hamburg-Eppendorf, Neuropathologie, Hamburg, Germany

Objective

Recent reports on medulloblastoma (MB) in adults suggest different risk stratification based on biological findings as well as prognostic expectations. We intend to illustrate that this seemingly rare entity requires new clinical trials to establish the prognostic impact and expected clinical outcome for adult patients with MB based on molecular investigations.

Methods

Neuropathological analysis of the tumor samples included conventional stains, immunohistochemistry and genome-wide DNA methylation profiling using an 850k Illumina EPIC array and classified by the DKFZ brain tumor classifier. Clinical records were examined concerning age at diagnosis, clinical symptoms, MRI-studies, surgical procedures and adjuvant therapy.

Results

We show the data of 5 adults diagnosed with MB in 2019 at our medical center. The median age at diagnosis was 38.2 years. The main clinical feature was hydrocephalus in all cases, headache, nausea, gait disturbance and walking disorder. MRI scans revealed a tumor in the posterior fossa, in one case associated meningeosis and spinal metastasis. All patients underwent surgery. Gross total resection was performed in 4 patients, in one patient only a stereotactic biopsy seemed reasonable. Histology showed 3 cases of sonic hedgehog (SHH), all of desmoplastic subtype, whereof 2 indicated TP53 wt and 2 cases of wingless (WNT) MB with just one TP53 wt. None of the tumors showed N-MYC or C-MYC gene amplification. The MGMT Promoter was found unmethylated in all cases. All patients receive adjuvant radiochemotherapy accordingly NOA 07 with slight individualized modification after stem cell mobilization in 4 cases.

Conclusion

These cases of MB in adults correspond to the adult MB series reported to date but display an epigenetic profile differing from the widely understood childhood counterparts. Moreover, these cases illustrate that the development of detailed molecular analyses and the molecular understanding of rare entities provided nowadays enable detailed planning and coordination of upfront clinical trials to evaluate treatment options particularly in respect to chemotherapy regimen.

Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P134

Der STAMPE2-Score eignet sich zur Abschätzung des postoperativen Epilepsie-Risikos bei Meningeompatienten in einer unabhängigen Kohort

The STAMPE2 score is suitable to estimate postoperative seizures in meningioma patients in an independent cohort

P. Baumgarten¹, M. Sarlak¹, A. Spyranis¹, F. Geßler¹, M. Wagner², P. N. Harter³, V. Seifert¹, T. Freiman⁴

¹Universitätsklinikum Frankfurt am Main, Klinik und Poliklinik für Neurochirurgie, Frankfurt am Main, Germany

²Universitätsklinikum Frankfurt am Main, Neuroradiologie, Frankfurt am Main, Germany

³Johann Wolfgang Goethe-Universität Frankfurt am Main, Edinger Institut, Neuropathologie, Frankfurt am Main, Germany

⁴Universitätsklinikum Frankfurt am Main, Klinik und Poliklinik für Neurochirurgie, Frankfurt am Main, Germany

Objective

Seizures are one of the most common symptoms of Meningioma patients. However, it still remains unclear whether prophylactic preoperative anticonvulsive treatment is reasonable. The STAMPE2 score has been implemented by Wirsching et al. to estimate the postoperative seizure-risk. We aimed to evaluate this score in our independent cohort.

Methods

In total 556 patients (female 375 / male 181) were included. WHO grade at primary resection in 331 patients was grade I, in 197 patients grade II and in 9 patients grade III. Recurrences were also included as well. Modified STAMPE2 score was applied to our cohort and points were added as follows: Sensorimotor deficit (1pt), tumor progression (1pt), age < 55 years (1pt), major surgical complication (2pts), preoperative epilepsy (2pts) and edema (1pt).

Results

In our cohort, 58 patients showed tumor recurrence after a mean of 36 months (range 3 – 277 months) and 82 of all patients developed postoperative seizures. Setting a cut off at 4 points there was a significant difference in the occurrence of postoperative seizures between the two groups ($p < 0.0001$, seizure risk 23% vs 49%). The seizure free survival and thus the occurrence of either early or late seizures did not correlate with the STAMPE2 score.

Conclusion

Investigating the STAMPE2 score on an independent cohort underlines that it is well suitable to estimate the seizure risk of meningioma patients and should be taken to design further studies for prophylactic anticonvulsive treatment in meningioma patients.

Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P135

Evaluation von Referenzgenen für RT-PCR Analysen in Meningiomen in Abhängigkeit der Therapie und des Tumorgades

Evaluation of reference genes for real-time quantitative RT-PCR analysis in meningiomas with respect to treatment status and histopathological tumour grade

M. Kauke, B. Krschek, R. H. Goldbrunner, M. Timmer

Universitätsklinikum Köln, Klinik für Neurochirurgie, Köln, Germany

Objective

Gene expression profiling of brain tumors has yielded valuable information about prognostic markers and bears great value for improving patient individualized clinical management. Real-time quantitative RT-PCR is a reliable method that allows parsing the transcriptome of neoplastic material. Normalization genes that are stable under the influence of e.g. tumor grade and treatment status are important to avoid misinterpretation of gathered transcriptomic data.

Methods

We tested a batch of six commonly used reference genes (ACTB, GAPDH, MRPL19, SDHA, EIF2B1, RPL37A) with respect to the expression stability and variation under the influence of tumor grade (WHO[°]I-III) and treatment status (naïve vs. recurrent) in 52 tissue samples. Seven groups were selectively investigated and subjected to comparative analysis: naïve WHO[°] I; recurrent WHO[°] I; naïve WHO[°]II; recurrent WHO[°] II; naïve WHO[°]III; recurrent WHO[°]III and control tissue.

Results

The expression of the reference genes was heterogeneous across all experimental groups with RPL37A and MRPL19 showing the highest and ACTB and EIF2B1 showing the lowest inter- and intra-group variability. Treatment naïve meningiomas showed a tendency for higher relative expression of the reference genes when compared to control and recurrent meningiomas. Across all experimental groups, a combination of GAPDH and EIF2B1 showed the highest stability value as determined by the NormFinder algorithm.

Conclusion

Tumor grade and treatment status seem to influence the expression of ACTB, GAPDH, MRPL19, SDHA, EIF2B1, and RPL37A. Reference genes should be carefully chosen with respect to tumor grade and treatment status in order to avoid misinterpretation of qPCR data in meningioma tissue samples.

Neuroonkologie – Meningeome und andere Entitäten I/*Neurooncology – meningiomas and others I*

P136

Analyse und Weiterentwicklung eines verbalen Gedächtnistests für die Verlaufsbeobachtung deutschsprachiger Hirntumorpatienten *Verbal learning memory testing for longitudinal assessment of German brain tumour patients*

D. Klütsch¹, K. Jonas², C. Schröter¹, R. H. Goldbrunner¹, C. Weiß Lucas¹, N. 1. Studiengruppe^{1,3,4,5,6,7,8,9,10,11,12,13}

¹Universitätsklinikum Köln, Zentrum für Neurochirurgie, Köln, Germany

²Universität zu Köln, Humanwissenschaftliche Fakultät, Abteilung Heilpädagogik und Rehabilitation, Köln, Germany

³Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

⁴Universitätsklinikum Würzburg, Neurochirurgische Klinik und Poliklinik, Würzburg, Germany

⁵Universitätsmedizin Mainz, Neurochirurgische Klinik und Poliklinik, Mainz, Germany

⁶Universitätsklinikum Carl Gustav Carus Dresden, Klinik und Poliklinik für Neurochirurgie, Dresden, Germany

⁷Donau Isar Klinikum, Neurochirurgie, Wirbelsäulenchirurgie, Interventionelle Neuroradiologie, Deggendorf, Germany

⁸Universitätsklinikum Regensburg, Neurochirurgie, Regensburg, Germany

⁹HELIOS Kliniken Schwerin, Neurochirurgie und Wirbelsäulenchirurgie, Schwerin, Germany

¹⁰Klinikum Chemnitz gGmbH, Klinik für Neurochirurgie, Chemnitz, Germany

¹¹Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

¹²Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Lübeck, Germany

¹³Universitätsklinikum Heidelberg, Klinik für Neurochirurgie, Freiburg, Germany

Objective

Due to its relative simplicity in comparison to other verbal learning memory tests (VLMT) the revised Hopkins VLMT (HVLMT-R) is used most often for the assessment of brain tumour patients. The German version of the HVLMT-R consists of a translation of the original English HVLMT-R, using exactly the same items – without acknowledging language-specific linguistic parameters of standardization. We analysed the comparability of the parallel German word lists regarding different levels of word processing and memorization.

Methods

Ninety patients with primary glioblastoma ($m = 53$, age range: 24-81 years) were included. Two different parallel versions of the HVLMT-R consisting of twelve nouns grouped in three semantic categories were administered to the patients on two consecutive days. After three learning trials with immediate recall, delayed recall and word recognition (from a read-out list of 24 items including 12 distractors) were assessed. Kendall's rank correlation coefficient b was calculated to compare the test results between parallel versions.

Results

In a descriptive linguistic analysis the German wordlists of the HVLMT did not conform to parallelized item sets concerning linguistic parameters (e.g. number of syllables, word frequency, morphological and/or phonological complexity, lexicosemantic ambiguity) e.g., the total number of syllables varies between 18 and 30 and mean word frequency ranges from 5.25 to 28.9. The retest-reliability for the overall learning trial as well as for the late recall trial showed a moderate correlation ($b=0.5 - 0.6$; $p<0.001$), whereas the retest-reliability for the percentage of retention was weak ($b=0.40$, $p<0.001$).

Conclusion



Our preliminary results support our hypothesis that the translated parallel versions of the HVLMT-R do not compare well regarding linguistic parameters, which might be one major reason for a only weak to moderate parallel-test reliability. This underlines the need for a linguistically standardized construction of native-language based word lists. Such alternative, parallelized word lists developed by our group are currently under pre-clinical evaluation.

Neuroonkologie – Meningeome und andere Entitäten I/Neurooncology – meningiomas and others I

P137

Konfokale Laserendomikroskopie– eine histologische Gegenüberstellung seltener Tumore *Confocal laser endomicroscopy – a histological work-up of rare tumours*

D. Breuskin, J. Oertel

Universitätsklinikum des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

Objective

Confocal laserendomicroscopy (CLE) is a novel investigational technique in neurosurgery. Since the clarification of tumour histology during surgery can be crucial, neurosurgeons need to rely on frozen sections in order to gain a first evaluation. Confocal laserendomicroscopy allows neurosurgeons to evaluate tissue on a microscopic level and gain first estimates of what tumour entity is present. While we have already presented data on more common tumour entities, we aim at providing information on tumours that are rarer and could pose more difficulties for evaluation.

Methods

We have investigated 306 cases of CNS tumours with CLE. Of these, we present cases of the rarer tumor types, namely paraganglioma (n=1), pituitary adenoma (n=7), AVM (n=2), cavernoma (n=4), lymphoma (n=4), plexuspapilloma (n=1), gliosarcoma (n=1) and neuroblastoma (n=1) together with the histological work up in order to make this technology more comprehensible as well as more approachable.

Results

We were able to compare confocal laserendomicroscopic data with histological HE stained specimen in order to evaluate the images. Our work up highlights the specific characteristics of these different tumour types and draws parallels in order to make the correct diagnostic choice.

Conclusion

Confocal laserendomicroscopy can help neurosurgeons to acquire first information on tumour entities before frozen sections are available. As soon as some knowledge and experience are acquired, CLE may become a strong complementary tool for neurooncological surgery.

Neuroonkologie – Gliome II/Neurooncology – Gliomas II

P138

Intratumorale Heterogenität der dielektrischen Eigenschaften beim Glioblastom *Intratumoral heterogeneity of dielectric properties in glioblastoma*

M. Proescholdt¹, J. Falter¹, A. Haj¹, C. Doenitz¹, A. Brawanski¹, P. Eberl¹, A. Lohmeier², E. M. Störr², Z. Bomzon³, H. S. Hershkovich³

¹Universitätsklinikum Regensburg, Neurochirurgie, Regensburg, Germany

²Universitätsklinikum Regensburg, Klinik und Poliklinik für Neurochirurgie, Regensburg, Germany

³Novocure GmbH, Haifa, Israel

Objective

Recently, tumor treating fields (TTFields) were established for the treatment of newly diagnosed glioblastoma (GBM). One of the most crucial parameters defining the treatment efficacy of TTFields is the electric field intensity, which depends on the dielectric properties of the tumor tissue. In this study we determined the dielectric properties of GBM by analyzing resected tissue following a fast acquisition protocol. To account for the intratumoral heterogeneity, different regions of the tumor were analyzed separately.

Methods

A cohort of 38 patients with newly diagnosed GBM were analyzed. Tissue samples were acquired from the vital tumor area and perinecrotic compartment. The tissue was measured immediately to avoid artifacts. A fragment was dissected from each tissue sample and was placed into a cylindrical cell with a known diameter. The impedance was recorded at frequencies 20Hz-1MHz using a software specifically developed for this study, which controls the LCR meter. The measured impedance was translated into dielectric properties of the sample (conductivity and relative permittivity) based on the parallel plate model, the recorded complex impedance and the geometry of the samples. Each tissue sample was fixed, and stained with H&E to visualize cellularity, luxol fast blue to analyze the myelinated fiber content and factor VIII related antigen to assess tumor vascularity.

Results

We found significant differences between the conductivity and permittivity of tissue samples from each individual tumor (mean conductivity [S/m]: 0.302; range: 0.607 – 0.100; mean permittivity [Farad/m]: 3519.8; range: 11182.5 – 135.7). Consistently, the perinecrotic areas displayed lower conductivity values compared to the solid tumor compartments. Histological analysis revealed significantly higher cellularity and lower myelinated fiber content in tissue samples with high conductivity and permittivity.

Conclusion

The dielectric properties of GBM show a high intratumoral heterogeneity which correlates with the extent of cellularity and myelin fiber content within the tissue.

Neuroonkologie – Gliome II/Neurooncology – Gliomas II

P140

Intraoperative mechanische Vermessung der Gewebemechanik von Gehirntumoren *Intraoperative mechanical measurement of tissue biomechanics in brain tumours*

M. Matthiae¹, J. Kren¹, D. Theisen-Kunde², R. Brinkmann^{2,3}, S. Buschschlüter⁴, M. M. Bonsanto¹

¹Universitätsklinikum Schleswig-Holstein, Abteilung für Neurochirurgie, Lübeck, Germany

²Medizinisches Laserzentrum Lübeck GmbH, Lübeck, Germany

³Universität zu Lübeck, Institut für Biomedizinische Optik, Lübeck, Germany

⁴Söring GmbH, Quickborn, Germany

Objective

Tactile intraoperative information is important for the neurosurgeon's decision in tumor surgery. The haptic experience together with visual inspection through the microscope enables the surgeon to distinguish tumor tissue from healthy brain tissue. In this study, a standardized intraoperative indentation measurement is carried out to detect elasticities of tumor tissue quantitatively. This study is part of a comprehensive BMBF project (FKN: 13N14664) aimed at optimizing the resection of brain tumors through novel solutions, while minimizing surgical risks of functional damage.

Methods

In vivo-detected tumor elasticities of fresh tissue samples are measured within 5 minutes directly in the operating room. For this purpose, a metallic test specimen with cylindrical dimensions is pressed into the soft tissue and the counterforce is determined with respect to indentation depth. An objective measure of tumor elasticity is Young's modulus which is determined by indentation for different specimens of each tumor. The resulting elasticities are correlated with neuropathological tissue properties, preoperative MRI imaging and the tactile impressions of the surgeon.

Results

The indentation measurements are carried out on gliomas, metastases and meningiomas. There is a strong heterogeneity of local elasticity within each tumor. Generally, however, there is a systematic link between measured tumor elasticities and tactile findings. The intraoperative mechanical elasticity measurements of this study open up possibilities for distinguishing between healthy and tumor tissue. It is thus an alternative method to established intraoperative online elastographic ultrasound and MR elastography.

Conclusion

As far as the current scientific state of the art is concerned, there is no elastic data from indentation measurements of brain tumors measured in vivo. Thus, for the first time, such a reference system for tumor elasticity in brain tumors is to be established, which is the basis for an automated intelligent intraoperative detection of tumor tissue. For example, the automated adaptation of the supplied ultrasound energy during the resection of brain tumors is a possible application.

Neuroonkologie – Gliome II/Neurooncology – Gliomas II

P142

Ein neuartiges Glioblastom-Invasionsmodell unter Verwendung menschlicher Hirnschnittkulturen *A novel glioblastoma invasion model using human brain slice cultures*

V. M. Ravi, K. Joseph, N. Neidert, J. Beck, U. G. Hofmann, O. Schnell, D. H. Heiland

Universitätsklinikum Freiburg, Klinik für Neurochirurgie, Freiburg, Germany

Objective

Over the past several decades, therapies to combat malignant glioma that appeared promising in mice models have failed during clinical trials amongst others due to the differences encountered during translation of research from model organisms to humans. To partially mitigate these difficulties in translation, we present a human cortical organotypic culture based GBM model, which allows us to manipulate individual components of the tumour environment in order to investigate the influence of different cell types in the immunosuppressive tumour microenvironment.

Methods

Human neocortical tissue (at least 2 cm away from the tumour core) or entry cortex from epilepsy surgery, was cultured for up to 21 days post resection using advanced culture conditions. The cultured tissue was further injected with patient derived human GBM cells to create an *ex vivo* human model of glioblastoma. The role of astrocytes in tumour microenvironment was studied using a microglia loss of function model. Tumour growth was monitored using fluorescence microscopy and microglia crosstalk was studied using flow cytometry and RNA-sequencing analysis.

Results

Our data corroborate differences between astrocytes in human and murine models in different reactive states, showing that the glioblastoma microenvironment is difficult to be accurately modelled using murine models. Results from microglia depletion showed ample evidence of crosstalk between GBM cells, astrocytes and microglia showing the increased intensity of anti-inflammatory cytokine IL-10 and TGF β when microglial depletion was carried out.

Conclusion

This model therefore has potential applications to the fields of neuroscience, neuro-oncology and pharmacotherapy.

Neuroonkologie – Gliome II/Neurooncology – Gliomas II

P143

Funktionelle Reorganisation von kortikalen Motorik-Arealen in Gliom-Patienten untersucht mit navigierter transkranieller Magnetstimulation

Functional reorganisation of cortical motor areas in glioma patients as examined by navigated transcranial magnetic stimulation

S. Ille, M. Grziwotz, A. Schröder, B. Meyer, S. Krieg

Technische Universität München, München, Germany

Objective

Glioma-induced functional reorganization (FR) is recently being discussed more frequently. However, there are only a few prospective longitudinal studies. The present study therefore investigates FR of cortical motor areas after the resection of motor-eloquent gliomas by navigated transcranial magnetic stimulation (nTMS).

Methods

We included 10 patients (mean age 49 ± 16 years) with motor-eloquent gliomas (6 low- and 4 high-grade) scheduled for microsurgical resection. nTMS motor mappings and measurements of clinical motor function were performed preoperatively as well as 3, 6, and 12 months after surgery.

Results

Functional motor areas in terms of nTMS motor mappings shifted in comparison to the preoperative situation on the antero-posterior axis within the same hemisphere (mean 8.2 ± 2.1 mm), and away from the resection cavity. The shifting was mainly observed at the 3 and 6 months follow-up but also continues 12 months after surgery. We also found a shift of the motor function to the unaffected hemisphere in one patient, resulting in a right-sided cortical area showing nTMS-induced motor evoked potentials (MEPs) of right-sided hand muscles. The excitability of the motor system, measured by the resting motor threshold (rMT), has shown to be very robust and reproducible in case of an intact motor system (mean difference 4.27 V/m). In contrast, the rMT decreased in patients with an improvement of clinically investigated motor function and increased in those, who showed a worsening motor function postoperatively (mean difference 12.82 V/m).

Conclusion

Our preliminary results show that nTMS is an appropriate technique to visualize FR in glioma patients. Further patients must be investigated to confirm these first results and to draw further conclusions on the impact of FR and plasticity.

Neuroonkologie – Gliome II/Neurooncology – Gliomas II

P144

Tumor-infiltrierende Effektor-T-Zellen und falsch-positive Diagnose eines Tumorprogresses im MRT und 18FET-PET nach Vakzinierung mit dendritischen Zellen bei Patienten mit neudiagnostiziertem Glioblastom
Tumour-infiltrating effector T-cells and false-positive identification of tumour progression by MRI and 18FET-PET after dendritic cell vaccination in newly-diagnosed glioblastoma patients

M. Rapp¹, A. Datsi², J. Felsberg³, N. Galldiks⁴, M. A. Kamp¹, R. V. Sorg², M. Sabel¹

¹Universitätsklinikum Düsseldorf, Neurochirurgie, Düsseldorf, Germany

²Universitätsklinikum Düsseldorf, Institut für Transplantationsdiagnostik und Zelltherapeutika, Düsseldorf, Germany

³Universitätsklinikum Düsseldorf, Institut für Neuropathologie, Düsseldorf, Germany

⁴Universitätsklinikum Köln, Neurologie, Köln, Germany

Objective

In the phase II GlioVax trial, patients with newly diagnosed glioblastoma are treated with dendritic cell vaccination as add-on to standard radiochemotherapy after fluorescence-guided surgery. Currently, it is not clear, whether dendritic cell vaccination results in effector T cell infiltration of the tumor, whether such infiltrates may mimic tumor progression and whether 18FET-PET imaging may contribute to discriminate progression from an immune response. Therefore, vaccinated 3 patients with suspected tumor recurrence based on MRI have been studied.

Methods

In the event of suspected tumor recurrence based on MRI, vaccinated patients received additional 18FET-PET imaging. When tumor recurrence was confirmed, patients were subjected to surgery and tumor samples assessed histopathologically. In addition, tumor-infiltrating lymphocytes were isolated immunomagnetically and expression of interferon- γ as well as transcription factors (T-bet, FoxP3, GATA3) was determined by flow cytometry.

Results

After diagnosed tumor recurrence by MRI, 3 patients received additional 18FET-PET imaging. In 1 patient, it did not confirm recurrence, whereas in 2 of the patients, tumor recurrence was apparently confirmed and patients subjected to surgery. Histopathological examination, however, did not confirm tumor progression, but revealed therapy induced changes. Patients showed high frequencies of CD4+ (40.9/31.9%) and CD8+ (53.6/37.8%) interferon- γ producing tumor-infiltrating T cells, which express the transcription factor T-bet, but not FoxP3 or GATA3. In non-vaccinated patients, such cells were present in low frequencies only (1-5%). This indicates that infiltrating TH1 and Tc1 effector T cells are present in the tumor after vaccination.

Conclusion

Dendritic cell vaccination appears to result in a substantial infiltration by interferon- γ producing TH1 and Tc1 effector T cells. The presence and activity of these effector T cells may lead to a misinterpretation of MRI (pseudoprogression), which not in all cases can be resolved by additional 18FET-PET imaging.

Neuroonkologie – Gliome II/Neurooncology – Gliomas II

P145

Intraoperatives Neuromonitoring – hochfrequente monopolare Stimulation versus 60 Hz Stimulation für eloquent gelegene Hirntumore – ein chirurgisches Assessment

Relevance assessment of intraoperative neuromonitoring-monopolar stimulation combined with 60 Hz or 60 Hz stimulation only

F. Staub-Bartelt, M. Rapp, D. Hänggi, H. J. Steiger, M. A. Kamp, M. Sabel

Universitätsklinikum Düsseldorf, Neurochirurgie, Düsseldorf, Germany

Objective

Intraoperative neuromonitoring (IONM) is required for resection of eloquently located cerebral lesions. Speech monitoring with bipolar stimulation is widely used during awake surgery, whereas monopolar stimulation in combination with extended IONM including SSEP, MEP and ECG monitoring most frequently is applied for motor mapping in asleep patients. In our neurooncological department both techniques are used either combined or separately for surgery of eloquent brain tumours. Here, we present data concerning assessment of intraoperative relevance of both techniques.

Methods

We prospectively enclosed data of all patients undergoing surgery using any IONM method between 01/19-11/19 (n=104). Retrospectively evaluation of relevance of the chosen intraoperative techniques was conducted. Postoperative neurological outcome and grade of resection evaluated by post-OP MRI were analysed as proof of concept.

Results

68% of the patients underwent awake surgery. Awake surgery with 60 Hz stimulation only was assessed to be adequate in 24 % (n=25) mostly in strict left temporal lesions. 43 % (n=45) of the surgeries required either planned or additional monopolar stimulation or extended IONM mostly due to lesions of the right hemisphere in planned non-awake surgeries or non-adequate awake patients in awake surgery. In 20 % of the patients (n=21) combination of both methods was evaluated as useful or relevant mostly in patients when monopolar stimulation only showed indifferent results or lesions were located parietotemporal. In 13 % (n=13) none of the methods were relevant mostly due to indifferent or intraoperative loss of IONM signals or non-adequate awake patients when speech testing was obligate. 4 patients (4%) suffered from a permanent deficit linked to resection. Complete resection was intraoperatively evaluated in 77 patients (79%), after matching with post-OP MRI 16% showed a residual tumor volume.

Conclusion

Adequate IONM techniques depend on various factors such as localisation, required testing parameters and patients' compliance. Monopolar stimulation was found to be essential for eloquent tumours of the right hemisphere in non-awake or inadequately awake patients for motor mapping. 60 Hz stimulation only was sufficient for strict temporal lesions without vessel conflicts. Combination was useful in patients with parietotemporal lesions or when monopolar motor mapping showed indifferent results. Extended IONM was only crucial in lesions conflicting cerebral vessels.

Neuroonkologie – Gliome II/Neurooncology – Gliomas II

P146

Operative Therapie von intraventrikulären, neuroepithelialen Tumoren *Surgical treatment of intraventricular neuroepithelial tumours*

A. K. Aftahy¹, M. Barz¹, P. Krauss¹, F. Liesche², B. Wiestler³, S. E. Combs⁴, C. Straube⁴, B. Meyer¹, J. Gempt^{1,5}

¹Klinikum rechts der Isar München, Klinik und Poliklinik für Neurochirurgie, München, Germany

²Klinikum rechts der Isar München, Abteilung für Neuropathologie am Institut für Pathologie, München, Germany

³Technische Universität München, Neuroradiologie, München, Germany

⁴Klinikum rechts der Isar München, Klinik und Poliklinik für Strahlentherapie, München, Germany

⁵Klinikum rechts der Isar München, Neurochirurgische Klinik und Poliklinik, München, Germany

Objective

Intraventricular neuroepithelial tumors (IVT) are rare lesions, such as ependymomas (EP), subependymomas (SE) and central neurocytomas (CN). The treatment of choice is neurosurgical resection. Here we describe a large series of IVTs, postoperative outcomes and surgical approaches.

Methods

We included patients that underwent resection of an IVT (between 3/2009 – 05/2019) emphasizing on surgical approach, extent of resection, clinical outcome and perioperative complications.

Results

45 IVTs were resected from 03/2009-05/2019: 13 EP, 21 SE, 10 CN and one gliependymal cyst (GEC). Median age was 52,5 (±17,1) years with 25 (55,6%) male and 20 (44,4%) female patients. Complete removal was achieved in 42/45 cases (93,3%), 84,6% (11/13) EP, 100% (21/21) SE, 90% (9/10) CN and one GEC. Rate of postoperative new neurological deficits was 26,6% (12/45), from which 58,3% were permanent during follow-up. Postoperative KPS was 90% (IR 80-100). 14 (31,1%) patients improved, 22 (48,9%) remained unchanged and nine (20%) declined. Adverse events rate was 20%. One patient with 4th ventricle SE died due to central lung artery embolism. Rate of shunt-dependent hydrocephalus was 13,3% (6/45). Mean follow-up was 26,9 (±30,1) months. 20 frontal-keyhole, 22 median suboccipital telovelar and three other approaches were performed. No statistically significance was detected regarding predictive factors and approaches.

Conclusion

Our surgical findings emphasize complete resection both safe and feasible, if institutional experience is given. Satisfying long-term survival and cure is possible by complete removal. Gross total resection should always be performed under function-remaining aspects due to mostly benign or slow growing nature of IVTs.

Neuroonkologie – Gliome II/Neurooncology – Gliomas II

P147

Analyse des Einflusses der Kortextemperatur auf die Patientenkognition während einer Wachoperation – Pilotstudie

Analysis of influence of cortex temperature on patient cognition during awake-surgery – a pilot study

J. Knipps, M. A. Kamp, M. Rapp, D. Hänggi, M. Sabel

Universitätsklinikum Düsseldorf, Neurochirurgische Klinik, Düsseldorf, Germany

Objective

During skull trepanning, it is possible to observe an intraoperative heat loss at the brain surface due to convection as well as thermal radiation. This effect is intensified involuntarily, when rinsing fluid adapts to room temperature during surgery, or intentionally, when cerebral seizures are stopped by active ice-water rinsing. However, the patient's active cognitive cooperation is essential, especially during awake phase. The aim of this pilot study is to investigate the influence of cortex temperature on cognition during awake-surgery.

Methods

During an awake-surgery, the complete course of the cortex's temperature was analysed continuously by an imaging camera. This was performed with 8 patients at a total of 52 measuring points. The body's core and the cortical temperature changes were determined over time – split into phases where no water, warm flush (36°C) or ice water was used. As a surrogate for the cognitive performance of patients, a reaction time test was performed intraoperatively on the patient.

Results

During the first measurement the cortex's temperature was 37.1°C (36.2-37.5°C). The cortex's surface temperature approached room temperature (median: 26.2°C) without proper regular irrigation (mean - 1.1°C in the first 10 min, mean - 2.4°C in the first 15 min).

Average reaction time was 742 milliseconds. At the same time, average reaction time at a cortex temperature < 35°C was 1421 milliseconds, at a cortex temperature 35°C 572 milliseconds ($p < 0.05$). At a cortex temperature < 35°C, reaction time improved again after rinsing with warm liquid.

Conclusion

Our pilot study suggests a continuous drop in the cerebral cortex's temperature during (awake) phase of surgery. Furthermore, the average reaction time correlated with the temperature of the cortex significantly. The brain's temperature may have significant impact on the cognitive performance of patients during the awake phase. This possible connection should be investigated in further studies.

Neuroonkologie – Gliome II/Neurooncology – Gliomas II

P148

Primäre und sekundäre Gliosarkome – Unterschiede bei der Behandlung und den Ergebnissen *Primary and secondary gliosarcoma – differences in treatment and outcome*

B. Hong¹, M. Lalk², B. Wiese², R. Merten¹, H. E. Heissler², P. Raab², C. Hartmann³, J. K. Krauss⁴

¹Medizinische Hochschule Hannover, Klinik für Strahlentherapie und Spezielle Onkologie, Hannover, Germany

²Medizinische Hochschule Hannover, Klinik für Diagnostische und Interventionelle Neuroradiologie, Hannover, Germany

³Medizinische Hochschule Hannover, Institut für Pathologie, Hannover, Germany

⁴Medizinische Hochschule Hannover, Klinik für Neurochirurgie, Hannover, Germany

Objective

Gliosarcoma - regarded as a rare variant of glioblastoma - has been observed in approximately 2% of patients with malignant gliomas. While treatment and outcome of patients with gliosarcoma has received more attention over the past decade, only few studies compared differences in primary versus secondary gliosarcoma. In this report we aimed to analyze the impact of surgical resection on the one hand and to evaluate outcome comparing patients with primary versus secondary gliosarcoma on the other.

Methods

Twenty patients underwent microsurgical resection for supratentorial gliosarcoma within a period of 10 years at our institution. Patients with primary gliosarcoma (n=10) were compared to patients with secondary gliosarcoma (n=10). Treatment history of gliosarcoma, including surgical resection and adjuvant postoperative therapy were retrospectively reviewed. Follow-up data, progression-free survival (PFS) and overall survival (OS) were evaluated.

Results

The mean age of patients with primary gliosarcoma was 60.0 ± 15.0 years, and that of patients with secondary gliosarcoma was 54.8 ± 12.2 years. The median follow-up time of all patients was 18 months. The median PFS in patients with primary gliosarcoma was significantly higher than in patients with secondary gliosarcoma (10.5 months vs. 4.0 months; $p=0.01$). The 6-month PFS rates were 80.0% in patients with primary and 30.0% in patients with secondary gliosarcoma. Upon recurrence, 6 patients with primary gliosarcoma and 4 patients with secondary gliosarcoma underwent repeat surgical resection. At the last follow-up, 18 patients had succumbed to the disease and 2 patients were still alive. The mOS of patients with primary gliosarcoma was significantly higher than that of patients with secondary gliosarcoma (13.5 months vs. 6.5 months; $p=0.01$). The 1-year and 2-year survival rate in patients with primary gliosarcoma was 70.0% and 20.0%, respectively, in patients with secondary gliosarcoma it was 10.0% and 10.0%, respectively. The mOS of patients with primary gliosarcoma who underwent repeated surgery for tumor recurrence was significantly higher than that of patients with secondary gliosarcoma (18 months vs. 8 months; $p=0.016$).

Conclusion

Patients with primary gliosarcoma benefit much more from surgical resection in comparison to those with secondary gliosarcoma who already presented with a recurrent tumor - both with regard to PFS and mOS. In case of tumor recurrence, patients with secondary gliosarcoma have an unfavorable prognosis with limited further options.

Neuroonkologie – Gliome II/Neurooncology – Gliomas II

P149

Die vergleichende Transkriptom-Analyse von temozolomid-resistenten GBM-Stammzellen und GBM-Residiven offenbart Carbonic Anhydrase 2 (CA-2) als vorrangigen Resistenz-Faktor
Comparative transcriptomic analysis of temozolomide resistant GBM stem cells and recurrent GBM reveals carbonic anhydrase 2 (CA-2) as a major resistance factor

J. Bartsch¹, K. Zhao¹, R. Hannen¹, B. Carl¹, A. Pagenstecher², C. Nimsky¹

¹Philipps-Universität Marburg, Klinik für Neurochirurgie, Marburg, Germany

²Philipps-Universität Marburg, Neuropathologie, Marburg, Germany

Objective

About 95 % of GBM patients show tumor relapse leaving them with limited therapeutic options as recurrent tumors are often resistant to temozolomide (TMZ). GBM-like stem cells (GSCs) are considered to be the major obstacle in therapy resistance, so that characterization of their response to TMZ is helpful in identifying genes associated with TMZ resistance.

Methods

GSCs were isolated from GBM patients (n=5) and characterized by IF-staining for GFAP and Nestin. GSCs from 3 different GBM patients were continuously exposed to TMZ treatment similar to patient treatment intervals (10 mM, 5 out of 7 days) over a period of 20 weeks. Dose-response curves were generated to determine IC50 values for TMZ. RNAs from resistant cell clones were subjected to RNA sequencing. Expression changes of candidate genes were analyzed by qPCR, western blotting, and immunohistochemistry in resistant GSCs and in matched patient samples (GBM vs. recurrent GBM).

Results

RNA sequencing analysis revealed 49 genes dysregulated in TMZ resistant cell clones. By qPCR analyses of the most prominent 10 genes (up- or downregulated), we found that only the gene encoding for Carbonic Anhydrase 2 (CA-2) was consistently upregulated in all GSCs cell clones and in recurrent GBM vs. GBM. Further analyses confirmed a strong expression of CA-2 in GBM tissue and in GSCs. No expression of CA-2 was observed in differentiated patient-derived GBM cell lines. This also applies for other CAs identified in GBM such as CA-9 and CA-12. Furthermore, we used an inhibitor for Carbonic Anhydrases, Acetazolamide (ACZ) in conjunction with TMZ and observed a significant sensitization of GSCs ($p < 0.01$) for TMZ in all GSCs cell lines tested.

Conclusion

To minimize the occurrence of GBM recurrence, it is essential to eliminate GSCs, which are particularly resistant to standard therapy. Here we provide a rationale for a specific and potent inhibition of Carbonic Anhydrase 2 as a means to optimize the existing chemotherapy of GBM.

Neuroonkologie – Gliome III/Neurooncology – Gliomas III

P150

Chirurgische Behandlung von WHO Grad I Gliomen – Bedeutung der Tumorlokalisation auf das Outcome *Surgical treatment of WHO grade I gliomas – implications of tumour localisation on outcome*

M. Scherer¹, C. Jungk¹, A. El-Damaty¹, M. Bendszus², A. W. Unterberg¹

¹Universitätsklinikum Heidelberg, Heidelberg, Germany

²Universitätsklinikum Heidelberg, Heidelberg, Germany

Objective

WHO grade I intracranial gliomas are usually referred to as benign tumors and complete surgical resection is supposed to improve outcome. Unlike other types of glioma however, WHO^oI tumors often affect patients at a younger age and are preferentially located within the posterior fossa (PF) which renders surgical treatment particularly demanding. This study assessed surgical and clinical outcome in WHO^oI gliomas with emphasis upon PF tumors.

Methods

We retrospectively reviewed all consecutive WHO^oI glioma resections from 06/2009-12/2017 at our institution. All resections were done under 1,5 tesla intraoperative MRI guidance. Extent of resection (EOR) was assessed volumetrically under consideration of cystic/solid proportions and T1 and FLAIR lesion size. Progression free survival times (PFS, either clinically or radiologically) of supratentorial and PF tumors were compared and Kaplan-Maier and multivariate Cox regression was calculated for the variables of PFS.

Results

We identified 76 WHO^oI gliomas (53 pilocytic astrocytomas, 13 gangliogliomas, 6 DNETs, 4 subependymomas) with 29 (38%) located in the PF. Median age was 16 (range 1-73), 75% of cases were <25y at the time of surgery. Compared to supratentorial lesions, PF tumors were younger (mean age 16.2±13.6y vs. 25.3±16.6y, p=0.009), more often cystic (66% vs. 38%, p=0.017), more likely to show new neurologic symptoms postoperatively (28% vs. 15% p<0.0001) as well as at the 3-month follow-up (6% vs. 2%, p<0.0001) and had more wound complications (29% vs. 6%, p=0.018), respectively. EOR was comparable according to T1w images (97% vs. 96%, p=0.58) and FLAIR images (94% vs. 94%, p=0.77). PF tumors showed significantly longer mean PFS (93.6m vs. 64.0m, p=0.006). In multivariate regression, supratentorial location (OR 51.7, 95% C.I. 4.4-606.2, p=0.002) and age <18y (OR 9.9, 95% C.I. 1.8-54.3, p=0.008) were independently associated with earlier progression. Histology, recurrent tumors or EOR were not associated with PFS.

Conclusion

We evaluated the surgical treatment of WHO^oI gliomas corroborating PF resections to be more complex procedures with higher postoperative morbidity. However, we observed marked discrepancies in PFS despite a comparable EOR in favor of PF tumors. This implies that there is a probability for differences in the biologic behavior between tumors in the PF and supratentorial tumors within the benign histology of these gliomas. Careful monitoring and evaluation of adjuvant treatment options might be warranted particularly in younger patients with supratentorial WHO^oI gliomas.

Neuroonkologie – Gliome III/Neurooncology – Gliomas III

P151

Präoperative Einschätzung des Risikos von Kurzzeitüberleben bei Glioblastom-Patienten – der SHORT score *The SHORT score for preoperative assessment of the risk for short-term survival in glioblastoma*

D. Pierscianek¹, Y. Ahmadipour¹, K. Kaier², M. Darkwah Oppong¹, A. Michel¹, S. Kebir³, M. Stuschke⁴, M. Glas³, U. Sure¹, R. Jabbarli¹

¹Universitätsklinikum Essen, Klinik für Neurochirurgie und Wirbelsäulenchirurgie, Essen, Germany

²Albert-Ludwigs-Universität Freiburg, Institut für Medizinische Biometrie und Medizinische Informatik, Freiburg, Germany

³Universitätsklinikum Essen, Klinik für Neurologie, Abteilung für Klinische Neuroonkologie, Essen, Germany

⁴Universitätsklinikum Essen, Klinik für Strahlentherapie, Essen, Germany

Objective

Despite recent improvements in treatment of glioblastoma (GBM), some patients still show a short survival. In this study, we sought to develop a new risk score for preoperative assessment of short-term survival (STS, < 6 months) in GBM patients.

Methods

All adult patients, who underwent surgical resection of GBM between 2004 and 2014 were included (n=379). Various demographic and clinical parameters, which are available at admission, were assessed. Variables were evaluated in univariate and multivariate analyses. The score was validated in a separate GBM cohort selected for biopsy (n=170).

Results

The following independent predictors of STS were integrated into a new score: body height (*Small*, <169 cm, 1point), arterial *Hypertension* (1point), patients' age (*Older*: ≤54 years – 0points, 55-74 years – 1point, ≥75 years – 2points), and poor clinical status (*Reduced* Karnofsky performance status scale: ≤60% – 2points, 70-80% – 1point, ≥90% – 0points). Therefore, the new risk score (**SHORT [Term]**) ranged from 0 to 6 points and showed a good accuracy of risk estimation for STS in GBM (AUC: 0.715). STS rates were 9.7%, 23.1% and 70% in GBM patients scoring <2 points, 2-4 points and >4 points respectively ($P<0.0001$). The score was successfully validated (AUC: 0.792).

Conclusion

This study suggests a new risk score for preoperative assessment of STS risk in GBM patients. Still, this risk score needs external validation in larger patients' cohorts. Our score might be a tool to facilitate treatment decisions in GBM patients prior to surgery.

Neuroonkologie – Gliome III/Neurooncology – Gliomas III

P152

Sicherheit und Operationsdauer – roboterassistierte Serienbiopsie und klassische Stereotaxie im Vergleich *Safety and time efficiency of robot-guided surgery versus classic frame-based stereotaxy*

A. Spyranthis¹, J. Quick-Weller¹, A. Cattani¹, L. Willems², T. Woebbecke¹, A. Constantinescu¹, V. Seifert¹, T. Freiman¹

¹Johann Wolfgang Goethe-Universität Frankfurt am Main, Neurochirurgie, Frankfurt am Main, Germany

²Johann Wolfgang Goethe-Universität Frankfurt am Main, Neurologie, Frankfurt am Main, Germany

Objective

With the introduction of the robotic surgery assistant (ROSA) in our department in 2015, we have acquired an alternative to classic stereotactic surgery. In this study, we compare robot-assisted and stereotactic biopsies regarding safety and time efficiency for different intracranial target areas.

Methods

All patients who underwent guided biopsy from 01/2015 to 12/2018 were included, 148 patients had ROSA guided surgery, 258 patients were operated using the Leksell stereotactic frame. Referencing was carried out by a laser-scan of the face for the ROSA system and by thin-layer computer tomography (CT) for the Leksell frame.

Results

We performed 151 robot-guided biopsies in 148 patients. We identified 10 postoperative hemorrhages, 5 of them clinically silent. In 5 patients, neurological deficits due to postoperative hemorrhages were diagnosed (3%). The average overall procedure time including anesthesia was 169 min. With the Leksell frame, 266 stereotactic biopsies in 258 patients were performed. Complications included 20 postoperative hemorrhages, 8 of them relevant (3%). Seizures occurred in 2 patients (< 1%) and wound infections in 3 patients (1%). The average time was significantly longer and amounted to 179 min ($p = 0,01$). Particularly interesting was the fact that robot-guided surgery required significantly less time in the biopsy of temporal targets (161 min, $n = 25$) than stereotactic surgery (188 min, $n = 39$), $p < 0,001$.

Conclusion

The procedure time could be shortened by using the ROSA system, in particular in temporal biopsies. The time saving is most likely due to the sparing of the transport to the thin-layer CT and its fusion. In particular, temporal biopsies are difficult to plan due to the positioning of the frame, which shall not interfere with the biopsy trajectory.

Neuroonkologie – Gliome III/Neurooncology – Gliomas III

P153

Tumorprogress bei unbehandelten Glioblastomen *Growth progression in untreated glioblastoma*

J. Kren, E. Ducho, M. M. Bonsanto

Universitätsklinikum Schleswig-Holstein, Neurochirurgie, Lübeck, Germany

Objective

Little is known about growth of glioblastoma. While meningiomas tend to grow proportionally slow, glioblastoma volume tends to explode in a short period of time. Since these tumours are highly aggressive, operative resection, if possible, should be planned shortly after diagnosis.

How long should a waiting period for glioblastoma resection be at most for optimal outcome?

Methods

In this retrospective, preliminary study the data of 102 patients were screened for diagnostic and pre-operative MRI-scans, which lay at least 7 days apart. Tumour volume was estimated in 27 cases. Diagnostic MRI-scans and pre-operative MRI-scans were compared. Volume was estimated using the BrainLab® cranial planning tool (Smart Brush). Waiting time and tumour growth were estimated, as were means and standard deviations (SD).

Results

In 27 cases, patients waited longer than 7 days for surgery, the least waiting time was 8 days, at most patients waited for 63 days. Mean and SD of waiting time between diagnostic MRI and pre-operative MRI were $21,33 \pm 12,75$ days. The mean age was 64 ± 12 years. Sizes of the tumours ranged from 0,18 to 55,9 cm³ with a mean of $21,48 \pm 16,12$ cm³ in diagnostic scans and from 0,8 to 56,1 cm³ with a mean of $25,99 \pm 17,92$ cm³ in pre-operative scans. 23 tumours grew significantly while 3 shrunk. Mean absolute growth was $4,5 \pm 7,59$ cm³ (from -16,6 cm³ to 25,9 cm³), while relative growth was $97,65 \pm 222,94$ % (from -54,6 to 1111,1 %). Correlation is moderately high with 0,57 between waiting time and tumour growth.

Conclusion

Not only time seems to determine tumour growth, but also factors, which are not visible in MRI scans. That is why an operative resection of possible glioblastoma should be planned as soon as possible to prevent exponential growth, which leads to greater neurological damage and could make resection quite more difficult. Further studies should focus on patient's outcome.

Neuroonkologie – Gliome III/Neurooncology – Gliomas III

P156

Das Volumen von niedriggradigeren Gliomen ist indirekt proportional zur Expression bestimmter molekularer Marker

Volume of lower-grade gliomas is inversely proportional to molecular features

A. Krigers, J. Kerschbaumer, M. Demetz, C. Thomé, C. F. Freyschlag

Medizinische Universität Innsbruck, Universitätsklinik für Neurochirurgie, Innsbruck, Austria

Objective

Volumetric expansion is known to be a prognostic factor for the survival of LGG patients. The aim of our study was to correlate incidental discovery of LGG with tumour volumetry and imaging parameters including the WHO grades, presence of anaplastic foci and molecular markers.

Methods

From our database we could identify 99 consequent patients with histologically proven lower-grade gliomas. All underwent their first resection in our institution. The volume on MRI was measured in T1 CE and native, T2, FLAIR and DWI sequences. Molecular markers, neuropathological, epidemiological and clinical data were analysed in correlation to volumetric assessment.

Results

In our series 47 (47%) tumours were diffuse (WHO°II), 16 (16%) showed focal anaplasia (WHO°II-III) and 26 (26%) were anaplastic (WHO°III). IDH1 was mutated in 51 (71%) and wildtype in 21 (29%) cases. ATRX was expressed in 34 (62%) and lost in 21 (38%) LGG samples. Patients with IDH1 mutation were significantly younger with a mean age of 41 years (SE ±2) vs. 53 years (SE ±4, p=0.004).

The tumours with IDH1 mutation showed significantly lower level of anaplastic features – 24/51 vs 16/21, p=0.007; and had a trend towards loss of ATRX expression 17/37 vs. 3/16, p=0.061. Surprisingly, no significant differences were found regarding EGFR expression.

IDH1 mutation demonstrated a significant impact on volume in preoperative MRI compared to wildtype: in T1 – median 34.6 cm³ vs. 14.0 cm³ (p=0.035); in T2 – 33.7 cm³ vs. 14.3 (p=0.012), in FLAIR – 46.5 cm³ vs. 18.4 cm³ (p=0.021). The contrast enhancement tended to be less advanced in IDH1 mutated tumours, however, this difference was not significant, p=0.093. The tumours with ATRX loss were significant larger on preoperative MRI scans and had less CE.

The extent of resection did not differ considering IDH1 or ATRX status with median complete resection and mean – 95% (SE ±3) for CE volumes and 83% (SE ±3) for not enhancing volumes in T1 sequence. Consequently, the resected volume of the tumour was larger in case of loss of ATRX expression and IDH1 mutation. In cases with IDH1 mutation the clinical PFS after the resection was significantly higher with a mean 77 months (SE ±4) vs. 59 months (SE ±2), p<0.05.

Conclusion

Tumour volumes were inversely proportional to molecular markers. IDHwt gliomas seem to be diagnosed earlier with lower volumes as compared to IDHmut. The extent of resection was uninfluenced by the molecular strata of the tumours.

Neuroonkologie – Gliome III/Neurooncology – Gliomas III

P157

"NanoPaste" zur Therapie von Glioblastom Rezidiven

"NanoPaste" therapy as potential treatment option for recurrent glioblastoma

M. Schwake, O. Grauer, M. Mütter, A. K. Bruns, S. Schipmann, W. Stummer

Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

Objective

We recently showed that intracavitary thermotherapy with superparamagnetic iron-oxide nanoparticles can induce persistent inflammatory reactions which might lead to long-term stabilization of recurrent glioblastoma (GBM) patients.

Methods

Here, we report data from a series of ten recurrent GBM WHO IV patients (IDH WT, MGMT: methylated 30%, unmethylated 70%; median age: 59 years) who were treated with intracavitary thermotherapy after coating the resection cavity wall ("NanoPaste") with NanoTherm® (MagForce AG, Berlin, Germany). All patients underwent six 1-hour semi-weekly hyperthermia sessions in an alternating magnetic field (mean maximum temperature 52.3° C (+/- 6.0 °C), and six patients also received concurrent radiotherapy at a dose of 39.6 Gy (5 x 1.8 Gy/week).

Results

No major side effects were observed during active treatment. However, all patients developed cerebral edema and increasing clinical symptoms during treatment follow-up (median 92 days, range 73 to 144). Patients were treated with dexamethasone and, if necessary, underwent re-surgery to remove nanoparticles (n=5). Histopathology revealed sustained necrosis and large amounts of nanoparticles without evidence for tumor activity and a proinflammatory reaction with increased T-cell and myeloid cell infiltration. Median overall survival (mOS) for the study population was 10.1 months (CI 95% 8.0 to 12.2). A survival advantage could be observed for patients who were treated at first recurrence (n=5) when compared to patients treated at the second recurrence or later (mOS = 20.6 vs 9.4 months). Patients, who received both thermotherapy and re-irradiation (n=6) had better mOS than patients treated with thermotherapy alone (17.3 vs 8.6 months). Two patients had long-lasting treatment responses > 23 months with one patient who is still alive 3.5 years after treatment without receiving any further therapy.

Conclusion

These results warrant further investigations. A European clinical registry will be set up to further evaluate the potential of "NanoPaste" therapy for patients with recurrent glioblastoma.

Fig 1

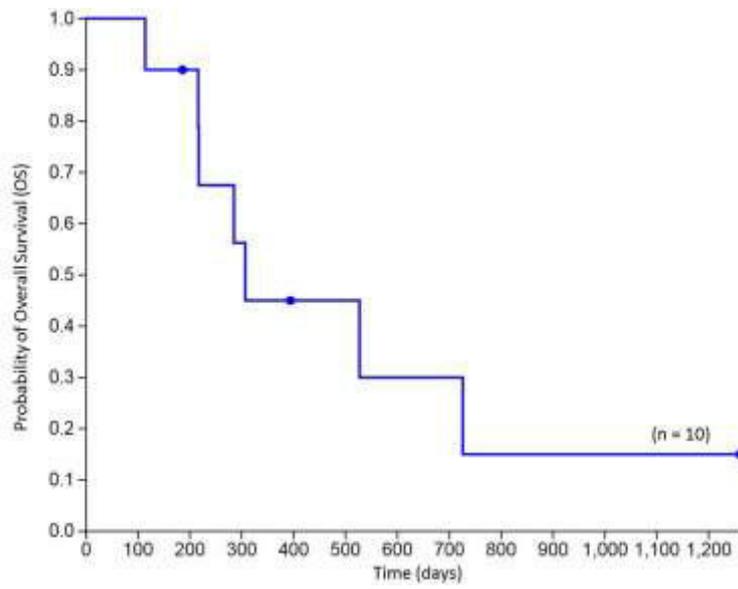
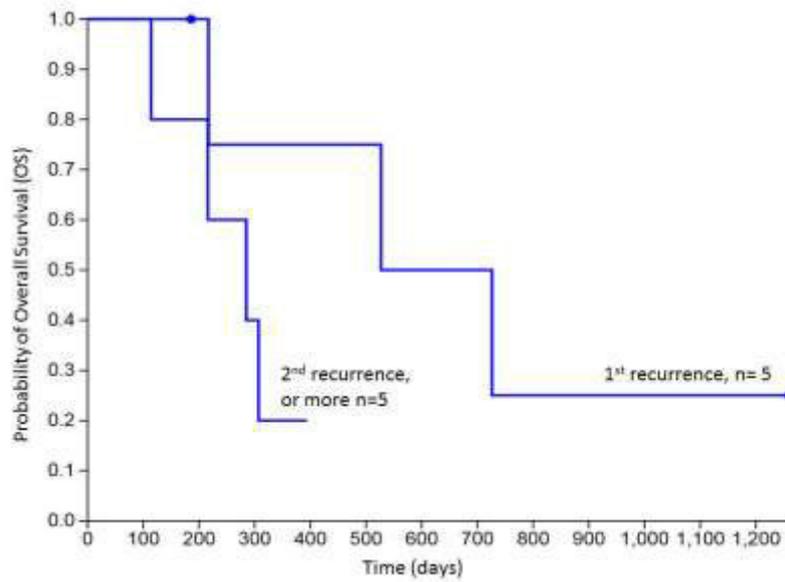


Fig 2



Neuroonkologie – Gliome III/Neurooncology – Gliomas III

P158

Synergistische Effekte der Blockade des CXCL2/CXCR2 Signalwegs und gleichzeitiger Temozolomid-Therapie im Glioblastoma multiforme als kombinierter Therapieansatz

Synergistic effects of blocking the CXCL2/CXCR2 pathway in combination with Temozolomide therapy in glioblastoma multiforme as a combined therapeutic approach

C. Jelgersma, J. Zollfrank, S. Brandenburg, P. Vajkoczy, G. Acker

Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

Objective

Blocking of the CXCL2/CXCR2 pathway has been shown to reduce glioma growth and the standard therapy Temozolomide (TMZ) is known to induce changes in this chemokine network in glioma cell lines. Thus, the aim of our study was to investigate possible synergistic effects of TMZ in combination with CXCR2 antagonist (SB225002).

Methods

GL261 glioma cells were implanted intracranially in C57/B6N mice and the treatments (Control with Aqua ad iniectabilia i.p., SB225002 via osmotic pump, TMZ i.p. and SB225002+TMZ; n= 7-8 per group) were initiated after 14 days and carried out for 7 consecutive days. Tumor volume was verified using MRI before and after the treatment period. Immunofluorescence staining was performed on the tumor tissue with focus on angiogenesis, tumor-associated macrophages (TAMs) and proliferation. One-way Anova with Bonferroni correction was used for statistical analysis ($p \leq 0.05$).

Results

Tumor volume was significantly reduced by 61% after TMZ and by 75% after combined treatment in comparison to control tumors on day 21 (mean volumes (in mm^3) were: control 30.22 ± 19.64 ; SB225002 alone: 16.04 ± 6.81 ; TMZ alone 11.75 ± 6.82 ; combination: 7.51 ± 2.97). The difference in tumor growth between the combination therapy and TMZ or SB225002 did not reach a significant level. The immunostainings showed significantly reduced proliferation in TMZ and combination group vs. control and combination vs. SB225002. Apoptosis, TAM accumulation and CXCL2/CXCR2 do not seem to be affected significantly by any of the treatments, while SB225002 induced alterations in tumor vascularisation. No side effects were observed amongst all treatment groups.

Conclusion

TMZ in combination with SB225002 was well tolerated and reduced the tumor volume significantly most likely due to impaired proliferation. However, as the impact of the combination therapy in comparison to TMZ alone was not impressive within the observation time, survival experiments are needed to clarify the real benefit of the combination treatment.

Neuroonkologie – Gliome III/Neurooncology – Gliomas III

P160

Die miRNA-181a reguliert die IDH1 Expression im Glioblastom und dient als prognostischer Marker für den klinischen Verlauf der Erkrankung

MiRNA-181a regulates IDH1 expression in glioblastoma and is a prognostic marker for the clinical course of the disease

C. Sippl¹, S. Louisa², R. Ketter², S. Urbschat², J. Oertel²

¹Universitätsklinikum des Saarlandes, Neuropathologie, Homburg, Germany

²Universitätsklinikum des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

Objective

The prognosis of WHO grade IV gliomas is still very poor. IDH1 mutation plays a crucial role in prognosis of high grade Glioma. Patient with a mutation (R132H) in the IDH1 gene show an ameliorated overall survival. In previously published literature miRNA-181a was identified as a regulator of IDH1 expression. This study therefore evaluates the expression of miRNA-181a as a potential prognostic marker in glioblastoma.

Methods

Using qRT-PCR, 74 GBM specimens were analysed for the expression of miRNA-181a calculated as fold change (FC). The results of the analysis were correlated with individual clinical data. All further molecular and clinical characteristics like MGMT-Methylation, extent of resection and Karnofsky-Index were considered.

Results

In the cohort at hand 11/74 (14,9%) patients displayed an IDH1 mutation. 69/74 (85,1%) showed an IDH1 wild type. Patients with an IDH1 mutation showed a significantly longer overall survival ($p = 0.004$). Expression of miRNA-181a (FC) was significantly higher in patients harbouring an IDH1 mutation ($p = 0.004$). In patients with IDH1 wild type expression high miRNA-181a expression is significantly prognostic of a more favourable clinical course with increased overall survival ($p=0.019$). This effect was not observable in patients with an IDH1 mutation.

Conclusion

The miRNA-181a seems to be a promising prognostic marker in glioblastoma patients with IDH1 wild type characteristics and should be further evaluated.

Neuroonkologie – Gliome III/Neurooncology – Gliomas III

P161

Epidemiologische, klinische und molekulargenetische Charakteristika einer Single-Center Kohorte von 556 Glioblastomen

Epidemiological, clinical and molecular characteristics of a single-centre cohort of 556 glioblastoma

D. Pierscianek, J. Rodemerck, M. Darkwah Oppong, A. Michel, R. Jabbarli, U. Sure, K. H. Wrede

Universitätsklinikum Essen, Klinik für Neurochirurgie und Wirbelsäulen Chirurgie, Essen, Germany

Objective

Glioblastoma is the most common malignant brain tumor in adults. The treatment consists of surgical reduction of the tumour mass, radiation and chemotherapy. A definitive cure cannot currently be achieved. In general, mean survival times range from a few months without treatment to around 15 months with combined radio-chemotherapy. Only patients with specific molecular changes in the tumour cells can achieve significantly longer overall survival.

Methods

All patients treated in our university hospital between January 2012 and December 2018 were eligible for our study. Patients' records were reviewed for demographic (age, gender), clinical (location, side, surgery vs. biopsy, postoperative treatment, overall survival) and molecular (IDH1 mutational status, MGMT promotor methylation, ki67 index) characteristics. Statistical analyses were conducted using SPSS version 26.0.

Results

A total of 556 patients treated for glioblastoma were included. Mean age at diagnosis was 62,71±12,25 (range 21-91) years. 326 patients were male (58,6%), 235 tumours were located in the left hemisphere and 23 tumours had developed on both sides. The majority of patients underwent open surgery (N=434, 78,1%). Molecular analysis revealed IDH1/2 mutations in 4,2% of patients (N=21) and MGMT promotor methylation in 218 patients (42,9%). Median overall survival was 242,5 days. A combination of IDH1/2 mutation and MGMT promotor methylation was seen in 14 cases. Kaplan-Meier analysis demonstrated a significantly better survival for patients with IDH1/2 mutation ($p<0,001$) and with MGMT promotor methylation ($p=0,001$). Patients with IDH1/2 mutations or MGMT promotor methylation were significantly younger than patients with wild-type IDH1/2 gene or unmethylated MGMT promotor ($p<0.001$; $p=0.046$). 65,2% of patients underwent postoperative treatment with combined chemo-radiotherapy, whereas only radiotherapy, only chemotherapy was applied in 19,3% and 8,5% of patients, respectively. 39 patients received only best supportive care.

Conclusion

We present one of the largest contemporary single centre cohorts of glioblastoma patients. The incidence of molecular tumour features (IDH1/2 and MGMT) are in line with published data.

Neuroonkologie – Gliome III/*Neurooncology – Gliomas III*

P012

Post-Hoc Analyse der EF-14 Phase III Studie – TTFIELDS beeinflussen die Tumorwachstumsraten *EF-14 Phase III post-hoc analysis – TTFIELDS affect tumour growth rates*

A. Kinzel¹, N. Urman², G. Lavy-Shahaf³, S. Levi³, Z. Bomzon³

¹Novocure GmbH, Root D4, Switzerland

²Novocure GmbH, Portsmouth, NH, United States

³Novocure GmbH, Haifa, Israel

Objective

The pivotal EF-14 study on newly diagnosed glioblastoma (nGBM) patients demonstrated that combining TTFIELDS with maintenance temozolomide significantly extends progression-free survival (PFS) compared to temozolomide treatment alone (6.7 vs 4.0 months, $p < 0.001$). It can be hypothesized that TTFIELDS treatment leads to local tumor control and significantly decreased tumor growth rates. In order to test this hypothesis, we analyzed patients from the EF-14 phase III study who received only a biopsy.

Methods

Our analysis included patients from the EF-14 study who received biopsy and showed radiological progression (treatment: N=37/60, control: N=12/29). In a first step, the volumes of the enhancing tumors were segmented on T1c MRIs both at baseline and later at progression. In a second step, we calculated the tumor growth rate as following:

$\text{growth_rate} = (\ln(v_0) - \ln(v_1)) / dt$. (v_0 - tumor volume at baseline), v_1 - Tumor volume at progression, dt - days to progression).

This models tumor volume as increasing exponentially over time. Finally, we compared the median growth rates between control and treatment arm.

Results

The calculations demonstrate that the median growth rate was lower in the treatment arm compared to the control. (control: 0.14 ± 0.12 mL/month, TTFIELDS -0.011 ± 0.11 mL/month, $p < 0.008$ Wilcoxon rank-sum).

Conclusion

Our post-hoc analysis of EF-14 demonstrated that tumor growth rates are reduced in the combined TTFIELDS+TMZ arm when compared to TMZ alone. The analysis only included patients that received a biopsy. The reason for this is that defining the volume of a tumor in resected patients is ambiguous because of the fact that part of the tumor was removed. In summary, our results suggest that TTFIELDS enhances local tumor control.

References:

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Neuroonkologie – Gliome III/Neurooncology – Gliomas III

P155

Eine rapide Methode zur reproduzierbaren Herstellung von gut charakterisierten Gold-Nanopartikeln zur Transfektion von 3D Hirntumor-Zellkulturen

A rapid one-pot synthesis method for the reproducible generation of well-defined gold nano-carriers to transfect brain tumour 3D cultures

B. Giessen¹, A. C. Nickel², A. G. Manjón³, A. Vargas-Toscano², C. Scheu³, C. Janiak¹, U. D. Kahlert²

¹Heinrich-Heine-Universität Düsseldorf, Mathematisch-Naturwissenschaftliche Fakultät, Düsseldorf, Germany

²Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany

³Max-Planck-Institut für Eisenforschung GmbH, Düsseldorf, Germany

Objective

Glioblastoma is an aggressive disease with currently limited treatment options available. GBM cells with stem cell (=GSCs) properties are thought to be responsible for the initiation and propagation of the disease. There is a great clinical need for efficient therapy delivery to GSCs. In this work, we developed a novel method to synthesize fluorescent gold nanoparticles as potential drug and gene delivery systems able to penetrate three-dimensional *in vitro* systems.

Methods

Four different procedures aiming to synthesize gold (Au) nanoparticles (NPs) in polyethylene imine (PEI) solution as stabilizer, as well as fluorescein isothiocyanate (FITC) as a fluorescent marker were applied *incorporating* a fast microwave-assisted reaction. NP characterization was performed employing transmission electron microscopy (TEM), scanning transmission electron microscopy (STEM), dynamic light scattering (DLS), ultraviolet–visible spectroscopy (UV-VIS), fluorescence spectroscopy and thermogravimetric analysis (TGA). NP purification *via* dialysis was performed. The amount of incorporation into GSC using a panel of GSC cell lines was quantitatively assessed via FACS and cytotoxicity assessed with cell growth assay. "False-positive" cells due to surface-bound NP were distinguished from cell internalization using a dye-quenching step before FACS.

Results

Resulting core sizes of NPs range from 3 to 6 nm. Our repetitive analysis resulted in an average internalization efficacy of up to 53% of all the exposed GSCs (500.000 cells, 1 mg/L NPs) with minimal cytotoxic effects (>75% cell growth as compared to control treatment).

Conclusion

We developed a straight-forward, reproducible one-pot synthesis method for Au-NPs as nanocarriers. Those NPs are able to efficiently transfect GSCs. The limited per se cytotoxicity of the particles may be beneficial in order to reduce off-target effects to no cancer cells upon functionalization of Au-NPs with anti-GSC specific targeting moieties. Given the particularly high therapy resistance of GSCs, this technology may be useful for developing novel treatment strategies to manage this disease.

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P162

Ausgezeichneter Hörerhalt bei der Resektion kleiner Akustikusneurinome und Variationen des Hörerhalts bei Anwendung unterschiedlicher Gradierungssysteme
Favourable hearing preservation rates in small acoustic neuroma surgery and variations due to different grading systems

K. Rössler¹, Y. Bozhkov², J. Feulner³, S. Rampp², J. Shawarba², H. Iro³, U. Hoppe³, M. Buchfelder²

¹Medizinische Universität Innsbruck, Neurochirurgische Klinik, Wien, Austria

²Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

³Hals-Nasen-Ohren-Klinik-Erlangen, Erlangen, Germany

Objective

Acoustic neuroma (AN) surgery is routinely performed on patients with various tumor sizes inappropriate for wait & scan or radiosurgery. Preoperatively, grading systems are applied for estimation of postoperative hearing preservation (HP) rates.

Methods

A retrospective single-centre analysis of 138 retrosigmoid operated ANs between 2014 to 2017 was performed. Patients gender was well balanced, mean tumor size was 20.4 mm (+/- 7.6 mm SD) with complete fundus infiltration in 67.4%. The overall resection rate was 93.5 %, with a low surgical complication rate of 3.6%. Tumors were classified preoperatively on T1 contrast and T2 axial MRI scans using the 3- tier Erlangen Grading System dependent on size (10.1% Grade 1 < 12mm, 65.2% Grade 2 between 12 and 25mm, 24.6% Grade 3 > 25mm) or the anatomically based 4- tier Koos Grading System (2.9% Grade 1, 40.6% Grade 2, 31.2% Grade 3 and 25.4% Grade 4).

Results

Preoperative serviceable hearing was found in 70.3% of patients and was significantly correlated to tumor size ($p=0.001$). An average mean postoperative serviceable HP rate of 38.6% was achieved (83.3% for tumors <12 mm, 38.5% for tumors between 12 and 25mm and 5.3% for tumors larger than 25mm according to the Erlangen Grading system). On the contrary, applying the Koos Grading System preoperatively instead, postoperative serviceable HP rates were 100% for Koos Grade 1 (meatal), 35.6% for Koos Grade 2 (cisternal), 23.1% for Koos Grade 3 (cisternal with brain stem contact) and 21.7% for Koos Grade 4 tumors (brain stem compression). Additionally, we found a trend to better HP rates in left sided tumors or when the fundus was tumor free. The rate of normal or nearly normal postoperative facial function in the total cohort was 75.3% (House and Brackmann (HB) Grade 1/2). Grade 3 paresis was found in 4.3% and severe facial deficits were apparent in 5.1% of patients (HB Grade 4).

Conclusion

This study showed that 1. Performing surgery on small tumors can achieve excellent hearing preservation rates and that 2. the application of different grading systems has significant influence on the reporting of postoperative HP.

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P163

DMD Deletionen stellen die häufigsten genomischen Alterationen bei Esthesioneuroblastomen dar *Intragenic DMD deletions are the most common recurrent genomic alterations in esthesioneuroblastoma*

T. Juratli^{1,2}, N. Nayyar³, M. Young⁴, M. Subramanian³, E. Willimas⁵, D. Cahill², P. Brastianos³, D. Linn⁶

¹Universitätsklinikum Carl Gustav Carus Dresden, Klinik für Neurochirurgie, Dresden, Germany

²Massachusetts General Hospital, Abteilung für Neurochirurgie, Boston, MA, United States

³Massachusetts General Hospital, Division of Neuro-Oncology, Department of Neurology, Boston, MA, United States

⁴Massachusetts General Hospital, Division of Neuro-Oncology and Hematology/Oncology, Departments of Medicine and Neurology, Boston, MA, United States

⁵Massachusetts General Hospital, Department of Pathology, Boston, MA, United States

⁶Massachusetts Eye and Ear Hospital, Department of Otolaryngology, Boston, MA, United States

Objective

Esthesioneuroblastoma (ENB) is a rare, malignant neuroectodermal tumor of the olfactory epithelium. Due to its rarity, our knowledge about the genomic landscape of ENB has remained opaque and to date, a few recurrent genetic alterations have been identified. Here, we sought to examine the genomic signature on a series of clinically well-characterized aggressive ENB samples.

Methods

We performed whole-exome sequencing (WES) in a cohort of 26 ENB samples from 12 patients, containing 11 matched primary-metastatic samples. In addition, targeted sequencing was carried out in all samples to determine *TERT* promoter hotspot mutations. Furthermore, we performed immunohistochemistry (IHC) using an antibody that recognizes the dystrophin central rod domain in all available specimens.

Results

Our cohort consisted of 9 male and 3 female patients with a median age of 66 years at first diagnosis (4- 77 years). One patient was staged Kadish B at the time of diagnosis and eleven were staged Kadish C. The median overall survival was 3.85 years (0.3 – 16 years). Consistent with previous findings, each tumor exhibited a different mutational signature and the mutational landscape appears to be predominantly driven by copy number variations. Interestingly, we detected intragenic deletions in the Duchenne muscular dystrophy gene (*DMD*) as the most common and consistent alteration in ENB patients (in 11 of 12 patients, 91.6%). *DMD* deletions, when identified within the primary ENB, were preserved in all subsequent metastatic lesions. Moreover, *DMD* deletions were concurrently identified in three cases with multiple metastases. IHC revealed the concurrent loss of dystrophin expression, the protein encoded by *DMD*, in all cases with *DMD* deletions. Otherwise, no other recurrent genomic findings were detected, including *TERT* promoter mutations.

Conclusion

Our findings validate previously described *DMD* deletions as the most common recurrent genomic alteration in primary ENB. Furthermore, our data demonstrate that *DMD* deletions were perpetuated in subsequent metastatic lesions, and when identified in any metastasis, were present in other metastases from the same patient

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P165

Lebensqualität nach Hämangioblastom-Operation in der Neurochirurgie – Von-Hippel-Lindau-Syndrom (VHL) versus Nicht-Von-Hippel-Lindau-Syndrom (NVHL)

Quality of life after neuro-surgery for haemangioblastoma – Von-Hippel-Lindau-Disease (VHL) versus Non-Von-Hippel-Lindau-Disease (NVHL)

C. Karadag¹, D. Hänggi², J. F. Cornelius²

¹Universitätsklinikum Düsseldorf, Neurochirurgie, Düsseldorf, Germany

²Universitätsklinikum Düsseldorf, Neurochirurgische Klinik, Düsseldorf, Germany

Objective

This study focuses on life quality of patients after operations for hemangio-blastoma, with particular regard to von-Hippel-Lindau disease.

Methods

Retrospective study of patients operated for hemangioblastoma in a tertiary neurosurgical centre in the period from 2003 to 2018. All patients were asked to fill out modified Short Form (36) Health Surveys (SF-36) to assess current quality of life (QoL).

Results

70 patients operated for one or multiple hemangioblastomas were identified. Out of these 9 patients were dead, 10 not contactable, 2 domiciled abroad and one patient not of legal age. A total of 40 patients, 22 male and 18 female with an average age of 59.6 years replied to the query. 85% of these patients had a cerebellar, 12.5% a spinal cord and 2.5% a brainstem location. Participation in the study was averaged 78.4 months after the latest hemangioblastoma surgery. 12 patients (30%) currently suffer from von-Hippel-Lindau disease. NVHL-patients showed a physical sum score of 44,23% on SF-36 while VHL-patients averaged 46,83% (P= 0,679). In Mental Sum Score patients without VHL-disease reached 44,23% whereas VHL-patients reached 46,83% (P= 0,03).

Conclusion

The present study showed no differences in quality of life of VHL-patients vs. Non-VHL-patients. Although von-Hippel-Lindau patients suffer from an incurable disease and often undergo multiple surgeries, they have potential to attain good quality of life. This information is helpful for patient counseling and organization of psycho-oncological care.

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P166

Korrelation von radiologischen, histologischen und mikroskopisch intraoperativen Befunden bei der Resektion von Hirnmetastasen

The correlation of microscopic intraoperative aspects, histological and radiological diagnostics in surgery of brain metastases

L. Dybowski¹, K. Engellandt², M. Meinhardt³, D. Krex¹

¹Universitätsklinikum Carl Gustav Carus Dresden, Klinik für Neurochirurgie, Dresden, Germany

²Universitätsklinikum Carl Gustav Carus Dresden, Institut für Neuroradiologie, Dresden, Germany

³Universitätsklinikum Carl Gustav Carus Dresden, Institut für Pathologie, Dresden, Germany

Objective

Metastases are the most frequent malignant brain tumors with an even rapidly increasing incidence. While chemo- immunotherapy gets more and more important primarily in the therapy of the underlying disease but also for brain metastasis treatment in general, the standard of care is an interdisciplinary therapeutically approach consisting of surgical resection of single or up to three metastasis followed by focal radiation in case of incomplete resection. Therefore, the postoperative MRI diagnosis is crucial. However, we frequently envisage questionable findings where a complete resection versus tumor remnant cannot be distinguished. In the present analysis we tried to address that issue.

Methods

Retrospective analysis of 100 patients with supratentorial metastasis of any origin. In addition to documentation of basic clinical data the focus was laid on the surgeon's estimation (SE) of the extent of resection according to the surgical report, the report from early postoperative MRI diagnosis (MRI) and the histological analysis of probes (HA) taken from the tumor border zone. Follow-up MRI were recorded, also. Further, all pre- and early postoperative MRI were re-reviewed by an experienced neuroradiologist.

Results

In a primary cohort of 40 patients we found a correlation between SE and MRI in 48%. A discrepancy between MRI and second review by a neuroradiologist was found in 16% of cases. There were no more tumor-cells found in the HA of the border zone in 63%. A correlation between detection of tumor cells in HA and MRI was found in 75%. In the follow-up analysis, 39% of the patients with a tumor –remnant in MRI developed a local recurrence. 22% of patients with no remnant in MRI developed no recurrent tumor, while 18% did.

Conclusion

Taken that the data from our primary population of brain metastasis patients are confirmed by the analysis of the entire cohort, there is a surprisingly low sensitivity and specificity in the diagnosis of a postoperative local status when SE, MRI and HA are taken into account either in combination or each item alone. This clearly needs to be improved for example by consequent histopathological analysis of the tumor border zone and novel MRI protocols.

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P167

Der Nutzen der endoskopisch assistierten Chirurgie für Meningeome der vorderen Schädelgrube *The value of endoscopy-assisted surgery in anterior fossa meningiomas*

S. Müller, J. Oertel, S. Linsler

Universitätsklinikum des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

Objective

Keyhole approaches for the skull base are currently under investigation for skull base tumour surgery. A lower complication rate is to be expected with the same successful resection rate. A good visualization of the target is the major aspect of the procedure to achieve a high resection rate and also a low complication rate. Here the endoscope is a second imaging tool for better visualization of the target intraoperatively and detecting remnant tumour tissue. In this study the authors report their current series of procedures in anterior skull base meningiomas, which were operated in an endoscopy assisted microsurgical procedure.

Methods

Between January 2012 and December 2016, 28 patients with anterior skull base meningiomas underwent microsurgical, endoscopy assisted procedures. The procedures were video recorded. The cases were prospectively followed. The surgical technique was carefully analyzed. Special attention was paid to the necessity of switching the operation strategy, complications, surgical radicality, relief of symptoms.

Results

In all cases an adequate visualization of the tumor was possible. So there was no necessity to switch to another approach. The authors detected in 12 of the 28 cases remnant tumor at the end of the microsurgical procedure with angled or 0° scopes following further resection. In 27 cases (96%) a resection Simpson grade 1 was possible and in the postoperative MRI no remaining tumour was visualized after a 6 and 18 months follow-up. In one case there was a deterioration of vision. In one case a recurrence of the meningioma was shown in the 18 months MRI follow-up. No further complications or complaints were reported.

Conclusion

The endoscopy assisted resection of skull base meningiomas has been shown to be safe and successful with a higher possible radicality and only minor complications. Further cases are necessary to analyze the value of the endoscope in skull base procedures and to compare this with other techniques.

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P168

Der erweiterte endoskopische Zugang zur Sellaregion und zur Schädelbasis – Ist ein Nasenloch ausreichend? *The extended endoscopic approach to perisellar and skull base lesions – Is one nostril enough?*

S. Linsler, S. Senger, J. Oertel

Universitätsklinikum des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

Objective

The extended endonasal endoscopic approach to the skull base is still under investigation. The main advantage of using this technique is to approach lesions in a minimally invasive manner thereby avoiding brain retraction. Here, the authors present the results of extended endonasal endoscopic surgery via one nostril.

Methods

All skull base procedures performed via an endonasal approach at the author's Department between January 2011 and May 2017 were analysed prospectively. Special attention was paid to complications, radicality, advantages and disadvantages of the endoscopic technique. In addition, the application of various telescopes and the technique of dural closure were analysed.

Results

Sixty-two patients were operated on various lesions of the skull base via an extended endonasal approach. Seven lesions were resected via a binostril technique. All other lesions could be visualized by the monostril technique. In 2 of 62 cases, the authors had to switch to the binostril technique. MRI revealed radical gross total resection in 93% of all cases when intended. Overall complication rate was 16% (9/55) in the monostril and 57% (4/7) in the binostril cohort. Seven patients in the monostril cohort (13%) versus three patients in the binostril cohort (43%) complained of postoperative nasal congestion.

Conclusion

This clinical report shows that many extended skull base lesions can be treated by a monostril endonasal approach. In selected cases, this technique might represent an alternative to the binostril approach. Nevertheless, the binostril technique offers a better range of manipulation and exposure and should be preferred in difficult and very extended cases.

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P169

Vorteile der navigierten zervikalen Korpektomie und ventralen Verplattung im Bereich der unteren Halswirbelsäule

Advantages of navigated anterior cervical corpectomy and plating of the lower cervical spine

J. Perrin, S. Georgiev, A. Karakoyun, N. Etmiran, F. Enders

Universitätsklinikum Mannheim, Neurochirurgische Klinik, Mannheim, Germany

Objective

Cervical corpectomy with anterior plating is a common applied treatment option for severe degenerative spinal disease or cervical spinal tumours. Optimal implant positioning is often challenging especially in the lower segments of the cervical spine. Although commonly practiced the rate of perioperative complications and postoperative morbidity remains relatively high due to misplacement of implants. The aim of this study was to optimize implant positioning by applying spinal navigation for the anterior cervical reconstructive surgery.

Methods

After standard supine positioning for an anterior cervical approach, an additional Mayfield clamp with an attached reference array was fixed to the patient's head. An intraoperative Dyna-CT with a 3D robotic C-arm was then performed followed by an autoregistration process. The surgical approach to the anterior spine, the corpectomies and screw placement for anterior plating were all performed with navigational guidance. Cages were placed under fluoroscopy. Cranial-caudal, midline, anterior-posterior and lateral borders of the cages and plates were verified with the navigation to assess final positioning. If necessary, objects, e.g. tumours or vessels, were segmented on preoperative CT scans and fused with the intraoperative images. We then conducted comparative analysis with postoperative images.

Results

A total of 16 patients, 9 women and 7 men, underwent navigated anterior cervical reconstructive spine surgery at our department from June 2017. Of these 16 cases 11 patients were treated due to degenerative spine disease and 5 had metastasis of the cervical spine. 3 patients underwent anterior cervical reconstruction between the levels C6 and Th1, 9 patients between C5 and C7 and 4 between C4 and C6. No perioperative complications in respect to implant displacement were detected. Postoperative scans revealed optimal positioning of the cages, screws and plates respectively in all patients. Surgical time was merely increased by 6 Minutes on average.

Conclusion

This study demonstrates that the use of spinal navigation for cervical anterior reconstructive surgery seems advantageous for optimal implant positioning. This technique can potentially reduce the risks of implant associated peri- and postoperative complications or iatrogenic morbidities especially of the lower cervical segments.

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P170

Klinische, radiologische und histopathologische Prädiktoren für die postoperative Langzeitprognose von atypischen Meningiomen

Clinical, radiological and histopathological predictors for long-term prognosis after surgery for atypical meningiomas

E. M. S. Streckert¹, K. Heß², P. B. Sporns³, A. Adeli³, C. Brokinkel³, J. Kriz⁴, M. Holling¹, H. T. Eich⁴, W. Paulus², D. C. Spille¹, A. T. Van Eck⁵, D. R. Raleigh⁶, M. W. McDermott⁷, W. Stummer¹, B. Brokinkel²

¹Universitätsklinikum Münster, Klinik und Poliklinik für Neurochirurgie, Münster, Germany

²Universitätsklinikum Münster, Institut für Neuropathologie, Münster, Germany

³Universitätsklinikum Münster, Institut für Klinische Radiologie, Münster, Germany

⁴Universitätsklinikum Münster, Klinik für Strahlentherapie und Radioonkologie, Münster, Germany

⁵Gamma Knife Zentrum Krefeld, Krefeld, Germany

⁶University of California San Francisco, Department of Radiation Oncology, San Francisco, CA, United States

⁷University of California San Francisco, Department of Neurological Surgery, San Francisco, CA, United States

Objective

Although considerable rates of recurrence and mortality can be found in atypical meningiomas, reliable predictors for evaluating a long-term prognosis are unclear. On the other hand, determinations of molecular alterations known to correlate with recurrence have not yet been established in routine neuropathological analyses. Therefore, we aimed to determine clinical, radiological and histological risk factors for progression available from routine perioperative data.

Methods

Associations of radiological, clinical and histological variables with recurrence and mortality were retrospectively analyzed by uni- and multivariate analyses.

Results

138 patients consisting of 64 females and 74 males (46% and 54%, median age 62 years) underwent surgery for intracranial atypical meningioma between 1991 and 2018 were included. Gross total resection (GTR, Simpson grade I+II) could be achieved in 81% of all cases, whereas subtotal resection (STR, Simpson grade \geq III) was achieved in 19%. Within a median follow-up of 62 months, recurrence occurred in 52 (38%) and death in 22 (16%) cases. In patients who did not receive adjuvant irradiation, recurrence rates were higher after STR than after GTR (32% vs 63%, $p=.025$). In univariate analyses, only intra-tumoral calcifications on preoperative MRI ($p=.012$) and the presence of brain invasion in the absence of other histological grading criteria ($p=.010$) were correlated with recurrence. In multivariate analyses, only patient age was positively (HR: 1.03, 95%CI 1.04-1.05; $p=.018$), and the presence of brain invasion as the only grading criterion (HR: .37, 95%CI .19-.74; $p=.005$) was negatively associated with progression, while increasing age at the time of surgery (HR: 1.07, 95%CI 1.03-1.12; $p=.001$) was prognostic for mortality.

Conclusion

Reliable clinical predictors for both progression and mortality in patients with atypical meningiomas are difficult to determine. However, both gross total resection and, after STR, adjuvant irradiation might improve

local tumor control rates. PFI was longer in brain-invasive but otherwise histologically benign meningiomas and in tumors displaying calcifications on preoperative MRI.

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P171

Somatostatinrezeptor-Radiotherapie für Kopf-/Hals-Paragangliome *Somatostatin receptor targeted radioligand therapy in head and neck paraganglioma*

M. Mütter¹, W. Roll², B. Zinnhardt², E. Suero Molina¹, M. Schäfers², M. Weckesser², K. Rahbar², W. Stummer¹

¹Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

²Universitätsklinikum Münster, Klinik für Nuklearmedizin, Münster, Germany

Objective

Surgical resection is the therapy of choice in head and neck paraganglioma (HNPG), however associated with significant morbidity depending on tumor size and localization. In cases of progressive residual or recurrent disease, novel and less aggressive therapeutic options are warranted. Somatostatin receptor (SSTR) targeted radioligand therapy poses a promising alternative, as SSTRs are upregulated in paraganglioma. However, only few studies provide evidence on indications, safety and effectiveness. The aim of this study was to provide a case series on peptide receptor radionuclide therapy (PRRT) with ¹⁷⁷Lu-DOTATATE for HNPG in a single center setting.

Methods

Retrospective case series on all PRRT with ¹⁷⁷Lu-DOTATATE for HNPG from 2015 to 2019; protocol according to PRRT guidelines established for neuroendocrine tumors. Therapy response was assessed by pre- and three-month post-therapy ⁶⁸Ga-DOTATATE-PET-CT (threshold set at 41% SUVpeak) and MRI volumetric analysis. Therapeutic uptake was classified on ¹⁷⁷Lu-DOTATATE scintigraphies 48h p.i. according to the Krenning scale. Longer-term clinical outcome and MRI follow-ups were evaluated.

Results

A total number of seven patients (mean age 60 years; range 14 - 84) with HNPG (3 carotid body tumors, 4 jugulotympanic paragangliomas) were included in this retrospective analysis. Patients received a median of 4 cycles (IQR 3 - 5) of ¹⁷⁷Lu-DOTATATE PRRT. Comparison of pre- and post-therapy imaging showed an increase in PET volumes only in one patient; technical reasons did not allow for a meaningful comparison with MRI in this patient. Tumor uptake in 48h p.i. ¹⁷⁷Lu-scintigraphies was moderate to high in all patients (median Krenning scale 3, IQR 2-4). None of the patients showed progressive disease during a median follow-up time of 28 months. Symptoms improved in 2/7 patients. Sensorineural hearing loss is the symptom less likely to improve after PRRT. No adverse events were noted.

Conclusion

SSTR-targeted therapy using ¹⁷⁷Lu-DOTATATE shows promising effectiveness for growth stabilization at high safety profile. Quantitative ⁶⁸Ga-DOTATATE-PET complements morphological standard MRI / CT skull base imaging, especially in cases of previous surgery or irradiation.

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P172

Die prognostische Rolle des Simpson Grads in Meningeomen – nach 62 Jahren noch relevant? *The prognostic role of Simpson grading in meningioma – still relevant after 62 years?*

F. Behling¹, C. K. Fodi¹, I. Gepfner-Tuma^{1,2}, K. Machetanz¹, K. Kaltenbacher², M. Renovanz¹, M. Skardelly¹, G. Tabatabai^{1,2}, J. Schittenhelm³, M. Tatagiba¹

¹Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

²Universitätsklinikum Tübingen, Klinik für Neurologie, Tübingen, Germany

³Universitätsklinikum Tübingen, Institut für Neuropathologie, Tübingen, Germany

Objective

Since the proclamation of the Simpson grading for the extent of resection in meningiomas in 1957, many more insights have been gained regarding the biology, histopathological classification and treatment of meningiomas. Until today the Simpson grading determines the intraoperative course during meningioma resection, believing that a Simpson grade II resection is better for the patient than grade III for example. In the light of the established prognostic factors in meningiomas, this retrospective analysis aims to clarify to what extent the Simpson grading in its single cutoffs is still of prognostic significance for our patients.

Methods

We analyzed the clinical and histopathological data of 429 meningiomas that were surgically resected in the authors' institution between 04/2011 bis 12/2015. Operative reports were reviewed regarding the extent of resection according to the Simpson grading system. Meningioma subtype according to the WHO classification of 2016 as well as histopathological brain invasion and time of progression were retrieved from clinical records. Univariate and multivariate analyses were applied.

Results

Altogether 49 meningiomas showed tumor recurrence (49/429, 11.4%) after a mean follow-up of 31 months (1.7-95.7 months). The rate of recurrence increased with each Simpson grading step. Meningiomas operated according to Simpson grade I showed only 4.4% recurrences (4/90) while grade II and III had high rates of 5.5% (7/126) and 12.6% (12/95). Tumors resected according to Simpson grade IV, meaning a subtotal resection, had the highest rate of recurrence with 23.3 % (24/103) (Pearson's chi-squared test, $p < .0001$). Multivariate analysis including WHO grade and Simpson grade at all different cutoffs revealed that next to the WHO grading ($p = 0.0443$) only the cut off at Simpson grade 3 and 4 has independent prognostic value ($p = 0.0423$). Cut offs between Simpson grade 1 and 2 as well as 2 and 3 have no independent prognostic significance.

Conclusion

Incomplete tumor resection after microsurgical meningioma resection remains an independent prognostic factor with a higher rate of tumor recurrence. The multivariate analysis of this cohort does not show a prognostic benefit between Simpson grades 1/2 and 2/3, suggesting that the efforts we make and the risks we take when encountering the dural attachment of meningiomas have a questionable prognostic impact.

Neuroonkologie – Meningeome und andere Entitäten II/*Neurooncology – meningiomas and others II*

P173

Einfluss der ABO Blutgruppe auf thromboembolische Komplikationen und postoperative Nachblutungen nach Resektion intrakranieller Meningeome

The impact of ABO blood group on thromboembolic and haemorrhagic complications after resection of intracranial meningiomas

C. Beynon¹, V. Rösner¹, L. Albrecht², U. Müller², K. Zweckberger¹, A. W. Unterberg¹

¹Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

²Institut für Klinische Transfusionsmedizin und Zelltherapie Heidelberg gemeinnützige GmbH und Institut für Immunologie, Heidelberg, Germany

Objective

Recent studies have suggested an impact of the ABO blood group on thromboembolic and haemorrhagic events following trauma or surgical procedures. However, only limited data are available on the impact of the ABO blood group in neurosurgical patients. The goal of the present study was to evaluate the role of the ABO blood group on the rate of thromboembolic and haemorrhagic events in patients treated surgically at our institution for intracranial meningioma.

Methods

We retrospectively analysed the medical records of consecutive patients undergoing resection of intracranial meningiomas at our institution during a period of 12.5 years (2006-2018). Clinical characteristics, modalities of surgical treatment, histopathological results and the postoperative course of patients were analysed with specific focus on ABO blood group typing result, need for transfusion of blood products, events of postoperative thromboembolism and intracranial re-haemorrhage requiring surgical revision, as well as in-hospital mortality.

Results

A total of 1781 patients were included in this study. Corresponding to their ABO blood type, patients were subdivided into four categories: Blood group A (n=774; 43%); blood group B (n=220; 12%); blood group AB (n=87; 5%); and blood group O (n=700; 39%). Thromboembolic events such as pulmonary embolism occurred in a total of 29 patients (1.6%) and univariate analysis revealed no significant differences between ABO blood groups (A: 1.6%; B: 1.4%; AB: 0%; O: 2.0%). Intracranial re-haemorrhage requiring re-craniotomy and haematoma evacuation occurred in a total of 48 patients (2.3%) and no significant differences were observed between the ABO blood groups (A: 2.5%; B: 2.3%; AB: 2.2%; O: 3.1%). The overall in-hospital mortality rate was 0.17% (n=3).

Conclusion

Patients with blood group O had higher rates of thromboembolism and postoperative haemorrhage than other blood groups, but these differences failed to reach statistical significance. These findings suggest a limited impact of the ABO blood group on postoperative complications after resection of intracranial meningiomas.

Neuroonkologie – Gliome IV/*Neurooncology – Gliomas IV*

P174

Die CCL18/CCR8 Signalkaskade fördert das humane Glioblastomwachstum in Abhängigkeit von gliom-assoziierten Monozyten

The CCL18/CCR8 signalling cascade promotes the growth of human glioblastoma in dependence on glioma associated monocytes

Y. Huang¹, Y. Yuan¹, L. Kuhrt¹, X. Pengfei¹, M. Schnauss¹, M. Synowitz², H. Kettenmann¹, C. Flüh^{2,1}

¹Max-Delbrück-Centrum für molekulare Medizin, Zelluläre Neurowissenschaften, Berlin, Germany

²Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Kiel, Germany

Objective

With an average survival of 14 months and an incidence of 3.2 cases per 100.000 persons per year, glioblastoma multiforme is the most frequent and most malignant primary human brain tumor. Up to 40% of the tumor mass consists of tumor-associated microglia/macrophages (GAMs). GAMs are known to have a profound effect on tumorigenesis in glioma. There are various known interaction pathways between GAMs and glioma cells, which have been studied mostly in mice. Chemokine C-C motif ligand 18 (CCL18) is a chemokine, which predominantly is expressed by microglia and activated monocytes. Chemokine (C-C motif) receptor 8 (CCR8) is a receptor for CCL18, which is expressed on glioma cells. Both, ligand and receptor are expressed in human, but not in mice.

Methods

We performed an expression analysis using The Cancer Genome Atlas (TCGA) database and identified a direct association between high CCL18 expression level and survival time in GBM (12,7 vs. 14.7 months). We confirmed that CCL18 expression was higher in GAMs isolated by magnetic-activated cell sorting (MACS) for CD11b from human glioma resections, while CCR8 expression was higher in the CD11b-negative fraction (predominantly the glioma cells) as assessed by qrtPCR and Western blot. To test the impact of CCL18 signaling on glioma growth, we developed a humanized brain slice model by replacing the intrinsic microglia in a cultured mouse brain slice by human THP-1 derived monocytes. After an incubation time of 5 days, we inoculated the human glioma cell lines U251MG, U87 and LN229 into the murine slice.

Results

Comparing slices with and without THP-1 derived monocytes showed that the human THP-1 cells promoted the growth of the human glioma cell lines, confirming our previous observation from the murine system that microglia promote glioma growth. The promotion of U87 and LN229 glioma growth by THP-1 could be attenuated by either a specific CCR8 neutralizing antibody or a CCL18 neutralizing antibody, indicating that THP-1 glioma interaction is mediated by the CCL18-CCR8 axis.

Conclusion

The CCL18/CCR8 signaling pathway between GAMs and tumor cells could be an interesting target for future therapeutic regimens in glioblastoma multiforme.

Neuroonkologie – Gliome IV/Neurooncology – Gliomas IV

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Humane Gliomzellen erwerben Temozolomid-Resistenz durch DNA-Fehlpaarungsreparatur Dysfunktion *Human glioma cells acquire temozolomide resistance via DNA mismatch repair dysfunction*

K. Yamashiro, S. Ohba, K. Nakao, Y. Hirose

Fujita Health University, Neurosurgery, Aichi, Japan

Objective

In the management of malignant glioma, the resistance to chemotherapeutic agents by the tumor cells could be a big problem. Although temozolomide (TMZ) has been used as a major compound in the treatment for this kind of tumor, the average survival time has been extended only a few months. While O6-methylguanine-DNA methyltransferase (MGMT) is a well-known TMZ resistance mechanism, some of the glioblastomas shows low MGMT expression. Even glioblastomas with decreased MGMT expression come to acquire resistance to TMZ, elucidation of the mechanism of TMZ resistance caused by factors other than MGMT is therefore necessary. Previous studies have shown that TMZ induces prolonged arrest of human glioma cells in the G2/M phase of the cell cycle followed by a senescence-like phenomenon or mitotic catastrophe. These findings suggest that the G2 checkpoint is linked to DNA repair mechanisms. In the present study, based on the above stated background, we aimed to elucidate the mechanism of TMZ resistance in glioblastomas with low MGMT expression and thereby to solve this problem.

Methods

We generated TMZ-resistant (TR) clones with low MGMT expression by repeatedly administrating TMZ to human glioma U87MG cells. We evaluated TMZ-induced cell cycle arrest, expression of MSH6 which is a key component of mismatch repair system (MMR), and effect of Chk1- and Cdc2-inhibitors in TR-clones.

Results

While TR clones obtained after 2-3 months exposure to TMZ (TR-s) underwent transient G2 arrest after TMZ treatment, longer (4-6 months) exposure to TMZ enriched the proportion of TR-clones that underwent only minimal G2 arrest following TMZ treatment (TR-l). The expression of p-chk1, p-chk2, and p-cdc2, which are key event in TMZ-induced G2 arrest, were not observed after TMZ treatment in TR-l clones. MGMT was not detectable, however, MSH6, a major MMR component, was reduced in TR-l clones. None of Chk1- and Cdc2-inhibitors could resensitize TR-l clones to TMZ.

Conclusion

Our result suggested that longer drug treatment may induce the development of cells highly resistant to DNA damaging agent(s) by means of MMR modification. Further investigation on the mechanism of acquired resistance to TMZ by glioma cells could provide a key to developing rational drug treatment. It has been shown that the development of new treatments for MMR-deficient tumors is required, on the other hand, in order to achieve great treatment results, it might be important to intensify treatment before the tumor develops a MMR deficiency.

Neuroonkologie – Gliome IV/*Neurooncology – Gliomas IV*

P175

Infiltration der subventrikulären Zone durch niedriggradige Gliome – molekulare Marker, Behandlung und Therapieergebnisse

Infiltration of the subventricular zone in low-grade gliomas – molecular markers, management and outcome

P. Karschnia¹, J. Weller¹, J. Blobner¹, V. M. Stoecklein¹, L. Von Baumgarten², D. B. Nasseh³, M. M. Dorostkar⁴, J. Dietrich⁵, J. Tonn¹, N. Thon¹

¹Klinikum der Ludwig-Maximilians-Universität München, Klinik für Neurochirurgie, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, Klinik für Neurologie, München, Germany

³Klinikum der Ludwig-Maximilians-Universität München, Comprehensive Cancer Centre, München, Germany

⁴Klinikum der Ludwig-Maximilians-Universität München, Klinik für Neuropathologie, München, Germany

⁵Massachusetts General Hospital, Clinic of Neurology, Boston, MA, United States

Objective

The subventricular zone (SVZ) represents the largest adult neural stem cell niche. Primary involvement of the SVZ is associated with decreased survival in high-grade glioma, however, clinical experience with low-grade glioma (LGG) is limited.

Methods

We retrospectively reviewed our institutional database of the Division of Neuro-Oncology for patients with LGG, WHO grade II°. We recorded imaging findings; histopathological as well as molecular information; therapeutic approaches; and outcome.

Results

182 patients treated for LGG were identified, including 97 oligodendrogliomas and 85 astrocytomas. 78 of the 182 patients (43%) were found to have SVZ-involving LGG. Age, sex ratio, histopathology, MGMT promotor methylation status, and IDH mutation status did not differ between SVZ-involving LGG and non-SVZ-involving LGG. Symptoms were non-specific in both groups, and attributed to tumor mass effect. First-line therapeutic approaches included surgery, radiotherapy, chemotherapy, and wait-and-scan approaches, and did not differ between both groups. Mean follow-up time was 59 months. Overall, 43 patients (24%) showed malignant progression to high-grade glioma during follow-up. Involvement of the SVZ predicted shorter time to malignant progression ($p = 0.002$). Only in LGG involving the SVZ, there was a trend that therapy other than wait-and-scan might be associated with longer time to malignant progression ($p = 0.078$). Median overall survival was not reached after ten years. Twelve patients with SVZ-involving LGG had died at database closure, whereas only six patients with non-SVZ-involving LGG died (7% vs. 3%). SVZ involvement correlated negatively with overall survival ($p = 0.023$). MGMT promotor methylation ($p = 0.001$) and IDH mutation ($p = 0.001$) were positive prognostic markers for survival among LGG involving the subventricular zone.

Conclusion

SVZ involvement may convey a risk factor for malignant progression and outcome in LGG patients. Aggressive first-line therapy might be recommended in LGG involving the SVZ. MGMT promotor methylation status and IDH mutation status may be useful tools to further guide therapeutic approaches in such tumors.

Neuroonkologie – Gliome IV/Neurooncology – Gliomas IV

P176

Die Bedeutung von 5-ALA induzierter PpIX-Fluoreszenz während der chirurgischen Resektion spinaler Ependymome

The value of visible 5-ALA induced PpIX fluorescence during surgery for spinal ependymomas

P. A. Mercea¹, M. Millesi¹, B. Kiesel¹, M. Mischkulnig¹, V. Mazanec¹, T. Roetzer², A. Woehrer², S. Wolfsberger¹, J. Herta¹, K. Roessler¹, E. Knosp¹, G. Widhalm¹

¹Medizinische Universität Innsbruck, Neurochirurgie, Wien, Austria

²Medizinische Universität Innsbruck, Klinisches Institut für Neurologie und Neuropathologie, Wien, Austria

Objective

Gross total resection (GTR) is the treatment of choice in the majority of cases suffering from spinal ependymomas. The extent of resection is considered the most important factor for patient prognosis and the risk of recurrence. However, incomplete resection is not uncommon leading to an increased risk of tumor recurrence. One important aspect leading to such an incomplete resection is insufficient visualization of tumor tissue during surgery. Therefore, we investigated the value of 5-aminolevulinic acid (5-ALA) induced protoporphyrin IX (PpIX) fluorescence in a consecutive series of spinal ependymomas.

Methods

Since 2009, 5-ALA was administered in a total of 31 patients with spinal ependymomas. A conventional white-light microsurgical resection of the tumor was performed in all cases. In addition to this standard procedure, the PpIX fluorescence status of each tumor was evaluated during surgery repeatedly using a modified neurosurgical microscope. In intramedullary tumors, if GTR was feasible and assumed, the resection cavity was investigated for potential residual fluorescing foci.

Results

In all patients, the application of 5-ALA was feasible and no side effects occurred. PpIX fluorescence was observed in the majority of spinal ependymomas (n=25, 81%). In contrast, no fluorescence was noted the remaining 6 patients (19%). After assumed GTR in intramedullary tumors (n=15), residual fluorescing foci within the resection cavity could be detected in 5 cases (33%).

Conclusion

5-ALA is a promising marker for intraoperative visualization of spinal ependymomas with the majority of cases showing visible PpIX fluorescence. Residual fluorescing foci could be identified in 33% of intramedullary tumors after assumed GTR under conventional white-light. Therefore, 5-ALA induced PpIX fluorescence may be useful in increasing the extent of resection in intramedullary ependymomas and thus in future may reduce the risk of recurrence.

Neuroonkologie – Gliome IV/Neurooncology – Gliomas IV

P177

Einfluss der initialen Mittellinienverlagerung beim Glioblastom auf das Überleben – Ist der Würfel schon gefallen?

Impact of initial midline shift in glioblastoma on survival – Alea iacta est?

J. Wach, M. Hamed, P. Schuss, E. Güresir, U. Herrlinger, H. Vatter, M. Schneider

Universitätsklinikum Bonn, Neurochirurgie, Bonn, Germany

Objective

Limited data are available with regard to the impact of baseline midline shift (MLS) on long-term survival and progression in glioblastoma (GBM). Objective of this study was to analyze the influence of mass effect on survival and progression with due regard for the patient demographics, operative techniques, molecular pathology and postoperative treatment.

Methods

198 patients with GBM were analyzed retrospectively. MLS was measured on preoperative T2-weighted magnetic resonance images (MRI) at the level of the septum pellucidum. Patients were dichotomized in groups with low (< 10 mm) and high (\geq 10 mm) MLS. Both MLS-groups were compared with regard to survival, progression-free survival (PFS) and postoperative course of Karnofsky Performance Status (KPS). Possible correlations were investigated using univariate -, binary logistic regression-, and Kaplan-Meier analyses.

Results

Two-sided Fisher's exact test revealed no statistically significant differences of the confounders between low- and high-MLS group.

Median survival was 18.0 months (95% CI=15.3-20.7) in the low-MLS group (n=173), and 9.0 months (95% CI=4.8-13.2) in the high-MLS group (n=25), respectively (p=0.045).

59.1% (13/22) with an initial high-MLS had a KPS of < 70% after 3 months, whereas 20.5% of the the low-MLS group had a KPS of < 70% (p<0.001).

Binary logistic regression analysis including the MGMT status, Extent of resection, baseline KPS, and MIB-I index revealed low-MLS as the only predictor for survival at 12 months (p=0.046, OR=2.70, 95% CI=1.0-7.2).

Median PFS was 6.0 months in the high-MLS group and 9.0 months in the low MLS-group (log-rank test; p=0.08).

Conclusion

Initial midline shift \geq 10 mm seems to be an imaging characteristic which independently predicts the survival rate in glioblastoma.

Neuroonkologie – Gliome IV/Neurooncology – Gliomas IV

P178

Anfallsoutcome in der Glioblastomchirurgie des Temporallappens – Lobektomie als ein supra-totales Resektionsregime übertrifft die konventionelle Gross-Total-Resektion

Seizure outcome in temporal glioblastoma surgery – lobectomy as a supra-total resection regime outclasses conventional gross-total resection

M. Schneider¹, G. Aydin¹, I. Ilic¹, A. Rácz², E. Güresir¹, H. Vatter¹, P. Schuss¹, M. Hamed¹, V. Borger¹

¹Rheinische Friedrich-Wilhelms-Universität Bonn, Abteilung für Neurochirurgie, Bonn, Germany

²Rheinische Friedrich-Wilhelms-Universität Bonn, Abteilung für Epileptologie, Bonn, Germany

Objective

Both pre-and postoperative seizures constitute severe side effects in glioblastoma patients that negatively impact patient quality of life. Therefore, postoperative seizure freedom represents an important secondary outcome measure in glioblastoma surgery. Recently, supra-total glioblastoma resection in terms of anterior temporal lobectomy (ATL) has gained growing attention with regard to superior long-term disease control for temporal-located glioblastoma compared to conventional gross-total resections (GTR). However, the impact of ATL on seizure outcome in these patients is unknown. We therefore analyzed ATL and GTR as differing extents of resection in regard of postoperative seizure control in patients with temporal glioblastoma and preoperative symptomatic seizures.

Methods

Between 2012 and 2018, 31 patients with preoperative seizures underwent GTR or ATL for temporal glioblastoma at the authors' institution. Seizure outcome was assessed 12 months after tumor resection according to the International League Against Epilepsy (ILAE) classification and stratified into favorable (ILAE class 1) versus unfavorable (ILAE class 2-6).

Results

Overall, 23 out of 31 patients (74%) with preoperative seizures achieved favorable seizure outcome following resection of temporal-located glioblastoma. For the ATL group, postoperative seizure freedom was present in 12 out of 13 patients (94%). In comparison, respective rates for the GTR group were 11 out of 19 patients (58%) ($p < 0.05$, OR 8.7, 95% CI 0.9-81.5).

Conclusion

ATL in terms of a supra-total resection strategy was associated with superior favorable seizure outcome following temporal glioblastoma resection compared to GTR. Regarding abovementioned survival benefit following ATL compared to GTR, ATL as an aggressive supra-total resection regime might constitute the surgical modality of choice for temporal-located glioblastoma.

Neuroonkologie – Gliome IV/*Neurooncology – Gliomas IV*

P179

Zugang innovativer Medizintechnik zum Leistungskatalog gesetzlicher Krankenversicherung in Deutschland und anderen Ländern am Beispiel der Tumortheraiefelder (TTFields)

Access of innovative medical technologies to compulsory health insurance reimbursement in Germany and other countries by example of tumour treating fields (TTFields)

C. Proescholdt

Novocure GmbH, Root D4, Switzerland

Objective

To highlight the challenges and differences in access of breakthrough medical device technologies to the compulsory health insurance in Germany and other countries, by example of a novel cancer treatment using Tumor Treating Fields (TTFields).

Access challenges for innovative medical devices vary by country. Common issues for novel device technologies are the difficulties to classify the treatment in the respective country's health care system and the according ability to develop a value-based reimbursement pathway.

Methods

We reviewed access pathways and reimbursement decisions of payers in several countries. We assessed their classification of the device delivering TTFields in the respective country, the flexibility of their health care framework and the way the technology was implemented.

Results

All countries were able to implement the novel technology delivering TTFields their respective health care systems. 3 countries consider the technology to be an outpatient treatment delivered by durable medical equipment, one country classifies it a hospital dispensed medical device, one country as an extended medical service and the last country as rehab services.

The differential fitting of the novel technology in the respective country's health care system allows each of the countries to take a positive, value-based reimbursement decision for this breakthrough technology. Generally, the speed of payer adoption varied based on the ability of the healthcare system to evaluate the clinical data supporting its use, rather than focusing on more technical aspects of how the device is delivered to patients.

Conclusion

Classification of a breakthrough technology delivered through a medical device in the traditional framework of health care systems is challenging and handled differently by each country. All countries with a flexible approach regarding this novel oncological treatment modality however, were able to reach positive reimbursement decisions by classifying the technology in the category most suitable in the respective country's health care system.

Neuroonkologie – Gliome IV/Neurooncology – Gliomas IV

P180

Das Verhalten von niedriggradigen Inselgliomen unterscheidet sich von anderen Tumoren – eine MRT-Volumetriestudie unter Einbeziehung neuropathologischer molekularer Marker
Insular lower-grade gliomas behave differently – a volumetric MRI and neuropathological retrospective analysis

C. F. Freyschlag, A. Krigers, M. Demetz, J. Kerschbaumer, C. Thomé

Medizinische Universität Innsbruck, Klinik für Neurochirurgie, Innsbruck, Austria

Objective

The location of lower-grade gliomas[c1] (LGG) showed a preference for eloquent regions within the brain, especially involving the insula. With the constant development of MR imaging and the diagnostic prioritisation of molecular markers plus the increased detection of anaplastic foci within LGG, therapeutic strategies need to be tailored. The aim of our study was to correlate tumour volumetry and imaging parameters of insular tumours with the WHO grades, presence of anaplastic foci and molecular markers.

Methods

From our database we could identify 99 consecutive patients with histologically proven lower-grade gliomas, 13 (13%) of which were exclusively insular tumours. All underwent their first resection in our institution. The volume on MRI was measured in T1 CE and native, T2, FLAIR and DWI sequences. Molecular markers, neuropathological, epidemiological and clinical data were analysed in correlation to the non-insular cohort.

Results

There were no significant differences in preoperative tumour volumes in MRI T1, T2, FLAIR and DWI sequences as well as considering contrast enhancement compared to tumours with different localization. However, the remnant volume of the insular tumours in postoperative MRI was significantly larger in T1 Sequences – median 26.7 cm³ (IqR 9.2 ÷ 53.3) vs. 44.8 cm³ (IqR 15.5 ÷ 83.0), p=0.048; and tended to be larger in T2 and DWI. Five[c1] patients with insular LGG with progressive disease showed minor relative growth from their last MRI compared to tumours in other localizations: in T1 – median 67% (IqR 17 ÷ 251) vs. 3% (IqR -26 ÷ 16), p=0.006; in T2 – 35% (IqR 20 ÷ 71) vs. 6% (IqR -22 ÷ 14), p=0.004; in FLAIR Sequence – 33% (IqR 16 ÷ 68) vs. 4% (IqR -25 ÷ 16), p=0.004. We could not find any significant differences considering preoperative symptoms, epidemiological data, WHO Grade, ATRX or IDH1 Status, PFS and OS.

Conclusion

Extent of resection in insular gliomas is worse than in more superficial tumours, however, growth rates upon recurrence / regrowth seem to be lower than in frontal or temporal tumours.

Neuroonkologie – Gliome IV/Neurooncology – Gliomas IV

P181

Die Claudin-1-Downregulation spielt eine wichtige Rolle in der Pathophysiologie invasiver Hypophysen-Makroadenome

Claudin-1 downregulation plays a major role in the pathophysiology of invasive pituitary macroadenomas

M. Mohme¹, R. Rotermund¹, K. C. Mende¹, T. Burkhardt², J. Matschke³, M. Westphal¹, J. Flitsch¹, W. Saeger³

¹Universitätsklinikum Hamburg-Eppendorf, Klinik für Neurochirurgie, Hamburg, Germany

²Friedrich-Ebert-Krankenhaus Neumünster, Neurochirurgie, Neumünster, Germany

³Universitätsklinikum Hamburg-Eppendorf, Institut für Neuropathologie, Hamburg, Germany

Objective

Pituitary adenomas are generally completely resectable, and thus can be cured. However, certain adenomas are invasive and complete resection is difficult. Until now it is unclear, which phenotype leads to invasion into the cavernous sinus. We hypothesize that the expression of Claudin-1 could play a role in the pathophysiology of invasive macroadenomas.

Methods

We prospectively collected tissue from 120 patients with invasive or non-invasive macroadenomas of the pituitary. When available, differential tissue analysis from the peripheral and central tumor areas was performed. Tumor tissue was evaluated for Claudin-1, a tight junction molecule, expression and Ki-67 index. Invasiveness was evaluated by the surgeon's intraoperative assessment and radiological finding, as defined by the Knosp Score.

Results

We included 32 cases of acromegaly (78.1% invasive), 71 hormone inactive adenomas (HIA)(63.4% invasive), seven with cushing adenomas (57.1% invasive) and 10 prolactinomas (20% invasive)($p < 0.001$). Radiologically tumors presented in 15.4% with Knosp °I, 35.9% °II, 29.1% °III and 19.6% °IV.

We found a negative correlation for peripheral Claudin-1 expression with higher Knosp Grades (°III and °IV, $p = 0.02$). Knosp °I-II Claudin-1 positivity was (+) in 27.3%; (++) in 31.8% and (+++) in 40.9% of cases. Knosp °III-IV Claudin positivity was (+) in 51.4%; (++) in 35.1% and (+++) in 13.5%. Peripheral Claudin-1 positivity was associated with a higher grade of resection, as 40.9% Claudin-1 (+++) tumors and 31.8% of Claudin-1 (++) tumors could be completely resected, opposed to 46.7% of Claudin-1 (+) tumors in incomplete resection ($p = 0.03$). The same was found for the histological diagnosis of invasiveness in hormone HIA, which was also inversely correlated with Claudin-1 positivity ($p = 0.02$). There was no significant difference in tumor volume concerning claudin positivity. Intraoperative evaluation of invasiveness was inversely correlated with Claudin positivity as was radiological evaluation of invasiveness ($p = 0.01$).

Conclusion

Claudin-1 expression was inversely correlated to the invasiveness of pituitary macroadenomas. Our study supports the hypothesis, that a dysregulation of cell-cell adhesion contributes to the invasive nature of invasive pituitary macroadenomas. Claudin-1 expression should be assessed in larger cohorts in order to assess its impact on the outcome of macroadenomas.

Neuroonkologie – Gliome IV/Neurooncology – Gliomas IV

P182

Optische Charakterisierung von Fluorescein *in vitro* und *ex vivo* *Optical characterisation of fluorescein in vitro and ex vivo*

R. Xu¹, F. Frenzel², W. Teich³, J. Rösler³, K. Hoffmann², M. Misch³, P. Vajkoczy³, U. Resch-Genger², J. Onken³

¹Charité – Universitätsmedizin Berlin, Berlin, Germany

²Bundesanstalt für Materialforschung und -prüfung (BAM), Institut für Biophotonik, Berlin, Germany

³Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

Objective

The utilization of fluorescein-guided biopsies and resection has been discussed as a suitable strategy to improve and expedite operative technique for the discrimination between contrast-enhancing and healthy tissue. However, little is known about the optical characteristics of fluorescein after biological metabolization in tumor tissue.

Methods

Tumor tissue was obtained from a study cohort of a prospective observational study on the utilization of fluorescein-guided biopsy and resection (n=6) and compared to the optical properties *in vitro* and tumor tissue of glioma patients (n=5) without *i.v.* application of fluorescein. Tissue samples were fixed in 4%PFA overnight at 4°C, immersed in 30% sucrose, embedded in OCT and cut to 10µm sections. The dye-exposed tumor tissues were used for optical measurements to confirm the detectability of fluorescein emission signals *in vitro*. Confocal laser scanning was conducted using an APD for light detection and filters for separation of green (545±12.5nm) and red (655±20nm) emission. Spectra measurements at 488nm excitation were performed under same conditions using an emCCD camera.

Results

Optical measurements of fluorescein in 0.9%NaCl under *in vitro* conditions showed an absorption maximum of $\lambda_{max\ abs}=479\text{nm}$ as detected with spectrophotometer Specord200 and an emission maximum of $\lambda_{max\ em}=538\text{nm}$ as recorded with the emCCD detection system of a custom-made microscope-based single particle setup using a 500nm long-pass filter. Under *ex vivo* conditions, the fluorescein tumor samples revealed a broadening of the emission band. This can be explained by the high pH sensitivity of fluorescein, that can exist in the three different protonation states "neutral", "monoanion", and "dianion", accounting for the different characteristics of fluorescein molecules located in the acid extracellular milieu of the tumor, which most likely exist mainly as monoanions, compared to fluorescein molecules sensing a more basic environment. The latter can result in the formation of the dye's dianion.

Conclusion

Biological metabolization of fluorescein within the scope of preoperative *i.v.* leads to a change in the optical properties of the dye, particularly a broadening of the emission band. This underlines that a profound understanding of the *ex vivo* optical properties of fluorescein is crucial for applications such as intravital microscopy and immunofluorescence staining protocols for localization studies.

Neuroonkologie – Gliome IV/Neurooncology – Gliomas IV

JM–JNS09

Gen-Expressionsprofil von Glioblastomzellen von langzeitüberlebenden, Patienten, die mit einer dendritischen Zell-Immuntherapie behandelt wurden

Gene expression profile of glioblastoma cells from patients with long-term survival treated with dendritic cell immunotherapy

J. Takei^{1,2}, Y. Kamata¹, Y. Akasaki², R. Mori², Y. Yamamoto³, T. Tanaka⁴, M. Murahashi¹, Y. Murayama²

¹The Jikei University School of Medicine, Division of Oncology, Research Centre for Medical Sciences, Tokio, Japan

²The Jikei University School of Medicine, Department of Neurosurgery, Tokio, Japan

³Jikei University Daisan Hospital, Department of Neurosurgery, Tokio, Japan

⁴Jikei University Kashiwa Hospital, Department of Neurosurgery, Chiba, Japan

Objective

Glioblastoma is the most malignant brain tumour of the central nervous system tumours. Dendritic cells (DCs) perform an essential role in the immune system as antigen-presenting cells. Immunotherapy with DCs for glioblastoma is expected to improve the therapeutic outcome for patients by inducing tumour-specific cytotoxic T cells. Previously we reported the effectiveness of immunotherapy with fusion cells (FCs) obtained by merging DCs and patient-derived tumour cells in a phase I/II clinical trial. In this trial, median overall survival reached 30 months for the patients with newly diagnosed glioblastoma. The main aim of this study was to investigate the differences in gene expression and tumour characteristics between patients with long and short survival times.

Methods

We collected patient-derived tumour samples from adults with a newly diagnosed glioblastoma who underwent immunotherapy with FCs from 2006 to 2014. Total RNA was extracted from patient-derived tumour cells using RNeasy plus kit (QIAGEN). mRNA was extracted using Dynabeads mRNA DIRECT Micro kit (Thermo Fisher) and the library was prepared using Ion Total RNASeq kit v2 (Thermo Fisher). Ion chef (Thermo Fisher) and Ion Proton (Thermo Fisher) were used to perform next generation sequencing for whole transcriptome analysis. The samples were divided into two groups in accordance with the patient's overall survival, long-term survivors' samples (group L, 3 years or more survival period) and short-term survivors' samples (group S, less than 3 years survival period). Differential expression analysis between the two groups was carried out using CLC Genomics Workbench (QIAGEN). Genes with fold change > 2 were identified as differentially expressed genes. Gene Ontologies (GO) were assigned and enrichment analysis was carried out using CLC Genomics Workbench.

Results

Whole transcriptome analysis was performed for 6 samples, out of which 2 belonged to group L and 4 belonged to group S. GO enrichment analysis revealed that GO terms for "anatomical structure formation involved in morphogenesis" and "cell differentiation" were over-represented in Group L and Group S, respectively. The GO terms of group L had 7 differentially expressed genes, while the group S had 27 differentially expressed genes.

Conclusion

Patients treated with FCs immunotherapy using patient-derived glioblastoma cells which had high expression of cell differentiation-related genes might tend to have a poor prognosis.

Spinale und zerebrale Metastasen II/*Spinal and cerebral metastases II*

P184

Outcome nach Behandlung von Patienten mit primären und sekundären anaplastischen Meningeomen *Outcome following treatment of patients with de novo and secondary anaplastic meningiomas*

T. Juratli, S. Hennig, T. Pinzer, G. Schackert

Universitätsklinikum Carl Gustav Carus Dresden, Klinik für Neurochirurgie, Dresden, Germany

Objective

Anaplastic meningiomas World Health Organization (WHO) Grade III meningiomas are rare and represent 1%–2% of all meningiomas. They are characterized by significant morbidity and mortality. Anaplastic meningiomas are nowadays considered either to arise de novo (primary anaplastic meningiomas: PAM) or to progress from a lower-grade tumor (secondary anaplastic meningiomas: SAM). In this study, we sought to analyze clinical parameters that may influence progression-free (PFS) and overall survival (OS) following treatment of PAM and SAM.

Methods

Clinical data from patients who underwent resection of an anaplastic meningioma between 1995 and 2018 were evaluated. Kaplan-Meier and Cox regression analyses were performed to determine the impact of different clinical characteristics and different treatment modalities on survival.

Results

We identified 29 patients with an anaplastic meningioma (10 female and 19 male patients). The median age at first diagnosis was 70 years (23 – 85 years). Ten patients had a SAM and 19 patients a PAM. The majority of tumors (n= 18, 62%) were located at the brain convexity. While complete resection (Simpson Grade I) was achievable in 84% (n = 16) of the primary anaplastic meningiomas, only 60% of the secondary anaplastic meningiomas received a complete resection. The PFS of SAM patients was significantly shorter (12.3 months, 95% CI 3.1 – 21.5) compared with PAM patients (56.1 months, 95% CI 0.5 – 119.6, p= .004). All patients received radiotherapy, while only three patients received an adjuvant chemotherapy. In the multivariate analysis, none of the treatment modalities nor other demographic or clinical factors showed a significant influence on patients' outcome (PFS and OS).

Conclusion

Our study highlights the different prognoses of de novo and secondary anaplastic meningiomas. Moreover, it demonstrates that surgery is an effective treatment for secondary and primary anaplastic meningiomas.

Spinale und zerebrale Metastasen II/*Spinal and cerebral metastases II*

P185

Kolloidzyste des dritten Ventrikels – Fallbericht einer spontanen Rückbildung *Colloid cyst of the third ventricle – a rare case of spontaneous regression*

M. E. Weidemeier, H. W. S. Schroeder, J. Baldauf

Universitätsmedizin Greifswald, Klinik und Poliklinik für Neurochirurgie, Greifswald, Germany

Objective

A case report of spontaneous regression of a colloid cyst is presented. Additionally, a review on the present literature is discussed.

Methods

We report about a 48-year-old man who initially presented with a 12-month-history of daily intermitting headache and quotidian self-limiting visual blurriness in the morning. A MR imaging showed a cystic, sharp-edged lesion close to the left foramen of Monro which appeared isointense on T1-weighted images, slightly hyperintense on T2-weighted images and no gadolinium enhancement thus being highly suggestive for a colloid cyst. Since there was no sign of cerebrospinal fluid (CSF) flow obstruction, serial neuroimaging as follow-up was performed. Over the course of three years with ongoing symptoms of recurring headaches and visual impairment follow-up MR imaging demonstrated no changes in the cyst configuration. However, after four years the regular follow-up MRI demonstrated the disappearance of the cyst without the patient having undergone any treatment in the meantime. The headaches kept their intermittent pattern, the patient did not describe any other alteration or acute temporary deterioration of symptoms.

Results

Our case is an extraordinary rare example of a spontaneous resolution of a colloid cyst. Colloid cysts are commonly located in the third ventricle close to the foramen of Monro. Due to growth they may obstruct the foramen and thus the circulation of CSF consecutively causing an obstructive hydrocephalus. However, not all cysts demand for neurosurgical resection since both size and location might not interfere with CSF flow. In rare cases, even a spontaneous regression seems possible and is reported in four cases worldwide to date. The actual reason for cyst resolution remains unclear.

Conclusion

This is the fifth case since 2002 reported about a spontaneous regression of a colloid cyst. The underlying mechanism is thought to be of a spontaneous release of the cyst content by rupture possibly leaving remnants like a cystic wall behind. Being a benign lesion, colloid cysts may be found incidentally but may also present with neurological symptoms and sudden death. In asymptomatic patients follow-up with serial neuroimaging is sufficient as only few cases will demand neurosurgical intervention later on. The presented case is rare but has to be kept in mind when surgical indication is discussed for colloid cysts.

Spinale und zerebrale Metastasen II/*Spinal and cerebral metastases II*

P186

Automatische Detektion und Segmentierung von Hirnmetastasen in Patienten mit malignem Melanom durch ein Deep Learning Model

Performance of an advanced deep learning model in fully automated detection and segmentation of brain metastases in patients with malignant melanoma

L. Goertz, J. Borggreffe, R. Shahzad, B. Kricschek, R. Goldbrunner, L. Pennig

Universitätsklinikum Köln, Köln, Germany

Objective

Cerebral metastases represent an advanced stage of malignant melanoma and requires an adjustment of the oncological treatment concept. Magnetic resonance imaging (MRI) is the imaging modality of choice for detection and follow-up of brain metastasis. Owing to an increasing workload, physician fatigue with the inherent risk of misdiagnosis is a relevant concern, which can affect patient diagnosis, treatment and outcome. The purpose of this study was to develop and evaluate a deep learning model (DLM) based on convolutional neuronal networks that detects and segments brain metastases fully automatically on multiparametric MRI from diverse referring institutions, scanners and vendors in patients with malignant melanoma.

Methods

A total of 54 multiparametric MRI scans (T1-weighted, T1-weighted contrast-enhanced, T2-weighted, Fluid-attenuated inversion recovery sequences) from 54 patients with brain metastasis (mean age: 63.54 ± 13.83 years, 24 females) were used to train and validate the DLM. Independent manual segmentations of the metastases was performed in a voxel-wise manner by two experienced radiologists and served as the ground truth. A three-dimensional convolutional neural network architecture based on DeepMedic (Biomedica, Singapore), which was originally established for detection and segmentation of glioblastoma, was used and underwent dedicated training using five-fold cross validation (5-FCV).

Results

At the time of initial diagnosis, the patients had 102 brain metastases. The average metastasis volume was 2354.27 ± 7809.15 mm³, as determined by the ground truth. Before 5-FCV, the glioblastoma-trained DLM achieved a detection rate of 0.47 (median dice coefficient: 0.64). After 5-FCV, the sensitivity of the DLM increased to 0.87 ($p < 0.05$), with a corresponding median dice coefficient of 0.74 ($p < 0.05$).

Conclusion

After dedicated training using 5-FCV, our DLM detects brain metastases of malignant melanoma in MRI with high accuracy and achieves sufficient segmentation rates despite diverse scanner data. Therefore, it may pose a valuable adjunct for radiologists in cancer imaging.

Spinale und zerebrale Metastasen II/*Spinal and cerebral metastases II*

P187

EC-IC und IC-IC Bypass bei neuroonkologischen Erkrankungen – eine Serie von 3 Patienten *Extracranial to intracranial (EC-IC) and intracranial to intracranial (IC-IC) revascularisation procedures on patients with malignant brain tumour – a series of 3 patients*

A. Tortora¹, H. J. Steiger², J. F. Cornelius², D. Hänggi², M. Sabel², A. Petridis²

¹Kantonsspital Aarau AG, Neurochirurgie, Aarau, Schweiz

²Heinrich-Heine-Universität Düsseldorf, Klinik für Neurochirurgie, Düsseldorf, Germany

Objective

Arterial occlusion during neuro-oncological procedures is a feared complication. While some cortical vessels feeding non-eloquent brain regions or having leptomeningeal collateralization may be sacrificed without resulting neurological deficits, occlusion of small perforators and major vessels usually results in infarction. EC-IC and IC-IC reconstruction techniques can restore blood flow in non-perforating cerebral or cerebellar arteries. We present a series of 3 patients treated with bypass surgery after spontaneous or iatrogenic irreversible arterial occlusion during resection of a malignant brain tumor.

Methods

The data were retrieved from our database of patients treated with cerebral revascularization between January 2016 and August 2019. Only patients with a malignant brain tumor were included.

Results

Between January 2016 and August 2019 we performed 3 revascularizations on patients with malignant brain tumor. A double barrel end-to-end superficial temporal artery to medial cerebral artery anastomosis was performed on insular segment (M2) of a patient with insular WHO IV glioma and spontaneous thrombosis of the middle cerebral artery's main bifurcation. The patient underwent subtotal tumor resection after the bypass in the same procedure. A double barrel EC-IC end-to-end bypass using the occipital artery as donor was constructed after symptomatic occlusion of M1 on a previously operated WHO III glioma patient with exophytic cisternal growth pattern. The recipient arteries were found on cortical M4 branches of MCA. In a third patient with a sylvian metastasis, we created a double IC-IC bypass after an injury of the superior trunk's first bifurcation that was encased in a tumor with hard consistence. The bypass consisted of an end to end and an end to side anastomosis. All procedures were successful. Bypass patency was postoperatively confirmed by imaging without evidence of infarction in the revascularized territories.

Conclusion

Cerebral revascularization for neuro-oncological patients with malignant tumors is a safe procedure in high volume centers where bypass surgery is routinely performed. Positive clinical outcome in our small series encourages aggressive resection even in tumors adherent to or infiltrating major vessels.

Spinale und zerebrale Metastasen II/*Spinal and cerebral metastases II*

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Eine *in vitro* Technologie zur Abschätzung der Effektivität und des Risikopotentials von Substanzen zur Behandlung von Hirntumoren

An in vitro technology to score therapeutic efficacy and risk-potential of substances for targeting brain tumours

K. Koch¹, R. Hartmann², N. Tsiampali¹, C. Uhlmann¹, X. He³, M. A. Kamp¹, M. Sabel¹, R. Barker³, D. Willbold^{2,4}, H. J. Steiger¹, J. Maciaczyk^{1,5}, U. D. Kahlert¹

¹Heinrich-Heine-Universität Düsseldorf, Neurochirurgie, Düsseldorf, Germany

²Forschungszentrum Jülich, Institute for Complex Systems (ICS-6), Structural Biochemistry and JuStruct, Jülich, Germany

³University of Cambridge, Clinical Neurosciences, Cambridge, United Kingdom

⁴Heinrich-Heine-Universität Düsseldorf, Physikalische Biologie, Düsseldorf, Germany

⁵University of Otago, Surgical Sciences, Dunedin, New Zealand

Objective

The upregulation of anabolic processes to maintain high rates of cellular turnover is considered the cancers Achilles' heel. The intervention in altered metabolic pathways of cancer cells have emerged as a promising strategy to develop new treatments and diagnostic procedures. Thereby, the development of pharmacological inhibitors of metabolic enzymes plays a central role due to its effectiveness in targeting cancer cells. Nevertheless, severe adverse effects hinder the efficient clinical translation of promising metabolic enzyme inhibitors and causes a burden on patients and funding bodies. Improved early stage risk-assessment to characterize the specificity of test substances is therefore highly warranted. Here we present a metabologenomic *in vitro* tool to assess therapeutic efficacy and perform risk assessment of pharmacological glutaminase (GLS) inhibitors in the context of neuro-oncology.

Methods

A panel of glioblastoma stem-like cell models grown as neurospheres (GSCs) are treated with inhibitors of GLS. Mode of action was characterized by performing various functional *in vitro* assays such as quantification of cellular growth, clonogenicity, and analysis of cell cycle. Moreover, quantification of the abundance of intracellular metabolites in GSCs subjected to substance treatment, was used to estimate the efficacy of the GLS inhibitor.

Results

Treatment with small molecule inhibitors compound 968 and CB839 effectively diminished cell growth and *in vitro* clonogenicity of glioblastoma 3D cultures. However, metabolic monitoring revealed that only CB839 inhibited GLS enzymatic activity thereby limiting the influx of glutamine derivatives into the TCA cycle. Nevertheless, the effects of both inhibitors were highly GLS specific, since treatment sensitivity markedly correlated with GLS protein expression. Strikingly, we found GLS overexpressed in *in vitro* GSC models as compared to non-cancerous neural stem cells (NSC).

Conclusion

Pharmacologic GLS inhibition is a promising strategy to eradicate GSCs. The incorporation of a multi-parameter mode of action analysis as well as the inclusion of *in vitro* control systems into early stage substance testing is helpful in identifying test compounds with elevated off-target risk. The application of metabologenomics may be helpful in early stage drug development to evaluate toxicity or precision medicine.

Spinale und zerebrale Metastasen II/*Spinal and cerebral metastases II*

P189

Häufigkeit und Verteilung der Fehlerqualitäten beim Sprachmapping – ein Vergleich zwischen direkter kortikaler Stimulation und rTMS

Incidence and linguistic quality of speech errors – a comparison of TMS to intraoperative direct cortex stimulation reveals low reliability

K. Faust^{1,2}, P. Vajkoczy³, M. Münch³, J. Bährend³, T. Picht³, R. Moshourab³, H. Schneider³

¹Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

²Charité – Universitätsmedizin Berlin, Berlin, Germany

³Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

Objective

Due to the inter-individual variance of functional language anatomy, risk prediction based merely on anatomical data is insufficient in language area related brain tumor surgery, implicating a necessity for direct cortical and subcortical mapping during awake surgeries. Reliable non-invasive preoperative methods for language localization hold the potential to reduce the necessity for awake procedures, and may improve patient counselling and surgical planning. Repetitive navigated transcranial magnetic stimulation (rTMS) is an evolving tool for localizing language eloquent areas. The aim of our study was to investigate the reliability of rTMS in locating cortical language sites.

Methods

Prospectively, 25 patients with brain tumors in speech-related areas were evaluated with preoperative navigated transcranial rTMS (5Hz train of five, 105% RMT) and navigated direct cortical stimulation (DCS, 50Hz, 6-8mA, 200µs pulse width) during awake surgeries, employing a picture-naming task. Positive and negative stimulation spots within the craniotomy were documented in the same MRI data set. TMS and DCS language positive areas were compared with regards to their spatial overlap, their allocation into a cortical parcellation system and their linguistic qualities.

Results

There were 2.5-fold more positive language spots within the exposed area in rTMS than in DCS. The comparison of positive rTMS and DCS overlaps revealed a low sensitivity (36%) and a low positive predictive value (16%), yet a high specificity (90%) and a high negative predictive value (96%). Within the overlaps, there was no correlation in error quality. In DCS, 71% of language positive spots were located in the pars opercularis and pars triangularis of the frontal operculum and 27% within the supramarginal gyrus and dorsal portion of the superior temporal gyrus, while in rTMS language positivity was distributed more evenly over a large number of gyri.

Conclusion

The current protocol of rTMS for language was able to confine language negative sites with good dependability, yet was unable to allocate language positive spots. Further refinements of the technique are needed to establish rTMS language mapping as a useful clinical tool.

Spinale und zerebrale Metastasen II/*Spinal and cerebral metastases II*

P190

Frühes postoperatives MRT zur Evaluierung des Resektionsausmaßes bei Gehirnmastasen – Erfahrung an einem spezialisierten Zentrum

Early postoperative MRI to assess the extent of resection in brain metastasis – a single-centre experience

B. Kiesel, J. Furtner, R. Prihoda, M. Mischkulnig, M. Borkovec, T. Rötzer, A. Berghoff, M. Preusser, K. Rössler, G. Widhalm

Medizinische Universität Innsbruck, Wien, Austria

Objective

Neurosurgical resection of brain metastasis represents an important treatment option in the multimodal patient management. The extent of resection according to early postoperative MRI is known to be a crucial factor for patient prognosis and overall survival in gliomas. In brain metastasis the value of early postoperative MRI still remains unclear and no standards for postoperative imaging have been established so far. The aim of our study is thus to analyze the extent of resection in brain metastasis after surgery with early postoperative MRI in a large patient cohort.

Methods

Our study cohort included all patients who underwent resection of a brain metastasis followed by an early postoperative MRI between 2008 and 2017 at the Department of Neurosurgery, Medical University Vienna. T1-weighted sequences with and without contrast media were used to assess the extent of resection. In addition, the intraoperative impression of the performing neurosurgeon with regard to the extent of resection were compared with postoperative imaging data.

Results

Altogether, 95 resections of 98 brain metastasis were performed in 94 patients. Lung cancer was the most frequent primary tumor (49%) followed by breast cancer (14%) and melanoma (12%). According to the neurosurgeon's estimation, complete resection was achieved in 88% of cases. However, early postoperative MRI detected a distinct residual tumor in 30% of cases. Our data indicated an unexpected residual tumor on postoperative MRI in 27% of cases.

Conclusion

Our single center analysis demonstrate a high frequency of unexpected residual tumor after resection of brain metastasis. Since incomplete resection of brain metastasis affects patient prognosis, a standardized postoperative imaging protocol to routinely assess the extent of resection is warranted also in such tumors.

Spinale und zerebrale Metastasen II/*Spinal and cerebral metastases II*

P191

Zerebrale Metastasierung bei Schilddrüsenkarzinom – chirurgische Therapie und Ergebnisse *Brain metastases from thyroid carcinoma – surgical treatment and outcome*

M. Esmaeilzadeh, J. A. M. Müller, M. P. Polemikos, E. J. Hermann, F. Bengel, J. K. Krauss

Medizinische Hochschule Hannover, Neurochirurgie, Hannover, Germany

Objective

Intracranial metastases from thyroid cancer are rare. Although the prognosis of thyroid cancer patients is generally favorable, the prognosis of patients with intracranial metastases from thyroid cancer has been considered unfavorable having a lower survival rate than those without intracranial involvement. Many questions about their management remain unclear. The aim of this study is was to analyze the characteristics, treatments, and outcomes of patients with brain metastases from thyroid cancer.

Methods

Among 4320 patients with thyroid cancer recorded in our institutional databases between 1989 and 2019, 20 patients with brain metastasis were retrospectively collected and analysed. The clinical characteristics, histological type of primary cancer and metastatic brain tumor, additional previous distant metastasis, treatment modalities, locations and characteristics on radiologic findings, time interval between the first diagnosis of the primary thyroid cancer and brain metastasis, thyroglobulin level at the first detection of intracranial metastasis and survival were analyzed.

Results

The mean age at initial and diagnosis was 59.4 years and at the manifestation of cerebral metastasis 64.0 years. The histological types of the primary thyroid cancers were papillary in ten patients, follicular in seven, and poorly differentiated carcinoma in three. The average interval between the diagnosis of thyroid cancer and brain metastasis was 4.4 years (range, 0–15 years). The Karnofsky Performance Status (KPS) at the time of diagnosis of brain metastases was more than 80 % on average. Twelve patients had a single intracranial lesion, 5 patients had 2 or 3 lesions, and 2 patients had 4 and 5 lesions, respectively. Fifteen patients underwent surgical resection. Whole-brain radiotherapy or tyrosine kinase inhibitors were applied as postoperative adjuvant treatment, and radiotherapy and stereotactic radiosurgery was performed in 4 patients. Overall survival time ranged between 0.5 and 77 months after diagnosis of intracranial metastasis.

Conclusion

Patients with thyroid cancer can develop brain metastasis even after many years. An early diagnosis appears important to achieve a better prognosis. Surgical resection and adjuvant treatments in the contemporary era could improve survival time as compared to historical data.

Spinale und zerebrale Metastasen II/*Spinal and cerebral metastases II*

P192

Gibt es einen Stellenwert für die früh-postoperative MRT nach intrakranieller Metastasenresektion? *Is there a role for early postoperative MRI after resection of brain metastases?*

N. Mokhtari¹, B. Berger², M. Simon¹, A. Grote¹

¹Evangelisches Krankenhaus der Stiftung Bethel, Klinik für Neurochirurgie, Bielefeld, Germany

²Evangelisches Klinikum Bethel, Klinik für Neuroradiologie, Bielefeld, Germany

Objective

While glioma patients routinely undergo early postoperative MRI, the role of postoperative and in particular MR imaging following surgery for brain metastases is not clear. In the present study, we have therefore reviewed our institutional experience with early routine postoperative MRI after metastasectomy.

Methods

Pertinent demographic, clinical and imaging data from 230 consecutive adult patients undergoing surgery for brain metastases between 01/2016 and 10/2019 were retrospectively analyzed. In 96 cases early postoperative MRI was performed within the first 72 hours after surgery. Residual tumor was categorized using the RANO criteria as follows: "no residual tumor", "non-measurable residual tumor" and "measurable residual tumor".

Results

54 (56.3%) patients were female and median age was 58.1 years. The most frequent primary tumor sites were lung and breast (respectively 39 [40.6%]; 17 [17.7%]). 63 (65.6%) patients had a single metastasis. 19 (19.7%) cases were diagnosed with 2 and 14 (14.6%) with ≥ 3 metastases. Postoperative MR imaging revealed no hemorrhagic or other complication requiring revision surgery, but 9 (9.4%) ischemias resulting from perforator or small vessel occlusion, and cerebral venous sinus thrombosis in 5 (5.2%) patients. "Measurable residual tumor" was identified in 12 patients (12.5%). Four of these patients had a second surgery and resection of the tumor remnant. "Non-measurable residual tumor" was seen in 17 cases (17.7%), i.e. a complete resection proven by postoperative imaging was performed in only 67 procedures (69.8%). The postoperative MRI study showed residual tumor in 19/91 (20.9%; 7 measurable, 12 non-measurable) patients who had a presumably complete resection according to the operating surgeon's impression. Median follow up was 9.4 months. Residual tumor had no statistically significant impact on overall survival.

Conclusion

Routine postoperative MR imaging following resection of brain metastases might have some value for the diagnosis and management of vascular complications. Importantly, early postoperative MRI identifies a surprisingly large number of cases with unexpected incomplete resections. Future studies will have to define a potential impact of residual tumor on patient survival.

Spinale und zerebrale Metastasen II/*Spinal and cerebral metastases II*

P193

Der tumorbedingte Querschnitt – Analyse einer individuellen und interdisziplinären Erstbehandlung *Tumour-related paraplegia – analysis of an individual and interdisciplinary initial treatment*

T. Liebscher^{1,2}, M. Kreuzträger¹, T. Lübstorf², T. Auhuber³, G. Wüstner⁴, A. Ekkernkamp⁵, M. Kopp^{2,6}

¹Unfallkrankenhaus Berlin, Behandlungszentrum für Rückenmarkverletzte, Berlin, Germany

²Charité – Universitätsmedizin Berlin, Klinik für Neurologie und Abteilung für Experimentelle Neurologie, Berlin, Germany

³Unfallkrankenhaus Berlin, Medizinmanagement, Berlin, Germany

⁴Unfallkrankenhaus Berlin, Controlling, Berlin, Germany

⁵Unfallkrankenhaus Berlin, Klinik für Unfallchirurgie und Orthopädie, Berlin, Germany

⁶Berliner Institut für Gesundheitsforschung, QUEST- BIH Center for Transforming Biomedical Research, Berlin, Germany

Objective

The initial treatment of spinal cord injury (SCI) is based on the concept of comprehensive care. Due to its surgical severity and acute spinal paralysis, initial spine surgery represents a major challenge for spine centres. Due to the exceptional conditions of tumour-related SCI, its treatment requires individual and interdisciplinary approaches. The aim of the study is the descriptive analysis of treatment, outcome, duration of stay and costs compared to traumatic and inflammatory SCI.

Methods

Within the scope of monocentric care research, parameters of patients with acute paraplegia were analyzed from 2011 to 2017. A total of 365 patients (traumatic n=246; inflammatory n=64; tumorous n=55) were included and descriptively analysed.

Results

Characteristic for tumor-related SCI were the higher age (MW: 68 years) and the high proportion of incomplete SCI at admission (71%), which was similar to inflammatory SCI (Fig. 1). In 50% of the cases the thoracic spine was affected. In 87% of the cases spine surgery was performed. The spine surgery complications (9%) were lower compared to the more complex injury patterns after traumatic SCI (24%). Due to the more incomplete tumor-related SCI cases and the non-inflammatory cause, the urinary tract infections, lung infections and the multi-resistant pathogen detection (13%, 9% and 7%) were lower in comparison (Fig.1). 16% of patients died during initial treatment and 88% of these patient's will was documented. Due to the oncological further treatment, the time of the first treatment (mean 23 days) and the associated total costs (mean 19300,- €) were comparatively low (Fig.2).

Conclusion

Patient will and therapy objectives are the foundation of the initial treatment of a tumor-related paraplegia. Spine surgery, tumor board and paraplegiology should closely collaborate to achieve optimal patient care with low SCI-associated complications in the palliative situation.

Fig 1

Baseline characteristics	traumatic n=246	inflammatory n=64	tumorous n=55
Age, median (IQR)	62 (43-77)	72 (62-80)	68 (61-75)
Sex, w, %	29	47	31
AIS at admission, A : B : C : D, %	42 : 6 : 13 : 36	11 : 8 : 17 : 50	22 : 7 : 16 : 55
neurological level at admission, cervical : thoracic : lumbosacral, %	59 : 20 : 18	17 : 16 : 52	24 : 51 : 25
Rate of complications	traumatic n=246	inflammatory n=64	tumorous n=55
Spine surgery complications, %	24	9	9
Bladder infection, %	74	45	13
Pulmonary infection, %	50	39	7
Pressure ulcer, %	19	16	13
Thrombosis, %	7	0	0
Heterotopic ossification, %	2	0	0
Multi-resistant organisms, %	31	33	7
Death during initial treatment, %	8	19	16

Fig 2

	traumatic n=246	inflammatory n=63	tumorous n=55
Total length of stay in days, M (IQR)	79,6 (48,8-113,5)	54,3 (22,2-94,4)	23 (17-32)
	traumatic n=226	inflammatory n=49	tumorous n=40
Surgery costs in €*1000, M (IQR)	5,7 (3,1-8,4)	5,3 (3-8,2)	5 (2,6-6,9)
Total costs in €*1000, M (IQR)	57,2 (33,8-97,9)	43,5 (24,8-80)	19,3 (15,4-27)

Freie Themen/*Free topics*

P194

Ergometrische Verbesserung des Operationsarbeitsplatzes zur Steigerung der Leistungsfähigkeit und Erhalt der Gesundheit des OP-Personals

Ergometric improvement of working place in the OR to improve capability and physical health for OR staff

C. Ewelt¹, V. Lanwer², M. Yavuz², S. Zawy Alsofy¹, W. Stummer², R. Stange³, M. Klingenhöfer⁴

¹Sankt Barbara-Klinik Hamm-Heessen, Klinik für Neurochirurgie, Hamm, Germany

²Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

³Universitätsklinikum Münster, Abteilung für Muskuloskeletale Medizin, Münster, Germany

⁴Städtisches Klinikum Dresden, Klinik für Orthopädie, Dresden, Germany

Objective

Working place of spine surgeons in the operating room (OR) requires permanent standing occupation in a monotone constrained posture. The static load is often aggravated by burden of an X-ray lead gown. Working times in excess of 10 hours are not rare due to economic reasons. The ergonomic arrangement of the working place in the OR is therefore an important measure to improve and preserve capability and physical health for surgeons and assisting staff.

Methods

In a prospective, oligocentre observational study with N=30 participants evaluation was carried out, whether the use of a polyurethane foot mattress of 2 cm thickness would influence subjective capability and physical health. According to a standardized questionnaire, subjective parameters before, during and after the working process in the operating room were recorded. N=4 questionnaires with versus without use of a foot mattress of each study participant were analysed. Further, N=10 participants were included for anatomical and ergonomical evaluation. In addition, electronical plantar footprint measurement and optical pedobarography and gravity loading for each foot were revealed by using a sensoric sole, which analysed 5-minute-standing and movements in a simulated working situation, comparable to reality in the OR.

Results

83% of N=30, so in 120 consecutive questionnaires, participants reported a positive effect as well as an improvement of capability by using a polyurethane foot mattress independent of the duration of use. A reduction of weariness, leg pain and lower back pain was reported for use of a foot mattress in excess of 4 hours ($p<0,05$). Pedobarography for a 5-minute-simulation of standing and working in the OR revealed an improvement concerning centre of pressure in the analysed feed. The mean pressure was 26% lower with a significant improvement of $P<0.05$.

Conclusion

Ergonomic arrangement of the individual working place is an established matter of course according to the guidelines of workers compensation board. Working place of spine surgeons and operating staff leads to a wearing and constrained posture. The flexible standing position on a polyurethane foot mattress leads to a significant performance enhancement and improvement of physical health of the spine surgeon and the operation staff.

Freie Themen/*Free topics*

P195

Risikobewertung bei chronischen subduralen Hämatomen bei 148 Patienten – ein einfacher Wert für die Vorhersage von Rezidiven
Risk assessment in chronic subdural haematoma evaluated in 148 patients – a simple score for predicting recurrence

E. Suero Molina¹, L. Borscheid¹, M. Freistühler², W. Stummer¹, S. Schipmann-Miletic¹

¹Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

²Universitätsklinikum Münster, Controlling Department, Münster, Germany

Objective

Chronic subdural hematoma (CSDH) is a frequent disease in neurosurgical practice. However, a considerable recurrence rate keeps this condition challenging to treat. We aimed to provide a simple tool for risk assessment in these patients.

Methods

We conducted a retrospective analysis of surgically treated patients with chronic subdural hematomas. In addition to patients' demographics, radiological assessment included volume, thickness, midline shift and density of hematomas. Statistically significant variables in univariate analysis were further analyzed in a multivariate logistic regression model to create a risk score for recurrence of CSDH.

Results

A total of 148 patients were identified and included for analysis. 50.7% (n=75) were older than 76 years of age. The overall hematoma recurrence rate requiring surgery was 23.6% (n=35). Preoperative hematoma thickness >30mm, as well as preoperative thrombocytopenia, midline shift >6 mm, hematoma volume >80ml and overall hematoma density >45 Hounsfield Units (HU), were significantly more frequent in the recurrence group. Furthermore, after multivariate assessment, preoperative hematoma thickness, thrombocytopenia, postoperative midline shift and hematoma density were independent risk factors and included in the risk assessment tool. Patients were divided into 3 risk groups corresponding to the total scores.

Conclusion

We provide a simple risk-score assessment for predicting recurrence of subdural hematoma. However, since therapy algorithms differ remarkably between neurosurgical services, it remains to be seen if these results are applicable to other institutions. A prospective study that evaluates the reliability and validity of this risk-score in different institutions is therefore needed to assess the clinical value of this tool.

Freie Themen/*Free topics*

P196

Obstruktion moderner Titan- und Silikon-Shuntventile durch arachnoidale extrazelluläre Matrix-Membranen *Modern titanium and silicone shuntvalve implants and internal tissue obstructions by arachnoid extracellular matrix membranes*

H. C. Ludwig¹, C. Reitemeyer¹, H. C. Bock¹, M. Sigler²

¹Universitätsmedizin Göttingen, Neurochirurgie, Schwerpunkt Pädiatrische Neurochirurgie, Göttingen, Germany

²Universitätsmedizin Göttingen, Pädiatrische Kardiologie und Intensivmedizin, Göttingen, Germany

Objective

Shunt valves imply the demand for high performance rates and life long function. To overcome traditional silicone materials adjustable and gravity adapted titanium valves still occlude and cause dysfunction. Even high experienced departments treating the most delicate and vulnerable preterm with PHHC, valve complications in this group occur quite often. The aim of the present study was to investigate silicone and titanium valves for occupation with cellular and proteinous materials inside the housings.

Methods

19 explanted shunt valves from children between 2 and 182 months of age were investigated following obstruction. After fixation in formalin and embedding in hardresin, the specimens were cut and slices were ground to a thickness of 5-30 microns. Histology and immunohistochemistry was performed using antibodies with markers for microglia, astrocytes, platelets, monocytes and the matrix proteins laminin, fibronectin, collagen IV.

Results

Traces, layers and plaques could be demonstrated in every investigated silicone or titanium valve with an implantation time of more than 6 days. Most of the tissue was found adjacent to silicone and titanium surfaces of the inner housing, the rotor for the adjustment and the ball in cone system. Staining with markers for micro- and astroglia was positive in 40%-60% of the specimen, mostly demonstrating a proteinous layer positive for laminin (80%), fibronectin (30%) and collagen IV (30%).

Conclusion

Tissue reactions and colonisations with cellular and proteinous material are common in silicone and inside titanium shunt valves causing serious obstruction in PHHC. Obstructive layers consisting of extracellular matrix resemble astrocytic repair mechanisms of subventricular polarized astrocytes adjacent to the basal membrane. The knowledge of these typical arachnoid pattern of tissue colonisation is a prerequisite for developing future shunt devices.

Freie Themen/*Free topics*

P197

Kognitive Fähigkeiten und neuronale Aktivität im medialen präfrontalen Kortex nach Läsion des *Nucleus fastigii* im Rattenmodell

Lesion of the fastigial nucleus in juvenile rats affects cognitive function and neuronal activity in the prefrontal cortex

Y. Al Krinawe, S. Helgers, S. Al-Afif, M. Alam, E. J. Hermann, K. Schwabe, J. K. Krauss

Medizinische Hochschule Hannover, Neurochirurgische Klinik, Hannover, Germany

Objective

Cerebellar cognitive affective syndrome, with persistent deficits in motor, cognitive and emotional domains, may result from various types of cerebellar midline injuries. It is, however, not exactly known which anatomical structures are involved. Here we investigate whether bilateral fastigial nucleus lesions early in life would affect limbic and cognitive-associative related functions later in life in a rat model. Furthermore, potential changes in the neuronal activity in the medial prefrontal cortex (mPFC) were tested.

Methods

The fastigial nucleus was lesioned bilaterally by thermocoagulation via stereotaxically implanted electrodes in 23-day old male Sprague Dawley rats. Electrodes were inserted without application of electric current in a sham-lesion group. Together with naïve rats they served as controls. All groups underwent standardized examinations investigating locomotive activity (open field) and coordination (rotarod) during development, as well as anxiety behavior (elevated plus maze), and cognitive-associative functions (radial maze and oddball paradigm) when they had become adult. Thereafter, electrophysiological recordings were performed in the mPFC. Finally, lesions and recording sites were histologically verified.

Results

In rats with lesions of the fastigial nucleus motor coordination on the rotarod was disturbed during development until adulthood, whereas locomotive behavior was only reduced until postsurgical day 7. As adults, lesioned rats were more anxious on the elevated plus maze, and showed mild impairment in learning the oddball paradigm and the radial maze test as compared to both control groups. Electrophysiological recordings showed a pattern change in mPFC single unit activity in lesioned and sham lesioned rats. Furthermore, the coherence between the mPFC local field potential and the electrocardiogram over the sensorimotor cortex was enhanced across delta, theta, alpha and beta frequency bands in lesioned rats as compared to the control groups.

Conclusion

Enhanced anxiety and reduced cognitive functions together with altered firing patterns and low frequency band oscillations in the mPFC after lesions indicate an important role of the fastigial nucleus in the context of the cerebellar cognitive affecting syndrome.

Freie Themen/*Free topics*

P198

Der Finde-das-Symbol-Test – Normierung eines Neglekttests mit fünf Parallelversionen, entwickelt für die klinische Verlaufsbeobachtung von Hirntumorpatienten

The find-the-symbol test – a normative study comparing five parallel versions of a modified Bells neglect test designed for clinical monitoring of brain tumour patients

C. Schröter¹, A. Wagner¹, S. Kochs¹, R. H. Goldbrunner¹, _ . NOA-19 Studiengruppe^{2,3,4,5,6,7,8,9,10,11,12}, C. Weiß Lucas¹

¹Universitätsklinikum Köln, Allgemeine Neurochirurgie, Köln, Germany

²Universitätsklinikum Münster, Neurochirurgie, Münster, Germany

³Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

⁴Universitätsklinikum Würzburg, Neurochirurgie, Würzburg, Germany

⁵Universitätsklinikum Mainz, Neurochirurgie, Mainz, Germany

⁶Universitätsklinikum Carl Gustav Carus Dresden, Neurochirurgie, Dresden, Germany

⁷Klinikum Chemnitz gGmbH, Neurochirurgie, Chemnitz, Germany

⁸Universitätsklinikum Schleswig-Holstein, Neurochirurgie, Schleswig-Holstein, Germany

⁹Helios Kliniken, Neurochirurgie, Schwerin, Germany

¹⁰Universitätsklinikum Regensburg, Neurochirurgie, Regensburg, Germany

¹¹Universitätsklinikum Freiburg, Neurochirurgie, Freiburg, Germany

¹²Donau Isar Klinikum, Neurochirurgie, Deggendorf, Germany

Objective

The assessment of neurocognitive functions in brain tumour patients suffers from the limited availability of sensitive and validated instruments to detect even slight or moderate impairments. The Bells cancellation test is most widely used for assessing neglect in brain tumour patients but does not offer the option of parallel testings and is rather demanding for the in general cognitively and emotionally affected brain tumour patients. Therefore, a simplified version of the Bells cancellation test titled "Find the symbol!" test (FST) was designed and evaluated in five parallel versions.

Methods

192 healthy volunteers (96 male, 96 high general education level, median age 54 yrs [18-89 yrs]) were tested with the five parallel versions of the FST and additional standard tests (i.e., Bells cancellation test, Apples test, line bisection test) in pseudo-randomized sequence. Motivation and distress level were assessed prior to testing, test results, duration and subjective difficulty level were assessed for each test. The influence of subjective factors on outcome was assessed using ANOVA., parallel-test reliability between FST versions and the validity of the FST compared to standard tests were analysed.

Results

The FTS test result i.e. the percentage of expected cancellations decreased with high age ($F[1,153]=28.4$, $p<0.001$) and was higher in females ($F[1,153]=7.5$, $p<0.01$)., test duration depended on age ($F[1,153]=111.2$, $p<0.001$) and educational level ($F[1,153]=14.1$ $p<0.001$). The subjective difficulty level was slightly influenced by the patients motivation alone ($F[1,153]=4.7$, $p<0.05$). The FTS results were well comparable across the five FTS parallel versions (95.5 ± 2.5 % of expected cancellations). Compared to the standard Bells tests, the FTS was had a shorter administration time (70 ± 30 vs. 102 ± 43 s, $p< 0.001$) and was better accepted as reflected by a subjective difficulty rating of 2.4/10 versus 3.4/10 ($p<0.001$).

Conclusion

The FTS provides a brief and well-tolerated alternative to the commonly used Bells cancellation test for neglect assessment, offering five parallel versions suited for longitudinal studies.

Freie Themen/*Free topics*

P199

Nutzen oder Last? – verstellbare Ventile beim Normaldruckhydrozephalus *Benefit or burden? – adjustable valves in normal pressure hydrocephalus*

S. Kalb, F. Ringel, A. Gutenberg

Universitätsmedizin Mainz, Klinik und Poliklinik für Neurochirurgie, Mainz, Germany

Objective

There is dispute if ventriculo-peritoneal shunting (VPS) with adjustable valves (AV) should be recommended in patients with normal pressure hydrocephalus (NPH), as positive response to valve pressure adjustment is often lacking over time.

Methods

We retrospectively analyzed the clinical effect of valve pressure adjustments during the postsurgical course in NPH.

Results

71 patients with presurgical positive spinal tap test were operated between January 2007 and December 2016 for NPH, in whom an AV was implanted. 42 were male, mean age at shunt surgery was 73 years. 8 patients were excluded for statistical analyses as follow-up time was less than 3 months. For 63 patients the mean follow-up time was 52.1 months. A total of 364 follow-up visits was analyzed, 77% of these were regular scheduled controls. During these controls, 127 adjustments of AV opening pressures were performed in 43 patients (median of 3 adjustments per patient). Only 20 (31.5%) of these adjustments lead to improvement of symptoms. Three groups of patients were identified: (1) 16% never benefited, (2) 27% only transiently improved and (3) 57% permanently profited from VPS. In 64.8% of group (2) and 66.7% of (3), improvement of symptoms was achieved by valve pressure adjustments, only. Median time to permanent deterioration of symptoms in group (2) was 10.9 months. There were no differences in the outcome associated with comorbidities, the kind of AV, the initial valve pressure chosen or presence of a gravitational unit.

Conclusion

As already known from previous publications, only half of patients with NPH have a long-lasting benefit from shunt placement with a certain decline of symptoms after about 11 months. However, the amount of patients with a beneficial long-term outcome can be doubled by repetitive AV adjustments.

Freie Themen/*Free topics*

P200

Quantitative 3D-Analyse der Grubenbildung der Schläfenregion nach Kraniektomie und Kranioplastie *Quantitative assessment and localisation of the hollowing of the temple after craniectomy and cranioplasty*

M. Kosterhon, F. Ringel, M. Jägersberg

Universitätsmedizin Mainz, Neurochirurgische Klinik und Poliklinik, Mainz, Germany

Objective

Conventionally offered computer-aided design (CAD) cranioplasty implants are shaped with respect to the bony defect. Temporal muscle atrophy and displacement following decompressive craniectomy and time delayed cranioplasty are not taken into account, resulting in a typical residual contour defect at the temple, despite surgical efforts of temporal muscle restoration. This can present a considerable esthetic discomfort for patients and their surroundings. The aim of this work was to assess the precise localization and volume of the hollowing defect after cranioplasty, to path the way for a surgical corrective during future cranioplasties.

Methods

We analyzed CT data of patients who had undergone both craniectomy and conventional CAD cranioplasty in our institution between 2012 and 2018. All of these patients had had surgical efforts to restore temporal muscle during cranioplasty. Out of these, all cases with CT datasets suitable for 3D analysis of the skin surface prior to craniectomy and at least 6 weeks after cranioplasty were searched. In these patients, the two respective datasets were fused following a dedicated algorithm and software (Amira, Thermo Fisher Scientific). This allowed to visualize the shape of the hollowing defect as a volume, to quantify its volume and to localize the center of the defect volume (defined as the thickest part of the volume) in reference to the skull.

Results

91 patients had undergone both procedures between 2012 and 2018. Of these, 26 patients had suitable datasets. In ten of these patients, 3D visualization did not show an apparent esthetic defect of the temple. Sixteen patients had an apparent defect and their datasets were analyzed as described above. The average volumetric esthetically relevant temple defect volume was 5.0 ml (SD: ± 4.5 ml). The localization of this defect was centered around the area behind the zygomatic process of the frontal bone and just below the superior temporal line, approximately 3x3 cm².

Conclusion

This work supplies evidence for the indication of a surgical corrective during cranioplasty of an expectable hollowing defect of the temple. This defect is of relatively small volume, but at an esthetically critical area, where conventional surgical techniques fail to restore soft tissue volume. Based on this 3D data analysis, we are planning surgical strategies to improve esthetical results fast and with an approved material, e.g. PMMA bone cement adaptation or CAD prosthesis modification.

Freie Themen/*Free topics*

P202

HWK2-3 Wirbelkörperersatz – Operationstechnik und Literaturübersicht *C2-C3 replacement surgery – a technical note and review of the literature*

S. Ridwan, A. Grote, M. Simon

Evangelisches Klinikum Bethel, Neurochirurgie, Bielefeld, Germany

Objective

Anterior C2 replacement alone or in combination with C3 is infrequently performed in daily neurosurgical practice. Here we report an illustrative case and a review of the literature.

Methods

A 24-year old male presented with acute tetraparesis after suffering a stair fall. Initial CT Imaging revealed partial osteolysis of C2 and 3. Subsequent MRI showed additional spinal cord compression due to a ventral epidural mass. Emergency dorsal decompression and instrumentation surgery was performed. Motor function improvement (mild upper limb paresis) was rapid and almost complete. The histological work-up revealed an osteoblastoma. We felt that definitive surgical management was mandatory. A posterior release through rod removal was performed, followed by a high anterior ventral approach to C2-3 with corpectomy and fusion using a screw fixated custom-made mesh-implant and finally posterior fixation C1-7. Given the patient's young age, initial C0-7 instrumentation was reduced to C1-7. A review of the literature was performed.

Results

Postoperative imaging confirmed complete resection and proper implant placement and alignment. We found 10 reports with 1-11 cases in the pertinent literature addressing this matter. All described combined anterior-posterior approaches. A few described the high anterior cervical approach used in this case, others performed transmandibular or transoral surgery. One reported additional Halo-Fixation. Fusion techniques included autologous bone grafts or mesh-implants with or without anterior fixation. Revision and fusion rates were up to 14% and $\geq 90\%$ respectively. A high anterior cervical approach and custom-made mesh-implants with additional screw fixation may offer some advantages over more traditional surgical management strategies.

Conclusion

A high anterior cervical approach for C2-3 replacement utilizing a screw fixated custom-made mesh-implant can be performed without a transmandibular or transoral approach with satisfying results possibly reducing surgical morbidity. We feel that a combined approach with additional posterior fixation is mandatory.

Freie Themen/*Free topics*

P203

Low-tech Methode zur Kraniotomieplanung an der Schädelkonvexität *Low-tech method for craniotomy planning of convexity targets*

M. Jägersberg, F. Ringel

Universitätsmedizin Mainz, Neurochirurgische Klinik und Poliklinik, Mainz, Germany

Objective

Computer navigation for precise craniotomy planning is widely available. Nonetheless, in case of navigation breakdown or limited resources, for educational purposes and surgeon's confidence, every neurosurgeon should be able to hark back to a conventional technique to locate a target on the convexity with acceptable precision.

We present here a method to localize a target based on fundamental geometry with inexpensive and globally available tools (conventional 2D imaging in one single plane, calculator, divider).

Methods

The distances of a defined target from two distinct landmarks (eg. nasion, porion) are assessed in a CT or MR data set with a conventional image viewer within one single plane and by means of Pythagoras' theorem. The two distances from the landmarks are marked as circles onto the head of the patient with the help of a divider. The intersection defines the target. The congress presentation will include illustration and proof of the geometrical background and a step-by-step video of the procedure.

Results

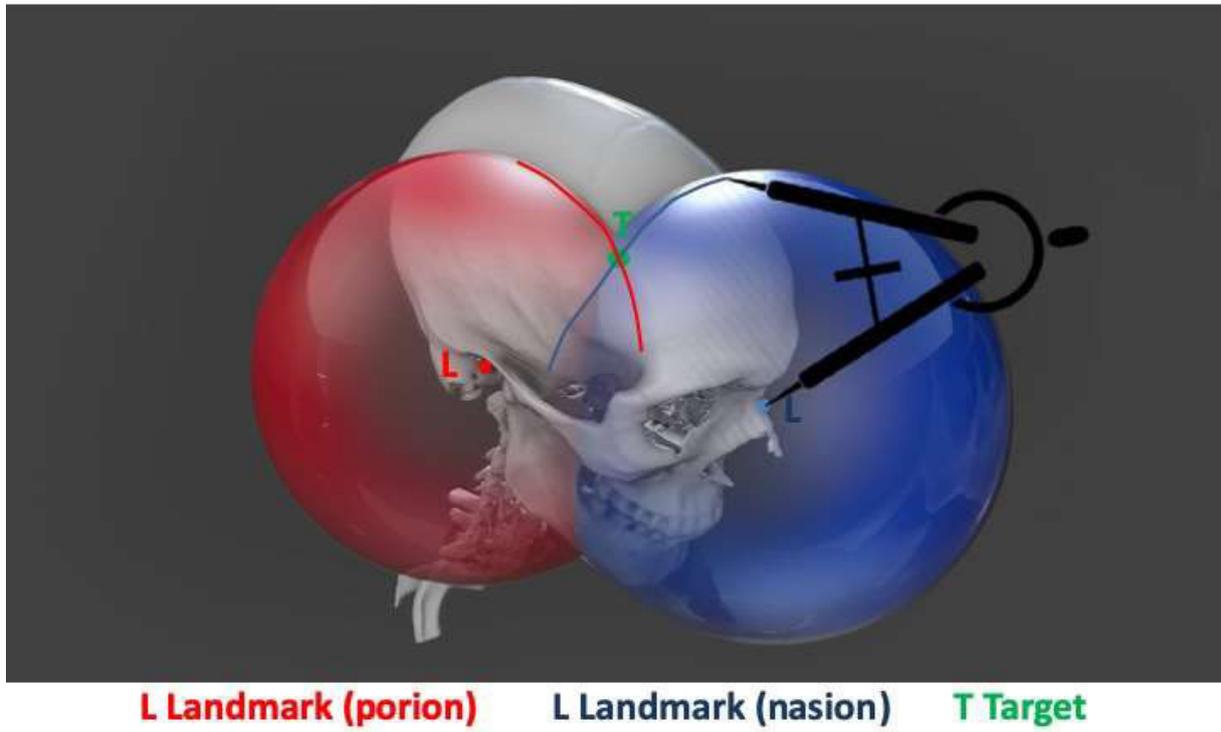
In a first step, 20 radio-opaque targets were placed on a saw bone skull prior to CT scanning. Targets were then assessed with the here described method and with navigation as gold standard. The mean offset between the measured target and the real target was 3.2 ± 2.4 mm in this series. The mean offset between computer-navigated target and real target was 1.8 ± 1.1 mm in this series (BrainLab Colibri Cart 1.1, $p < 0.05$).

With regard to this successful saw bone model a clinical study was executed. In 15 patients undergoing navigated cranial procedures, 100 targets were set randomly over the convexity in a navigation tool and localized with the here presented method and then with navigation. The mean offset was 10.9 ± 5.2 mm, with a confidence interval of 9.9 – 11.9 mm ($\alpha = 0.05$).

Conclusion

This is a low-tech procedure for localization of a radiological target on the convexity of the patient's head in short time and with inexpensive and globally available tools, with satisfying precision for many procedures.

Fig 1



Freie Themen/*Free topics*

P204

***In vitro* Testung explantierter VP-Shuntventile mit vermuteter Dysfunktion**

In vitro testing of explanted shunt valves in hydrocephalic patients with suspected valve malfunction

C. Bettag¹, C. Von der Brelie¹, F. Freimann¹, U. W. Thomale², V. Rohde¹, I. Fiss¹

¹Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

²Charité – Universitätsmedizin Berlin, Neurochirurgie/Pädiatrische Neurochirurgie, Berlin, Germany

Objective

Diagnosis of symptomatic valve malfunction in hydrocephalic patients treated with VP-Shunt (VPS) is still a challenge. Clinical symptoms such as headache or nausea are unspecific, hence cerebrospinal fluid over- or underdrainage can only be suspected but not proven. Knowledge concerning valve dysfunction is still limited. We aim to provide data on the flow characteristics of explanted shunt valves in patients with suspected valve malfunction.

Methods

An *in vitro* shunt laboratory setup was used to analyze the explanted valves under conditions similar to those in a ventriculo-peritoneal shunt system. The differential pressure (DP) was adjusted stepwise to 20, 10, 6 and 4 cmH₂O. The flow rate of the explanted and the regular flow rate of an identical reference valve were evaluated at the respective DPs.

Results

Twelve valves of different types (three Codman CertasPlus, four Miethke gravity-regulated Shuntassistant, three Codman Hakim programmable valve, two DP-components of the Miethke proGAV 2.0 valve) from eight patients (four male) with internal hydrocephalus were explanted between 2016 and 2017. Four patients suffered from idiopathic normal pressure (iNPH), three patients from posthemorrhagic and one patient from obstructive hydrocephalus. Bonferroni-adjusted post-hoc analysis revealed a significant difference ($p < 0.001$) of the flow rate between each explanted shunt valves and their corresponding reference valve, at each DP.

Conclusion

In all patients with suspected valve malfunction, significant alterations of flow rates were demonstrated, verifying a valve deficiency, which could not be objectified by the diagnostic tools used in the clinical routine. In cases with obscure clinical VPS insufficiency, valve deficiency should be considered.

Freie Themen/*Free topics*

JM–JNS10

Längswirkungen der kombinierten Bypass-Chirurgie auf abnorme Nebenkanäle bei der Moyamoya-Krankheit *Longitudinal effects of combined bypass surgery on abnormal collateral channels in moyamoya disease*

S. Yamamoto, D. Kashiwazaki, E. Hori, N. Akioka, N. Kuwayama, S. Kuroda

University of Toyama, Department of Neurosurgery, Toyama, Japan

Objective

In moyamoya disease (MMD), dilated perforating arteries such as lenticulostriate arteries and thalamic perforators, and anterior and posterior choroidal arteries often abnormally anastomose with medullary arteries in periventricular area and retrogradely supply collateral blood flow to ischemic cerebral cortex. These abnormal collateral channels have been recognized as the potential bleeding source in hemorrhagic MMD. Therefore, to regress the abnormal collateral channels is one of the purposes of surgical revascularization for MMD, especially hemorrhagic type. Present study was aimed to clarify if our surgical procedure, superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis and encephalo-duro-myo-arterio-pericranio-synangiosis (EDMAPS) can regress the abnormal collateral channels in adult and pediatric patients with MMD.

Methods

Suzuki's angiographical stage and development of three subtypes of collateral channels including lenticulostriate, thalamic, and choroidal channels were evaluated on cerebral angiography before and 3-6 months after combined bypass surgery. Development of abnormal collateral channels was categorized into 3 grades (Grade 0, 1, and 2) based on degree of their extension. Postoperative advancement of Suzuki's stage and regression of abnormal collateral channels were statistically analyzed.

Results

Present study included 63 involved hemispheres of 44 adult patients and 29 of 17 pediatric patients with MMD who underwent combined bypass surgery and cerebral angiography before and after surgery. Suzuki's angiographical stage was significantly advanced after surgery in both adult and pediatric hemispheres ($P=0.042$ and $P<0.001$, respectively). Lenticulostriate, thalamic, and choroidal channels were significantly regressed in adult hemispheres after surgery ($P<0.001$, $P=0.012$, and 0.0028 , respectively, **Fig. 1A**). In pediatric hemispheres, lenticulostriate and choroidal channels were significantly regressed ($P=0.0050$, 0.034 , respectively, **Fig. 1B**). Representative case is shown in **Fig. 2**. No ischemic and hemorrhagic stroke occurred during follow-up periods (40.2 ± 25.5 and 54.9 ± 19.7 months in adult and pediatric patients, respectively).

Conclusion

STA-MCA anastomosis and EDMAPS was effective to prevent not only ischemic symptoms but also hemorrhagic event through remarkably regressing the abnormal collateral channels that can be the hemorrhagic source in MMD.

Fig 1

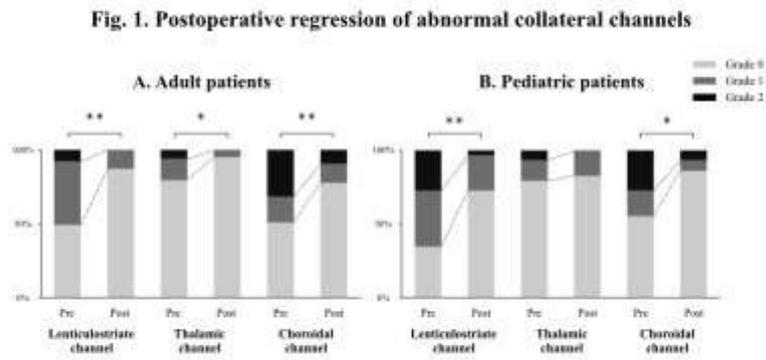
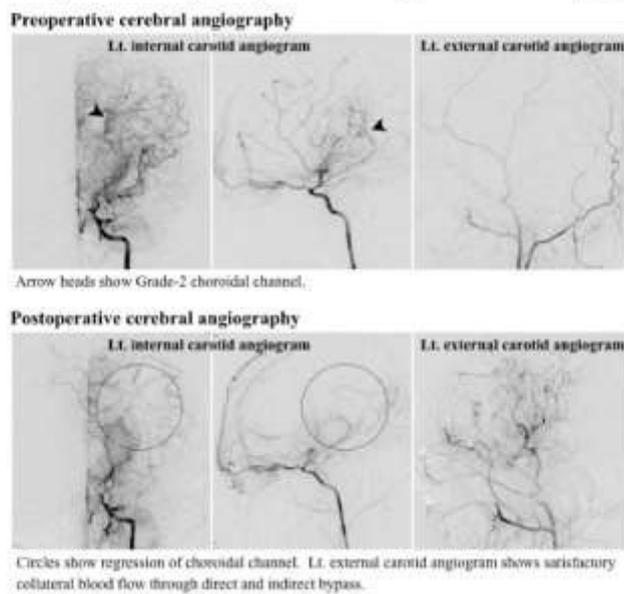


Fig 2

Fig. 2. Preoperative and postoperative findings on cerebral angiography



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P205

Closed-loop (auto-) vagus Nervstimulation – maßgeschneiderte Therapie oder ungerichtete Behandlung – eine Fallserie

Closed-loop (auto-) vagus nerve stimulation – patient-tailored therapy or undirected treatment – a case series

P. Spindler, P. Vajkoczy, U. C. Schneider

Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

Objective

In multi-drug-resistant epilepsy vagus nerve stimulation (VNS) is an efficacious additional treatment to reduce seizure frequency and –severity. A recently developed cardiac-based seizure detection (CBSD) algorithm triggers additional stimulation upon heart rate increases of at least 20% (Model AspireSR). Yet, long term sensitivity and specificity of the CBSD-algorithm remain unclear. We present a case series of 11 adult patients with epilepsy with AspireSR

Methods

Individual VNS data and seizure diaries were reviewed. Open- and closed-loop VNS was active in all patients. We reviewed CBSD-settings, operating hours and battery status of the devices. Percentage of auto-stimulation was assessed in comparison to continuous but intermittent stimulation. If seizure diaries were available, we verified whether a high rate of auto-stimulation was present during the documented seizures

Results

We reviewed 11 patients with a mean age of 28 years (± 18 y). Mean duration since implantation was 43 months (± 13 m). Mean operating time was 4908 hours (1766-8907h), CBSD-thresholds ranged between 30% and 70%. Battery status was 75% in all patients. No correlation between CBSD-thresholds and number of auto-stimulations was seen. Of 2.471.370 detected stimulations 100.448 (4,1%) were auto-stimulations according CSDB-algorithm. Proportion of auto-stimulation varied substantially. While 7 patients had a mean of 2.4% (± 2.2 %), 4 patients had a significantly higher proportion of auto-stimulation 9.3% (± 3.2 %). Seizure-frequency was higher in patients with more auto-stimulation, according to data from seizure diaries (eligible in 5 patients, only). Adverse events occurred in none of the patients

Conclusion

High sensitivity (>80%) of seizure-detection was described in short time observations. In another study 35% of detected seizures were treated with auto-stimulation. Here we provide long-term results for sensitivity and specificity of the CBSD algorithm. While sensitivity seems to be high, we presume specificity to be weak. An extremely high number of auto-stimulations is supposedly false-positive. Yet, treatment was well tolerated by the patients without any adverse events and battery life did not seem to be compromised, despite the high number of auto-stimulations. CBSD is a promising development, yet the algorithm should be revised to provide a better specificity

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P206

Stimulationssystem bezogene Komplikationen bei Tiefenhirnstimulation an einem großen Patientenkollektiv von 586 Operationen im Langzeit-Follow-up – häufigeres Auftreten bei Tourette und Dystonie
Long-term hardware-related complications of deep-brain stimulation in a large cohort of 586 surgeries – more frequent in Tourette' and dystonia

J. Runge¹, A. Saryyeva², M. Wolf³, C. Blahak³, C. Schrader⁴, T. M. Kinfe⁵, H. Bänzner³, M. Abdallat², J. K. Krauss²

¹Medizinische Hochschule Hannover, Neurochirurgie, Hannover, Germany

²Medizinische Hochschule Hannover, Neurochirurgie, Hannover, Germany

³Universitätsklinikum Mannheim, Neurologie, Mannheim, Germany

⁴Medizinische Hochschule Hannover, Neurologie, Hannover, Germany

⁵Universitätsklinikum Bonn, Neurochirurgie, Bonn, Germany

Objective

In this retrospective study we determined the frequency of hardware-related complications of deep brain stimulation in a large series of patients.

Methods

586 surgeries for DBS electrode implantation were performed from 1997 to 2018. All procedures were performed or supervised by the same neurosurgeon in three different centers using the same technique. The median follow-up was 3.7 years with the longest follow up of 16.9 years. Hardware-related complications within this time were documented and analysed.

Results

In 27 cases (4.5%) we could detect hardware complications. There were 11 lead fractures which in reimplantation of the leads in 10 cases, while one patient refused to undergo another surgery. Three of these patients had fractures of both leads. Fifteen patients had fractures in the extension cables connecting the lead with the implanted pulse generator (IPG). Malfunction of the IPG resulted in IPG replacement before battery depletion in one case. These complications became manifest between 1 month and 6.4 years after surgery, at a mean of 3.7 years. We found a significantly higher rate of fractures (lead and extension) in patients with Tourette syndrome (21.3 % of Tourette-patients, $p=0.007$). Also patients with dystonia got a significantly higher concurrency of lead fractures (3.7%, $p=0,043$).

Conclusion

Sustained or repetitive muscle contractions in dystonic patients or motor tics in patients with Tourette syndrome cause a higher physical exposure for DBS hardware resulting in a higher rate of fractures.

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P207

Langzeitergebnisse nach Tiefenhirnstimulation bei Zwangserkrankung – klinische Befunde und Lebensqualität nach 4–8 Jahren
Long-term deep brain stimulation in treatment-resistant obsessive-compulsive disorder – outcome and quality of life at 4–8-year follow-up

A. Saryyeva¹, L. Winter², K. Schwabe¹, H. E. Heissler¹, J. Runge¹, M. Alam¹, I. Heitland², K. Kahl², J. K. Krauss¹

¹Medizinische Hochschule Hannover, Neurochirurgie, Hannover, Germany

²Medizinische Hochschule Hannover, Psychiatrie, Sozialpsychiatrie und Psychotherapie, Hannover, Germany

Objective

Deep brain stimulation (DBS) has been proposed as a promising treatment for patients with treatment refractory obsessive-compulsive disorder (trOCD). However, the optimal site for stimulation is still a matter of debate, and clinical longterm follow-up observations including data on quality of life are sparse. We here present 6 trOCD patients who underwent DBS with electrodes placed in the bed nucleus of the stria terminalis/ anterior limb of the internal capsule (BNST/ALIC), followed for 4-8 years after lead implantation.

Methods

In this prospective observational study, 6 patients (4 men, 2 women) aged 32-51 years suffering from severe to extreme trOCD underwent DBS of the BNST/ALIC. Symptom severity was assessed using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), and quality of life using the World Health Organization Quality of Life assessment scale (WHO-QoL BREF). Follow-up was obtained at least for 4 years in all patients.

Results

With chronic DBS for 4 - 8 years 4/6 patients had sustained improvement. Two patients remitted, and two patients responded (defined as > 35% symptom reduction), while the other two patients were considered non-responders on longterm. Quality of life markedly improved in remitters and responders. We did not observe periinterventional side effects or adverse effects of chronic stimulation.

Conclusion

Chronic DBS of BNST/ALIC provides longterm benefit up to 4 - 8 years in trOCD, although not all patients take profit. Quality of life improves in DBS responders, documented by improved QoL scores and, even more important, by regaining of autonomy and improving psychosocial functioning.

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P208

Multi Recharge – eine multizentrische, offene, kontrollierte Studie zur Akzeptanz, Anwendbarkeit und Komplikationen bei wiederaufladbaren Neurostimulatoren zur Tiefen Hirnstimulation
The Multi Recharge Trial – a multicentre, open-label, controlled trial on acceptance, convenience, and complications of rechargeable internal pulse generators for deep brain stimulation

M. Jakobs¹, A. K. Helmers², M. Synowitz², P. J. Slotty³, J. Anthofer⁴, J. Schlaier⁴, M. Kloß⁵, A. W. Unterberg¹, K. Kiening¹

¹Universitätsklinikum Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

²Universitätsklinikum Schleswig-Holstein, Neurochirurgische Klinik, Kiel, Germany

³Universitätsklinikum Düsseldorf, Stereotaktische und Funktionelle Neurochirurgie, Düsseldorf, Germany

⁴Universitätsklinikum Regensburg, Neurochirurgische Klinik, Regensburg, Germany

⁵Universitätsklinikum Heidelberg, Neurologische Klinik, Heidelberg, Germany

Objective

Rechargeable neurostimulators for deep brain stimulation have been available since 2008, promising longer battery life and fewer replacement surgeries compared to non-rechargeable systems. Long-term data on how recharging affects movement disorder patients are sparse. This is the first multicenter, patient-focused, industry-independent study on rechargeable neurostimulators.

Methods

Four neurosurgical centers sent a questionnaire to all adult movement disorder patients with a rechargeable neurostimulator implanted at the time of the trial. The primary endpoint was the convenience of the recharging process rated on an ordinal scale from "very hard" (1) to "very easy" (5). Secondary endpoints were charge burden (time spent per week on recharging), user confidence, and complication rates. Endpoints were compared for several subgroups.

Results

Datasets of 195 movement disorder patients (66.1% of sent questionnaires) with Parkinson's disease (PD), tremor, or dystonia were returned and included in the analysis. Patients had a mean age of 61.3 years and the device was implanted for a mean of 40.3 months. The overall convenience of recharging was rated as "easy" (4). The mean charge burden was 122 min/wk and showed a positive correlation with duration of therapy; 93.8% of users felt confident recharging the device. The rate of surgical revisions was 4.1%, and the infection rate was 2.1%. Failed recharges occurred in 8.7% of patients, and 3.6% of patients experienced an interruption of therapy because of a failed recharge. Convenience ratings by PD patients were significantly worse than ratings by dystonia patients. Caregivers recharged the device for the patient in 12.3% of cases. Patients who switched from a non-rechargeable to a rechargeable neurostimulator found recharging to be significantly less convenient at a higher charge burden than did patients whose primary implant was rechargeable. Age did not have a significant impact on any endpoint.

Conclusion

Patients with movement disorders rated recharging as easy, with low complication rates and acceptable charge burden.

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P209

Ausschalten und Aufdecken – stimulationsinduziertes zerebelläres Syndrom unter VIM/DRT-THS bei essentielltem Tremor

Turn'em off – to identify stimulation-induced cerebellar syndrome in VIM/DRT-DBS for essential tremor

B. Sajonz¹, G. Blazhenets², I. Walz^{3,4}, M. Frommer¹, J. Thurow², C. Maurer³, M. Rijntjes³, P. Meyer², V. Coenen¹

¹Universitätsklinikum Freiburg, Funktionelle und Stereotaktische Neurochirurgie, Freiburg, Germany

²Universitätsklinikum Freiburg, Klinik für Nuklearmedizin, Freiburg, Germany

³Universitätsklinikum Freiburg, Klinik für Neurologie und Neurophysiologie, Freiburg, Germany

⁴Albert-Ludwigs-Universität Freiburg, Institut für Sport und Sportwissenschaft, Freiburg, Germany

Objective

Up to 20 % of patients with DBS of the VIM/dentato-rubro-thalamic bundle (DRT) for essential tremor develop a stimulation-induced cerebellar syndrome, which is difficult to treat and has effects on the quality of life. While the exact cause is elusive, different theories have been discussed. Among them is the (supratherapeutic) co-stimulation of further cerebellar output pathways in addition to the DRT (Groppa et al., Brain 2014) and antidromic stimulation of the cerebellum (Reich et al., Brain 2016). A thorough diagnostic work up was performed in affected patients and multi-modal data were retrospectively analyzed to identify common symptom patterns and potential causes.

Methods

In eight patients who complained about recurrent tremor and cerebellar symptoms after VIM/DRT-DBS a cerebral [¹⁸F]FDG PET, tremor (accelerometer & EMG) and gait (video-based markerless motion capture system) analyses were performed with activated DBS (DBS_{ON}) and 72 hours after deactivation (DBS_{OFF_72h}); gait and tremor were also analyzed directly after deactivation (DBS_{OFF}). Exploratory PET analyses (categorical comparisons and correlations) were done with SPM.

Results

Across all patients, we found a significantly increased metabolism of the thalamus and dentate nucleus and a decreased metabolism of the cerebellar hemispheres with DBS_{ON} ($p < .01$). Thalamic metabolism correlated positively with the metabolism of the dentate nucleus (both conditions pooled, ($p < .01$). The coefficient of variation (CoV) of step length (a marker of gait ataxia) with DBS_{ON} correlated negatively with the change in metabolism of the right cerebellar hemisphere (DBS_{ON}-DBS_{OFF_72h}; $p < .01$). The drop of frequency of postural tremor of the right hand upon deactivation of DBS (DBS_{OFF}-DBS_{ON}) correlated with gait ataxia (CoV_{step length}) with DBS_{ON} ($p < .05$). The frequency of postural tremor on the right showed a differential course across patients.

Conclusion

We observed differential changes of neuronal activity in the dentate nucleus and cerebellar hemispheres according to stimulation state (DBS_{ON}-DBS_{OFF_72h}). Increased neuronal activity of the thalamus with DBS_{ON} correlated positively with the increase of neuronal activity of the dentate nucleus, supporting the theory of antidromic stimulation, while reduced activity of the cerebellar hemispheres correlated with gait ataxia. The course of tremor frequency before and after deactivation of DBS may help to identify patients developing a stimulation-induced cerebellar syndrome

Fig 1

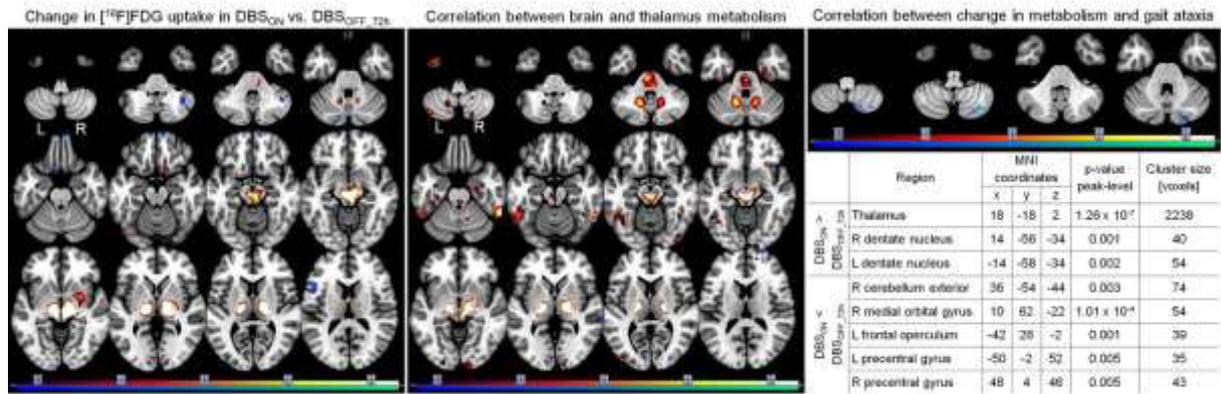
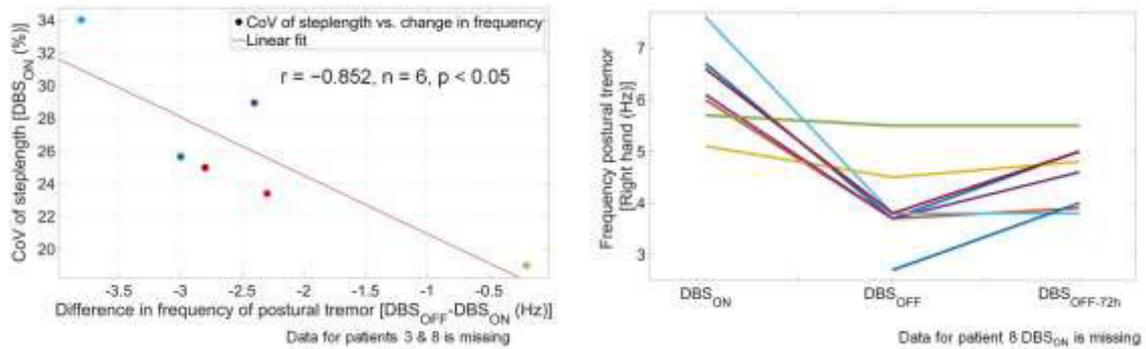


Fig 2



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P211

Dorsalganglien Stimulation (DRGS) verringert chronische neuropathische Schmerzen unter gleichzeitiger Abnahme der kortikalen Gamma-Aktivität

Dorsal root ganglion stimulation (DRGS) relieves chronic neuropathic pain along with a decrease in cortical gamma power

M. Morgalla, Y. Zhang, M. Fortunato, M. Tatagiba, G. Lepski, B. Chander

Eberhard Karls Universität Tübingen, Neurochirurgische Klinik, Tübingen, Germany

Objective

Chronic neuropathic pain (CNP) may be associated with hyperexcitability of the nociceptive system. Previously, we have shown the recovery of laser evoked potentials (LEP) after 6 months of dorsal root ganglion stimulation (DRGS) therapy of CNP patients. This possibly happened due to the increase in signal to noise ratio resulting from relieving hyperexcitability of the nociceptive system. Therefore, we hypothesize that DRGS may relieve CNP also through a decrease in the broadband cortical gamma power as a reflection of hyperexcitability.

Methods

Here we performed resting-state electroencephalography (EEG) and LEP assessment of 9 patients (2 females) ranged from 36 to 77 years ($M = 56.78$, $SD = 12.80$) diagnosed with CNP who received DRGS therapy. The average power spectrum is computed from 5s segments of preprocessed EEG data. EEG channel (C3 or C4) over the sensory-motor cortex contralateral to the limb affected with CNP was selected for the assessment of gamma power before the onset of DRGS and 1 week after DRGS. Additionally, assessment of LEP and ongoing CNP rating were performed before the onset of DRGS and after 1 week of DRGS.

Results

Assessment of resting state gamma power revealed a significant decrease in low gamma power between 30 – 45 Hz ($t(8) = 3.076$, $p = .015$) from day 1 ($M = 0.614$, $SD = 0.416$) to day 7 ($M = 0.248$, $SD = 0.102$) after DRGS. LEP assessment revealed a significant increase ($U(8) = -2.67$, $p = .008$) in the LEP amplitude after 1 week ($Mdn = 7.60$, 95% CI = [7.12, 9.99]) of DRGS when compared to previous DRGS ($Mdn = 3.27$, 95% CI = [2.75, 3.81]). Recovery of LEP amplitude was accompanied by a significant decrease in CNP rating ($U(8) = -2.669$, $p = .007$) after 1 week ($Mdn = 2$, 95% CI = [1.79, 2.88]) when compared to previous DRGS ($Mdn = 7$, 95% CI = [6.79, 7.88]). Furthermore, we found a significant correlation of low gamma power ($rs(18) = .495$, $p = .037$) with CNP rating.

Conclusion

DRGS therapy for CNP decreased broadband gamma power in addition to LEP recovery and a decrease in CNP rating. Thus, in addition to the recovery of LEP, a decrease in broadband gamma power may be considered as further evidence in favour of a reduction of hyperexcitability of the nociceptive system in response to DRGS therapy as a potential mechanism of CNP relief. Therefore, a positive correlation between gamma power and CNP rating suggests that gamma power may serve as a marker for tuning the DRGS parameters for optimal CNP relief as a clinical application.

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Reduziertes schmerzfreies Intervall nach Thermokoagulation des Ganglion Gasseri zur Behandlung von Trigemineuralgie bei Patienten mit multipler Sklerose
Pain-free interval after radiofrequency rhizotomy of the Gasserian ganglion in trigeminal neuralgia is reduced in patients with multiple sclerosis

T. Greve, J. Tonn, J. H. Mehrkens

Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik und Poliklinik, München, Germany

Objective

In trigeminal neuralgia (TN) refractory to conservative treatment, invasive therapeutic options depend on the underlying cause. Patients with TN and multiple sclerosis (MS-TN) are usually subjected to percutaneous radiofrequency rhizotomy (RF) of the gasserian ganglion due to a different pathomechanism of pain compared to idiopathic TN (ITN). There are controversial reports on pain-free interval (PFI) after RF in patients with MS-TN compared to ITN. We systematically compared PFI in a single-center retrospective cohort of all patients receiving RF of the gasserian ganglion as primary neurosurgical therapy.

Methods

Between 01/2012 and 10/2016, 232 patients were treated with RF for TN (318 procedures). Only patients with RF as primary neurosurgical treatment option with a minimum follow-up of 36 months were included. Based on these criteria, 157 patients were included. 37 (23.6%) of those had MS-TN (18f, 57.6 ± 10.8 years, 3 patients over 75 years) and 120 (76.4%) had ITN (62f, 70.2 ± 10.7 years, 43 patients over 75 years). Median follow-up was 39.2 months [range 36.1 – 91.1 months].

Results

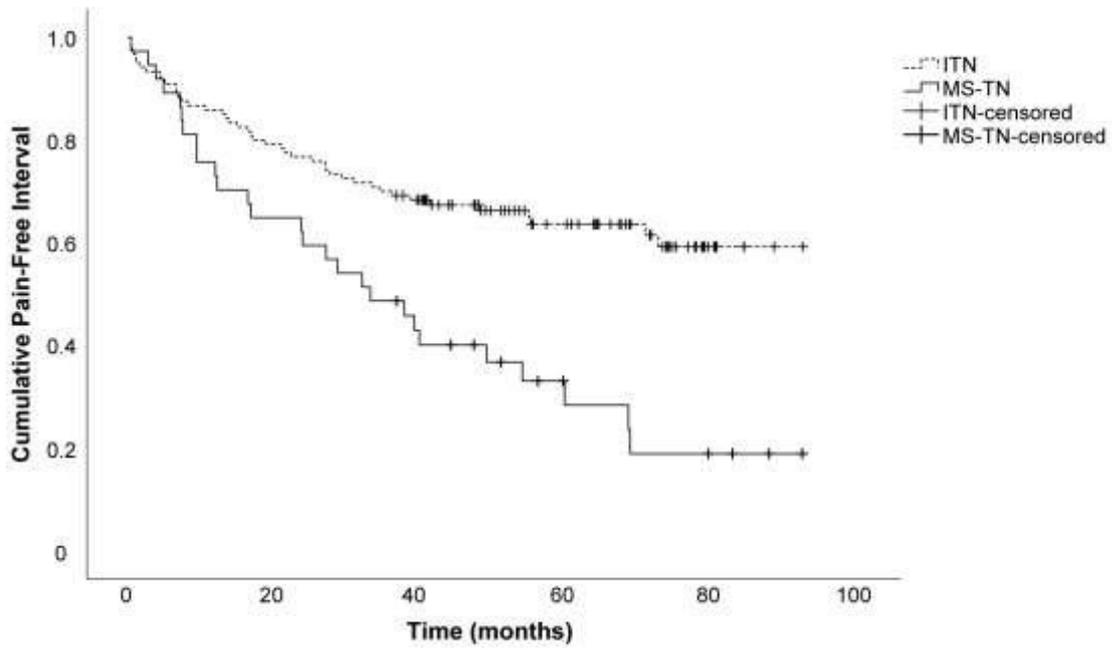
In the MS-TN group, 27 (73%) patients showed a recurrent TN after 25.7 ± 20.5 months [range 0.4 – 68.6 months]. In the ITN group, 44 (36.7%) patients showed a recurrent TN after a median of 20.7 ± 16.6 months [range 0.5 – 72.0 months]. In MS-TN, the proportion of pain-free patients was 67.7% at 1 year, 40.0% at 2 years and 18.9% at 3 years. In ITN patients, the proportion of pain-free patients was 90.0% at 1 year, 80.0% at 2 years and 70.0% at 3 years. Kaplan-Meier analysis demonstrated a significant difference in PFI in MS-TN compared to ITN (41.1 vs. 64.8 months, $p < 0.001$). Within the ITN group, no significant difference in PFI was noted between patients above and below 75 years of age.

Conclusion

In contrast to previously published literature, we report a significant reduction in PFI when patients with TN secondary to multiple sclerosis are subjected to RF compared to patients with idiopathic TN.

Figure 1 Kaplan-Meier analysis of pain-free interval after radiofrequency rhizotomy.

Fig 1



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P213

Neuromagnetische Hirnantworten als Prädiktor für das Outcome der mikrovaskulären Dekompression bei der Trigeminalneuralgie
Neuromagnetic brain responses as a predictive marker for the outcome of microvascular decompression in trigeminal neuralgia

B. Kretzschmar¹, A. Jin¹, A. Rupp², M. Jakobs¹, D. Haux¹, A. W. Unterberg¹, R. Ahmadi¹

¹Universitätsklinikum Heidelberg, Heidelberg, Germany

²Universitätsklinikum Heidelberg, Neurologische Klinik, Heidelberg, Germany

Objective

While some patients with trigeminal neuralgia (TN) respond to drug treatment, there are still patients with refractory symptoms. The most common cause of classical TN is assumed to be a neurovascular conflict of the trigeminal nerve and the superior cerebellar artery. Current imaging techniques show low specificity for relevant nerve compressions since neurovascular conflicts can also be observed in healthy individuals. Information on the functional aspect of nerve damage is still lacking. Electro- and magnetoencephalography (EEG/MEG) allow the functional investigation of the nociceptive system by means of laser-evoked brain responses. In an effort to find specific patterns of neural damage we disentangled cortical generators and assessed frequency-specific oscillations in patients before and after microvascular decompression (MVD) using MEG.

Methods

We applied 30 noxious laser pulses (Nd:YAP, λ 1340nm, 3 ms, 5mm, 1.75/2.00J) at the affected trigeminal dermatoma (V2/V3) and its corresponding contralateral region in patients with classic, drug-refractory TN before and after MVD ($n=8$, 2 were excluded due to strong muscle artifacts). After each single pulse, patients were instructed to evaluate the perceived pain intensity on a numerical rating scale. Gradients of magnetic fields were recorded using a 122-channel whole-head MEG system inside a magnetic shielded room. For source analysis of the evoked fields we used a distributed source model and evaluated nociceptive-induced oscillations using a wavelet analysis. Non-responders with persistence of pre-existing symptoms (2/8) were identified by evaluation of the German pain questionnaire.

Results

The cortical reconstruction revealed pronounced bilateral activity in the primary and secondary cortex (S1/S2) as well as in the posterior and anterior insula (pIC/aIC). The spectrotemporal analysis mainly showed changes in the low frequency range in contralateral S1. At the control site we observed an oscillatory response in the theta/alpha range within a time interval of 200–500ms after stimulus onset. In the group of responders, this activation was delayed or attenuated to the control site and, interestingly, resembled the contralateral site postoperatively again. Nonresponders showed theta/alpha activation already preoperatively.

Conclusion

Our results elucidate the functional dynamics of neural damage in S1 and might serve as a promising marker for the development of novel diagnostic concepts in the future.

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P214

Perkutane Radiofrequenz-Thermokoagulation bei persistierendem idiopathischem Gesichtsschmerz – eine monozentrische retrospektive Analyse

Percutaneous radiofrequency thermocoagulation for persistent idiopathic facial pain – a retrospective monocentric analysis

B. Al Barim, L. Lemcke, S. Schipmann, W. Stummer

Universitätsklinikum Münster, Neurochirurgie, Münster, Germany

Objective

Persistent idiopathic facial pain (PIFP), previously termed atypical facial pain, is a debilitating chronic pain condition with pain radiating to one or more of the trigeminal dermatomes. Typically there are no pathologies that can be identified during workup and causal therapies are not available. Therapy is symptomatic and various medical and interventional approaches are used. The aim of this study was to evaluate the effectiveness of percutaneous radiofrequency thermocoagulation (PRTC) of the Gasserian ganglion (GG) in patients with PIFP and the duration of pain relief, as well as the identification of clinical and surgical factors associated with its success.

Methods

Data on all patients with PIFP between 2009 through 2019 that have been treated with PRTC of GG were included into the study. PRTC was performed under intermittent propofol sedation via puncture in the middle third of the edge of the mandible and entering the foramen ovale through the skull base under fluoroscopic control. After lifting propofol sedation the GG was stimulated and PRTC was performed in a range of 55 to 90°C after resuming sedation. Outcome was assessed with a six tiered score from 1 (complete remission) to 6 (no benefit). Chi-square test and univariate logistic regression was used for categorical and continuous variables, respectively. Odds ratio was obtained with 95% confidence intervals. Log-rank test was used for time to event analyses. Statistical significance was defined as $p < 0.05$.

Results

57 Patients were included with a median of 69 years. 61.4% of patients experienced pain relief after initial PRTC lasting for a median of 120 days. The second intervention was successful in 78.1% of patients, further procedures were successful in 84.4%. 13.8% could end all other treatments (Score 1), 29.3% experienced significant pain relief (Scores 2 and 3), 27.5% of Patients experienced mild pain relief (Scores 4 and 5). The remaining patients did not benefit (Score 6). Patient sex, number of repetitions, and number of affected branches were predictive factors for pain relief.

Conclusion

PRTC as an interventional form of therapy for PIFP appears a beneficial form of symptomatic treatment showing good pain relief, especially for patients with former pain relief through PRTC. Minimal invasiveness makes a repeatable intervention for patients suffering from PIFP. Further studies have to be performed to understand predictive factors in light of retrospective limitations of this study.

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P215

Intraventriculäre Baclofentherapie für die Behandlung der Dystonie – Indikationen, Methode und Outcome *Intraventricular baclofen for dystonia – indications, technique and outcome*

M. Abel¹, M. Kudernatsch¹, S. Persits¹, C. Onyinz¹, L. Gunz¹, C. Zeches², S. Berweck²

¹Schön Klinik Vogtareuth, Neurochirurgie, Vogtareuth, Germany

²Schön Klinik Vogtareuth, Fachzentrum für pädiatrische Neurologie, Neuro-Rehabilitation und Epileptologie, Vogtareuth, Germany

Objective

Intrathecal baclofen (ITB) has been commonly used as treatment for dystonia. However, in rare cases, the use of ITB is not possible. For these patients, intraventricular baclofen (IVB) is a valid alternative. Up to now, most published case series made use of an endoscopic approach for implantation of the intraventricular catheter. Reducing the cortical manipulation to a minimum, implantation of IVB catheters with navigated frameless stereotaxy is the most minimal invasive approach feasible. For this, literature is scarce. Therefore, the aim of the study was to evaluate indications, surgical technique, complication rate and outcomes of IVB application with navigated frameless stereotaxy as an effective alternative for ITB in patients with severe generalized secondary and hereditary dystonia.

Methods

A retrospective analysis of all patients who were treated with IVB in our institution in the period between 2009 and 2019 was performed. All intraventricular catheters were implanted by navigated frameless stereotaxy. Intraoperatively, application of contrast agents was used to verify the correct placement of the catheter.

Results

Thirteen patients (six males, seven females) with severe generalized secondary and hereditary dystonia were treated with IVB. The mean age of the patients was 12.5 years (range 2-23 years). Indications for the use of IVB included preceding infection of the spinal catheter with intrathecal adhesions, insufficient ITB response, dystonic storms with a predisposition for spinal catheter dislocation, conservatively managed as well as surgically instrumented anatomical deformities of the spine and thereby maintaining the possibility to undergo a spinal surgery procedure in the future. Twelve catheters were located into the third ventricle and one catheter was positioned into the lateral ventricle. In our cohort, no perioperative or technical complication occurred. The mean follow up was 16 months. Dystonia improved in 12 of 13 patients. One child who did not respond to IVB had not responded to previous ITB as well. As side effects nausea and vomiting were observed after the implantation of IVB. One child developed a pump infection and required pump removal.

Conclusion

Our study indicates, that IVB aided by navigated frameless stereotaxy is an effective, minimally invasive and safe therapeutic option with only few side effects in the management of rare cases with severe dystonia, when ITB drug delivery is not feasible.

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P216

Direktionale versus klassische DBS-Elektroden – eine retrospektive Analyse *Directional versus conventional DBS leads – a retrospective cohort analysis*

P. Fricke¹, R. Nickl¹, L. Massa¹, H. Christin¹, F. Lange², P. Capetian², M. Reich², R. I. Ernestus¹, J. Volkmann², C. Matthies¹

¹Universitätsklinikum Würzburg, Neurochirurgische Klinik und Poliklinik, Würzburg, Germany

²Universitätsklinikum Würzburg, Neurologische Klinik und Poliklinik, Würzburg, Germany

Objective

Deep brain stimulation is a well-established treatment for Parkinson's Disease. Directional deep brain stimulation (dDBS) leads offer the opportunity of steering current in horizontal and vertical directions and expands the therapeutic window in individuals compared to ring mode. Till present day, evaluation of directional leads compared to conventional leads (cDBS) in implantation strategies, programming advantages and clinical outcome is an ongoing process. Here we focus on a retrospective description of our non-matched pre-/post dDBS-era cohort of patients with PD.

Methods

The period from 2013 -2018 was chosen because of very uniform DBS technology applied in 43 (14 female) patients with PD by STN-DBS in our institution. Since 2016, 24 of these were implanted with directional DBS leads. We retrospectively analyzed lead deviation compared to the planned target one year after surgery, motor outcome according to UPDRS-III scores and stimulation parameters for both groups.

Results

19 patients were in the cDBS group (5 female) and 24 in the dDBS-group (9 female). Age differed significant for both groups with cDBS 55.9 years and dDBS 64.4 y ($p < 0.01$). Precision of lead position was comparable in both groups ($p = .366$). Patients' UPDRS-III scores improved similarly in both groups with a Stim-ON/Med-OFF improvement of 75% of the initial levodopa response, with similar rates of good to excellent responders. After one year, 20 of 46 D-leads in the dDBS-group were activated in ring mode and 26 of 46 D-leads in directional mode; of those 11 leads were activated also with vertical steering. D-mode stimulation needed less current (2.9mA) than conventional mode (3.7mA), $p = .04$.

Conclusion

This is the first retrospective cohort analysis of directional vs. conventional DBS leads. Accuracy of the implantation at one year post surgery was similar in both groups. The stimulation amplitude was smaller in the dDBS group, reflecting previous results, providing a larger therapeutic window for directional stimulation. 75% of the dDBS patients were stimulated with at least one lead with horizontal steering for the best clinical effect at one year post surgery indicating a benefit of this programming option. On a group level, UPDRS-III improvement was comparable in both groups, although the dDBS group was significantly older. To address advantages of horizontal and/ or vertical steering for the future, we recommend a prospective evaluation in matched groups.

Funktionelle Neurochirurgie und Schmerzchirurgie II/Functional neurosurgery and pain surgery II

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Abhängigkeit der Präzision der roboterassistierten, stereotaktischen Chirurgie von der präoperativen Bildgebungsmodalität

Accuracy of stereotactic robot-assisted surgery depends on preoperative imaging modality

K. Machetanz, F. Grimm, A. Gharabaghi, M. Tatagiba, G. Naros

Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

Objective

The accuracy of stereotactic robot-assisted surgery is still under debate. As every neuronavigation system, the accuracy of the robot-assisted technology depends on the registration process. Modern stereotactic robots allow several different registration methods: i) laser-based surfaces registration (LSR) and ii) (bone) fiducial-based registration (BFR). While LSR depends on the quality of surface representation of the preoperative imaging, BFR has been shown to be very accurate but invasive. The present study aimed to determine the impact of these registration methods on the accuracy of robot-assisted stereotactic procedures.

Methods

This prospective study enrolled 29 patients who underwent a robotic-assisted stereotactic procedure (e.g. SEEG implantation, intracranial biopsy). Every patient received a preoperative T1 MR image (resolution 1 mm, isovoxel) for trajectory planning. In 7 cases this image was used for intraoperative MRI-LSR. Another 7 case received an additional CT (resolution 1mm) for intraoperative CT-LSR. Finally, 15 patients received a preoperative CT (resolution 1mm) after bone fiducial implantation for intraoperative BFR. Surgical approach was performed with a 2.1 mm drill. Entry point error (EPE) was assessed by the position of the drill hole on the postoperative CT scan.

Results

The mean EPE was 1.0 ± 0.9 mm [range: 0-3.4]. There was a significant main effect of the registration process on the EPE ($X^2=6.61$, $p=0.037$; Kruskal-Wallis). Follow-up test revealed no statistical difference between CT-LSR (0.9 ± 0.8 [0-2.1] mm) and BFR (0.7 ± 0.3 [0.2-1.1] mm) ($X^2=0.40$, $p=0.525$; Kruskal-Wallis). In contrast, both CT-LSR and BFR had a smaller EPE than MRI-LSR (2.2 ± 1.1 [0.8-3.4] mm) ($X^2=4.34$, $p=0.037$ and $X^2=5.78$, $p=0.016$; Kruskal-Wallis).

Conclusion

The present study proves that the accuracy of robot-assisted stereotactic procedures depends on the applied registration process. T1-based MRI-LSR led to a higher EPE than CT-LSR and BFR. If MRI-LSR is necessary, sequences (e.g. T2) with better surface depiction should be used.

Funktionelle Neurochirurgie und Schmerzchirurgie II/*Functional neurosurgery and pain surgery II*

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Effekte von Harmalin auf die neuronale Aktivität von Purkinje-Zellen des Kleinhirns in einem genetischen Mausmodell für Tremor

Effect of harmaline on neuronal activity in cerebellar Purkinje cells in a genetic mouse model of tremor

M. Alam¹, X. Jin², S. Helgers¹, J. K. Krauss¹, K. Schwabe¹, E. Schneider³

¹Medizinische Hochschule Hannover, Abteilung für Neurochirurgie, Hannover, Germany

²Zhongda Hospital Southeast University China, Abteilung für Neurochirurgie, Nanjin, China

³Medizinische Hochschule Hannover, Institut für Pharmakologie, Hannover, Germany

Objective

Harmaline-induced tremor by activation of GABAA receptors is a commonly used model of essential tremor. Clinical and experimental findings suggest that altered cerebellar function is involved in tremor generation. The atypical chemokine receptor 1 (Ackr1) is exclusively expressed in cerebellar Purkinje cells (PCs). It has been shown that Ackr1^{-/-} knock out (KO) mice are sensitive to develop harmaline induced tremor.

To investigate potential differences in cerebellar neuronal activity of PCs in wild type (Wt) and Ackr1^{-/-} KO mice, and the effect of harmaline.

Methods

We recorded single unit (SU) activity together with local field potentials (LFPs) under urethane anesthesia (1.6 g/kg, i.p.) in Ackr1^{-/-} KO mice (N=8) and Wt control mice (N=9) before and after harmaline injection (15mg/kg).

Results

A total of 1736 cerebellar PCs were recorded from Wt and KO mice. The PCs neuronal firing rate was higher and the dispersion of index as a measure for irregularity was lower in Wt mice compared to KO mice (P<0.001). Harmaline decreased the firing rate and increased the dispersion index without differences in KO and Wt mice (P<0.001). The percentage of regular firing patterns was lower and the burst pattern was higher in KO compared to Wt mice (P<0.001). Injection of harmaline increased the burst patterns in both Wt and KO mice (P<0.05). The relative power of cerebellar theta, alpha, and beta band activity was lower, while gamma was higher in KO as compared to Wt mice. Harmaline-injection enhanced theta band activity in both Wt and KO mice (P<0.001), whereas beta band activity was enhanced, and gamma band activity was reduced only in KO mice (P<0.001).

Conclusion

Neuronal activity of PC cells differed between Wt and KO mice both with regard to single unit firing patterns and relative power of oscillatory activity. Overall, harmaline-injection affected neuronal activity, which was not specific for KO mice.

Funktionelle Neurochirurgie und Schmerzchirurgie II/*Functional neurosurgery and pain surgery II*

P219

Neuraler Aufbau des Septum verum

Neural architecture of the septum verum – a fibre dissection study

L. Bárány¹, O. Ganslandt², M. Buchfelder³, P. Kurucz^{2,3}

¹Semmelweis University, Department of Anatomy, Histology and Embryology, Budapest, Hungary

²Katharinenhospital Klinikum Stuttgart, Neurochirurgische Klinik, Stuttgart, Germany

³Friedrich-Alexander-Universität Erlangen-Nürnberg, Neurochirurgische Klinik, Erlangen-Nürnberg, Germany

Objective

The septum verum is the ventral part of the human septum that contains well developed nuclei, such as the bed nucleus of stria terminalis (BNST) as well as the septal nuclei. The BNST is a potential target of deep brain stimulation (DBS) in patients with various psychiatric disorders, such as drug resistant obsessive-compulsive disorder or anorexia nervosa. The nuclei septales were proposed as possible targets of DBS in patients with traumatic brain injury. The comprehensive description of the three-dimensional anatomy of the septum verum, its connections and the adjacent structures is lacking in the literature.

Methods

Six cadaveric human brains (12 hemispheres) were involved in this study. Five of them were fixed in 5% formalin and frozen on -30 °C according to the well-known method of Klingler. The brains were halved and dissected from medial to lateral and from inferior to superior direction. The fiber dissection was carried out with microsurgical instruments and with the aid of an operating microscope. The macroscopic findings were controlled and verified with histology in one brain.

Results

The septum verum is located under the septum pellucidum, in the ventral part of the septum telencephalic that separates the two lateral ventricles. The following connections were successfully identified: 1) the precommissural fibers of the fornix; 2) the fasciculus inferior of the septum pellucidum; 3) the stria medullaris of thalamus; 4) the stria terminalis; 5) the ventral amygdaloseptal fibers; 6) and the stria olfactoria medialis. The postcommissural fibers of the fornix, the mammillothalamic fascicle, the cingulum as well as the inferior and anterior peduncles of the thalamus were demonstrated in all cases. Fibers originating from the stria medullaris of thalamus and crossing through the massa intermedia as well as fibers between the postcommissural portion of the fornix and the stria medullaris of thalamus were constant findings during the dissections.

Conclusion

Understanding the three-dimensional anatomy of the septum verum may help to improve the accuracy of electrode implantation during DBS as well as interpretation the side effects that originate from incorrect electrode placement.

Funktionelle Neurochirurgie und Schmerzchirurgie II/*Functional neurosurgery and pain surgery II*

P220

Resting-state fMRT Konnektivität – ein Netzwerk Kontext für hochauflösende Sprachkartierung der Broca-Region mittels transkranieller Magnetstimulation

Resting-state fMRI connectivity – a network context for high-resolution language mapping of Broca's region with transcranial magnetic stimulation

J. Ort¹, K. Sakreida², J. Kernbach¹, H. R. Clusmann¹, G. Neuloh¹

¹Universitätsklinikum RWTH Aachen , Klinik für Neurochirurgie, Aachen, Germany

²Universitätsklinikum RWTH Aachen , Klinik für Psychiatrie, Psychotherapie und Psychosomatik, Aachen, Germany

Objective

Navigated transcranial magnetic stimulation (TMS) language mapping yields focal results. For extended interpretability, we correlated resting-state functional MRI connectivity of Broca's region with a previously found cluster of TMS susceptibility in object naming close to the inferior frontal junction area.

Methods

Twelve healthy, left-dominant native German speakers underwent both magnetic resonance imaging (MRI) and high-resolution TMS language mapping with a 30-target grid systematically covering Broca's region. Resting-state activity was acquired at 3 Tesla for a duration of 10 minutes. fMRI data were analyzed using the SPM Toolbox CONN with standard preprocessing. Seed-to-network brain connectivity was analyzed based on 30 seed volumes originating from TMS stimulation sites and with the Harvard-Oxford predefined networks as ROIs (excluding the language network of the left inferior frontal gyrus (IFG) to avoid self-correlation). The clustering of seed ROIs was performed using a farthest point algorithm and correlated with previous clustering results based on TMS susceptibility in object naming.

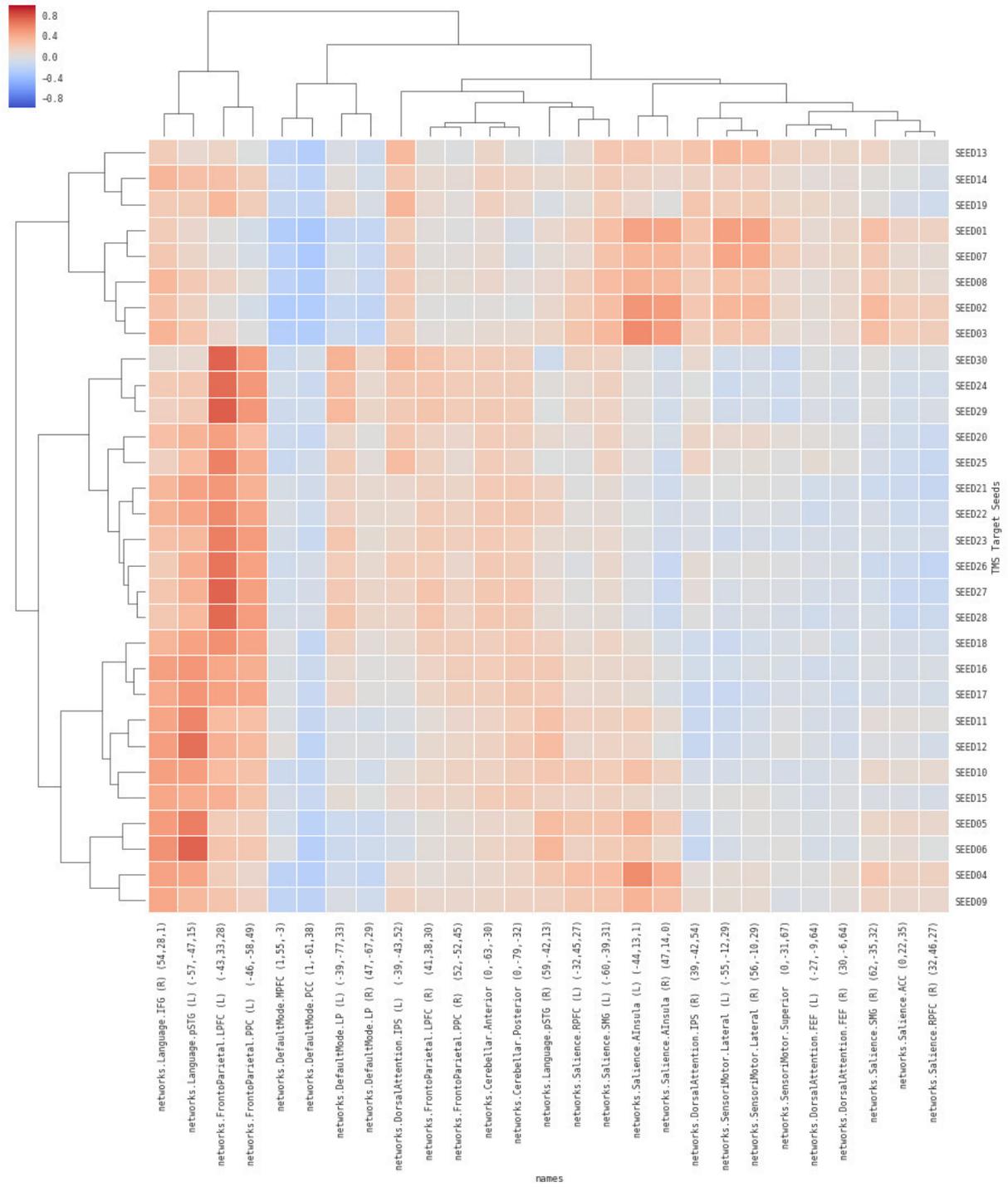
Results

Our clustering approach revealed three coherent clusters (cluster 1: posterior, cluster 2: anterior ventral, cluster 3: dorsal). Cluster 1 showed strong connectivity to lateral senso-motoric networks as well as to parts of the salience/attentional network (e.g. ipsi- and contralateral insula). There is also a distinctive anticorrelation to the default mode network (DMN). Cluster 2 displays connectivity to the classical language networks (e.g., contralateral IFG and ipsilateral superior temporal gyrus). The dorsal Cluster 3 showed connectivity to the ipsilateral frontoparietal networks involved in cognitive control. The focus of TMS inhibition in naming overlapped with clusters 1 and 3 only.

Conclusion

Parcellation of Broca's region according to TMS and resting-state fMRI reveals different patterns of functionally coherent subregions with only partial overlap. In this study, the focus of TMS susceptibility in naming suggested inhibition of salience processing, cognitive and sensory-motor control rather than language processing proper. In presurgical planning, resting-state fMRI may provide an important complementary network context for focal TMS mapping results.

Fig 1



Funktionelle Neurochirurgie und Schmerzchirurgie II/*Functional neurosurgery and pain surgery II*

P222

Anwendung von MEG, Neuronavigation und intraoperativer Bildgebung für Reoperationen von nicht anfallsfreien Patienten nach primärer OP

Reoperation in failed epilepsy surgery using MEG, neuronavigation and intraoperative MR imaging

J. Shawarba¹, B. Kasper¹, S. Rampp¹, R. Coras¹, I. Blümcke¹, M. Buchfelder¹, K. Rössler²

¹Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

²Medizinische Universität Innsbruck, Neurochirurgische Klinik, Wien, Austria

Objective

Reoperations in patients with failed epilepsy surgery are still challenging although a reasonably good seizure outcome seems possible. Advanced imaging and intraoperative MR tomography may contribute to a better postoperative seizure outcome in this patient group.

Methods

We investigated 27 patients (13 female/14 male/ mean age at first surgery 29.4 yrs) with a mean seizure history of 14 years mean (from 1-35 yrs). The mean time between first surgery and reoperation after failure was 3.8 years (from 0-13 yrs). Additionally, to the standard preoperative investigations, 35 magnetoencephalography (MEG) investigations were performed and 17 patients had intraoperative neuronavigation and MR imaging during reoperation.

Results

Histologically, reoperated patients included 7 with unspecific gliosis (25.9%), 6 with gangliogliomas (22.2%), 6 with focal cortical dysplasia (22.2%), 4 with hippocampal sclerosis and 4 other pathologies. The postoperative seizure outcome in the investigated patients after a second surgery was 67% Engel Grade I (18/27 patients, follow up time 4.9 yrs). Altogether, 78% of patients had a better seizure outcome than after the first surgery, 19% had an equal outcome and 3% a worse outcome. Integration of preoperative MEG and intraoperative MR imaging correlated positively with enhanced seizure outcome.

Conclusion

Our investigation demonstrated that patients with failed epilepsy surgery may have a favorable seizure outcome after a second surgery due to advanced preoperative imaging and intraoperative MR technology.

Funktionelle Neurochirurgie und Schmerzchirurgie II/*Functional neurosurgery and pain surgery II*

P223

Unterscheidung zwischen Meningeom, Dura mater und Überlappungsbereichen durch robotisierte, makroskopische Raman Spektroskopie (RS)

Differentiation between meningioma, dura mater and overlapping-areas by robotised, macroscopic Raman spectroscopy (RS)

G. Mirizzi¹, F. Jelke¹, F. Kleine Borgmann^{1,2,3,4}, A. Husch^{2,5}, R. Slimani⁴, M. Mittelbronn^{2,3,4}, F. Hertel^{1,2,5}

¹Universität des Saarlandes, Homburg, Germany

²University of Luxembourg, Medical Clinic IV Endocrinology, Esch an der Alzette, Luxembourg

³National Health Laboratory Luxembourg, Düdelingen, Luxembourg

⁴Luxembourg Institute of Health, Luxembourg, Luxembourg

⁵Hospital Centre of Luxembourg, National Department of Neurosurgery, Luxembourg, Luxembourg

Objective

Incomplete intraoperative excision of meningiomas from the dura mater is often the cause for tumor-recurrence. This problem requires a quick and precise intra- or perioperative diagnostic tool, which is able to accurately determine the tumor-infiltration zone. We use RS as a non-destructive procedure to trace precisely the tumor-borders directly inside the operating room.

Methods

We employed a fully robotized system equipped with a visible light imaging camera as well as a 785nm laser, for the analysis on native samples immediately after surgical excision. The samples are afterwards subjected to a full pathological diagnostic. The combined data are analyzed by custom MATLAB™ tools. We performed exploratory data analysis after dimensionality reduction by unsupervised learning. Supervised learning based on support vector machines was employed to train a classifier to discriminate the different tissue types. Additionally, we compared different peaks in areas characteristic for collagen.

Results

We were able to distinguish between healthy dura mater and meningioma with a sensitivity of 99.7% and a specificity of 95.9%. We were not able to distinguish sufficiently between different meningioma subtypes. Cluster-visualization by dimension reduction (TSNE) of dura mater and meningioma spectra forms distinct clusters, the measuring points that are scattered in between originated from infiltration zones. This could be used as basis for mapping of tumor-dura overlapping areas and was confirmed by retrospective pathological examination. Next to classification, the spectra can also indicate specific biochemical differences between tissue types. The disappearance of the most prominent peaks in the dura sample, after treatment with collagenase, suggests that these originate from collagen.

Conclusion

RS is a promising, complimentary and easily-usable diagnostic tool to distinguish perioperatively between healthy dura mater and meningioma without additional fixation and microscopy. In the near future, RS might be used to diagnose directly the tumor-borders as well as the tumor-origin of the sample. This could potentially reduce the number of left-over tumor-cells after surgical excision and, as a conclusion, decrease the number of recurrences.

Funktionelle Neurochirurgie und Schmerzchirurgie II/*Functional neurosurgery and pain surgery II*

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Reduzierung der Strahlendosis und deren Auswirkungen auf die Genauigkeit der Lokalisierung eines rahmengestützten Stereotaxie-Systems
Reduction of radiation dosage of intraoperative computed tomography and its effect on localisation accuracy of a stereotactic frame

M. Bopp, N. Kröncke, B. Carl, C. Nimsky

Universitätsklinikum Gießen und Marburg, Klinik für Neurochirurgie, Marburg, Germany

Objective

To perform deep brain stimulation (DBS) an accurate localization of anatomical target structures as well as the precise placement of the electrodes within the target structures is required. To map high-resolution preoperative data to the patient's anatomy stereotactic frame-based techniques are applied. Due to less geometric distortion often computed tomography (CT) imaging is used, especially when intraoperative CT systems are available. Nevertheless, standard CT protocols together with increased scan length due to the stereotactic frame and attached localizer box, resulting in high radiation dosage. To overcome this issue while keeping high accuracy of frame localization in this study various scan protocols ranging from high to ultra-low radiation were evaluated.

Methods

To analyze the accuracy of frame localization related to different scanning protocols, a stereotactic frame (Zamorano-Duchovny) including a CT localizer box was attached to a head phantom. The stereotactic system was aligned straight in the iso-center of the CT scanner (AIRO[®] iCT, Brainlab, Munich, Germany). Start and end of each scan was defined equally covering the localizer box and the stereotactic frame. Six protocols (helical acquisition) were used: Head, Orbit, Sinus, Sinus-50%, Sinus-80%, Newborn. Frame localization was performed using Brainlab Elements Stereotaxy (Brainlab, Munich, Germany). The radiation dosage and deviation of slice-by-slice detected points along each of the eleven rods from the given model was evaluated.

Results

Overall deviation from the underlying model of the localizer box was 0.18 ± 0.05 mm (Head), 0.17 ± 0.05 mm (Orbit), 0.17 ± 0.04 mm (Sinus), 0.17 ± 0.04 mm (Sinus-50%), 0.17 ± 0.04 mm (Sinus-80%) and 0.16 ± 0.04 mm (Neonate) revealing no significant difference in localization accuracy. With a scan length of about 20 cm the dose length product was 1624.37 mGy*cm (Head), 583.19 mGy*cm (Orbit), 358.41 mGy*cm (Sinus), 178.22 mGy*cm (Sinus-50%), 71.45 mGy*cm (Sinus-80%) and 12.84 mGy*cm (Newborn) showing a significant decrease, while keeping all relevant structures (localizer box, bony structures for image fusion) sufficiently available.

Conclusion

For frame-based stereotactic procedures applying CT imaging for frame localization as well as image fusion with high-resolution preoperative data to map frame, image and patient space, also ultra-low dosage scanning protocols can be applied without any loss of localization accuracy.

Funktionelle Neurochirurgie und Schmerzchirurgie II/*Functional neurosurgery and pain surgery II*

P225

Stereotaktische Ventrikelkatheterimplantation bei Patienten in den ersten 3 Lebensjahren – Eine sichere und präzise operative Methode?

Stereotactic catheter implantation in young children and infants – A feasible and accurate surgical method?

M. Schaper, F. S. Fritzsche, W. Hamel, J. Köppen, M. Westphal, G. Kammler

Universitätsklinikum Hamburg-Eppendorf, Klinik für Neurochirurgie, Hamburg, Germany

Objective

In general, there is no need to implant intraventricular catheters by means of frame based stereotactic surgery in very young children except for very special indications. Main concerns include skull fractures by fastening the stereotactic pins and possible shifting of skull and brain tissue. The purpose of this report is to analyze our case series of stereotactic catheter implantation in children of very young age to show the feasibility and accuracy of this method to place catheters in very narrow intraventricular spaces

Methods

During the period from 05/2017 to 05/2019 seven infants (4 female, 3 male, age range 13-38 months) with cerebral Ceroid-Lipofuszinose II (CLN2) received intrathecal enzyme replacement therapy via Rickham-Reservoirs and ventricular catheters implanted stereotactically because of the very narrow ventricles. The use of stereotactic surgery was approved by an ethical vote

Results

The operating procedures lasted in average 150 minutes. Postoperative CT-scans showed no intracerebral hemorrhage and no significant deviation of the intraventricular catheters from planning trajectory (0-2,2mm). The implantation depth of the catheter differed at mean 3,3 mm (range 0-8mm) from trajectory. In all 7 cases the postoperative CT-scans showed no impact on the skull

Conclusion

Our data demonstrate the feasibility and accuracy of stereotactic catheter placement in very small children (<38 months) as representing a patient group that in general is not considered for frame-based stereotactic procedures. Increasingly available intrathecal therapies may require such technology which appears to be safe

Funktionelle Neurochirurgie und Schmerzchirurgie II/Functional neurosurgery and pain surgery II

P227

Gestörte Synchronisation der sensomotorischen β -Oszillationen nach transkranieller Magnetstimulation bei chronischen Schlaganfallpatienten

Disturbed beta synchronisation after transcranial magnetic stimulation in chronic stroke

G. Naros, B. Trunk, A. Gharabaghi

Eberhard Karls Universität Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

Objective

The combination of neurostimulation (i.e. transcranial magnetic stimulation) and neuroimaging (i.e. electroencephalography, EEG) enable's insights in the cortical physiology after brain damage, such as stroke. However, the available data is sparse. In the present study, we applied TMS-EEG to probe cortico-cortical integrity in 17 severely affected chronic stroke patients as well as in ten healthy age-matched controls. Electrophysiological findings were compared to clinical outcome measures and lesion characteristics

Methods

For this purpose, we applied magnetic pulses over both the affected and the unaffected hemisphere of severely-affected stroke patients while concomitantly recording electroencephalographic (TMS-EEG) signal. Subsequently data was analyzed evaluating the time-locked brain response in the timeseries and frequency domain. TMS-EEG experiment was repeated on both hemispheres of ten age-matched healthy subjects.

Results

In the stroke patients, magnetic stimulation of the unaffected hemisphere leads to an early (0-100 ms) and late (250-300 ms after TMS) synchronization in the beta frequencies. This behavior was significantly attenuated over the affected hemisphere. While the reduction of the early beta synchronization was related to the involvement of motor cortex, late beta synchronization was conserved in patients with contralesional upper limb MEPs. There was no correlation between the TMS-EEG findings and lesion size. Finally, there were no hemispheric differences in age-matched healthy subjects.

Conclusion

We conclude that early beta synchronization after TMS might serve as a biomarker for cortico-cortical integrity while late beta synchronization might indicate cortico-spinal integrity. In severe chronic stroke the motor network fails to restore the physiological motor frequencies indicating a massive cortical dysfunction. TMS-EEG recordings could be used in future to evaluate cortico-cortical integrity before and after neurosurgical interventions.

Fluoreszenz-gestützte Hirntumorchirurgie/*Fluorescence-guided surgery for brain tumours*

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5-ALA fluoreszenz-kontrollierte Entfernung von primären und sekundären Hirntumoren mit Unterstützung augmentierter Realität

5-ALA for the fluorescence-guided resection of primary and secondary brain tumours – observational insights in an augmented reality setting

P. Charalampaki¹, M. Nakamura², A. Heimann³, P. Proskynitopoulos¹

¹Kliniken der Stadt Köln, Klinik für Neurochirurgie, Köln, Germany

²Kliniken der Stadt Köln, Klinik für Neurochirurgie, Köln, Germany

³Universitätsmedizin Mainz, Institut für Neurochirurgische Pathophysiologie, Mainz, Germany

Objective

Fluorescence-guided surgery with the use of five-aminolaevulinic acid (5-ALA) is the state-of-the-art treatment of high-grade gliomas. However, intraoperative visualization of 5-ALA under violet light remains challenging, especially when blood covers parts of the surgical field, thereby masquing fluorescence. Apart from that, continuous switching between the light modes has a negative effect on operation ergonomomy. To overcome these problems and combine the brightness of visible light with the information delivered by 5-ALA fluorescence, we implemented multispectral fluorescence (MFL) in a microscope, a technique that is able to project both information in real-time to the surgeon.

Methods

After observational testing of the software on 3 rats, we examined 25 patients with primary and secondary brain tumors who underwent surgery using the MFL technique. One patient was operated on two different regions and lesions in the same setting. The tumors comprised of 6 glioblastomas, 4 anaplastic astrocytomas, 1 anaplastic oligodendroglioma, 2 meningiomas, 11 metastatic tumors, 1 acoustic neuroma, and 1 ependymoma. The MFL technique with the real-time overlay of 5-ALA fluorescence and white light was compared intraoperatively to the classic blue filter detecting 5-ALA fluorescence.

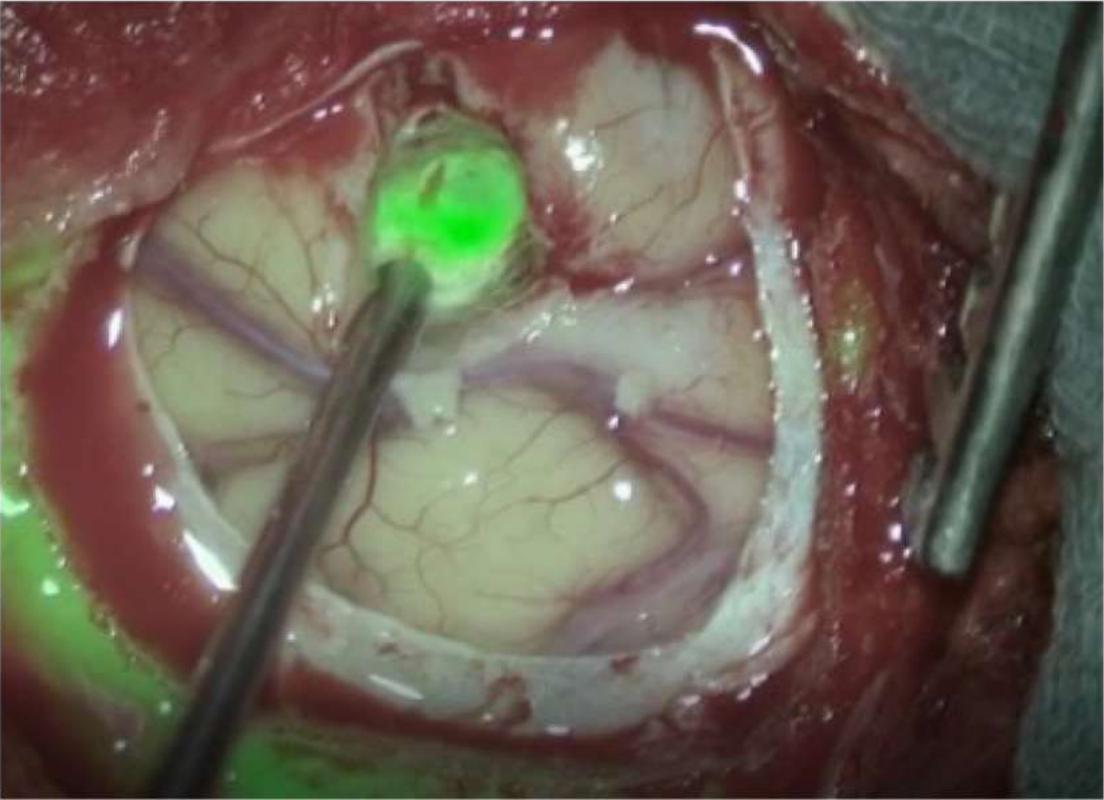
Results

The lesion was, in all cases, clearly visible and highlighted from the surrounding tissues. The pseudocolor we chose to visualize the lesion was green, representing 5-ALA fluorescence, with the surrounding brain tissue remaining in its original white color. In the cases where blood was covering the surgical field, orientation was easy to maintain, due to the additional information delivered from the white light image.

Conclusion

The MFL technique opens the way for precise and clear visualization of tumor 5-ALA fluorescence in real-time under white light. It can be easily implemented in the resection of all tumors accumulating 5-ALA. Drawbacks of classic 5-ALA fluorescence such as hidden fluorescence because of overlying blood could be overcome with the presence of additional white light and the clear visualization of the exposed brain. Furthermore, this new technique is a promising tool with the potential to significantly improve operation ergonomomy.

Fig 1



Fluoreszenz-gestützte Hirntumorchirurgie/*Fluorescence-guided surgery for brain tumours*

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5-ALA Kinetik in Meningeomen – vergleichende Analyse von Tumorfluoreszenz und PpIX Metabolismus *in vitro*

5-ALA kinetics in meningiomas – comparative analysis of tumour fluorescence and PpIX metabolism in vitro

E. C. Bunk¹, L. Stögbauer¹, A. Wagner², W. Paulus², W. Stummer¹, V. Senner², B. Brokinke¹

¹Universitätsklinikum Münster, Klinik und Poliklinik für Neurochirurgie, Münster, Germany

²Universitätsklinikum Münster, Institut für Neuropathologie, Münster, Germany

Objective

The utility of 5-aminolevulinic acid (5-ALA) mediated fluorescence-guided resection (FGS) of meningiomas is increasingly investigated in both in-vitro and in-vivo studies. However, kinetics of 5-ALA as well as expression of protoporphyrin (Pp) IX transport proteins (ABCG2 and ABCB6) and the Ferrochelatase (FECH) in meningiomas are largely unexplored.

Methods

Immortalized benign Ben-Men1 and malignant IOMM-Lee cells lines as well as primary grade I and II meningioma cells were treated with varying concentration of 5-ALA for 4h. PpIX fluorescence and expression of ABCG2, ABCB6 and FECH were analysed after 0, 2, 4 and 6 hours and compared with U87 glioblastoma cells.

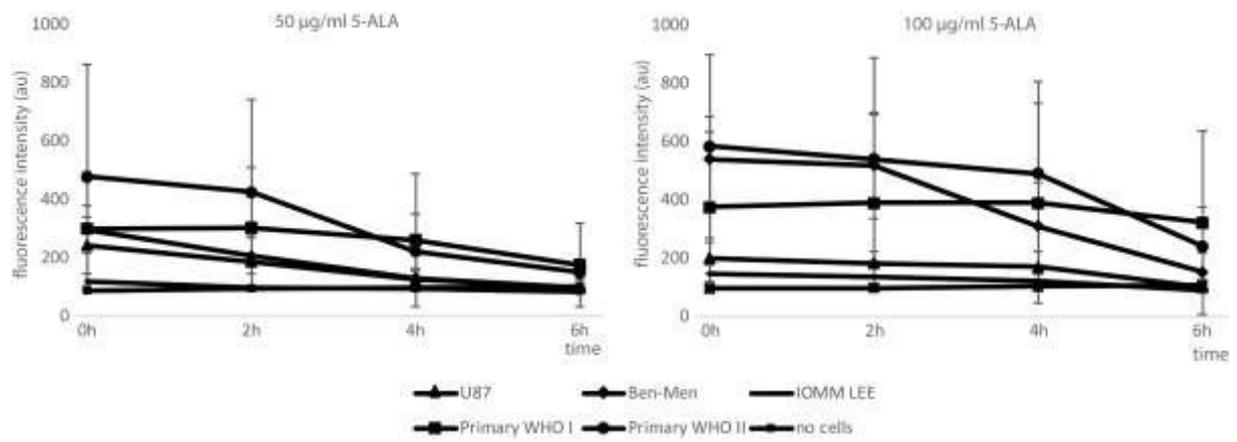
Results

Primary meningioma cells showed similar PpIX fluorescence intensity over time compared to Ben-Men1 and U87 cells after exposure to a medium dose of 5-ALA (50 µg/ml). In contrast to U87, exposure to 100 µg/ml 5-ALA lead to a significant increase of fluorescence in Ben-Men1 cells with a similar trend in primary meningioma cells. On the other hand, IOMM Lee cells did not show any relevant fluorescence. The attached figure illustrates the fluorescence intensity over time following administration of 50 or 100 µg/ml 5-ALA in primary meningioma, Ben-Men1, IOMM LEE and U87 cells (0=immediate measurement after finishing incubation). As a negative control empty 96-well plate wells (no cells) were used. Relative expression of the PpIX importer ABCB6 as well as FECH was increased in Ben-Men and primary meningioma cells compared to U87. Interestingly, also the relative expression level of the PpIX exporter ABCG2 was increased in primary meningioma cells while no expression could be detected in Ben-Men or IOMM-LEE cells.

Conclusion

Ben-Men1 but not IOMM-Lee cells were shown as valid models to study 5-ALA kinetics in immortalized meningioma cells. In contrast to glioblastomas, increase of 5-ALA dosage during FGS of meningiomas might help to overcome frequently reported intraoperative shortcomings such as heterogenous tumor fluorescence and lack of fluorescence of the dura tail. As expression of PpIX metabolism molecules is not necessarily correlated, other molecular mechanisms might alter fluorescence in meningiomas.

Fig 2



Fluoreszenz-gestützte Hirntumor Chirurgie/*Fluorescence-guided surgery for brain tumours*

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Echtzeit-Fluoreszenzkinetik von Protoporphyrin IX nach 5-ALA-Gabe und Faktoren, die die Fluoreszenz bei geringgradigem Gliom vorhersagen

Fluorescence real-time kinetics of protoporphyrin IX after 5-ALA administration and factors predicting fluorescence in low-grade glioma

E. Suero Molina¹, S. Kaneko^{1,2}, P. B. Sporns³, S. Schipmann-Miletic¹, D. Black⁴, W. Stummer¹

¹Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

²Hokkaido University Graduate School of Medicine, Department of Neurosurgery, Sapporo, Japan

³Universitätsklinikum Münster, Institut für Klinische Radiologie, Münster, Germany

⁴University of British Columbia, Canada

Objective

Five-Aminolevulinic acid (5-ALA) has been established as a compound for inducing fluorescence and assisting resection in high-grade glioma. However, in low-grade glioma (LGG) the clinical value of 5-ALA-induced fluorescence is unclear. Particularly, time-dependency and time kinetics have not been yet investigated. The purpose of this study was to investigate real-time kinetics of Protoporphyrin IX (PpIX) in LGG based on hyperspectral fluorescence-based measurements.

Methods

We evaluated patients harboring LGG surgically treated. Patients received 5-ALA at a standard dose of 20 mg/kg b.w. 4 hours prior to surgery. Assessments were performed utilizing a hyperspectral camera. Fluorescence intensity (FI) and PpIX concentration (CPpIX) were measured in the tumor tissue. We furthermore evaluated apparent diffusion coefficient (ADC)-based tumor cell density, Ki-67/MIB-1 Index, chromosomal 1p/19q co-deletion and ¹⁸F-fluoro-ethyl-tyrosine (¹⁸F-FET)-PET values and their role for predicting fluorescence.

Results

81 tissues from 25 LGG patients were included in this study. Tissues with fluorescence delivered a maximum of FI and CPpIX between 7-8 hours after 5-ALA administration. When visible fluorescence was available, peaks of FI and CPpIX were observed within a 7-8 hour time-frame regardless of MRI contrast-enhancement. GD-enhancement ($p=0.008$), Ki-67/MIB-1 Index ($p<0.001$), ¹⁸F-FET-PET uptake ratio ($p=0.038$) and ADC-based tumor cellularity ($p=0.017$) differed significantly between fluorescing- and non-fluorescing tissue. 1p/19q co-deletion was not reliable for predicting fluorescence. Logistic regression demonstrated ¹⁸F-FET-PET uptake and Ki-67/MIB-1 Index as independent variables for predicting fluorescence.

Conclusion

We report in a fluorescence-based assessment of CPpIX in human LGG tissues. ¹⁸F-FET-PET uptake and Ki-67/MIB-1 are independent strong factors for predicting fluorescence. Similar to previously reported in HGG, fluorescence peaked between 7-8 hours after 5-ALA application. In consequence, 5-ALA administration in patients with suspected LGG should be 4-5 hours prior to surgery and always adapted to the clinic's own logistics environment.

Fluoreszenz-gestützte Hirntumorchirurgie/*Fluorescence-guided surgery for brain tumours*

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Validierung eines neuen Filtersystems zur Visualisierung der 5-ALA-induzierten PPIX-Fluoreszenz in der Chirurgie maligner Gliome – eine Proof-of-Principle Studie

Validating a new generation filter-system for visualising 5-ALA-induced PPIX-fluorescence in malignant glioma surgery – a proof of principle study

E. Suero Molina¹, L. Stögbauer¹, A. Jeibmann², N. Warneke¹, W. Stummer¹

¹Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

²Universitätsklinikum Münster, Institut für Neuropathologie, Münster, Germany

Objective

The BLUE 400 filter system (Carl Zeiss Meditec, Oberkochen, Germany) has provided visualization of 5-ALA-induced fluorescence-guided surgery for more than 20 years. Nevertheless, constraints, e.g. limited background discrimination during hemostasis, obstruct fluency of surgery. A novel filter with improved background visualization was developed, requiring validation regarding fluorescence discrimination. The aim of this article is to determine diagnostic accuracy and perception of PPIX discrimination of a novel filter system with higher background illumination (BLUE 400 AR) compared to the gold standard, BLUE400.

Methods

A surgical microscope equipped with both BLUE 400 and BLUE 400 AR was used. Comparisons were performed on a biological basis and on the visual perception of margins. High-resolution images were compared during and after surgery by senior neurosurgeons. In a predefined biopsy algorithm, four biopsies per patient at tumor margins of PPIX fluorescence and adjacent brain were acquired using BLUE 400 AR only from regions intended for resection and assessed for cell count and density.

Results

Thirty-two patients with malignant gliomas were included in this study. BLUE 400 AR markedly enhanced the brightness of the surgical field, allowing superior discrimination of brain anatomy. A total of 128 biopsies from fluorescence margins were collected. PPV was 98.44% (95% CI, 90.06-99.77%) for malignant glioma. Residual median cell density in non-fluorescent tissue was 13% (IQR 13 to 31). Perception of the location of fluorescent margins on HD images was equivalent for both filter combinations.

Conclusion

BLUE400 AR demonstrated superior background compared to conventional BLUE 400 in malignant glioma surgery but comparable fluorescence margins and PPV. Therefore BLUE 400 AR can be considered safe and effective in supporting malignant glioma surgery.

Fluoreszenz-gestützte Hirntumor Chirurgie/*Fluorescence-guided surgery for brain tumours*

V199

Endoskopisch-assistierte fluoreszenzgestützte Resektion geht über den kontrastmittelaufnehmenden Tumoranteil hinaus

Endoscopic fluorescence-guided resection go beyond MR contrast-enhancement borders in glioblastoma surgery

C. Bettag¹, K. Schregel^{2,3}, P. Langer², D. Behme², V. Rohde¹, D. Mielke¹

¹Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

²Universitätsmedizin Göttingen, Neuroradiologie, Göttingen, Germany

³Ruprecht-Karls-Universität Heidelberg, Neuroradiologie, Heidelberg, Germany

Objective

Complete resection of the contrast-enhancing tumor tissue is a main surgical goal in patients with glioblastoma (GBM). Complete tumor removal can be increased from 36 to 65% by microscopic fluorescence-guided (FG) resection. Recently, a study was published showing that an endoscope being capable of inducing fluorescence, detects residual fluorescent tumor tissue not being visualized by the microscope, and increases radicality. However, the influence on the extent of resection has not yet been quantified.

Methods

A standard dose of 5-ALA (20 mg/kg) was given 4 hours before surgery. After completing microscopic FG resection, the resection cavity was scanned using the prototype of an endoscope with a blue light source to detect residual fluorescent tissue, being not visualized by the microscope. The residual fluorescent tissue was completely resected and imbedded separately for histopathological examination. Non-enhanced and contrast-enhanced 3D T1w datasets acquired before and within 48 hours after tumor resection were analyzed using 3D Slicer. Bias field corrected data were used to segment brain parenchyma, tumor, and resection cavity in order to derive their volume as well as the differences in parenchymal volume pre- and post-surgery. Thus, the postoperatively quantified brain parenchyma volume is equivalent to the overall resected fluorescent tissue.

Results

12 patients with GBM were included. The mean tumor volume was 52.22 cm³ (range 16.61- 122.40 cm³). The mean volume of the resection cavity was 33.15 cm³ and significantly smaller than the tumor volume ($p = 0.015$). However, the mean volume of the overall resected fluorescent tissue was 114.09 cm³ and thus, significantly larger than the mean tumor volume ($p < 0.001$), yielding a mean volume of non-enhancing but fluorescent tissue of 61.87 cm³. The mean relative size of the overall resected volume compared to the tumor volume was 244.41 % (range 101–419 cm³). In all cases, histopathological examination confirmed residual tumor tissue in the separately preserved biopsies.

Conclusion

Endoscopic FG-resection of GBM is a useful adjunct to the microscope and allows supramarginal resection due to the detection of residual fluorescent tumor tissue, not being visualized by the microscope.

Fluoreszenz-gestützte Hirntumor Chirurgie/*Fluorescence-guided surgery for brain tumours*

V200

Für freies Wasser korrigierte MRT-Diffusionsbildgebung verbessert die präoperative Beurteilbarkeit peritumoraler Faserbahnen der weißen Substanz bei Gliompatienten

Free-water correction in Diffusion MRI improves preoperative evaluation of peritumoral white-matter tracts in glioma patients

L. Weninger¹, K. Jütten², S. Koppers¹, V. Mainz³, M. Wiesmann⁴, H. R. Clusmann², D. Merhof¹, C. H. Na²

¹Rheinisch-Westfälische Technische Hochschule Aachen, Bildverarbeitung und Computer Vision, Aachen, Germany

²Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neurochirurgie, Aachen, Germany

³Rheinisch-Westfälische Technische Hochschule Aachen, Institut für Medizinische Psychologie und Medizinische Soziologie, Aachen, Germany

⁴Rheinisch-Westfälische Technische Hochschule Aachen, Institut für Diagnostische und Interventionelle Neuroradiologie, Aachen, Germany

Objective

Diffusion MRI with tractography-based estimation of fiber-connectivity is applied for surgical planning with the aim of maximal safe tumor resection, but preservation of functionally relevant white-matter (WM) tracts. Free-water (FW) partial volume effects however limit tracking algorithms at the boarder of cerebrospinal fluid or in the presence of vasogenic edema, which obscures WM estimates especially in peritumoral areas, endangering delineation of fiber displacement and tract identification. We compared a novel method for free-water correction of diffusion weighted imaging (DWI) to previous approaches on single- and multi-shell synthetic data and healthy adults, and applied it to a brain tumor patient database.

Methods

28 patients with cerebral glioma (mean age 51+/-17 yrs, 20 high-grade) were preoperatively examined using anatomical MRI and DWI. To determine the free-water volume fraction (FWVF), an artificial neural network (ANN) was trained on synthetic data generated from patient-specific DWI data. Voxels with known tissue properties (e.g. corpus callosum, ventricles, gray matter) were extracted, and by superposition of different voxels and varying tissue proportions, a synthetic dataset with known diffusion microstructure was composed. On this dataset, the ANN was trained to predict the FWVF, and then used to infer the FWVF of the whole brain. Finally, the diffusion signal uncontaminated by FW was determined.

Results

Evaluation of the exactness of the proposed method on the synthetic dataset showed similar results as compared to FW elimination for two-shell data, but better results as compared to other approaches for one- and three-shell data. Applying our novel FW correction algorithm on patient data, the predicted water compartment affected by edema ranged up to 30-40%. While FW correction resulted in corrected fractional anisotropy (FA) values within peritumoral edema, normal appearing white matter values were not altered. Peritumoral fiber-tracking improved and allowed delineation of fiber-tracts which were not depicted without FW correction (see figures).

Conclusion

We present a novel method for free-water correction in diffusion MRI, which is fast, independent of diffusion shells (b-values), and at no cost of additional acquisition time for the patient. Most importantly, it improves WM estimates and preoperative peritumoral fiber-tracking, which might be critical for surgical planning and postoperative functional outcome.

Fig 1

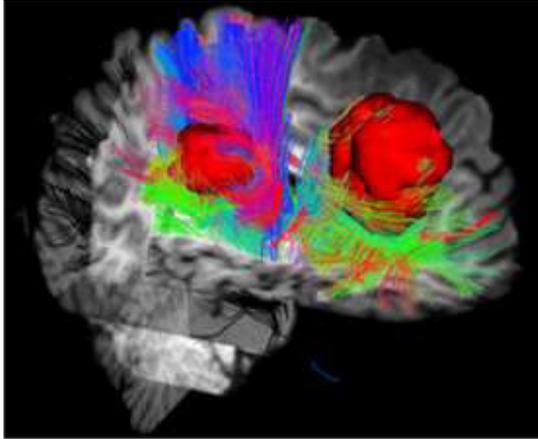


Figure 1: Peritumoral tracts without free-water correction

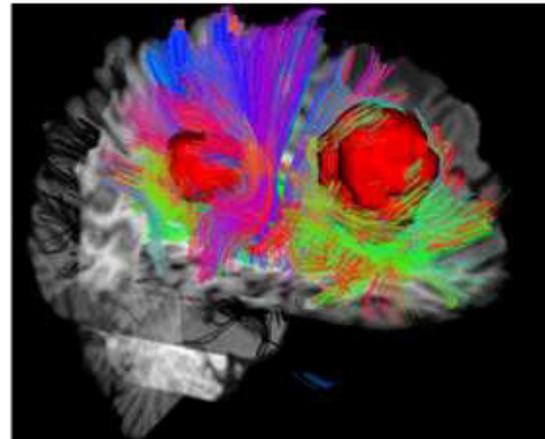


Figure 2: Peritumoral tracts after free-water correction

Neurointensivmedizin experimentell/*Neurocritical care experimental*

V201

Hämabbauprodukte nach einer Subarachnoidalblutung induzieren eine Verengung und Gefäßwandverdickung extraparenchymaler Hirnarterien von Mäusen

Haem degradation products after subarachnoid haemorrhage cause long-term vasoconstriction and vessel wall thickening of extraparenchymal brain arteries in mice

A. Joerk^{1,2}, S. C. Schröder^{1,3}, M. Ritter⁴, D. Freitag⁵, I. Ingrisch¹, D. Schulze⁴, G. Pohnert⁴, M. Westerhausen⁴, R. Kalff⁵, O. W. Witte^{1,2,3}, J. Walter⁵, K. Holthoff¹

¹Universitätsklinikum Jena, Klinik für Neurologie, Jena, Germany

²Universitätsklinikum Jena, Else Kröner-Forschungskolleg AntiAge, Jena, Germany

³Universitätsklinikum Jena, Else Kröner-Promotionskolleg JSAM, Jena, Germany

⁴Friedrich-Schiller-Universität Jena, Institut für Anorganische und Analytische Chemie, Jena, Germany

⁵Universitätsklinikum Jena, Klinik für Neurochirurgie, Jena, Germany

Objective

Delayed cerebral ischemia (DCI) caused by symptomatic cerebral vasospasm is the most important preventable cause of mortality and poor neurological outcome in subarachnoid haemorrhage (SAH) patients. We hypothesize that haem degradation products (HDPs), originating from the intracranial haematoma after aneurysm rupture, are involved in pathogenesis of delayed cerebral vasospasm by BK potassium channel inhibition. HDPs, comprising propentdyopents (PDP) and bilirubin oxidation products (BOX), are present in the cerebrospinal fluid of aneurysmal SAH patients and induced a short-onset vasoconstriction of cerebral arterioles in preclinical mouse models.

Methods

To study the long-term effect of HDPs on diameter and wall morphology of cerebral arteries, SAH was induced experimentally in adult wildtype and BK channel deficient mice (FVB/N) by the subarachnoid injection of autologous blood or PDP/BOX isomers into the cisterna magna. After the postinterventional days 7 or 14, mouse brains were removed and postfixed in 4% PFA for at least 48h. Subsequently, the diameter and vessel wall thickness of cross-sectioned artery segments in 40 µm brain slices were analyzed by confocal laser scanning microscopy after immunofluorescent staining with DAPI, anti-smooth muscle actin (SMA) and anti-CD 31.

Results

Two weeks after the subarachnoid injection of venous autologous blood (30 µl, $n=5$), PDP or BOX isomers (each 30 µl, 1 µM, $n=5$) the extraparenchymal located basilar artery (BA) and posterior communicating artery (PCA) were affected by a significant ($p<0.05$) increase of smooth muscle wall thickness in adult wildtype mice in comparison to control ($n=4$). This vessel wall remodelling was absent in PDP-treated BK knockout mice (30 µl, 1 µM, $n=4$). In addition, the wall thickness of the intraparenchymal located azygos pericallosal artery (APA) remained unchanged in all experimental groups ($p>0.05$). Focused on the diameter, blood as well as HDPs induced a significant vasoconstriction of PCA vessel segments in wildtype mice in comparison to control.

Conclusion

Besides the short-onset vasoactivity of HDPs, our data demonstrate for the first time a long-term vessel wall remodelling of brain base arteries which correlates in time with the onset of delayed vasospasm in SAH patients. In addition, the morphology changes were limited exclusively to extraparenchymal arteries and

dependent on BK channel expression. These findings may promote to a better pathomechanistic understanding of cerebral vasospasm.

Neurointensivmedizin experimentell/*Neurocritical care experimental*

V202

Das glymphatische Drainagesystem ist in der akuten Phase der experimentellen Subarachnoidalblutung beeinträchtigt

The glymphatic drainage system is impaired in the acute phase of experimental subarachnoid haemorrhage

T. P. Schmidt, S. Fontane, A. Bach, C. Conzen, H. R. Clusmann, U. Lindauer, G. A. Schubert

Universitätsklinikum RWTH Aachen, Neurochirurgie, Aachen, Germany

Objective

The glymphatic system was discovered as a supposed perivascular pathway clearing the brain from solutes by convective transportation along the vasculature. The impact of acute subarachnoid hemorrhage (SAH) on this important perivascular transport system is incompletely understood. Therefore we established a model for assessment of the glymphatic system in SAH.

Methods

The cisterna magna injection model for SAH in a rat was used to assess glymphatic drainage properties. Application of the fluorescence marker Alexa 594 was followed by autologous blood injection. Brains were then harvested at three different time points (15 minutes, 1 hour, 4 hours), followed by cryofixation and separation into 10 µm brainslices. Visualization was achieved via anti-GFAP (astrocytes) and anti-von Willebrand factor (anti-vWF, endothel) stainings.

Results

Subarachnoidal injection of Alexa 594 resulted in fluorescent signals between the anti-GFAP- (astrocytic endfeet) and anti-vWF- (endothelial layer) positive signals. Histogram analysis of different brain areas in SAH animals compared with sham operated animals showed a significant compromise of the newly identified transportation process.

Conclusion

In the acute phase after subarachnoid hemorrhage the glymphatic drainage system is severely compromised. These immediate alterations may play an imminent role in both early brain injury and delayed complications after SAH, warranting further analysis. Our animal model offers the possibility to analyze the impact of increased intracranial pressure and blood components on the glymphatic drainage.

Neurointensivmedizin experimentell/*Neurocritical care experimental*

V203

Monozyten-Polarisation in den protektiven Phänotyp nach aneurysmatischer Hirnblutung – ein neuer Therapieansatz

Skewing monocyte polarisation towards protective phenotype in aneurysmal subarachnoid haemorrhage (SAH) – a novel therapeutic approach

S. Muhammad^{1,2,3}, S. R. Chaudhry³, D. Hänggi¹

¹Heinrich-Heine-Universität Düsseldorf, Abteilung für Neurochirurgie, Düsseldorf, Germany

²University of Helsinki, Department of Neurosurgery, Helsinki, Finland

³Universitätsklinikum Bonn, Abteilung für Neurochirurgie, Bonn, Germany

Objective

State of the art research reveal critical role of inflammation during the phase of early and delayed brain injury after aSAH. Monocytes/macrophages being fundamental part of the innate immunity are the most important players to drive or inhibit inflammation. Monocyte induced inflammation depends on their polarization status either towards M1-type (pro-inflammatory) or M2-type (anti-inflammatory) monocytes. Monocytes polarization and their activation states after aSAH have still not been investigated in detail.

Methods

Peripheral venous blood from 15 SAH patients on day 1 and day 7, and once from 10 healthy controls was used for multicolour flow cytometry. Cells were stained with specific anti-human mouse monoclonal antibodies for 20 minutes and were then acquired on BD LSR Fortessa™. Monocytes were gated based on their intermediate side scatter and CD45 expression. Monocyte subsets were characterized based on differential CD14 and CD16 expression. Activation markers including CCR2, CX3CR1 and HLA-DR were used to quantify activation state of different monocyte subpopulations

Results

Analysis of monocyte sub-types based on differential CD14 and CD16 expression revealed that non-classical monocytes (M2-type) were significantly decreased compared to healthy controls on day 1. Moreover, intermediate monocytes were significantly higher on post-SAH day 1 compared to day 7. The CX3CR1+ intermediate and non-classical monocytes showed similar significant differences. Intriguingly, classical (M1-type) CCR2+ monocytes significantly increased on post-SAH day 1 as compared to controls and intermediate CCR2+ monocytes compared to post-SAH day 7. Finally, HLA-DR+ expression was impaired on all monocyte sub-population

Conclusion

Subarachnoid hemorrhage led to increased classical (M1-type) monocytes and decreased alternate (M2-type) monocytes. This imbalance of monocyte polarization towards M1-type cells may exacerbate inflammation mediated post-SAH complication. Skewing monocyte polarization towards M2-type cells after aSAH might be beneficial.

Neurointensivmedizin experimentell/*Neurocritical care experimental*

V204

Akutphase nach experimenteller traumatischer Hirnschädigung – Einfluss einer Überdosierung Dabigatran auf das Kontusionsvolumen und die diffus axonale Hirnschädigung – ein explorativer Tierversuch
Acute phase after experimental TB – influence of dabigatran overdose on contusion volume and diffuse axonal injury – an exploratory animal trial

B. Kremer¹, L. Liebenstund², S. Pinkernell¹, K. Nolte³, O. Grottko², M. Coburn², A. Höllig¹

¹Universitätsklinikum RWTH Aachen , Klinik für Neurochirurgie, Aachen, Germany

²Universitätsklinikum RWTH Aachen , Klinik für Anästhesiologie, Aachen, Germany

³Universitätsklinikum RWTH Aachen , Institut für Neuropathologie, Aachen, Germany

Objective

Direct oral anticoagulants (DOAC) are widely used and indications expand. Various advantages compared to phenprocoumon have led to a widespread use. However, there are also disadvantages as the renal elimination of some DOACs (particularly dabigatran) which entails the risk that older patients -susceptible to renal failure - are overdosed. Still there is scarce data on the natural course of patients on supramaximal concentrations of DOACs suffering from traumatic brain injury (TBI). We present experimental data on the acute phase after TBI with regard to contusion volume and signs of diffuse axonal injury (DAI).

Methods

Sprague Dawley rats received TBI by controlled cortical impact (CCI), either as a control group (no anticoagulation; n=3) or after pretreatment with dabigatran etexilate (n=7; 120mg/kg; target plasma dose of dabigatran > 800ng/ml). Baseline dabigatran plasma levels were determined. Three hours after TBI the animals were euthanized, brain were harvested, formalin fixed and afterwards embedded in paraffin. Slices at 2µm thickness then were stained with H&E, GFAP and SNTF. Contusion volume was measured using H&E stained slices, GFAP and SNTF positive areas accounted for DAI (analyses via ImageJ). Data from the control group was compared to the dabigatran group using a Mann-Whitney U Test (SPSS 25.0); p value was set ≤0.05.

Results

Contusion volumes did not differ between the two groups (p=1.0; Mann Whitney U Test). A significantly higher GFAP expression for the dabigatran animals was seen in the corpus callosum (p=.006), the ipsilateral and contralateral hippocampus (p<.001 each) and the mean GFAP expression on the trauma side. Higher GFAP expression in the control group was detected for the contralateral internal capsule (p=.003). Using SNTF as a very specific marker for DAI only the ipsilateral expression in the cingulum was significantly higher in the dabigatran animal (p<.001) and the mean expression in the left hemisphere differed significantly from the right one (p=0.048).

Conclusion

Animals with supramaximal dabigatran concentrations did not show larger contusions following TBI. However, signs indicating a DAI (in terms of higher GFAP expression) were more frequently seen in the dabigatran treated group, whereas SNTF expression on the ipsilateral side was only slightly higher in the dabigatran group. In the very acute phase after TBI, supramaximal dabigatran levels are preliminary associated with broader axonal lesion pattern, but not with larger contusion volume.

Neurointensivmedizin experimentell/*Neurocritical care experimental*

V205

Zusammenhang zwischen Herzfunktion und zerebraler Perfusion in einem Mausmodell der Subarachnoidalblutung

Correlation of myocardial function and cerebral perfusion in a murine model of subarachnoid haemorrhage

A. Neulen¹, M. Molitor², M. Kosterhon¹, T. Pantel¹, E. Holzbach¹, W. S. Rudi², S. H. Karbach², P. Wenzel², F. Ringel¹, S. C. Thal³

¹Universitätsmedizin Mainz, Neurochirurgische Klinik und Poliklinik, Mainz, Germany

²Universitätsmedizin Mainz, Zentrum für Kardiologie - Kardiologie I, Mainz, Germany

³Universitätsmedizin Mainz, Klinik für Anästhesiologie, Mainz, Germany

Objective

In rodent models of subarachnoid hemorrhage (SAH), the impact of cardiac function on cerebral perfusion (CP) is unclear. We therefore set out to investigate the interplay between cerebral perfusion and cardiac function in a murine endovascular filament perforation model of SAH. A further aim of this study was to record abnormal ECG and echocardiography recordings as a basis for future experimental studies on neurogenic stress cardiomyopathy (NSC), which occurs in a significant number of SAH patients.

Methods

20 female C57BL/6-N mice were randomized either to induction of SAH by endovascular filament perforation or to sham surgery. Cerebral cortical perfusion was imaged using laser SPECKLE contrast imaging, along with determination of intracranial pressure. Cardiac function was assessed with 1-lead ECG recordings and high frequency small animal echocardiography. Measurements were performed at baseline, and 15 min, 3 h, 24 h, 72 h and 7 days after surgery. Blood pressure was determined non-invasively using a tail-cuff system.

Results

Baseline parameters were similar between SAH and sham. SAH induction was associated with significant reduction of CP, which mostly recovered by 24 h. Blood pressure was similar between SAH and sham animals. Cardiac left ventricular function was enhanced during the first 72 h and reduced at 7 days compared to sham. In the SAH group, there was a significant positive correlation between left ventricular end-diastolic volume and CP between 3 and 72 h post-SAH. 3 SAH animals showed ECG-abnormalities e. g. a right bundle branch block 15 min and 3 h after SAH, which recovered by 24 h. In contrast to the overall increase in LVEF in the SAH group, 2 SAH animals showed a prominent decrease in LVEF 3 h after SAH, which recovered by 24 h.

Conclusion

In the murine SAH model, SAH influences cardiac function, and end-diastolic filling appears to influence cerebral cortical perfusion markedly in the early period after SAH. The abnormal ECG and echocardiographic findings observed in single animals resemble those found in SAH patients with NSC, indicating that the murine model is suited for functional studies on NSC after SAH.

Neurointensivmedizin experimentell/*Neurocritical care experimental*

V206

Rolle des acid-sensing ion channels 1a auf posttraumatischen Hirnschaden und funktionelles Outcome nach experimentellem Schädel-Hirn-Trauma

Role of acid sensing ion channel 1a in the development of posttraumatic brain damage and functional outcome after experimental traumatic brain injury

S. Cheng^{1,2}, M. Wostrack³, F. Ringel⁴, N. Plesnila^{1,2}, N. A. Terpolilli^{5,1,2}

¹Klinikum der Ludwig-Maximilians-Universität München, Institut für Schlaganfall- und Demenzforschung, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, München, Germany

³Technische Universität München, Neurochirurgie, München, Germany

⁴Universitätsmedizin Mainz, Neurochirurgie, Mainz, Germany

⁵Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgie, München, Germany

Objective

Traumatic brain injury (TBI) is a leading cause of death and disability among young adults and children and a major risk factor for neurodegenerative diseases and early-onset dementia. The mechanisms involved in the development of long-term consequences of TBI are not fully understood yet. Acid-sensing ion channel 1a is a voltage gated Na⁺- and Ca²⁺ channel located on the postsynaptic membrane of neurons in both central and peripheral nervous system; in the CNS, it is involved in mediating – among other things – synaptic plasticity. It also seems to be implicated in the development of post-ischemic brain damage. The role of ASIC1a in traumatic brain injury, especially for long-term consequences of TBI, has not been evaluated yet. In the current study, we investigated the effect of ASIC1a on lesion progression and functional outcome up to six months after experimental traumatic brain injury in a transgenic mouse model.

Methods

Male ASIC1a transgenic mice and their wildtype littermates were subjected to TBI using the controlled cortical impact model. Brain water content was assessed by the wet weight-dry weight method 24 hours after TBI. Body weight and motor function were measured 3 days before surgery, then 1, 3, 7, 14, 60, 90 and 180 days after TBI. Behavioral tests assessing memory and depression like behavior were performed 60, 90, and 180 days after CCI. Lesion volume was longitudinally observed with serial MRI scans 14, 60, 90, and 180 days after TBI. At the end of the observation period (180 days after TBI), brains were harvested for histological evaluation.

Results

ASIC1a deficiency did not affect survival rate, body weight, or fine motor skills after CCI. Brain edema formation 24 hours after TBI was significantly lower in homozygous ASIC1a animals compared to wildtype controls. Furthermore, homozygous ASIC1a mice showed significantly reduced lesion volume from 60 to 180 days and reduced hippocampal damage at 180 days after TBI, in MR as well as in histological assessment at six months after TBI. This translated into improved cognitive function at 180 days (as measured by Barnes Maze testing) and reduced depression-like behavior 60 to 180 days after TBI.

Conclusion

ASIC1a deficiency reduced brain edema formation early after TBI, significantly reduced posttraumatic brain damage and improved neurological outcome in the chronic phase after experimental traumatic brain injury. ASIC1a may therefore be a promising therapeutic target after TBI.

Neurovaskuläre Chirurgie I/*Neurovascular surgery I*

V207

Neuropsychologische Beeinträchtigung bei erwachsenen Moyamoyapatienten mit Moyamoya-Angiopathie – präoperative Beurteilung und Korrelation zu MRT und H₂¹⁵O-PET

Neuropsychological impairment in adults with moyamoya angiopathy – preoperative assessment and correlation to MRI and H₂¹⁵O-PET

P. Haas¹, M. Fudali¹, M. Milian¹, U. Ernemann², P. Meyer³, M. Tatagiba¹, N. Khan^{1,4}, C. Roder¹

¹Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

²Universitätsklinikum Tübingen, Diagnostische und Interventionelle Neuroradiologie, Tübingen, Germany

³Universitätsklinikum Freiburg, Klinik für Nuklearmedizin, Freiburg, Germany

⁴Universitätsspital Zürich, Moyamoya Center, Zürich, Switzerland

Objective

Patients with moyamoya angiopathy (MMA) are known to have an increased risk of impaired executive function (dysexecutive cognitive syndrome (DCS)). Number of moyamoya patients with DCS vary strongly in the literature, evidence of a correlation to affected vascular territories is low. This study aims to identify cognitive impairment in adult moyamoya patients and to correlate findings with imaging results. In addition, the predictive value of individual tests for the identification of DCS was analyzed.

Methods

Neuropsychological test data of 41 adult moyamoya patients was analyzed for a possible correlation with territorial hypoperfusion on H₂¹⁵O PET with acetazolamide (ACZ) challenge (cerebrovascular reserve – CVR) and infarction patterns observed in MRI. Each vascular territory was analyzed separately and correlated to neuropsychological test results and presence of DCS.

Results

41.5% of patients presented with DCS. Significant association of DCS and affection of the right MCA territory was seen for insufficient CVR in PET ($p=0.030$) and for patients with infarctions seen in MRI ($p=0.014$). Analysis of individual neuropsychological test results confirmed the main association with the right MCA territory, as well as some association with the right ACA territory. Analysis of a subgroup of patients with chronic disease on MRI (presence of large post-infarction gliosis and brain atrophy in affected territories) revealed a significantly higher risk for DCS (85% affected) than non-chronic patients (21% affected) ($p<0.001$).

Conclusion

Analysis of neuropsychological test data in this moyamoya cohort reveals DCS in 41.5% of all patients. Correlation between DCS and an impairment of CVR seen in PET and/or infarctions seen in MRI was significant for the right MCA territory. Patients with chronic disease had a significantly higher risk for DCS than non-chronic patients ($p<0.001$).

Neurovaskuläre Chirurgie I/Neurovascular surgery I

V208

Indocyaningrün Videoangiographie zur Bewertung und Selektion des Empfängergefäßes bei STA-MCA Bypass Revaskularisierung

Indocyanine green videoangiography for stratification of recipient vessel selection in STA-MCA bypass surgery

J. Goldberg^{1,2}, P. Vajkoczy¹, N. Hecht¹

¹Charité – Universitätsmedizin Berlin, Berlin, Germany

²Universitätsspital Bern, Bern, Switzerland

Objective

The identification of the ideal recipient in STA-MCA bypass surgery remains debatable because there are no objective selection criteria if multiple options exist. We aim to assess the value of indocyanine green videoangiography (ICG-VA) for recipient vessel selection in STA-MCA bypass surgery.

Methods

Sixty patients that underwent 65 STA-MCA bypass procedures with pre- and post-anastomosis ICG-VA were included. The primary surgeon was blinded towards the pre-anastomosis ICG-VA. First, pre-anastomosis white-light and ICG-VA were compared regarding the identifiability of potential recipients and pathological flow patterns. Second, the effect of definite recipient selection on flow increase within the recipient was analyzed according to initial flow within the recipient, the sequence of appearance and the vessel diameter in ICA-VA. Third, recipient flow increase was analyzed according to pre-anastomosis recipient flow direction and bypass graft orientation.

Results

ICG-VA permitted identification of a significantly higher number of potential recipients (median 4, range 1-9) than white-light (median 2, range 1-5; * $p < 0.001$) next to identification of pathological flow patterns in 20%. The recipient with the highest flow, earliest appearance and largest diameter was chosen in >45%. After bypass grafting, a significant recipient flow increase of $70 \pm 100\%$ (* $p = 0.001$) was noted. Interestingly, a higher flow increase occurred in recipients with initially low flow and late appearance (* $p = 0.01$), whereas the recipient diameter had no influence on recipient flow increase ($p = 0.09$). Further, a higher flow increase was noted in recipients with initially retrograde flow ($p = 0.02$), whereas no difference was found depending on graft orientation ($p = 0.44$).

Conclusion

ICG-VA facilitates identification of potential recipients and detection of pathological flow patterns in STA-MCA bypass surgery. Recipients with initially low flow, late appearance, and retrograde flow seem to bear the highest potential for flow increase, possibly due to a higher hemodynamic need for revascularization.

Neurovaskuläre Chirurgie I/*Neurovascular surgery I*

V209

Neue software-gestützte Bypassplanung und ihre Validierung durch transdurale ICG Videoangiographie *Novel software-derived workflow in EC-IC bypass surgery validated by transdural ICG videoangiography*

P. Dodier, W. T. Wang, G. Bavinzski, J. Frischer, K. Rössler

Medizinische Universität Innsbruck, Universitätsklinik für Neurochirurgie, Wien, Austria

Objective

The introduction of image-guided methods in bypass surgery resulted in optimized preoperative identification of recipients and in excellent patency rates, but recently presented methods are also resource-consuming. The objective was to present a cost-efficient planning workflow in extracranial-intracranial (EC-IC) revascularization in combination with transdural indocyanine green videoangiography (tICG-VA).

Methods

The study was a retrospective review at a single tertiary referral center from 2011 to 2018. A novel software-derived workflow was applied in 25 of 92 bypass procedures between 2011 and 2018. Precision and accuracy were assessed through tICG-VA identification of cortical recipients and by comparison of virtual and actual data. A control group of 25 traditionally planned procedures was additionally matched.

Results

Intraoperative transfer time of calculated coordinates averaged 0.8 min (0.4-1.9 min). The definitive recipients matched the targeted branches in 80%, and a neighboring branch was used in 16%. Our workflow led to a significant craniotomy size reduction in the study group compared to the control group ($p=.005$). tICG-VA was successfully applied in 19 cases. An average of two potential recipient arteries were identified transdurally, resulting in tailored durotomies and 3 craniotomy adjustments. Follow-up patency results were available for 49 bypass surgeries comprising 54 grafts. The overall patency rate was 91% at a median follow-up time of 26 months. No significant difference was found in the patency rate between both groups ($p=.317$).

Conclusion

Our clinical results validate the presented planning and surgical workflow and support the routine implementation of tICG-VA for recipient identification before durotomy.

Neurovaskuläre Chirurgie I/Neurovascular surgery I

V210

Vergleich von 968 Patienten mit intrakraniellen Aneurysmen und polyzystischer Nierenerkrankung aus der @neurIST Datenbank, der Kuopio Kohorte und einem Review der Literatur zu PKD-Patienten
Comparison of Autosomal Polycystic Kidney Disease patients with 904 patients with intracranial aneurysms from the @neurIST database and the review of the literature

J. Haemmerli, M. Georges¹ K. Schaller, P. Bijlenga

Genfer Universitätsspitäler, Klinik für die Neurochirurgie, Genf, Switzerland

Objective

Autosomal polycystic kidney disease (APKD) is a hereditary condition leading to vascular abnormalities. APKD patients are known to have more intracranial aneurysms (IA). The Kuopio cohort (Finland) is nowadays the largest cohort having compared demographic data and aneurysms characteristics between APKD- and non-APKD patients [1]. Characteristics of APKD patients has been reviewed after a systematic review of the literature in 2017 [2]. The @neurIST Aneurysm Data Bank (ADB) aims to collect information of patients diagnosed with IA. This study compares observation made in the ADB cohort, the Kuopio cohort and the literature review to have a better understanding of IA in APKD patients.

Methods

Information collected in the ADB on prospectively and consecutively recruited patients with ruptured and unruptured IA was studied. APKD patients were identified from it. Demographic data and aneurysm characteristics were analyzed and compared to the Kuopio cohort, which enrolled 6286 non-APKD IA and 102 APKD IA and the systematic review that reported information on 563 APKD patients, 679 IAs and location of 345 IAs.

Results

Between 2007 and 2017, 968 patients with IA were enrolled in the prospective and consecutive dataset of the ADB (947 non-APKD, 21 PKD) for a total of 1229 IA (1191 non-APKD and 38 APKD). PDK patients had significantly more IA in MCA arteries (OR 2.0, 95%CI 1.0-3.8) than other locations. Despite differences in the distribution of aneurysm according to location in different populations, the predominance of IA located in MCA arteries has been observed consistently. In all cohorts, APKD patients had more often multiple IA ($p < 0.05$) and were younger than non-APKD. APKD patients suffered more often from hypertension than non-APKD (Kuopio: 73.6% vs. 34.0%; ADB: 61.9% vs. 39.3%). No statistical difference was found in term of size of IA.

Conclusion

Patients suffering of APKD are more likely to suffer intracranial aneurysms than non-affected subjects. APKD patients diagnosed with IA are more likely to have multiple IAs and IAs are more likely to be located in MCA arteries. The precise role of loss of primary cilia function and blood hypertension on disease initiation, progression and severity still needs further investigations.

1. Nurmonen et al. 2017. Neurology
2. Cagnazzo et al. 2017. Acta Neurochirg

Neurovaskuläre Chirurgie I/Neurovascular surgery I

V211

Die Rolle der Kraniotomiegröße in alten Patienten mit traumatischen akuten subduralen Hämatomen – eine retrospektive Analyse

Same procedure every age? – The role of craniotomy size in elderly patients with traumatic acute subdural haematoma – A retrospective analysis

C. Unterhofer, M. Bauer, M. Unterhofer, C. Thomé

Medizinische Universität Innsbruck, Universitätsklinik für Neurochirurgie, Innsbruck, Austria

Objective

A retrospective study to compare standard (SC) or limited craniotomy (LC) was conducted in elderly patients with a traumatic acute subdural hematoma (aSDH). The aim of this study was to identify the role of craniotomy size in terms of clinical and radiological outcome.

Methods

Between 2000 and 2019 564 elderly patients were admitted harboring TBI. 69 Patients aged 75 or older with aSDH as sole pathology were retrospectively analyzed. SC was defined as a frontotemporoparietal craniotomy (>8cm) opposed to a temporoparietal craniotomy (<8cm, LC). Data were collected pre-and postoperatively including clinical (GCS) and radiological (hematoma depth (HD) and midline shift (MLS)) criteria. The primary outcome parameter was 30 day mortality. Secondary outcome parameters were radiological: residual HD and residual MLS.

Results

The mean age was 79 ($\pm 3,1$) years with no difference between groups. Mortality rate was significantly associated with preoperative HD $n = 19,9474 \pm 5,79294$ ($p=0.03$) and MLS $14,539 \pm 8,1613$ ($p=0.001$). A significantly higher mortality rate was found in the SC group $n=13$ (68,4%) ($p=0.045$). However, in this group patients scored significantly lower on the initial GCS ($p=0.026$). The preoperative HD ($p=0.08$) and the MLS ($p=0.09$) was significant higher in the SC group. The postoperative residual HD and MLS showed no significant difference between groups.

Conclusion

Size of craniotomy does not influence postoperative radiological outcome in elderly patients with aSDH. A LC is sufficient for adequate hematoma evacuation.

Schädelbasis/Skullbase

JM–JNS04

Endoskopische endonasale extradurale posteriore Clinoidektomie bei Schädelbasistumor *Endoscopic endonasal extradural posterior clinoidectomy for skull base tumour*

H. Ohata¹, T. Goto¹, A. Nagm¹, N. Rao², K. Nakajo¹, H. Morisako¹, H. Goto¹, T. Uda¹, S. Kawahara¹, K. Ohata¹

¹Osaka City University, Neurosurgery, Osaka, Japan

²Philipps-Universität Marburg, Neurosurgery, Bengaluru, India

Objective

The endoscopic endonasal approach for skull base tumors has become an important topic in recent years, but its use, merits, and demerits are still being debated. The objective of this study was to describe the surgical implementation and efficacy of the endoscopic endonasal extradural posterior clinoidectomy to obtain maximal tumor exposure.

Methods

The surgical technique included extradural posterior clinoidectomy following lateral retraction of the internal carotid artery at the paraclival segment and extradural pituitary retraction. In cases with prominent posterior clinoid process, the sellar dura was cut midline to facilitate extradural exposure of the process. Forty-four consecutive patients in whom this technique was performed between 2016 and 2018 at the authors' institution were reviewed. The pathology included 19 craniopharyngiomas, 7 chordomas, 6 meningiomas, 6 pituitary adenomas, 4 chondrosarcomas, and 2 miscellaneous. Utilization and effectiveness of this approach were further demonstrated with the radiological study of clinical cases.

Results

All cases were successfully operated using this procedure without any neurovascular injury, and it facilitated greater resection of the tumors. Four patients experienced transient postoperative abducens nerve paresis, and one patient experienced transient postoperative oculomotor nerve paresis; however, the deficits recovered within 3 months. On radiological examination, the surgical field was 2.2 times wider in cases with bilateral posterior clinoidectomy than in cases without posterior clinoidectomy.

Conclusion

The endoscopic endonasal approach with posterior clinoidectomy increases the working space and the maneuverability of the instruments to remove the tumor extended behind the posterior clinoid and dorsum sellae.

Schädelbasis/Skullbase

V214

Paradigmenwechsel in der Behandlung von Clivus Chordomen – von Midfacial Degloving zu endoskopischen Zugängen

Changing paradigm in surgical resection of clivus chordomas – from midfacial degloving to endoscopic approaches

K. Zweckberger, H. Giese, A. W. Unterberg

Ruprecht-Karls-Universität Heidelberg, Neurochirurgische Klinik, Heidelberg, Germany

Objective

Clivus chordomas are a rare tumor entity considered as low-grade malignancies. Treatment of choice encompasses radical surgical resection -if possible- followed by radiotherapy. Since the huge variety of tumor extension, different surgical approaches appear rational. Within the last ten years, however, coming along with the improved visual quality of the endoscopes, the transnasal endoscopic approach gained importance.

Methods

We retrospectively analyzed 69 surgical interventions in 49 patients with chordomas of the clivus between 2006-2019. We assessed tumor extension, the surgical approach, grade of surgical resection, neurological deficits prior and after surgery, and progression-free-survival in the primary and recurrent state.

Results

In 33 cases, we performed the primary surgery, in 36 cases, patients had already previous treatment. In primary cases, the most frequently used surgical approach was the navigation-guided transnasal endoscopic one (58%); in recurrences, however, the retrosigmoidal and the pterional approach dominated. Comparing the observation time between 2006-2012 versus 2012-2019, the endoscopic approach developed being the most dominant approach. In the group of primary surgery, we had no major complication; in recurrences, however, two patients had a post-operative hemorrhage and one was suffering from stroke. CSF leakage, as a minor complication, was seen in 11% of the entire cohort. In summary, we achieve progression-free survival over 5 years within 46%.

Conclusion

In surgical resection of clivus chordomas, the transnasal endoscopic approach has developed to the most preferred one, especially in primary surgery, however, considering the huge variety of tumor extension, alternative approaches are also necessary, especially in the recurrent state.

Schädelbasis/Skullbase

V215

Die Rolle der Neurochirurgie in der Behandlung von Patienten mit einer Pinealiszyste

The role of surgery in management of patients with pineal cysts – 25 years of experiences of a single-centre

B. Behmanesh, L. Imöhl, S. Y. Won, J. Quick-Weller, F. Geßler, V. Seifert

Universitätsklinikum Frankfurt am Main, Neurochirurgie, Frankfurt am Main, Germany

Objective

Pineal cysts are benign lesions, which mostly remain stable over years. Whether patients should be treated surgically or managed conservatively is still not fully understood. Hence, we report about of our experience, collected over 25 years and analyze the literature focusing on treatment modalities and benefit of surgery.

Methods

We conducted a retrospective study and included all patients treated from 1994 to 2019 in our department. A demographic analysis, radiological findings as well as maximum diameter, preoperative neurological status, duration of surveillance and overall outcome were conducted. Health status, pain level and sleep behavior were assessed prospectively using the EQ-5D 3L, SF -36 questionnaire, analog pain scale and Pittsburgh Sleep Quality Index.

Results

An overall of 97 patients were admitted for consultation and further treatment. Female to male ratio was 2.2 and the mean age was 31.5 years. The mean cyst diameter was 14.3 mm (range 2.1mm–23.1 mm). Only two patients (2.1 %) underwent surgical procedure, consisting of microsurgical cyst resection in one case and shunting in another case. After a mean follow-up time of 61.6 months clinical data represent no impairment of daily practice, work or physical activity. Increase in cyst diameter was seen in two patients. Data evaluating quality of life, pain level and sleep quality was available in 91 (93.4 %) patients and revealed a mean VAS of 1.5, the mean PSQI was 3.8 and EQ VAS of 83.9.

Conclusion

Based on the results of the present data as well as previously published data the indication for surgery should be evaluated very carefully. The "wait and see"-approach was tolerated very well in almost all patients.

Schädelbasis/Skullbase

V216

Zystische Kraniopharyngeome im Kindes- und Jugendalter - Stellenwert der Stereotaxie *Cystic craniopharyngioma in children and adolescents – the place of stereotactic treatment*

M. Schmutzner, S. Lietke, W. Rachinger, J. Tonn, F. W. Kreth, M. Kunz

Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik und Poliklinik, München, Germany

Objective

Treatment strategies for cystic craniopharyngiomas are still under debate particularly for the young population. We here present for the first time tumor control and functional outcome data after stereotactic (STX) and conventional surgical treatment.

Methods

From our prospective database, we identified pediatric and adolescent craniopharyngioma patients consecutively treated between 1990 and 2019. Treatment decisions in favor of microsurgery (transcranial/transsphenoidal) or STX treatment were made interdisciplinary. STX included aspiration of the cystic formation and/or implantation of an internal shunt catheter for continuous up- (ventricular system) and downstream (basal cisterns) drainage. Study endpoints were progression free survival (PFS), time to radiation, and functional outcome. The crossover rate from STX to microsurgical treatment was additionally analyzed. Functional outcome included ophthalmological, endocrinological and body-mass index (BMI) data.

Results

36 patients (median age 9.9 yrs) were analyzed including 33 (3) cystic (solid) tumors. STX was applied in 16, transsphenoidal (transcranial) microsurgery in 7 (13) tumors. Tumor volume reduction was achieved with either method (median 82 to 9cm³; p<0.001). Improvement of visual dysfunction was achieved in all patients independent of the applied treatment modality. Overall, 5-year PFS was 49% (median FU 81 months). 5-year PFS was 33%, 60%, and 67% after STX, transsphenoidal and transcranial resection, respectively (p=0.2). The 5-year crossover rate from STX to transcranial resection was 40% (median 106 months). The 5-year probability for external beam radiation was 5% (median 155 months) after initial treatment and not different among the applied treatment strategies. Endocrinological worsening/BMI increase) was most pronounced in patients undergoing external beam radiation (100%/8kg/m²), in-between after open tumor resection alone (63%/6kg/m²) and best in patients undergoing exclusively stereotactic treatments (22%/3kg/m²) (p=0.001). In multivariate analyses external beam radiation was associated with hypothalamic dysfunction (p=0.005).

Conclusion

STX represents a minimal invasive treatment option for cystic craniopharyngiomas and is associated with a favorable rate of functional deterioration. STX enlarges the therapeutic platform for predominantly cystic tumors. Personalized localized treatment options offer the chance to withhold radiation therapy in the vast majority of patients.

Gliome experimentell III/*Gliomas experimental III*

V217

Verstärkung der anti-neoplastischen Aktivität von photodynamischer Therapie mit 5-Aminolävulinsäure gegen Glioblastomzellen durch Hemmung von Bcl-2/Bcl-xL *in vitro*

Bcl-2/Bcl-xL inhibition enhances the anti-neoplastic activity of photodynamic therapy with 5-aminolevulinic acid against glioblastoma cells in vitro

C. Golla¹, J. Antonymuthu¹, A. Dwucet¹, M. Pruss¹, N. Bader², M. Hlavac¹, M. D. Siegelin³, M. A. Westhoff¹, T. Heiland¹, R. E. Kast⁴, C. R. Wirtz¹, F. Capanni², M. E. Halatsch¹, G. Karpel-Massler¹

¹Universitätsklinikum Ulm , Ulm, Germany

²Universität Ulm, Ulm, Germany

³Columbia University, New York, NY, United States

⁴IIAIGC Study Center, Burlington, VT, United States

Objective

In this study, we examined whether inhibition of the anti-apoptotic Bcl-2 family proteins Bcl-2 and Bcl-xL enhances the biological effects of photodynamic therapy with 5-aminolevulinic acid in an *in vitro* setting of glioblastoma.

Methods

Pre-clinical testing of microcontroller-based devices emitting light of 405 or 635 nm wavelengths in combination with exposure to 5-aminolevulinic acid and the Bcl-2/Bcl-xL inhibitor ABT-263 was performed in human established, primary cultured glioblastoma cells and glioma stem-like cells. We applied cell count analyses to assess cellular proliferation, annexin V/PI and TMRE staining to examine apoptosis, and Western blotting and specific knockdown experiments using siRNA to examine molecular mechanisms of action.

Results

Bcl-2/Bcl-xL inhibition had enhanced anti-proliferative effects in various types of glioblastoma cells when combined with photodynamic therapy. The combination treatment induced caspase-dependent apoptosis. On the molecular level, Bcl-2/Bcl-xL inhibition led to an upregulation of Mcl-1 which, however, was counteracted by an increased expression of NOXA when combined with photodynamic therapy.

Conclusion

These data suggest that Bcl-2/Bcl-xL inhibition enhances the susceptibility of glioblastoma cells towards photodynamic therapy. This observation is at least in part due to a cytotoxic effect of the combination treatment and likely linked to a shift of the cellular phenotype pro apoptosis in response to an increased NOXA/Mcl-1 ratio.

Gliome experimentell III/*Gliomas experimental III*

V218

Bestimmung des Abbruchkriteriums durch Analyse des Körpergewichtsverlaufs in einem Rattenmodell mit intrakraniellm Tumor

Body weight algorithm predicts humane endpoint in an intracranial rat glioma model

S. Helgers¹, S. R. Talbot², A. K. Riedesel¹, L. Wassermann², Z. Wu¹, J. K. Krauss¹, C. Häger², A. Bleich², K. Schwabe¹

¹Medizinische Hochschule Hannover, Abteilung für Neurochirurgie, Hannover, Germany

²Medizinische Hochschule Hannover, Institut für Versuchstierkunde und Zentrale Tieranlage, Hannover, Germany

Objective

Humane endpoint determination is fundamental in animal experimentation. Despite commonly accepted endpoint criteria for intracranial tumour models (20% body weight loss and deteriorated clinical score) some animals still die before being euthanized in current research. We here systematically evaluated other measures as surrogates for more reliable humane endpoint determination.

Methods

Adult male BDIX rats (n=119) with intracranial glioma formation after BT4Ca cell-injection were used. Clinical score and body weight were assessed daily. One subgroup (n=14) was assessed daily for species-specific (nesting, burrowing), motor (distance, coordination) and social behaviour. Another subgroup (n=8) was implanted with a telemetric device for monitoring heart rate (variability), temperature and activity. Body weight and clinical score of all other rats were used for training (n=34) and validation (n=63) of an elaborate body weight course analysis algorithm for endpoint detection.

Results

BT4Ca cell-injection reliably induced fast growing tumours. No behavioural or physiological parameter detected deteriorations of clinical state earlier or more reliable than clinical scoring by experienced observers. However, the body weight course analysis algorithm predicted endpoints in 97% of animals without confounding observer-dependent factors.

Conclusion

Clinical scoring together with the novel algorithm enables highly reliable and observer-independent endpoint determination in a rodent intracranial tumour model.

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Gliome experimentell III/*Gliomas experimental III*

V219

Der individuelle CpG-Methylierungsstatus im DMR-2 Abschnitt des MGMT-Promotors mithilfe der Sanger-Sequenzierung verbessert die prediktive Stratifizierung von Glioblastom-Patienten unter Chemotherapie mit Temozolomid

Individual CpG methylation status of the DMR-2 island of the MGMT promotor determined by Sanger sequencing improves predictive stratification of glioblastoma patients receiving temozolomide

S. Siller¹, M. Lauseker², J. Tonn¹, K. M. Niyazi³, S. Lietke¹, A. Giese⁴, S. Kreth⁵, F. W. Kreth¹

¹Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, Institut für Medizinische Informationsverarbeitung, Biometrie und Epidemiologie, München, Germany

³Klinikum der Ludwig-Maximilians-Universität München, Klinik für Radioonkologie, München, Germany

⁴Klinikum der Ludwig-Maximilians-Universität München, Zentrum für Neuropathologie und Prionforschung, München, Germany

⁵Klinikum der Ludwig-Maximilians-Universität München, Walter-Brendel-Zentrum für Experimentelle Medizin, München, Germany

Objective

Determination of *MGMT* promotor methylation usually relies on the evaluation of a limited number of CpG sites of the DMR-2 island. The predictive role of the remaining usually not analyzed CpG sites remains unknown. We here analyzed the individual methylation patterns of the DMR-2 island and their respective predictive impact in a large and homogeneously treated cohort of glioblastoma multiforme (GBM) patients undergoing radiotherapy plus concomitant and adjuvant temozolomide. The study protocol was approved by the institutional ethical board.

Methods

The individual methylation pattern of CpG-sites 74-98 was assessed by Sanger sequencing technique (SSeq) in 222 consecutive patients with histologically proven GBM assigned for radio-chemotherapy. In parallel, conventional methylation-specific PCR (MSP) was used for *MGMT* promoter methylation classification. Prognostic models were obtained from multivariate proportional hazards estimations.

Results

According to MSP, patients with methylated (MSP-positive) and unmethylated (MSP-negative) tumors experienced a median overall survival (OS) of 21.3mos and 12.5mos, respectively ($p < 0.001$). Individual methylation patterns as determined by SSeq were heterogeneous: Among MSP positive tumors, methylation level was highest in CpG sites 79-94 & 98 (median methylation rate: 82%), intermediate in CpG sites 74-78 (median methylation rate: 60%), and lowest in CpG sites 95-97 (median methylation rate: 33%) indicating a site-dependent methylation propagation. Correlation analyses additionally demonstrated a neighborhood-dependent methylation propagation: the methylation status of a given CpG site usually matched that of its neighborhood. Multivariate prognostic/predictive modelling indicates the cumulative number of methylated CpG sites to be linearly associated with OS ($p < 0.001$). Stratification of MSP-positive tumors indicates that median OS ranged from as low as 17.5 months (<18 methylated CpG sites) to as high as 27 months (≥ 18 methylated CpG sites).

Conclusion

Site- and neighborhood-dependent methylation propagation contribute to heterogeneous methylation patterns. Extensive analyses of CpG sites in the DMR-2 island improves predictive stratification of GBM patients, which can be used for more precise treatment concepts. SSeq overcomes limitations of conventional techniques such as MSP and can be implemented in daily clinical practice.

Gliome experimentell III/*Gliomas experimental III*

V220

Abstammungsverfolgung von gliom-assoziierten myeloiden Zellen mit multidimensionalen Techniken *Lineage tracking of glioma-associated myeloid cells by high-dimensional techniques*

N. Neidert, K. Joseph, V. M. Ravi, S. P. Behringer, J. P. Maier, J. Beck, O. Schnell, D. H. Heiland

Universitätsklinikum Freiburg, Klinik für Neurochirurgie, Freiburg, Germany

Objective

In malignant brain tumours, crosstalk and adaptation of brain resident and infiltrating myeloid cells form an immunosuppressive environment that causes dysfunctional activation of the T cells and leads to an inadequate immune response. Most recently, checkpoint inhibition (PD-1) failed to rescue the lost T cell response, highlighting that dysfunctional/exhausted T-cell activation in glioma is insufficiently understood. Here, we used single-cell RNA-sequencing analysis and cell-cell coactivation models to map cell fate decisions in T-cell activation.

Methods

The diversity of different myeloid cell-types was explored by multi-channel FACS analysis. Single-cell RNA-sequencing of 4 patients was performed by magnetic-bead enrichment of CD3 positive cells and removal of dead-cells by negative selection (MACS dead-cell removal) resulting in a stable vital cell population between 90-98%. The single-cell emulsion was formed by a microfluidic device and cells were barcoded by encapsulated gel beads containing unique molecular identifiers. After library construction and next-generation sequencing, we used a novel machine learning approach to model lineage development and cell fate decisions as well as cell-cell interactions.

Results

After quality control, 17.705 cells remained with an average of ~20.000 reads per cell. After batch removal and adaptation of stress-induced pathway activation we identified 15 clusters highly associated to T-cell lineages (CD4+/CD8+/ $\gamma\delta$ T, Treg), macrophages (CD163+), microglia (TMEM119+), monocytes (LYZ+), dendritic cells and glial lineages (OPC and oligodendrocytes). Integrative data analysis identified cell fate decisions based on IL10 induced transformation in effector T-cells causing the dysfunctional state in T cells. Prolonged proliferation of a subset of dysfunctional T-cells induced apoptosis at a later stage. Dysfunctional activation was traced back to a distinct subpopulation within the microglia and macrophage cluster marked by high expression of *SPP1*.

Conclusion

We identified a novel subpopulation of the tumour microenvironment which aids the evolution of dysfunctional T-cells by IL10 release. Targeting of the tumour microenvironment may provide promising therapy strategies in the future.

Gliome experimentell III/*Gliomas experimental III*

V221

Der Transfer mononukleärer Zellen aus CMV latenten Mäusen führt zu einer PDGF-Rezeptor beta vermittelten tumorspezifischen Infektion im murinen Glioblastommodell

Transfer of mononuclear cells from seropositive CMV latent mice leads to PDGFR-beta mediated tumoritropic infection in a mouse glioblastoma model

H. Krenzlin^{1,2}, N. Keric², E. A. Chiocca³, S. Lawler³, F. Ringel²

¹Brigham and Women's Hospital, Abteilung für Neurochirurgie, Boston, MA, United States

²Universitätsmedizin Mainz, Mainz, Germany

³Brigham and Women's Hospital, Department of Neurosurgery, Boston, MA, United States

Objective

Cytomegalovirus (CMV) has been linked to glioblastoma for over a decade. However, mechanisms how CMV tumour infection occurs, are poorly understood. CMV is carried within a small percentage of mononuclear myeloid and dendritic cell progenitors in the healthy seropositive host. Here we identify a possible infection pathway, involving mononuclear cells und the platelet derived growth factor receptor-beta (PDGFR-beta).

Methods

In vivo, mononuclear cells from blood and bone marrow of CMV latent mice were harvested and transferred to CMV naïve animals carrying orthotopic G1261fluc glioblastoma. Viral infection was analysed using immunofluorescence. *In vitro*, viral entry into glioblastoma stem cells was monitored using viral fluorescence labelling (GFP CMV). Receptor expression was analysed using Western blot and qPCR. Receptor knockdown was performed via siRNA.

Results

Bone marrow and peripheral blood mononuclear cells from CMV latent animals stained CMV positive using two different immunofluorescence antibodies. Transfer of these cells into seronegative CMV naïve mice carrying G1261 orthotopic tumors led to tumor infection and viral spreading within the glioblastoma. The known CMV entry receptor PDGFR-beta was found to be expressed in PN GSCs, while it is virtually absent in MES GSCs. Using GFP labelled CMV, proneural (PN) glioblastoma stem cells (GSCs) exhibited green fluorescence as indicator of viral entry at lower MOIs (MOI 0.1) and with higher fluorescence intensity, compared to mesenchymal (MES) GSCs (MOI 1). Inhibition of PDGFR-beta in PN GSCs using the small molecule inhibitor Imatinib lead to a 82±4.9% ($p < 0.05$) decreased expression of GFP, while siRNA knock-down of PDGFR-beta decreased GFP expression by 95.8±0.5% ($p < 0.05$).

Conclusion

Mononuclear cells are a potential site of latent CMV infection from where infection can spread to glioblastomas. One mechanism of viral entry into GSCs involves the PDGFR-beta receptor. Blocking or down regulation of PDGFR-beta leads to impaired viral entry and might thus represent a novel therapeutic target in glioblastoma therapy.

Gliome experimentell III/*Gliomas experimental III*

V222

Methylierungsbasierte Klassifizierung von Hirntumoren durch extrazelluläre Vesikel-DNA ***Methylation-based classification of brain tumours through extracellular vesicle DNA***

C. Maire¹, I. Stevic¹, D. H. Heiland^{1,2}, L. Dührsen¹, M. Westphal¹, U. Schüller³, K. Lamszus¹, F. L. Ricklefs⁴

¹Universitätsklinikum Hamburg-Eppendorf, Neurochirurgie, Hamburg, Germany

²Universitätsklinikum Freiburg, Neurochirurgie, Freiburg, Germany

³Universitätsklinikum Hamburg-Eppendorf, Neuropathologie, Hamburg, Germany

⁴Universitätsklinikum Freiburg, Freiburg, Germany

Objective

Genome-wide methylation profiling has recently been developed into a tool that allows subtype tumor classification in central nervous system (CNS) tumors. Extracellular vesicles (EVs) are released by CNS tumor cells and contain high molecular weight tumor DNA, rendering EVs a potential biomarker source to identify tumor subgroups, stratify patients and monitor therapy by liquid biopsy. We investigated whether the DNA in glioma-derived EVs reflects genome-wide tumor methylation profiles and allows tumor subtype classification.

Methods

DNA was isolated from EVs secreted by cultured glioma stem-like cells (GSC) as well as from the cells of origin and from the original tumor samples (n=6 patients). EVs were classified by nanoparticle analysis (NTA), immunoblotting, imaging flow cytometry (IFCM), multiplex EV assays and electron microscopy. Genome-wide DNA methylation profiling was performed using an 850k Illumina EPIC array and results were classified according to the DKFZ brain tumor classifier. EV DNA was furthermore isolated from brain tumor patients (n=3) and healthy donors (n=3)

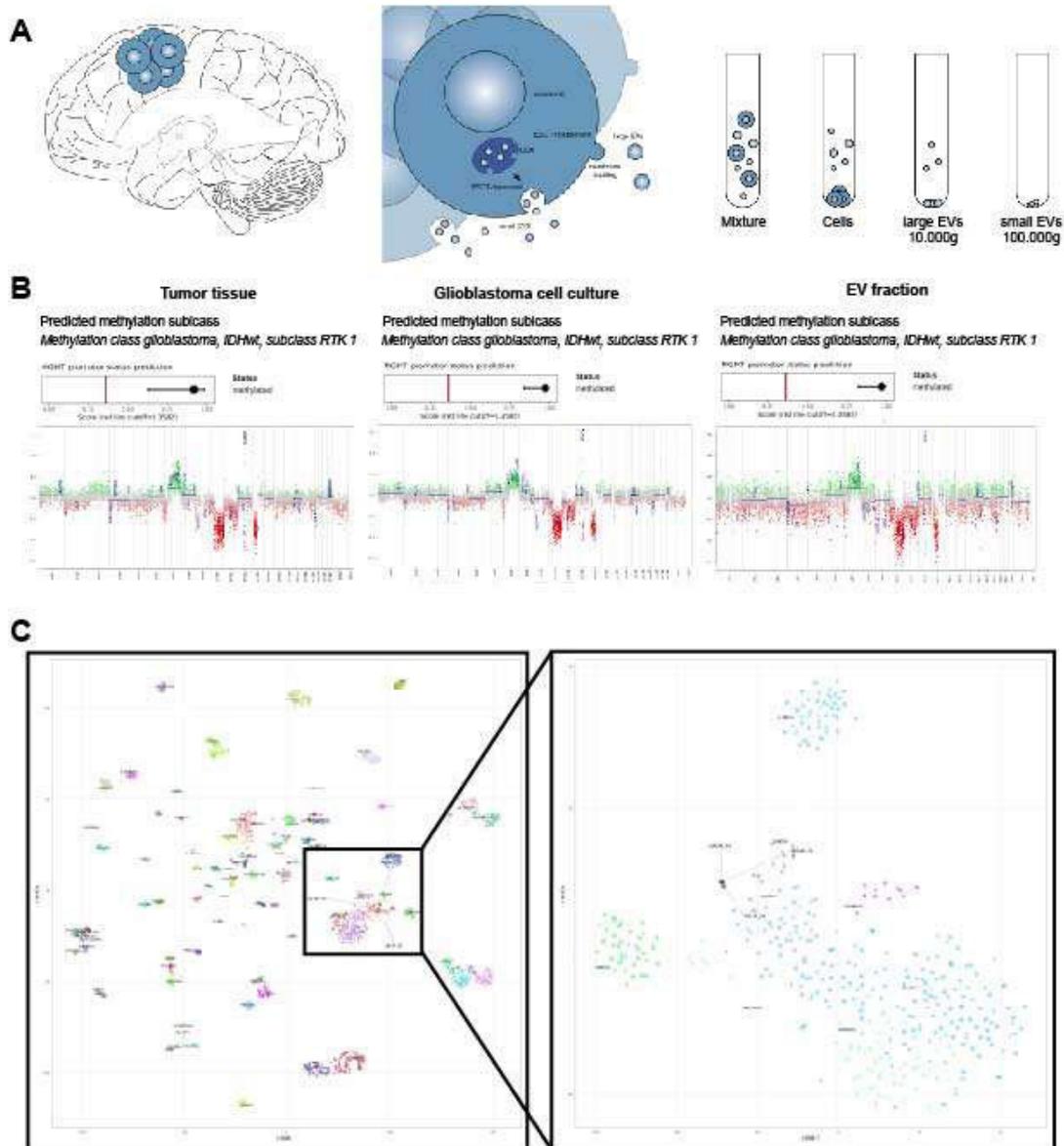
Results

The size range of GSC-derived EVs was 120-150 nm. The majority of secreted EVs exhibited high expression of common EV markers. Genome-wide methylation profiling of GSC-derived EVs correctly identified the methylation class of the original tumor, including information on the IDH mutation status and subclass classification (RTK1, RTK2). In addition, copy number alterations and the MGMT methylation status matched the pattern of the parental GSCs and original tumor samples. PCA analysis of methylation status of circulating EV DNA showed close relationship to the original tumor profile.

Conclusion

EV DNA faithfully reflects the tumor methylation class as well as the MGMT methylation status and copy number variations present in the parental cells and the original tumor. Methylation profiling of circulating tumor EV DNA could become a useful tool to detect and classify CNS tumors

Fig 1



Meningeome klinisch/*Meningiomas clinical*

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Erweiterung des radiomisch-semantischen Modells zur Wahrscheinlichkeitsvorhersage eines Rezidivs durch histopathologische Faktoren in WHO-Grad II Meningeomen

Augmentation of radiomic-semantic model of relapse prediction with histopathological features in WHO grade II meningioma

E. Kurz¹, D. Kalasauskas¹, A. Kronfeld², M. A. Brockmann², F. Ringel¹, N. Keric¹

¹Universitätsmedizin Mainz, Neurochirurgie, Mainz, Germany

²Universitätsmedizin Mainz, Neuroradiologie, Mainz, Germany

Objective

Atypical meningiomas (WHO grade II) comprise a relatively heterogeneous tumor entity. New molecular markers, associated with tumor aggressiveness have been recently introduced, whereas radiological criteria remain less defined.

Recently, we found that integration of radiomic and semantic features might be a promising tool to identify high-risk atypical meningiomas. In this study, we sought to evaluate the potential value of available histopathological data for the performance of this predictor model.

Methods

Primary atypical meningiomas with preoperative MRIs operated from 2003 to 2017 in our department were included in the study (n=76). Homogeneous radiomic data for contrast-enhanced T1 sequences was available for 52 patients. 25 radiomic, 11 histopathologic and 11 semantic features, potentially associated with tumor aggressiveness and clinical data including progression-free survival were used. Multiple imputation for the missing values was performed. We used univariate and multivariate regression for the outcome analysis and AUC for feature prediction.

Results

Mean age was 58,7 (SD 13,8) years, there were 59,2% women, the majority of tumors were localized on the convexity and falx, 13,2% could be resected completely (Simpson grade 1 or 2). Tumor relapse occurred in 22,4% of cases.

We found a predictive potential for Ki67 index (AUC 0,723, p=0,02 (difference entropy)) and brain invasion (AUC 0,706, p=0,004 (minimum)) using certain semantic characteristics. No association was detected between semantic and histological features. There were no tumor relapses occurring in cases with 5 or fewer mitoses per field. However, short follow up time must be taken into account. High cluster prominence was associated with tumor relapse (HR 5,9 (1,03-33,73)). High cellularity (HR 3,6 (95% CI 1,01-12,84)) and Cystic component (HR 9,77, 95%CI 3,14-30,41) were associated with shorter PFS. However, adding these histological criteria to the predictory model did not increase the classification power (AUC 0,853 vs. 0,855).

Conclusion

In this study, certain histological characteristics were associated with preoperative radiomic features. These additional information might be valuable for surgical strategy. Due to high classification power of integrated radiomic and semantic model, the histological criteria added little value.

Meningeome klinisch/*Meningiomas clinical*

V224

Hirninfiltration ist ein unabhängiger Risikofaktor für eine präoperative Epilepsie bei Patienten mit Meningeomen WHO Grad I und II

Brain invasion is an independent risk factor for preoperative seizures in meningioma WHO grade I and II patients

A. Biczok¹, J. Thorsteinsdottir¹, R. Egensperger², B. Suchorska¹, N. A. Terpolilli¹, J. Tonn³, C. Schichor³

¹Ludwig-Maximilians-Universität München, Neurochirurgie, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, Neuropathologie, München, Germany

³Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgie, München, Germany

Objective

Preoperative seizures are a common symptom in meningioma patients. Known risk factors include radiological features, localization but also WHO grading. Recently, brain invasion was added as an independent criterion for WHO II meningioma and its clinical importance was questioned in subsequent studies. Aim of our study was to evaluate whether brain invasion is an additional prognostic factor for seizures, independent from other histological grading parameters. The authors aim to investigate risk factors for preoperative seizure occurrence in patients with meningioma WHO grade I and II.

Methods

We retrospectively assessed meningioma patients receiving surgical resection between 2008 and 2017 at our institution for the association between preoperative seizures and sex, age, tumor location, WHO grade with special focus on histopathological features like mitotic count or brain invasion. WHO grade III meningiomas were excluded for a clearer stratification of the study population. All samples were reclassified according to the 2017 WHO criteria. Reference point of the study was the date of surgery. Date of last follow up was 05/2019. Multivariate regression was used to identify variables significantly associated with preoperative seizures.

Results

Overall, 997 patients were eligible for multivariate logistic regression analyses of preoperative seizures. Reclassified for the new WHO grading, 918 patients harbored a Meningioma WHO I, 79 meningioma WHO grade II. 37 patients showed histological signs of brain invasion. Preoperative epilepsy was found in 93 (9.33%) patients, seven patients with histologically proven brain invasion presented with epilepsy, 30 patients did not show any signs of preoperative seizures. In univariate analysis, preoperative epilepsy was independent from patient age and sex. In multivariate regression analysis, the risk of seizures was significantly higher in patients with brain invasion ($p=0.04$, $HR=2.369$, $CI=1.01-5.553$). In contrast, elevated mitotic count was not associated with higher risk of preoperative epilepsy.

Conclusion

In a large cohort of meningioma patients, brain invasion was identified as an independent risk factor for preoperative seizures, regardless of any other signs of atypia. Therefore, in patients presenting with preoperative seizures special focus should be put on the brain/meningioma interface from a surgical as well as from a histopathological point of view.

Meningeome klinisch/*Meningiomas clinical*

V225

Meningeome bei ≥ 75 Jahre alten Patienten – klinischer Verlauf und Validierung des SKALE-Scores *Meningiomas in patients ≥ 75 years of age – clinical outcome and validation of the SKALE score*

D. Monden¹, F. Raimann², P. N. Harter³, F. Keil⁴, T. Freiman⁵, V. Seifert¹, C. Senft¹, P. Baumgarten¹

¹Universitätsklinikum Frankfurt am Main, Klinik und Poliklinik für Neurochirurgie, Frankfurt am Main, Germany

²Johann Wolfgang Goethe-Universität Frankfurt am Main, Klinik für Anästhesiologie, Frankfurt am Main, Germany

³Johann Wolfgang Goethe-Universität Frankfurt am Main, Edinger Institut, Neuropathologie, Frankfurt am Main, Germany

⁴Universitätsklinikum Frankfurt am Main, Neuroradiologie, Frankfurt am Main, Germany

⁵Universitätsklinikum Frankfurt am Main, Klinik und Poliklinik für Neurochirurgie, Frankfurt am Main, Germany

Objective

Average life expectancy has increased and with it the number of very elderly meningioma patients.

Patients at age of ≥ 75 years show increased morbidity and mortality when undergoing intracranial surgery. Our aim was to evaluate whether very elderly meningioma patients benefit from surgery and to validate the SKALE score, which was designed for decision-making for these patients.

Methods

A total of 570 patients underwent meningioma resection between 2009 and 2016. Data of recurrent tumors reaching back to 1979 for primary resection were included as well. At primary resection, 46 patients were ≥ 75 years of age. We compared WHO grade, Karnofsky Performance Scale (KPS) change, intensive care unit (ICU) stay, Simpson score, progression free survival (PFS) and overall survival (OAS). Preoperative SKALE score (Sex, KPS, ASA, location and edema) was determined for elderly patients. SKALE ≥ 8 was set for dichotomization according to the first description.

Results

In 43 very elderly patients (male/female 21/22) all data were available. At first resection WHO grade $\geq II$ was found more frequently in elderly patients (57% vs 43%). Intended ICU stay of 1 day was only achieved in half of the patients, median stay was 2 days (range 1-46 days). Perioperative deterioration of KPS was more common in elderly patients ($p=0.0008$). Mean OAS was shorter in patients ≥ 75 years (75 vs. 269 months, $p<0.0001$). Analyses of the Kaplan Meier curves revealed differences in 1-year (0.88% vs. 25%) and 5-year mortality (4% vs. 50%) for very elderly patients. Multivariate analysis showed a significant survival benefit for patients with SKALE score ≥ 8 ($p=0.0166$) and for low Simpson grade ($p=0.0342$).

Conclusion

Very elderly meningioma patients face higher postoperative morbidity but have an increased risk for having higher WHO grade tumors. According to our data, even aggressive resection is reasonable. The SKALE score is a useful instrument regarding surgical indication.

Meningeome klinisch/*Meningiomas clinical*

V226

Das Rezidivrisiko von intrakraniellen Meningeomen – vergleichende Analyse zur Vorhersagekraft des postoperativen Tumolvolumens und der Klassifikation nach Simpson

Risk of tumour recurrence in intracranial meningiomas – comparative analyses of the predictive value of the postoperative tumour volume and the Simpson classification

D. C. Spille¹, K. Heß², E. Bormann³, C. Sauerland³, C. Brokinkel⁴, N. Warneke¹, W. Paulus², W. Stummer¹, B. Brokinkel¹

¹Universitätsklinikum Münster, Institut für Neurochirurgie, Münster, Germany

²Universitätsklinikum Münster, Neuropathologie, Münster, Germany

³Universitätsklinikum Münster, Biometrie, Münster, Germany

⁴Universitätsklinikum Münster, Radiologie, Münster, Germany

Objective

The Simpson grading has been widely established to quantify the extent of resection in meningiomas and to estimate the risk of postoperative tumor recurrence. However, grading is performed by the attending neurosurgeon and might suffer from bias and/or limited intraoperative view at the operative field. On the other hand, correlations between the postoperative tumor volume and the risk of recurrence are sparsely investigated and the value of postoperative imaging in meningiomas remains uncertain. We therefore compared the value of intraoperative assessment of the extent of resection with the tumor volume for the prediction of recurrence in a large series of meningiomas.

Methods

Tumor volume on initial postoperative MRI and the extent of resection according to the Simpson classification were determined for 939 patients with primary diagnosed intracranial WHO grade I-III meningioma (671 females, 268 males, median age of 58 years). Predictive values for recurrence were compared in uni- and multivariate analyses and the critical cut-off value of the tumor volume were determined in a tree-structured regression model.

Results

With a median follow up of 40 months, recurrence was observed in 12% of all 939 patients. The postoperative tumor volume was available in 423 patients and ranged between volumes of 0 ccm and 78.5 ccm. After designated gross total resections (Simpson grades I-III), residual tumor tissue could be detected in eight percent of the patients (range: 0.12 ccm – 33.5 ccm). In univariate analysis, both the Simpson grading ($p=0.004$) as well as the postoperative tumor volume (HR: 1.04, 95%CI 1.02-1.06, $p<.001$) strongly correlated with recurrence. Multivariate analysis adjusted for age, sex, tumor location, WHO grade, volume of tumor remnants and the extent of resection revealed high grade histology (HR: 3.95, 95%CI 2.00-7.77; $p<.001$) and postoperative tumor volume (HR: 1.05, 95%CI 1.02-1.08; $p=0.0001$), but not Simpson grade ($p=0.5859$) as predictive factors for recurrence. Regression Tree model revealed a postoperative tumor volume of >0.00 ccm as the significant threshold for predicting recurrence.

Conclusion

Postoperative MRI reveals residual tumor tissue in a considerable portion of meningioma surgeries.

Postoperative tumor volume is superior in predicting tumor recurrence compared to the Simpson classification. Risk of recurrence increases with any residual tumor tissue.

Meningeome klinisch/*Meningiomas clinical*

V227

Nutzen des präoperativen Routine-MRT zur Abschätzung des Risikos für Grad II/III Histologie und Rezidiventwicklung bei Patienten mit intrakraniellen Meningeomen

Predicting the risk of postoperative recurrence in patients with intracranial meningiomas using routine preoperative MRI

D. C. Spille¹, A. Adeli², P. B. Sporns², K. Heß³, E. M. S. Streckert¹, C. Brokinkel², W. Paulus³, W. Stummer¹, B. Brokinkel¹

¹Universitätsklinikum Münster, Klinik und Poliklinik für Neurochirurgie, Münster, Germany

²Universitätsklinikum Münster, Institut für Klinische Radiologie, Münster, Germany

³Universitätsklinikum Münster, Institut für Neuropathologie, Münster, Germany

Objective

Estimating the risk of recurrence is crucial during postoperative care of meningioma patients. However, risk factors for tumor recurrence or high-grade (grade II/III) histology available from routine preoperative imaging remain elusive.

Methods

Characteristics on preoperative magnetic resonance imaging (MRI) were chosen according to results of a recently published systematic review and included tumor and edema volumes, heterogeneity of the contrast-enhancement, enhancement of the tumor capsule, tumor location and intensity on T2-weighted images, disruption of the arachnoid layer, tumor shape and intratumoral calcifications, and were analyzed in 565 patients (406 females, 72%; 159 males, 28%; median age 59 years) with primary diagnosed intracranial meningioma. Correlations with tumor recurrence and high-grade histology were investigated in uni- and multivariate analyses.

Results

In univariate analyses, peritumoral edema volume (OR: 1.00, 95%CI 1.00-1.01; p=.003), heterogeneous contrast-enhancement (OR: 3.10, 95%CI 1.67-5.78; p<.001) and an irregular tumor shape (OR: 2.16, 95%CI 1.16-4.00; p=.015) were associated with high-grade histology. In contrast, the risk of high-grade histology tended to be lower in tumors not arising from the convexity (OR: .55, 95%CI .29-1.04; p=.066). Multivariate analyses confirmed peritumoral edema volume (OR: 1.00, 95%CI 1.00-1.01; p=.037) and heterogeneous contrast enhancement (OR: 2.51, 95%CI 1.20-5.25; p=.014) as independent predictors for WHO grade II/III histology. On the other hand, tumor volume (HR: 1.01, 95%CI 1.00-1.01; p=.045; AUC=.061), disruption of the arachnoid layer (HR: 2.50, 95%CI 1.36-4.61; p=.003), heterogeneous contrast enhancement (HR: 2.05, 95%CI 1.22-3.46; p=.007) and an irregular, mushroom-like tumor shape (HR: 2.57, 95%CI 1.51-4.37; p=.001) were positively correlated with recurrence. Multivariate analyses adjusted for age, sex, WHO grade and the analyzed radiological variables confirmed tumor volume (OR: 1.01, 95%CI 1.00-1.02; p=.032) and disruption of the arachnoid layer (HR: 2.44, 95%CI 1.21-4.92; p=.013) as independent radiological predictors for recurrence.

Conclusion

Routine preoperative MRI contains important information improving the estimation of prognosis in meningioma patients. Remarkably, risk factors for high-grade histology and recurrence were not necessarily congruent, raising the question of other underlying histopathological or molecular alterations.

Meningeome klinisch/*Meningiomas clinical*

V228

Tumorrezidiv und funktionelles Outcome nach chirurgischer Therapie spinaler Meningeome – institutionelle Erfahrung mit 123 Fällen

Tumour recurrence and functional outcome following spinal meningioma surgery – institutional experience with 123 cases

J. Wach, M. Banat, P. Schuss, E. Güresir, H. Vatter, J. E. Scorzin

Universitätsklinikum Bonn, Neurochirurgie, Bonn, Germany

Objective

Spinal meningiomas (SM) account for 2% of all meningiomas. Clinicoradiological and immunohistochemical factors were analysed with regard to the prediction of tumour recurrence and functional outcome.

Methods

Medical records of 123 patients who underwent surgery for SM between 2000 and 2019 were retrospectively reviewed with regard to demographic parameters, imaging features, surgical workflow, immunohistochemical items, neurological outcome and recurrence. Dural attachment, T2 hyperintensity of spinal cord, dural tail sign, tumour size, Simpson Grade, spinal level, medical history and histopathology were analysed to predict tumour recurrence and functional outcome. Neurological function was graded according to the Modified McCormick Scale (MMS) and dichotomized into to "good (I+II)" and "poor (III-V)" function.

Results

114 (92.7%) WHO grade I and 9 (7.3%) WHO grade II SMs were included in this study. Univariate analysis identified baseline T2 hyperintensity of the spinal cord, prolonged duration of baseline symptoms (≥ 4 weeks), age ≥ 66 years and dural tail sign as predictors of poor MMSs.

Baseline T2 hyperintensity of the spinal cord (OR=13.3, 95% CI=3.4-52.4, $p < 0.001$) and age ≥ 66 years (OR=10.3, 95% CI=2.6-41.1, $p = 0.001$) were the only independent predictors of poor MMSs at discharge in the binary logistic regression analysis.

Median (range) follow-up (including MRI surveillance) was 12.0 (3.0-120.0) months in 80 cases. 2 (1.6%) recurrences were observed. Kaplan-Meier analysis (log-rank test) showed that WHO grade II, cervical location, ventral tumour attachment, male sex, Diabetes, Simpson Grade (III&IV), and MIB-1 index $\geq 5\%$ were significant associated with an increased risk of recurrence.

Cox regression analysis revealed the MIB-1 labeling index $\geq 5\%$ as an independent risk factor for recurrence (HR: 1.77, 95% CI: 1.01-3.11, $p = 0.047$).

Conclusion

Baseline T2 hyperintensity, especially in the elderly patients should be reminded as far as functional outcome following surgical resection of spinal meningiomas is concerned. A policy of maximal safe resection of SMs prolongs recurrence-free survival in spinal meningiomas having high proliferative activity.

Zerebrovaskuläre Erkrankungen II/*Cerebrovascular diseases II*

V229

Das endogene Neuropeptid *Calcitonin gene-related peptide* nach spontaner Subarachnoidalblutung – ein psychoaktiver prognostischer Biomarker im Serum für Schmerz

The endogenous neuropeptide calcitonin gene-related peptide after spontaneous subarachnoid haemorrhage – a psychoactive prognostic serum biomarker for pain

E. Bründl¹, M. Proescholdt¹, E. M. Störr¹, P. Schödel¹, S. Bele¹, J. Höhne¹, F. Zeman², A. Brawanski¹, N. O. Schmidt¹, K. M. Schebesch¹

¹Universitätsklinikum Regensburg, Klinik und Poliklinik für Neurochirurgie, Regensburg, Germany

²Universitätsklinikum Regensburg, Zentrum für Klinische Studien, Regensburg, Germany

Objective

The pronociceptive neuromediator calcitonin gene-related peptide (CGRP) is associated with pain transmission and modulation. After spontaneous subarachnoid hemorrhage (sSAH), the vasodilatory CGRP is excessively released into cerebrospinal fluid (CSF) and serum and modulates psycho-behavioral function. In CSF, the hypersecretion of CGRP subacutely after good-grade sSAH was significantly correlated with an impaired health-related quality of life (hrQoL). Now, we prospectively analyzed the treatment-specific differences in the secretion of endogenous CGRP into plasma after good-grade sSAH and its impact on hrQoL.

Methods

26 consecutive patients (f:m=13:8; mean age 50.6 years) with good-grade sSAH were enrolled (drop out n=5): n=9 underwent endovascular aneurysm occlusion, n=6 microsurgery, and n=6 patients with perimesencephalic SAH received standardized intensive medical care. No patient developed any serious vasospasm-related ischemic or hemorrhagic complications. Plasma was drawn daily from day 1-10, at 3 weeks, and at the 6-month follow-up (FU). CGRP levels were determined with competitive enzyme immunoassay in duplicate serum samples. All patients underwent neuropsychological self-report assessment [36-Item Short Form Health Survey (SF-36) and ICD-10-Symptom-Rating questionnaire (ISR)] after the onset of sSAH (t_1 : day 11-35) and at the FU (t_2).

Results

During the first 10 days, the mean CGRP levels in serum ($.470 \pm .10$ ng/ml) were significantly lower than the previously analyzed mean CGRP values in CSF ($.662 \pm .173$; $p=.0001$). The mean serum CGRP levels within the first 10 days did not differ significantly from the values at 3 weeks ($p=.145$). At 6 months, the mean serum CGRP value ($.429 \pm .119$ ng/ml) was significantly lower compared to 3 weeks ($p=.0001$) and compared to the first 10 days ($p=.026$). Higher mean serum CGRP levels at 3 weeks ($p=.0001$) and at 6 months ($p=.0242$) correlated with a significantly poorer performance in the SF-36 item pain, and, at 3 weeks, with a higher ISR symptom burden regarding somatoform syndrome ($p=.0310$) at t_2 .

Conclusion

Our study reveals the first insight into the serum levels of endogenous CGRP in good-grade sSAH patients with regard to hrQoL. In plasma, upregulated CGRP levels at 3 weeks and 6 months seem to be associated with a poorer mid-term hrQoL in terms of pain. In migraineurs, CGRP receptor antagonists have proven clinical efficacy. Our findings corroborate the potential capacity of CGRP in pain processing.

Zerebrovaskuläre Erkrankungen II/*Cerebrovascular diseases II*

V230

Klinisches Outcome von Patienten mit früher im Vergleich zu später Implantation von ventrikuloperitonealen Shunts bei spontanen subarachnoidalen Blutungen

Clinical outcome in patients with early versus late ventriculoperitoneal shunting in spontaneous subarachnoid haemorrhage

J. F. Wojak, C. Ditz, J. Gliemroth, V. M. Tronnier, J. Küchler

Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Lübeck, Germany

Objective

Spontaneous aneurysmal subarachnoid hemorrhage (sSAH) is known to cause hydrocephalus in a subset of patients. Several studies discussed predictors for ventriculoperitoneal (VP)-shunting but only few is known about the ideal timing of definite implantation in cases of uncertain temporary closure trials of external drainage. Early VP-shunting might risk unnecessary surgery while late VP-shunting leads to an interruption of neurorehabilitation which might cause worse clinical outcome. Our study focused on the outcome of patients with early (within their first hospital admission) or late (after discharge for rehabilitation) VP-shunting and the occurrence of complications.

Methods

A retrospective 6-year study was conducted, reviewing 62 patients who underwent VP-shunting after good- or poor- (WFNS 1-3 or 4-5) grade sSAH. Based on the initial timing of VP-shunting, patients were subdivided into an early (before) or late (after discharge) VP-shunting group for further comparison. We collected clinical, demographic and follow-up data. All patients who did not fail temporary closure of external ventricular (EVD) or lumbar drainage (LD) were included for further observation of delayed shunting and elicitation of their mRS-Score after 3 and 6 months.

Results

43 female and 17 male patients met our inclusion criteria for further data analyses. We observed 43.5% good- (WFNS 1-3) and 53.2% poor-grade (WFNS 4-5) sSAH. 8 of 60 (13.3%) patients showed no initial hydrocephalus at admission. No significant differences were found in mRS after 3 or 6 months within both groups (p always >0.05). Revision surgery rate was tendentially higher with 11 (33%) patients before discharge compared to patients with later VP-shunting (15%) ($p= 0.09$). Regarding delayed complications, VP-shunting before discharge showed significantly more complications ($p<0.05$).

Conclusion

Regarding timing and clinical outcome of sSAH patients with hydrocephalus, there seems to be a wider time frame for definite VP-shunting without causing neurological aggravation than expected. Thus, giving patients the chance to start rehabilitation as soon as possible. Also, concerning delayed complications such as infections or shunt-dysfunction, we provide proof that implantation of a VP-shunt after discharge, in patients who initially did not fail temporary closure of external drainage, causes less complication rates. Further prospective studies with greater numbers should be accomplished to investigate this proposal.

Zerebrovaskuläre Erkrankungen II/*Cerebrovascular diseases II*

V231

Programmierbare Ventile bei chronischem Hydrocephalus nach Subarachnoidalblutungen – Ist es sinnvoll? *Programmable valves for chronic hydrocephalus following subarachnoid haemorrhage – Is it worthwhile?*

M. Darkwah Oppong, L. Droste, D. Pierscianek, K. H. Wrede, L. Rauschenbach, P. Dammann, A. Hertzen, U. Sure, R. Jabbarli

Universitätsklinikum Essen, Klinik für Neurochirurgie und Wirbelsäulen Chirurgie, Essen, Germany

Objective

Chronic hydrocephalus is a common complication following aneurysmal subarachnoid hemorrhage (aSAH) and is routinely treated with implantation of a ventriculoperitoneal shunt (VPS). Compared to fixed-pressure valves (FPV), adjustable-pressure valves (APV) might reduce the rates of over/underdrainage necessitating revision surgery. However, due to higher implant costs and vulnerability, the clinical utility of APV in neurosurgery is still the matter of debate. The aim of this study was to analyze the pros and cons of APV use in patients with aSAH.

Methods

From a large single center retrospective aSAH database containing over 900 patients treated between 2003 and 2016, all cases undergoing VPS placement for chronic hydrocephalus were eligible for this study. Multiple clinical and radiographic factors were tested for their influence on the need for revision surgery in case of shunt valve dysfunction or over/under drainage. Independent predictors were tested using multivariate analysis. Clinical outcome was analyzed at six months follow-up with mRS >3 defined as poor outcome.

Results

A total of 189 patients were included to the final analysis. FPV were implanted in the majority of patients (173/91.5%). Revision surgery due to over/underdrainage had to be performed in 8 (4,6%) cases with FPV and in no case with APV. Higher patients' age (>65 years, $p=0.011$; OR 10.36) and bone flap replacement following decompressive craniectomy ($p=0.044$; OR 6.53) independently predicted the need for revision surgery for over/under drainage. There was no difference in the occurrence of valve dysfunction between the two valve types (1 [6,3%] APV, 12 [6.9%] FPV), $p>0.99$. Patients requiring revision surgery for over/under drainage had a higher risk for poor outcome at six months follow-up ($p=0.009$).

Conclusion

In patients with aSAH and VPS placement, use of APV might reduce the need for revision surgery for over/under drainage, which is also associated with the functional outcome of SAH. Therefore, APV is a valuable option for aSAH individuals undergoing VPS implantation, particularly for elderly patients and those requiring decompressive craniectomy.

Zerebrovaskuläre Erkrankungen II/*Cerebrovascular diseases II*

V234

Einfluss von Komplikationen und Komorbiditäten auf die Länge des Aufenthaltes auf der Intensivstation nach aneurysmaler SAB

Impact of complications and comorbidities on the duration of intensive care after aneurysmal subarachnoid haemorrhage

A. Hammer¹, M. Hohenhaus², G. Ranaie¹, F. Erbguth³, H. H. Steiner¹, H. Janssen⁴

¹Paracelsus Medizinische Privatuniversität, Neurochirurgische Universitätsklinik, Nürnberg, Germany

²Paracelsus Medizinische Privatuniversität, Anästhesiologische Universitätsklinik, Nürnberg, Germany

³Paracelsus Medizinische Privatuniversität, Neurologische Universitätsklinik, Nürnberg, Germany

⁴Klinikum Ingolstadt, Institut für Neuroradiologie, Ingolstadt, Germany

Objective

In this study, we analysed a cohort of 164 cases of subarachnoid haemorrhage with the aim of detecting factors that influence the length of stay (LOS) in intensive care.

Methods

We analyzed the impact of complications and comorbidities on the length of stay (LOS) in intensive care with multiple linear regression methods. Moreover, binary logistic regression methods were used to examine whether the duration of intensive care is a predictor of outcome after 1 year. Patients who died during their stay in intensive care were excluded.

Results

Complications such as pneumonia ($p = 0.0031$), sepsis ($p = 0.0031$), hydrocephalus ($p = 0.0014$) and delayed cerebral ischemia (DCI) ($p = 0.038$) were critical factors affecting the LOS in intensive care as well as decompressive craniectomy ($p = 0.0077$). All analysed comorbidities such as hypertension, diabetes, hypothyroid, cholesterinemia, and smoking history had no significant impact on the LOS in intensive care. LOS in intensive care (OR = 1.09; $p = 0.0023$) as well as WFNS grade (OR = 3.72; $p < 0.0001$) and age (OR = 1.06; $p = 0.0061$) were significant factors that had an impact on the outcome after 1 year.

Conclusion

Complications during intensive care but not comorbidities are critical predictors of LOS in intensive care in our cohort. LOS in intensive care is a significant predictor of outcomes after subarachnoid haemorrhage.

Neurovaskuläre Chirurgie II/*Neurovascular surgery II*

V235

Die Anwendung der intraoperativen CT-Angiographie während des elektiven Aneurysmaclippings führt zu einer verbesserten Verschlussrate in der Aneurysmaversorgung

The use of intraoperative CT angiography during elective clipping of cerebral aneurysms improves complete aneurysm obliteration rates

J. Schwarting^{1,2}, R. Forbrig³, S. Siller³, J. Tonn¹, F. Dorn³, C. Schichor¹, J. Thorsteinsdottir¹

¹Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik und Poliklinik, München, Germany

²Ludwig-Maximilians-Universität München, Institut für Schlaganfall- und Demenzforschung, München, Germany

³Klinikum der Ludwig-Maximilians-Universität München, Abteilung für Neuroradiologie, München, Germany

Objective

Complete aneurysm occlusion is mandatory to prevent recurrent aneurysm formation. Up to now, the goldstandard still is postoperative angiography (pDSA) to confirm complete aneurysm occlusion and to rule out perioperative complications such as vasospasm or clip stenosis. As recent technical progress enables to perform intraoperative CT angiography (iCTA) in the clinical routine, we analyzed whether this method can improve obliteration rates by early detection of aneurysm remnants.

Methods

All patients treated with primary aneurysm clipping between 11/2012 and 10/2019 at our center receiving pDSA were retrospectively analyzed. Surgery was performed by 6 specialized vascular neurosurgeons. iCTA was routinely performed since 10/2016. Clinical outcome was assessed postoperatively, at discharge and at follow-up (last in 11/2019). iCTA and pDSA were analyzed by experienced neuroradiologists.

Results

A total of 293 patients were treated for aneurysm clipping within the mentioned time period. 45 patients without pDSA due to contraindications for pDSA (n=32), compliance (n=6), follow-up reasons (n=7) were excluded. Of the included 248 patients, 70 received iCTA and 178 did not. The two cohorts did not significantly differ in terms of age (54.6 vs. 57.3), sex (f/m: 56/14 vs. 121/57), and aneurysm size (6.8 vs. 6.9mm). The frequencies of surgeons were similar in both groups (p=0.12). Aneurysm location was equally distributed on MCA (57.1 vs. 57.9%) > ACOM (14.3 vs. 20.2%) > ACI (14.3 vs. 10.7%) > others (p=0.62). PDSA was described abnormal in 60 patients, judged as relevant in 22 cases, required revision in 3 cases, and judged as best achievable result for further observation in 35 cases. Patients who underwent elective clipping under iCTA guidance showed an abnormality on pDSA in 12.9% compared to 28.7% without iCTA guidance (p<0.009). In particular, an aneurysm remnant was described in 10.0 vs. 19.1% (p=0.08) of cases, resulting in surgical revisions in 1.4 vs. 1.1% (p=0.84). Clip stenosis was detected in 1.4 vs. 8.5% (p= 0.04) and vasospasm in 1.4 vs. 3.4% (p= 0.41). Clinical outcome did not significantly vary between groups: 95.7 vs. 93.3% (p=0.47) of patients had no permanent neurological deficit and average GOS at last follow-up was 4.9 vs. 4.9 (p=0.89).

Conclusion

The use of iCTA significantly improves complete obliteration rates in surgical aneurysm clipping.

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Geht die Behandlung von additionalen Aneurysmen nach vorangegangener Subarachnoidalblutung mit erhöhten Komplikations- und Morbiditätsraten einher?

Elective treatment of additional and recurrent aneurysms after previous subarachnoid haemorrhage – Are these patients at risk for complications and morbidity?

L. Goertz, G. Brinker, C. A. Hamisch, M. Hof, R. H. Goldbrunner, B. Krischek

Universitätsklinikum Köln, Köln, Germany

Objective

Microsurgical clipping and endovascular coiling are safe and efficient treatment options for both ruptured and unruptured intracranial aneurysms. We hypothesized that complication and morbidity rates would be increased in patients with a previous subarachnoid haemorrhage (SAH) that were treated for a recurrent or an additional, initially unruptured aneurysm on an elective basis.

Methods

This is a retrospective, single-center analysis of consecutive patients that underwent elective treatment for intracranial aneurysms by microsurgical clipping or endovascular therapy between 2010 and 2018. We analysed complications rates and functional outcome (modified Rankin scale, mRS) in patients with a previous SAH and compared the results to patients without history of SAH.

Results

A total of 301 patients were enrolled, 236 in the non-SAH group and 65 in the SAH group. Patients in the SAH group were younger (54.2 ± 12.0 vs. 50.8 ± 12.2 years, $p = 0.04$) and had a worse pre-procedural mRS score ($mRS \leq 1$: 79% vs. 93%, $p=0.01$) than patients in the non-SAH group. Procedure-related complications occurred in 15.4% among patients with previous SAH and in 12.7% among patients without SAH, which was not statistically significant ($p=0.6$). At the 6-month follow up, neurological worsening (defined as any increase on the mRS scale) was comparable between the SAH group (7.7%) and the non-SAH group (6.8%, $p=0.8$). A similar portion of patients achieved favourable outcome (mRS score > 2) in the SAH group (95.4%) and in the non-SAH group (98.3%, $p=0.17$). Moreover, among patients with a previous SAH, the choice of microsurgical clipping or endovascular treatment did not have a significant impact on clinical outcome at the 6-month follow-up.

Conclusion

Both surgical and endovascular treatment of recurrent or additional aneurysms in patients with a previous SAH is reasonably safe with similar complication rates and morbidity, when compared to patients without history of SAH.

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Ist eine verzögerte stationäre Aufnahme von Patienten mit aneurysmatischer Subarachnoidalblutung mit einem schlechteren Outcome assoziiert? – Ergebnisse einer Propensity Score-Untersuchung
Does delayed hospital admission of patients with aneurysmal subarachnoid haemorrhage translate into worse clinical outcome? – results of a single-centre propensity score analysis

L. Goertz, M. Pflaeging, R. H. Goldbrunner, G. Brinker, B. Krischek

Universitätsklinikum Köln, Köln, Germany

Objective

Early aneurysm embolization and standardized neurointensive care treatment within a neurovascular center are considered as key principles in the treatment of patients with aneurysmal subarachnoid haemorrhage (aSAH) in order to minimize secondary brain injury. In this study, patients with early (<24 hours; EHA) and delayed hospital admission (>48 hours; DHA) were compared in terms of baseline characteristics, treatment strategies, complications and clinical outcome.

Methods

Consecutive aSAH patients treated at a single neurovascular tertiary care center between 2009 and 2019 were reviewed. All patients were surveilled at a specialized neurointensive care unit, following a standardized aSAH management protocol. A 1:1 matching was performed based on individual propensity scores in order to account for diverging baseline characteristics.

Results

A total of 454 EHA patients and 55 DHA patients were included. DHA patients were significantly younger (52 ± 11 vs. 56 ± 14 years, $P=0.03$) and had lower World Federation of Neurosurgical Societies scores ($P<0.01$) than EHA patients. DHA patients were finally admitted due to persisting symptoms in 46%, progressive symptoms in 27%, recurrent symptoms after initial improvement in 15% and new neurological deficits in 13%. Endovascular coiling was more often performed in DHA patients (62%) than in EHA patients (42%, $P=0.03$). Propensity score matching revealed a higher infarction rate in the DHA group (49%) than in the EHA group (26%, $P=0.02$). Vasospasm occurred slightly more often in DHA patients (57%) than in EHA patients (42%), without reaching statistical significance ($P=0.12$). There was no significant difference in mid-term functional outcome between the two groups ($P=0.87$) as determined by the modified Rankin scale.

Conclusion

Delayed hospital admission is associated with an increased cerebral infarction rate, which might be predominantly related to vasospasm. Nevertheless, a favourable outcome can be obtained by state-of-the-art neurointensive care treatment within a highly specialized center.

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Charakterisierung von arteriosklerotischen Verschlussmustern bei zerebraler Revaskularisierung in der post COSS Ära

Characterisation of arteriosclerotic occlusion patterns in cerebral revascularisation in the post COSS era

L. Wessels, N. Hecht, P. Vajkoczy

Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

Objective

For the prevention of hemodynamic stroke, the COSS trial showed no benefit of STA-MCA bypass surgery compared to medical management. Despite these results, however, patients with arteriosclerotic internal carotid artery occlusion are still presented for evaluation of cerebral revascularization. Against this background, we analyzed the patient cohort that underwent STA-MCA bypass surgery in our Department for treatment of cerebral hemodynamic compromise due to arteriosclerotic cerebrovascular disease (ACVD) following the publication of COSS

Methods

Between 2011 and 2017, 132 patients underwent 136 STA-MCA bypass procedures for the treatment of cerebral hemodynamic compromise due to ACVD. Surgical eligibility required (1) unilateral (UVD) or multivessel (MVD) steno-occlusive ACVD, (2) recurrent TIAs under best medical management, and (3) impaired cerebrovascular reactivity (CVR). Demographic, clinical and radiographic data were retrospectively analyzed by an independent observer

Results

Out of 132 STA-MCA bypass surgeries, 118 unilateral and 7 bilateral procedures were performed. Nearly half (48%) of all patients suffered MVD with contralateral steno-occlusive disease in the anterior circulation and/or hemodynamically relevant stenosis in the posterior circulation. Compared to UVD, hemodynamic impairment in MVD was significantly greater due to bilaterally reduced CVR or hemodynamic steal (* $p < 0.0001$). Preoperatively, 57% suffered recurrent TIAs (UVD 55%; MVD 58%), 25% recurrent minor stroke (UVD 23%; MVD 27%) and 2% blood-pressure dependent neurological symptoms (UVD 1%; MVD 3%). Compared to the COSS inclusion criteria, only 16% had a single ischemic event in the last 120 days (UVD 21%; MVD 12%). Bypass patency rate at 1 year was 94%. The perioperative stroke rate at the time-point of discharge was 6% with a 3% risk of disabling stroke. The overall risk of ischemic stroke at 1 year was 7%. The median mRS at admission, discharge and follow-up at 1 year was 1 for both MVD (± 1.5) and UVD (± 0.8) and did not differ between groups or time points

Conclusion

Patients undergoing STA-MCA Bypass for ACVB in the post COSS era suffer more severe clinical symptoms than patients originally considered for COSS and nearly half of these patients suffer MVD with severest hemodynamic impairment. Considering the poor natural history of the disease, we, therefore, believe that STA-MCA bypass surgery remains justified in carefully selected patients

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Die Effektivität und langfristige Wirkung der Embolisation der *Arteria meningea media* bei chronischen Subduralhämatomen

Efficacy and long-term outcome of middle meningeal artery embolisation for chronic subdural haematoma

C. Onyino¹, M. Kudernatsch¹, C. Maurer², M. Abel¹, A. Berlis²

¹Schön Klinik Vogtareuth, Neurochirurgie, Vogtareuth, Germany

²Universitätsklinikum Augsburg, Neuroradiologie, Augsburg, Germany

Objective

Chronic subdural hematoma (CSDH) is a common neurosurgical condition and burr hole irrigation has been the mainstay of treatment. However, with uni- and multimodal treatment options available, consensus on this has not yet been established. Middle meningeal artery (MMA) embolization has recently been proposed as a promising adjunctive or alternative treatment, especially for patients on anticoagulant therapy. This study examined the efficacy and long-term results of MMA as a minimally invasive therapy in patients with CSDH.

Methods

Inclusion criteria in this retrospective study were patients diagnosed with CSDH in our institution between January 2018 and December 2019. They were divided into an embolization or a conventional group based on their treatment approach. The embolization cohort was subdivided into sole embolization treatment and embolization in combination with surgical treatment. Primary outcome was defined as the rate of surgical rescue and secondary outcome as the result at least 3 months after intervention.

Results

Thirty-one MMA embolizations were performed as a sole treatment in 15 patients (48.4%) and combined with burr whole irrigation in 16 patients (51.6%). Thirteen patients (41.9%) were followed-up with a mean follow-up period of 4.3 months. Spontaneous hematoma resolution was seen in 4 patients (30,8%), whereas 8 patients (61.5%) showed a minimal residue without mass effect or any clinical symptoms. Two patients (6.4%) needed hematoma evacuation after sole embolization treatment. Both patients were on anticoagulant therapy. The conventional group included 58 surgical treatments. In this group 38 patients (65.5%) were followed-up with a mean follow-up of 3.4 months. Spontaneous hematoma resolution was seen in 13 patients (43.2%), 20 patients (52.6%) showed a minimal residual hematoma without mass effect. In total, seven patients (12.1%) underwent a surgical rescue after the initial surgery, two patients because of an acute rebleeding during the hospitalization period and five patients due to hematoma reaccumulation with mass effect during the follow-up period. Five of these patients (71.4%) were on anticoagulant treatment.

Conclusion

MMA embolization has a positive therapeutic effect on CSDH, especially in patients on anticoagulant therapy. It seems to be more effective than conventional treatment alone, because of a lower complication rate in terms of acute rebleeding and hematoma reaccumulation.

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Implementation eines Hochdurchsatzverfahrens zur Medikamententestung in die Routineversorgung von pädiatrischen Hirntumoren – eine monozentrische Erfahrung in der personalisierten Neuroonkologie
Implementation of high-throughput drug screening into routine workflow for paediatric brain tumours – a single-centre experience in personalised neurooncology

T. Beez¹, C. Munoz-Bendix¹, A. Borkhardt², D. Hänggi¹, G. Reifenberger³, J. Bartl^{2,4}, M. Remke^{2,4}

¹Heinrich-Heine-Universität Düsseldorf, Klinik für Neurochirurgie, Düsseldorf, Germany

²Heinrich-Heine-Universität Düsseldorf, Klinik für pädiatrische Onkologie, Hämatologie und klinische Immunologie, Düsseldorf, Germany

³Heinrich-Heine-Universität Düsseldorf, Institut für Neuropathologie, Düsseldorf, Germany

⁴Deutsches Krebsforschungszentrum (DKFZ), Pädiatrische Neuro-Onkogenomik, Heidelberg, Germany

Objective

We have previously established and validated a highly specialized, semi-automated high-throughput drug screening (HTS) pipeline for pediatric brain tumors. Here we describe our experience in implementing this pipeline into routine workflow at a dedicated pediatric neuro-oncology center.

Methods

The pipeline is based on semi-automated devices, the D300e Digital Dispensers (Tecan Trading AG, Switzerland), that enable randomized distribution of active ingredients onto microtiter plates. It consists of 200 established chemotherapeutic agents and novel anti-cancer compounds currently in phase III and IV studies for a variety of tumor entities, not limited to brain tumors. The impact of the compounds on tumor cell viability was quantified after 72 hours of incubation using measurement of ATP level. Tumor samples of patients aged ≤18 years, who were primarily treated at our institution, were included after preoperative informed consent.

Results

Tumor samples (solid specimens and/or ultrasonic aspirator filtrate) of 164 primary tumors and 14 recurrent tumors were collected in the neurosurgical operation room and immediately transferred to the on-site laboratory, where processing and cultivation was performed. The main histological entities were pilocytic astrocytoma (N=31, 17%), medulloblastoma (N=28, 16%), glioblastoma (N=27, 15%) and ependymoma (N=21, 12%). Of these cases, 107 tumor cell cultures were established successfully and HTS was subsequently performed. Patient-specific drug screening results were categorized into absent/non-selective and selective activity of tested established chemotherapeutic agents and novel anti-cancer compounds.

Conclusion

The HTS pipeline was successfully implemented into our clinical routine workflow for pediatric brain tumors. As the tested drugs were selected for HTS based on clinical applicability, i.e. they were at least previously investigated in phase III and IV studies, personalized treatment options could be provided for 60% of pediatric brain tumors in the framework of future clinical studies.

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Die Bestimmung der Reorganisation des motorischen Areals mittels navigierter transkranieller Magnetstimulation (nTMS) bei Gliompatienten

Reorganisation of primary motor area in tumour patients examined by navigated transcranial magnetic stimulation (nTMS)

F. Roth, T. Picht, P. Vajkoczy, A. Zdunczyk

Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

Objective

Patients with brain tumors in motor eloquent areas are differently affected by motor deficits due to the lesion and surgical intervention. One reason for different dynamics of disease progression and surgical outcome could be an individual potential to compensate impairments of the motor cortex. The aim of the present study was therefore to examine reorganization capacity in patients with brain tumors using navigated transcranial magnetic stimulation.

Methods

The cortical motor representation area of the first dorsal interosseous muscle was mapped on both hemispheres in 25 patients with glioma WHO \geq II in primary and premotor cortex preoperatively and 6 months after surgery. The motor function was evaluated based on the British Medical Research Council Scale (MRC 1-5). Using nTMS the intracortical and corticospinal excitability was examined by determining the Resting Motor Threshold (RMT) and Recruitment Curve (RC). Intracortical inhibition was determined by the measurement of the Cortical Silent Period (CSP) and the cortical representation by mapping the motor area with 105% of the RMT.

Results

Mapping of the motor cortex was successful in all patients. Postoperatively 8 patients developed a new motor deficit (32%). Preoperatively, patients presented with an enlarged motor area on the affected hemisphere (AH) compared to the unaffected hemisphere (UH) (AH 430,8 mm² vs. UH 359,3 mm², $p < .05$). The preoperatively observed difference between the RMT ration of both hemispheres diminished after 6 months (preoperative 1,09 vs. follow up 0,96, $p < .05$). The corticospinal excitability of the affected hemisphere expressed by the RC also improved in the follow up period (AH RC slope preop 8,4 vs postop 12,5, $p < .05$). In trend, the cortical inhibition also decreased (preoperative AH 142,9 ms vs. follow up AH 127,1 ms, $p = ns$). In patients that did not recover, we observed no change in these parameters.

Conclusion

nTMS based motor mapping represents a valuable tool to measure tumor induced changes of corticospinal excitability and motor cortex reorganization. These results provide valuable information for individually tailored preoperative planning, risk stratification and postoperative follow up.

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Erhöhtes Blutungsrisiko nach elektiven Kraniotomien unter oralen Antikoagulanzen (OAK) und Thrombozytenaggregationshemmern (TAH)

Increased risk of bleeding after elective craniotomies by oral anticoagulants (OAC) and platelet aggregation inhibitors (PAI)

N. Karapetyan, S. Asgari

Klinikum Ingolstadt, Neurochirurgie, Ingolstadt, Germany

Objective

Postoperative intracranial hemorrhage (POIH) after craniotomies is associated with significant morbidity and mortality mainly if taking OAC and / or PAI. This retrospective study aims to find out whether intracranial hemorrhages are associated with the use of pre-operatively paused OAC and/or PAI after elective craniotomies.

Methods

In this study, 521 patients underwent elective craniotomies between June 2011 and February 2016. A group of 69 patients (group A) had taken OAC and/or PAI before surgery and were compared with the group of 452 patients (group B) without the use of those drugs, respectively. All anticoagulant and antiaggregant drugs had been paused before surgery. In this multivariate analysis several risk factors were considered as well.

Results

In 521 patients, 33 (6.33%) had POIH and 22 (4.22%) of these 33 patients were associated with clinical neurological deterioration. 9 patients (13%) of group A had suffered from POIH and mostly got a worse outcome. Contrarily, 24 patients of group B developed POIH (5.3%). The risk for POIH with neurological deterioration was 2.7-times higher for group A than for group B. This result was statistically significant (OR = 2.675, $p = 0.014$).

Conclusion

Despite pausing OAC and/or PAI before surgery and preoperative inconspicuous plasmatic coagulation and platelet count in the routine laboratory, there was a significantly increased risk of POIH with a worse clinical-neurological outcome among patients taking OAC and/or PAI previously. To minimize the risk of POIH in OAC and/or PAI patients and to reduce morbidity and mortality, it would be useful to perform more differentiated coagulation analysis and platelet function analysis before surgery.

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Postoperativ erhöhte Serumlaktatspiegel nach intrakraniellen Tumoroperationen sind unabhängig von der Tumorhistologie und werden durch die Steroidverabreichung und die Operationsdauer bestimmt
Postoperative elevated serum lactate levels after intracranial tumour surgery is independent from tumour histology and determined by steroid administration and surgery length

M. Mohme¹, J. Götttsche¹, N. Schweingruber², J. Grensemann³, J. Regelsberger¹, M. Westphal¹, P. Czorlich¹

¹Universitätsklinikum Hamburg-Eppendorf, Klinik für Neurochirurgie, Hamburg, Germany

²Universitätsklinikum Hamburg-Eppendorf, Klinik für Neurologie, Hamburg, Germany

³Universitätsklinikum Hamburg-Eppendorf, Klinik für Intensivmedizin, Hamburg, Germany

Objective

The aim of this study is to evaluate factors impacting postoperative elevated serum lactate levels after intracranial tumor removal. We hypothesized that tumor histology, together with intraoperative factors, such as steroid administration or surgery length are the major determinants for postoperative elevated serum lactate levels.

Methods

In total, we included 674 intracranially resected patients in this study. Tumor histology included glioblastoma (IDHwt, n = 284), astrocytoma (IDHmut, n = 184), 142 oligodendroglioma (n = 142), and meningioma (n = 100). Basic parameters, such as gender, age, tumor location, Ki67 index, WHO grade, surgery lengths, pre- and perioperative dexamethasone administration, as well as 17 postoperative metabolic and basic blood parameters on intensive care unit were analyze using a LMER and a linear statistic approach. Patients were subsequently stratified into high (>2mg/dl lactate) and low postoperative serum lactate level groups to analyze individual risk factors.

Results

Multivariate analysis showed that different tumor histologies did not correlate with an increase prevalence of postoperative elevated serum lactate levels. Increased serum lactate levels in the early postoperative course were primarily associated with surgery lengths and pre-/intraoperative steroid administration (p < 0.001). Lactate levels peaked at 12 hours and remained elevated within the first 24h postoperatively. The lab parameter profile of patients with elevated serum lactate levels was associated with a steeper drop in hemoglobin levels, presumably due to increase fluid administration, which was associated with a larger variance in blood pressure. Patients with elevated serum lactate levels also frequently presented with hyperglycemia, indicating a primary pathophysiological relevance of impaired insulin responsiveness in these patients. The impact of the surgery lengths on lactate levels was presumably mediated by increased blood loss and associated with increased need for metabolic recompensation.

Conclusion

We found that postoperative elevated serum lactate levels are primarily associated with the length of surgery and the pre- and intraoperative steroid administration but not with the histology or molecular subtype of the resected tumor.

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Perioperative Antikoagulation bei Patienten mit intrakraniellen Meningeomen – Kein erhöhtes Risiko intrakranieller Hämorrhagie?

Perioperative anticoagulation in patients with intracranial meningioma – no increased risk of intracranial haemorrhage?

F. Wilhelmy, A. Hantsche, J. Meixensberger

Universitätsklinikum Leipzig, Klinik und Poliklinik für Neurochirurgie, Leipzig, Germany

Objective

Anticoagulation (AC) is a critical topic in perioperative and post-bleeding management. Yet, there is a lack of data for a safe and reasonable use of prophylactic and therapeutic anticoagulation in regard of risk factors, cause and modality of brain tissue damage as well as for unfavorable outcomes, such as postoperative hemorrhage (PH) and thromboembolic events (TEE) in neurosurgical patients. In this paper we present retrospective data on perioperative anticoagulation in meningioma surgery.

Methods

Patient data of 286 individuals undergoing meningioma surgery between 2006 and 2018 were analyzed. We followed up on anticoagulation management, doses and time points of first application, laboratory values and adverse events like PH or TEE. Preexisting medication and hemostatic conditions were evaluated. Time course of patients measured as overall survival, re-admission for 30 days after surgery as well as Glasgow Outcome Scale (GOS) and Modified Rankin Scale (mRS). Statistical analysis was performed using multivariate regression.

Results

We carried out AC with Fraxiparin and, since 2015, Tinzaparin in weight-adapted recommended prophylactic doses. Delayed (216 ± 228 h) AC was associated with a significantly increased rate of thromboembolic events ($p=0.026$). Early (29 ± 21.9 h) prophylactic AC, on the other hand, did not increase the risk of PH. We identified additional risk factors for PH, such as blood pressure maxima, steroid treatment and increased white blood cell count. Patients' outcome was affected more adversely by TEE than PH (+3 points in modified rankin scale in TEE vs. +1 point in PH, $p=0,001$).

Conclusion

Early prophylactic AC is not associated with an increased rate of PH. The risks of TEE seem to outweigh those of PH. Early postoperative prophylactic AC in patients undergoing intracranial meningioma resection should be considered.

Fig 1

Characteristic	CG (n=269)	PH (n=17)	p value*
Demographic			
Gender	78 M (29%) 191 F (71%)	7 M (41.2%) 10 F (58.8%)	0.5
Age	61 ± 13 (50-72)	67 ± 14 (49-77)	0.5
BMI	27 ± 5 (24-30)	24 ± 3 (24-28)	0.5
Medical history			
Preexisting Anticoagulation	37 (13.8%)	4 (ASS, 23.5%)	0.5
Smoker	36 (13.4%)	1 (5.9%)	0.5
Steroid medication	136 (50.6%)	16 (94.1%)	0.001
Coagulation disorder	11 (4.1%)	3 (17.6%)	0.042
Event			
Length of surgery	270 ± 122 (192-358)	305 ± 156 (232-454)	0.5
Timepoint of anticoagulation	29 ± 22.4 (27-50)	69 ± 54 (28-96)	0.007
Timepoint of event (after surgery) in h		19 ± 16 (15-23)	
Laboratory values			
Maximum platelet count	267 ± 91.6 (222-321.5)	335 ± 129.4 (256.5-452)	0.013
Minimum platelet count	177 ± 57.6 (140-215.5)	142 ± 81.0 (119-201.5)	0.106**
Minimum hematocrit	0.381 ± 0.050 (0.273-0.335)	0.246 ± 0.060 (0.204-0.324)	0.011
Maximum blood pressure	155/65 ± 22/14 (140/60-170/75)	175/80 ± 19/12 (155/60 – 188/85)	Syst: 0.003 Diast: 0.053
White blood cell count at admission	7.5 ± 3.6 (6.2-9.8)	9.1 ± 3.2 (8.0-11.6)	0.045
Maximum white blood cell count	13 ± 5.6 (10-16.5)	17.6 ± 8.8 (13.2-24.0)	0.003
Creatinine at admission	70 ± 23.2 (63-81.5)	85 ± 15.4 (67.5-88.5)	0.016
Maximum creatinine	72 ± 27.9 (64-85.5)	90.0 ± 21.8 (76.5-115.5)	0.001
Minimum creatinine	55 ± 14.1 (48-65.5)	52 ± 11.4 (45-65.5)	0.553*

Table 2 Demographic description and risk factors for postoperative Hemorrhage (PH) in operated meningioma patients. 0.5 = not significant. * ordinal parameters; U-test, ordinal parameters; Chi square test **subgroup analysis of patients with surgically revised hemorrhage (PHR) was performed. In this group, a significant correlation for solid hemorrhage with minimal platelet count (CG 175 ± 59.2 vs. PHR 120 ± 93.6, p=0.007, OR 0.989 (CI 0.977-1.002)), as well as minimal creatinine (CG 55 ± 14 vs. PHR 45 ± 7.2, p=0.006, OR 0.939 (CI 0.892-0.990)) was found. The complete subgroup analysis is to be found in the appendix.

Fig 2

Time of PH (CT-diagnosis, h postoperative)	Time of first AC (in h postoperative)	Length of procedure (min)	Surgically revised	Type of AC	TEE
4	98	448	no	LMWH	no
4	78	233	no	LMWH	no
4	73	461	yes	LMWH	no
11	69	753	yes	LMWH	no
18	96	257	no	LMWH	ischemic stroke (168h postoperative)
18	72	305	no	LMWH	no
18	52	231	no	LMWH	no
18	51	329	no	LMWH	no
19	53	224	no	LMWH	no
19	none	335	no	none	no
20	240	169	yes	LMWH	DVT and LAE (after discharge)
22	112	375	yes	UFH	no
22	none	255	yes	none	no
24	28	216	yes	LMWH	no
40	26	504	yes	LMWH	no
53	24	584	yes	LMWH	no
64	26	250	yes	LMWH	no

Table 4 Patients with PH(I) and Time - point of Anticoagulation

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Der prädiktive Wert der D-Welle, der Handmuskel-MEPs und -SSEPs für das Outcome der Feinmotorik der distalen oberen Extremität nach spinalen intramedullären tumorchirurgischen Eingriffen

The predictive value of D-wave, hand-muscle MEPs and SSEPs for the distal upper limbs fine motor outcome after cervical intramedullary spinal cord tumour surgery

S. Siller, S. Zausinger, N. Muesken, J. Tonn, A. Szélényi

Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik, München, Germany

Objective

D-wave and muscle MEP monitoring during cervical intramedullary spinal cord tumour surgery (cIMSCT) is considered to be the gold standard for assessing potential injury to the corticospinal tract and indicating permanent postoperative para-/tetraparesis, but its predictive value for the distal upper limbs' fine-motor outcome in case of multimodal intraoperative neurophysiological monitoring (IONM) has not been addressed.

Methods

Intraoperative recording of epidural D-wave caudally to the surgical level, hand-muscle motor and median-nerve somatosensory-evoked potentials (hmMEPs/mSSEPs) was attempted in 11 patients (m/f: 6/5, median age: 41.4 years) undergoing cIMSCT surgeries. The following permanent IOM-alterations were considered significant: D-wave amplitude decrement $\geq 50\%$, hmMEPs amplitude decrement $\geq 80\%$ and mSSEPs amplitude reduction $\geq 50\%$ / latency increase $\geq 10\%$. Distal upper limb fine-motor function (manometrical hand-force measurement, Nine-Hole-Peg-Test) was assessed preoperatively and 6 weeks postoperative and correlated with IONM-findings.

Results

73% of the tumours were located above C4-level. Gross-total resection was accomplished in 73%. In all cases, bilateral hmMEPs and mSSEPs were present, D-Wave recording failed in 1 patient with severe preoperative paraparesis. Transient deterioration of hmMEPs resp. D-wave occurred in one patient each; none of these patients had a new neurological deficit postoperatively. However, despite corrective actions, persisting critical hmMEPs findings were present in 3 patients and mSSEPs findings in 1 patient, while a persisting deterioration of D-wave parameters did not occur. Two of these 3 patients postoperatively presented with a paresis of distal upper limb fine motor function but intact gait.

Conclusion

In cIMSCT surgery, unimpaired D-wave findings reliably predicted preserved motor function of the lower limbs, however, failed to sufficiently cover distal upper limb motor function, thus giving rise to false-negative findings. In cIMSCT, selective hmMEPs and mSSEPs alteration have to be observed since they might predict distal upper limb fine motor outcome.

Gliome klinisch II/*Gliomas clinical II*

V247

Gliosarkome – demographische, klinische, radiologische und molekulargenetische Charakteristika von Gliosarkomen und Unterschiede zu Glioblastomen

Primary gliosarcoma – demographic, clinical, radiographic and molecular-genetic characteristics and differences with primary glioblastoma

D. Pierscianek, M. Darkwah Oppong, A. Michel, K. H. Wrede, U. Sure, R. Jabbarli

Universitätsklinikum Essen, Klinik für Neurochirurgie und Wirbelsäulen Chirurgie, Essen, Germany

Objective

Primary Gliosarcoma (PGS) is a very rare variant of malignant primary brain tumors. Accordingly, data on the epidemiology and natural history of PGS is scarce. The treatment strategies for PGS are based on the studies on primary glioblastoma (PGB) patients. We aimed at analyzing the basic characteristics and clinical course of PGS patients and eventual differences to PGB.

Methods

All consecutive cases with PGS and PGB treated at our university hospital between January 2001 and December 2018, were eligible for this study. Demographic, clinical, radiographic and histological characteristics were collected. Univariate, multivariate (MVA) and propensity score matching analyses were performed.

Results

The final analysis consisted of 56 PGS and 1249 PGB cases. In univariate analysis, there was a trend towards longer OS under temozolomide (TMZ)-therapy, as compared to radiotherapy without TMZ ($p=0.0510$). But in MVA, only higher patients' age ($p=0.003$), preoperative KPS < 80% ($p=0.035$) and larger tumor size ($p=0.046$), but not TMZ-therapy ($p=0.576$) were independently associated with the OS of PGS. Compared to PGB, PGS patients showed temporal predilection ($p=0.006$), higher rates of concomitant eccentric cysts ($p=0.001$), lower profiles of GFAP staining ($p=0.006$) and MGMT methylation ($p=0.038$), as well as higher rates of P53 mutations ($p=0.006$). In the MVA for OS predictors, PGS patients showed significantly poorer outcome, when compared to the whole PGB cohort ($p=0.043$). However, when restricting the PGB cohort to the IDH1-WT cases, the outcome difference was no more significant.

Conclusion

Poorer outcome and response to TMZ-therapy in PGS patients is most likely related to less favorable IDH1 and MGMT methylation status of these individuals. As to other differences with PGB, there are PGS-specific anatomic characteristics like temporal predilection and presence of eccentric cysts.

Gliome klinisch II/*Gliomas clinical II*

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Entstehung von sekundären Gliosarkomen durch maligne Transformation – Inzidenz, Risikofaktoren und Prognose

Malignant transformation to secondary gliosarcoma – incidence, risk factors and prognosis

D. Pierscianek, M. Darkwah Oppong, A. Michel, K. H. Wrede, U. Sure, R. Jabbarli

Universitätsklinikum Essen, Klinik für Neurochirurgie und Wirbelsäulenchirurgie, Essen, Germany

Objective

Primary gliosarcoma (PGS) are rare malignant brain tumor entities. Even rarer is the occurrence of secondary gliosarcoma (SGS) due to malignant transformation, occurring mostly from primary glioblastoma (PGB). Current evidence regarding SGS is based on case reports or small case series. The aim of this study was to analyze the epidemiologic and clinical features of SGS patients based on large mono-centric series.

Methods

Of the institutional database, containing all consecutive patients with tumors of the central nervous system treated between 2001 and 2018, the cases with SGS were retrospectively collected. Demographic, clinical, radiographic and histological characteristics of the SGS patients were analyzed and compared to the counterpart cohorts with primary entities. Univariate and multivariate analyses were performed.

Results

During the observational period, SGS was documented in 20 cases, predominantly in male patients (60%). Mean age of the patients was 50.9 (± 17.8) and 54.7 (± 16.3) years at the time of primary diagnosis and malignant transformation respectively. The most common primary entity was PGB (50%), followed by 5 WHO-Grade III and 4 WHO-Grade II tumors, as well as 1 case of NOS CNS embryonal tumor. The incidence of SGS transformation was 0.8%, 0.6% and 0.6% for PGB, WHO Grade III and II tumors respectively ($p=0.6477$). The location of the tumor in the temporal lobe was significantly associated with the risk of SGS transformation among all WHO-Grade II-IV brain tumors (OR=5.0 [95% CI: 2.07 – 12.14], $p=0.0002$). Biological grading of the primary tumor inversely correlated with the timing of malignant transformation accounting in average 12.1 months, 12.7 and 138.6 months for PGB, WHO Grade III and II tumors respectively ($p=0.0107$). However, SGS survival after transformation was not associated with the primary WHO grading ($p=0.9158$). There was a trend towards decreasing rates of the MGMT methylation, when comparing PGB with PGS and SGS (38.6% vs 27.3% vs 16.7% respectively, $p=0.0829$).

Conclusion

Malignant transformation to SGC is a very rare complication of CNS tumors, which can occur between several weeks and many years after primary diagnosis. The risk of SGS development is not limited to PGB. Location of the tumor in the temporal lobe seems to increase the likelihood of SGS transformation.

Gliome klinisch II/*Gliomas clinical II*

V249

Monopolare und bipolare Stimulation während zerebraler Tumorresektionen – Ergebnisse einer ersten Serie hinsichtlich einer autonomen Anwendbarkeit eines neuen Monitoringgerätes durch den Chirurgen
First experiences with monopolar and bipolar brain mapping during awake and asleep surgery using a new device autonomously operated by the surgeon

F. Staub-Bartelt, M. Rapp, D. Hänggi, H. J. Steiger, M. A. Kamp, M. Sabel

Universitätsklinikum Düsseldorf, Neurochirurgie, Düsseldorf, Germany

Objective

Patients with eloquently located cerebral lesions require surgery using intraoperative motor or speech mapping with monopolar or bipolar stimulation. 50-60Hz stimulation with an Ojeman stimulator can mainly be performed by the surgeon independently, whereas monopolar stimulation requires additional trained personnel for handling of the intraoperative monitoring (IONM) system. Here, we report our first experiences using a device that can be operated by the surgeon autonomously for both intraoperative techniques.

Methods

For monopolar and bipolar cortical/subcortical stimulation two preset programmes were available and intraoperatively used. One enabling EMG real-time tracking of 8 muscles for monopolar mapping and a second programme for 60 Hz stimulation. Neither SSEP, MEP nor ECOG monitoring was available. Motor mapping was performed using a standard monopolar probe connected to the device. EMG signals were screened in real-time on the device monitor. For 60 Hz stimulation a standard bipolar stimulation probe was connected through a second port. Preoperative application of subdermal EMG needles as well as intraoperative handling of the device were performed by the surgeons independently. Postoperatively, evaluation of autonomous handling and feasibility of the device for chosen test parameters was conducted.

Results

From 04/19-11/19, 40 patients with eloquently located cerebral lesions underwent surgery using the device. Regarding setup and sufficiency for cortical/subcortical monopolar and bipolar mapping the new device was evaluated as independently usable for motor and language mapping in 34 patients. In 6 patients speech testing was performed using an Ojeman stimulator. Complete resection was intraoperatively evaluated in 27 patients (73%). After matching with post-OP MRI a residual tumor volume was demonstrated in 4 patients (15%), three patients postoperatively suffered from a new neurological deficit, two of them after using standard Ojeman stimulator, follow-ups are still pending.

Conclusion

The device was evaluated as sufficient in 85%. However, missing concurrent SSEP monitoring was seen as a severe limitation in special indications and led to exclusion of patients where extended IONM was required. Concerning grade of resection and neurological outcome results were comparable to IONM procedures using standard devices. In this first cohort surgeons were able to perform motor and speech mapping adequately and safely by independent use of the device.

Gliome klinisch II/*Gliomas clinical II*

V250

Chirurgische Ergebnisse bei diffusen niedergradigen Gliomen – aktuelle prospektive Daten des LoG-Glio Registers

Surgical outcome in diffuse low-grade glioma – contemporary prospective data from the LoG-Glio registry

J. Coburger¹, S. Rückriegel², M. Nadji-Ohl³, C. Von der Brelie⁴, C. Roder⁵, K. Faust⁶, D. Sachs³, M. Löhr², S. Grüninger⁷, P. Vajkoczy⁶, M. Tatagiba⁵, R. I. Ernestus², V. Rohde⁴, O. Ganslandt³, C. R. Wirtz⁷, A. Pala¹

¹Bezirkskrankenhaus Günzburg, Neurochirurgie, Günzburg, Germany

²Julius-Maximilians-Universität Würzburg, Neurochirurgie, Würzburg, Germany

³Klinikum Stuttgart, Neurochirurgie, Stuttgart, Germany

⁴Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

⁵Universitätsklinikum Tübingen, Neurochirurgie, Tübingen, Germany

⁶Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

⁷Universität Ulm, Neurochirurgie, Günzburg, Germany

Objective

Level of evidence for surgical management in low grade glioma (LGG) is low and mainly relies on retrospective series. Hence prospective contemporary assessment of surgical outcome is important to assure surgical quality control and to evaluate surgical strategies.

Methods

Prospective registry data from 2016 to 2019 was searched for diffuse LGG WHO°II and III with complete follow up assessment. Demographic data and the following outcome parameters were assessed at 3 months follow up: new permanent neurological deficits (NPND), NHISS score, ECOG, used surgical technique and presence of residual tumor (RT). Descriptive assessment and multivariate binary regression models for influence of RT and ND were calculated.

Results

96 patients (pts) were assessed. Median age was 40 yrs (min 18, max 78), 80 pts (90%) had no neurological deficit before surgery; tumors were in eloquent location in 57 pts (60%); median time to surgery was 1 month (min 0, max 27); stereotactic biopsy (STX) was performed in 10 (10%), intended subtotal resection (STR) in 33 (34%) and intended gross total resection (GTR) in 53 pts (55%). 17 pts (18%) had recurrent surgery. The following surgical techniques were used: awake surgery in 19 (20%), intraoperative monitoring/mapping (IOM) in 58 (61%), ultrasound in 29 (31%) and iMRI in 35 pts (37%).

NPND were found in 17 pts (23%). 5 pts (6%) had severe, while 12 (15%) had slight NPND. Highest rate of severe NPND was found in pts, who underwent intended STR (n=3 [11%]) compared to intended GTR with n=2 (5%). No NPNDs were found after STX. In multivariate assessment, none of the surgical techniques but eloquent location influenced presence of NPND. Perioperative complications other than NPND were found in 14 pts (15%). Most common was ischemia (n= 3 [3%]). After surgery, median ECOG remained stable as well as median NHISS. A deterioration was seen in 13 pts (18%) for ECOG, in 19 pts (27%) for NHISS. RT was found in 50 pts (53%) and in 14 pts (26%) with intended GTR. Surgical technique did not influence presence of RT in multi- and bivariate assessment.

Conclusion

Contemporary surgical outcome in diffuse LGG shows a high rate of NPND and a relatively low rate of radiologically complete tumor resection despite intended GTR. Hence, use of intraoperative monitoring/mapping and intraoperative imaging should be considered in any surgery of a diffuse LGG given the mostly eloquent lesions and the crucial importance of a complete tumor resection for these pts survival.

Gliome klinisch II/*Gliomas clinical II*

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Aktuelle Behandlung von diffusen niedergradigen Gliomen in sechs zertifizierten neuro-onkologischen Zentren – prospektive Daten aus dem LoG-Glio Register

Contemporary management of diffuse low-grade glioma from six certified neuro-oncological centres – prospective data from the LoG-Glio registry

J. Coburger¹, M. Nadji-Ohl², C. Von der Brölie³, S. Rückriegel⁴, C. Roder⁵, K. Faust⁶, D. Sachs², S. Grüninger¹, M. Löhner⁴, P. Vajkoczy⁶, M. Tatagiba⁵, R. I. Ernestus⁴, V. Rohde³, O. Ganslandt², C. R. Wirtz¹, A. Pala⁷

¹Universität Ulm, Neurochirurgie, Günzburg, Germany

²Klinikum Stuttgart, Neurochirurgie, Stuttgart, Germany

³Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

⁴Julius-Maximilians-Universität Würzburg, Neurochirurgie, Würzburg, Germany

⁵Universitätsklinikum Tübingen, Neurochirurgie, Tübingen, Germany

⁶Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

⁷Bezirkskrankenhaus Günzburg, Neurochirurgie, Günzburg, Germany

Objective

In recent years, some level of consensus for management of diffuse astrocytoma and oligodendroglioma was reached. Aim of the present study was to assess the current management of these lesions based on data from the LoG-Glio registry.

Methods

Prospective data sets of primary diagnosis of WHO^oII/III astrocytoma or oligodendroglioma registered from 2016 to 2019 in 6 certified neuro-oncological centers were retrieved and analyzed for type and timing of surgical treatment and planned adjuvant treatment. A descriptive assessment was performed.

Results

76 patients with histologically confirmed diagnosis were retrieved. 43 astrocytoma (74% WHO^oII) and 33 oligodendroglioma (91% WHO^oII) were found. 65 patients (78%) had surgery within 3 months after primary diagnosis (PD). Maximum time from PD to surgery was 5.6a. Open surgery was performed in 67 patients (87%), while stereotactic biopsy was done in 10 (13%).

Planned adjuvant treatment in IDH mutated astrocytoma with residual tumor (19) was "wait-and-scan" in 3 patients (16%), radiotherapy (RT) in 5 patients (26%), combined RT/temozolomid (TMZ) in 8 patients (42%), consecutive RT/TMZ in 2 patient (11%) and consecutive PCV in 1 patient (6%). IDH mutated astrocytoma without (w/o) residual tumor (11) were treated with "wait-and-scan" in 7 pts (63%), RT in 1 pts (9%) and combined RT/TMZ in 3 pts (27%).

IDH wildtype astrocytoma (14) were treated with combined RT/TMZ in 11 pts (79%). All others received "wait-and-scan".

Oligodendroglioma with residual tumor (16) had "wait-and-scan" in 1 pt (6%), RT in 6 (35%) PCV in 3 pts (18%), combined RT/TMZ in 3 pts (18%); and consecutive RT/PCV in 4 (24%). W/o residual tumor (17) had "wait-and-scan" in 11 pts. (69%), combined RT/TMZ in 1 (6%) and consecutive RT/TMZ in 1 pt and consecutive RT/PCV in 3 pts (19%).

Conclusion

While early surgical treatment was performed in the majority of cases, adjuvant treatment of low grade glioma remained largely heterogeneous in this contemporary cohort of patients treated in certified neurooncological centers. Especially, patients with oligodendroglioma and residual tumor were treated with consecutive RT and PC(V) only in ¼ of cases despite results of RTOG 9802. Hence an early update of the current glioma guidelines is recommended.

Gliome klinisch II/*Gliomas clinical II*

V252

Untersuchungen zur Neurokognition bei der Chirurgie temporaler niedriggradiger Gliome in Abhängigkeit vom Resektionsausmaß

Surgery for temporal low grade-glioma – Does extent of resection impair neurocognitive outcome?

I. Ilic¹, M. Schneider¹, J. Taube², G. Aydin¹, E. Güresir¹, V. Borger¹, H. Vatter¹, C. Helmstaedter², P. Schuss¹, M. Hamed¹

¹Rheinische Friedrich-Wilhelms-Universität Bonn, Abteilung für Neurochirurgie, Bonn, Germany

²Rheinische Friedrich-Wilhelms-Universität Bonn, Abteilung für Epileptologie, Bonn, Germany

Objective

With regard to superior long-term disease control, anterior temporal lobectomies (ATL) as a supra-total resection regime have gained growing attention in surgery for temporal lobe tumors. However, aggressive temporal tumor resection might be accompanied by an impairment of a patient's neurocognitive functioning. We therefore analyzed our institutional database with regard to postoperative changes in neurocognitive skills following surgical therapy of temporal-located low grade glioma depending on the extent of tumor resection.

Methods

Between 1999 and 2018, 33 patients were surgically treated for temporal-located low-grade gliomas via ATL or lesionectomy in terms of gross-total resection (GTR) at the authors' institution. Histopathological analysis revealed 7 grade-II pleomorphic xanthoastrocytoma, 19 grade-I pilocytic astrocytomas, 7 grade-II diffuse astrocytomas. Pre- and postsurgical neuropsychological examination included attention, language as well as verbal and figural memory functions. Language functions were assessed with the Token Test, and a phonemic verbal fluency task. Verbal and nonverbal memory was evaluated by the Verbaler Lern- und Merkfähigkeitstest and a revised five-trial version of the Diagnosticum für Cerebralschädigung, respectively.

Results

14 patients were surgically treated by ATL, whereas GTR was performed in 19 patients. Analysis of attention revealed deterioration of preoperative functioning for 21% of patients in the GTR group compared to 20% in the ATL group ($p=1.0$). Respective values for verbal and nonverbal memory were 37% and 23% ($p=0.5$) as well as 15% and 32% ($p=0.4$). Postoperative language functions were worsened in 53% of patients with GTR compared to 62% of patients with ATL ($p=0.8$).

Conclusion

With regard to ATL and GTR as differing oncosurgical approaches that did not exhibit significant differences in the rates of postoperative neurocognitive impairment, ATL in terms of a supra-total resection strategy constitutes a safe surgical treatment option for temporal-located LGG.

Schädelhirntrauma und Kranioplastie/*Traumatic brain injury and cranioplasty*

V253

Das deutsche Schädel-Hirn-Trauma Register – erste Daten aus der Pilotphase *The German national TBI-registry – preliminary data from the pilot period*

A. Younsi¹, A. W. Unterberg¹, P. Czorlich², A. H. Hussam³, D. Lindner⁴, M. Luchtman⁵, T. Lustenberger⁶, M. Maegele⁷, I. Marzi⁶, U. M. Mauer⁸, K. Schmieder⁹, M. Strowitzki¹⁰, E. Uhl¹¹, T. Westermaier¹², S. Wolf¹³, W. I. Steudel¹⁴

¹Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

²Universitätsklinikum Hamburg-Eppendorf, Neurochirurgie, Hamburg, Germany

³Universitätsklinikum RWTH Aachen, Neurochirurgie, Aachen, Germany

⁴Universitätsklinikum Leipzig, Neurochirurgie, Leipzig, Germany

⁵Universitätsklinikum Magdeburg, Neurochirurgie, Magdeburg, Germany

⁶Universitätsklinikum Frankfurt am Main, Unfallchirurgie, Frankfurt am Main, Germany

⁷Kliniken der Stadt Köln, Unfallchirurgie, Köln, Germany

⁸Bundeswehrkrankenhaus Ulm, Neurochirurgie, Ulm, Germany

⁹Universitätsklinikum der Ruhr-Universität Bochum, Neurochirurgie, Bochum, Germany

¹⁰Berufsgenossenschaftliche Unfallklinik Murnau, Neurochirurgie, Murnau, Germany

¹¹Universitätsklinikum Gießen und Marburg, Neurochirurgie, Gießen, Germany

¹²Universitätsklinikum Würzburg, Neurochirurgie, Würzburg, Germany

¹³Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

¹⁴Universitätsklinikum Homburg, Neurochirurgie, Homburg, Germany

Objective

Since nationwide data on the epidemiology, treatment characteristics and long-term outcome of severe traumatic brain injury (TBI) in Germany are lacking, neurosurgeons from the German Neurosurgery Society (DGNC) and traumatologists from the German Trauma Society (DGU) joined forces in 2016 to conceptualize a TBI module for the well-established Trauma Register of the DGU (TR-DGU), functioning as the German National TBI registry (GNTR). After funding for this endeavor was secured, the corresponding electronic case report forms were designed, ethical approval was obtained, and a one-year-long pilot period of the GNTR was initiated in February 2019.

Methods

Preliminary data from the pilot period of the GNTR which has been initiated in February 2019 and will continue until February 2020, aiming to enroll severe TBI patients in 22 neurosurgical as well as traumatological departments across Germany is presented. In the GNTR, TBI patients are prospectively enrolled when treatment on the ICU \geq 24h is indicated. A variety of clinical and radiological parameters are collected, and the outcome is assessed by the GOSE score at discharge as well as at 6- and 12 months follow-up.

Results

Details on the structure and data set of the GNTR as well as associated milestones and pitfalls during the conception and implementation phase are outlined. Demographic as well as clinical, laboratory and radiological characteristics of the TBI patients enrolled during the pilot period of the GNTR are presented, indicating the current epidemiology and care situation of severe TBI in Germany. In addition, mortality, as well as early functional outcome following severe TBI in Germany measured by the GOSE score, are described. If available, factors associated with an unfavorable outcome (GOSE 1-4) after severe TBI are assessed using uni- and multivariate regression analyses.

Conclusion

National TBI registries are needed to collect high quality, prospective data on the most severe form of this devastating condition. The preliminary results from the pilot period of the GNTR do not only depict the epidemiology of severe TBI in Germany but also allow to evaluate and compare factors associated with its long-term outcome, ultimately helping to improve its treatment.

Schädelhirntrauma und Kranioplastie/*Traumatic brain injury and cranioplasty*

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Rolle von Receptor interacting protein (RIP) 1 und 3 bei der langfristigen Entwicklung des posttraumatischen Hirnschadens

Role of receptor interacting proteins (RIP) 1 and 3 in chronic posttraumatic brain damage

A. Wehn¹, I. Khalin¹, N. Plesnila¹, N. A. Terpolilli^{2,1}

¹Klinikum der Ludwig-Maximilians-Universität München, Institut für Schlaganfall- und Demenzforschung, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgie, München, Germany

Objective

Traumatic brain injury (TBI) is a major cause of death and disability worldwide and often leads to progressive brain damage and, subsequently, increasing neurological deficits over time. A possible mechanism identified to play role in the development of post-TBI brain damage is necroptosis. The main mediators of this caspase-8 independent death pathway are receptor interacting proteins (RIP) 1 and 3, which form the necrosome complex. We previously demonstrated that knockdown of RIP1 and/or RIP3 leads to a reduction of neuronal cell death in vitro. In the current study, we therefore assessed the role of RIP 1 and 3 in vivo after experimental traumatic brain injury.

Methods

Transgenic RIP3 and RIP1 neuronal transgenic mice were subjected to controlled cortical impact (CCI) injury. Lesion volume and posttraumatic brain damage were assessed by magnetic resonance (MR) imaging 15 minutes, 24 hours, 7, 30, 60, and 90 days after CCI. At 90 days after TBI, brains were harvested for histopathological and immunohistochemical evaluation. Motor function was assessed by the Beam Walk test, memory function by the Barnes Maze paradigm, and depressive behavior assessed by the Tail Suspension test.

Results

Serial MR imaging showed that RIP1 as well as RIP3 deficient animals had significantly smaller lesion volumes compared to their respective controls, starting at one week and one month after TBI, respectively. Neuroprotection was most pronounced in the hippocampus where tissue loss was significantly reduced in transgenic animals in MRI as well as in histopathology. This decrease in lesion size did not translate into differences in motor function or neurobehavioral deficits, but led to a better performance in learning and memory tasks. Furthermore, astrogliosis and microglia coverage, especially in the hippocampus, were reduced in transgenic animals.

Conclusion

In conclusion, necroptosis mediated by RIP1 and RIP3-complex formation plays an important role in the development of long-term posttraumatic brain damage and could be a promising target for future neuroprotective therapies. Of note, significant reduction of lesion volume and neurobehavioral improvement was obvious only at later time points (< one week) suggesting that evaluation of posttraumatic brain damage exclusively at early time-points (e.g. 24h) after TBI is insufficient for conclusive assessment of neuroprotective interventions.

Schädelhirntrauma und Kranioplastie/*Traumatic brain injury and cranioplasty*

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Altersabhängiges Outcome nach akutem Subduralhämatom *Age-dependent outcome following acute subdural haematoma*

S. Bele, E. Bründl, K. M. Schebesch, A. Brawanski, N. O. Schmidt

Universitätsklinikum Regensburg, Klinik und Poliklinik für Neurochirurgie, Regensburg, Germany

Objective

With increasing numbers of elderly patients and tight resources concerning intensive care beds we examined the outcome following acute subdural hematoma (aSDH) according to age and initial GCS.

Methods

Charts of patients with aSDH between 2000 and 2017 were retrospectively checked for age, GCS on admission, midline shift, pathological coagulation and GOS at discharge and 6 months after hospital discharge. Only patients who either were treated surgically or at least for 24 h conservatively on an ICU were included. We built 2 age groups, a) patients ≤ 65 years and b) patients > 65 years. Adverse outcome was defined as GOS 1-3 and good outcome GOS 4-5.

Results

571 patients were included in this study. 264 patients were ≤ 65 years and 307 > 65 years. In the younger patients, 163 were GOS 1-3 and 101 were GOS 3-4 at hospital discharge. 6 months later a total of 156 patients ≤ 65 years showed good outcome. In the elderly patient group 244 of 307 were GOS 1-3, 90 patients of whom died during hospital stay. Only 63 elderly patients were in the good outcome group. The patients > 65 years also showed less improvement compared to the younger population as only 98 patients were in the GOS 4-5 group at 6 months after discharge, meaning only 35 patients improved over the months. When combined with primary GCS ≤ 5 on admission, 97% of the patients > 65 years were GOS 1-3, 63% of whom died during hospital stay. At 6 months after discharge an additional 15 % died. In the group of patients ≤ 65 years and GCS ≤ 5 on admission initially 92% were GOS 1-3 at discharge but clearly improved after 6 months with 67% remaining GOS 1-3.

Conclusion

In our examined population, patients > 65 years showed significantly worse outcome following aSDH than younger patients. Especially when the GCS on hospital admission was ≤ 5 , 63 % of the patients died during hospital stay and 34 % stayed in care centers. Thus, it should be very carefully decided if surgical treatment is the correct choice for patients > 65 years of age with aSDH and GCS ≤ 5 on admission since those patients either die or stay in nursing homes in clinically bad condition.

Schädelhirntrauma und Kranioplastie/*Traumatic brain injury and cranioplasty*

V256

"Es ist Teil meines Jobs, oder?" – emotionale Belastungen im intensivmedizinischen Behandlungsteam im Kontext von Entscheidungen zur Therapiezieländerung

"It's part of my job, right?" – emotional burdens in the intensive care team in the context of end-of-life-decisions

P. Czorlich¹, M. M. Mader¹, G. de Heer², S. Kluge², K. Kettmann³, B. Löwe³, M. Westphal¹, A. Weigel³

¹Universitätsklinikum Hamburg-Eppendorf, Klinik und Poliklinik für Neurochirurgie, Hamburg, Germany

²Universitätsklinikum Hamburg-Eppendorf, Klinik für Intensivmedizin, Hamburg, Germany

³Universitätsklinikum Hamburg-Eppendorf, Klinik für Psychosomatische Medizin und Psychotherapie, Hamburg, Germany

Objective

End-of-life-decisions (EOLD) are daily practice in the neurosurgical intensive care unit (ICU) setting. Non-clearly structured and documented EOLD can lead to conflict in the treatment team and have a negative impact on mental health and job satisfaction. With the aim of developing measures to improve or maintain mental health and job satisfaction, target group specific burdens and needs in EOLD need to be identified.

Methods

Between July to October 2018, physicians and nurses were asked about their subjective experience of the current definition, documentation and implementation of EOLD as well as their effects on job satisfaction and their emotion regulation with the help of semi-structured interviews in 12 ICU's of our institution. The answers were qualitatively evaluated according to the thematic analysis. In addition, the frequency of EOLD in everyday life and their significance for job satisfaction, perceived workload and emotional stress were quantified. A numerical rating scale was used to capture global satisfaction (0 = not at all satisfied to 10 = completely satisfied) with the current definition, documentation and implementation of EOLD.

Results

A total of 19 physicians (61%) and 12 (39%) nurses participated, half of whom (54%) had EOLD "daily" or "several times a week". Physicians were significantly more satisfied with the current definition, documentation and implementation of EOLD as the nursing staff (6.63 vs. 3.75; $p < .001$). The importance of job satisfaction was very high in both groups (8.16 vs. 8.42; $p = n.s.$), as well as the emotional stress (5.05 vs. 5.00; $p = n.s.$) and the workload (6.74 vs. 8.33; $p = n.s.$). Physicians addressed emotional stress caused by recurring escalation situations during weekend or overnight services, e.g. due to insufficient documentation that led to ethical conflicts, experienced helplessness or perceived disproportion of treatment. Nursing staff experiences emotional burden due to their lack of involvement in the EOLD process while still having to carry out the EOLD even if they do not agree. Reported measures for emotion regulation ranged from individual endurance to established rituals in the team.

Conclusion

The results of the present study indicate different needs of physicians over nurses in the context of EOLD. A reduction of emotional stress by EOLD could be achieved through a combination of structural measures and individual intervention to support emotional regulation.

Schädelhirntrauma und Kranioplastie/*Traumatic brain injury and cranioplasty*

V257

Systemische Entzündungsmarker wie C-Reaktives Protein und Procalcitonin sind bei EVD-assoziierten Infekten in Patienten mit hämorrhagischen Schlaganfällen nicht erhöht
Systemic inflammation markers like C-reactive protein and procalcitonin are not increased in ventriculostomy-related infections in patients with haemorrhagic stroke

S. S. Wang, E. Pietrzko, E. Keller, G. Brandi

Universitätsspital Zürich, Zürich, Switzerland

Objective

Ventriculostomy-related infection (VRI) is a serious complication in patients with hemorrhagic stroke. In such patients, early diagnosis of VRIs is complicated by blood contamination of CSF following ventricular hemorrhage. The role of serum-inflammatory markers in the diagnosis of VRIs is unclear. We therefore aim to evaluate the diagnostic potential of white blood cells count (WBC), C-reactive protein (CRP), and procalcitonin (PCT) in patients who developed VRIs after hemorrhagic stroke with an external ventricular drain (EVD) *in situ*.

Methods

A total of 347 patients with hemorrhagic stroke (spontaneous subarachnoid, intra-parenchymal or intraventricular hemorrhage) with EVD were analysed in this cohort study. 14 patients developed a VRIs ("VRI"), defined by positive CSF bacterial culture and increased WBC in CSF (larger than range of 200-250 cells/mcgl), and 115 patients without VRIs ("no-VRI") with serial CSF sampling were included in the analysis. Patients with CSF-contamination or suspected VRI (negative CSF cultures but antibiotic treatments) were excluded. WBC, CRP, and PCT were measured daily. CSF was sampled routinely twice a week or by $T > 38^{\circ}\text{C}$. For the analysis, mean peak values of WBC, CRP, PCT during the time of EVD *in situ* were compared between groups (t test). Data are expressed as mean with CI 95%.

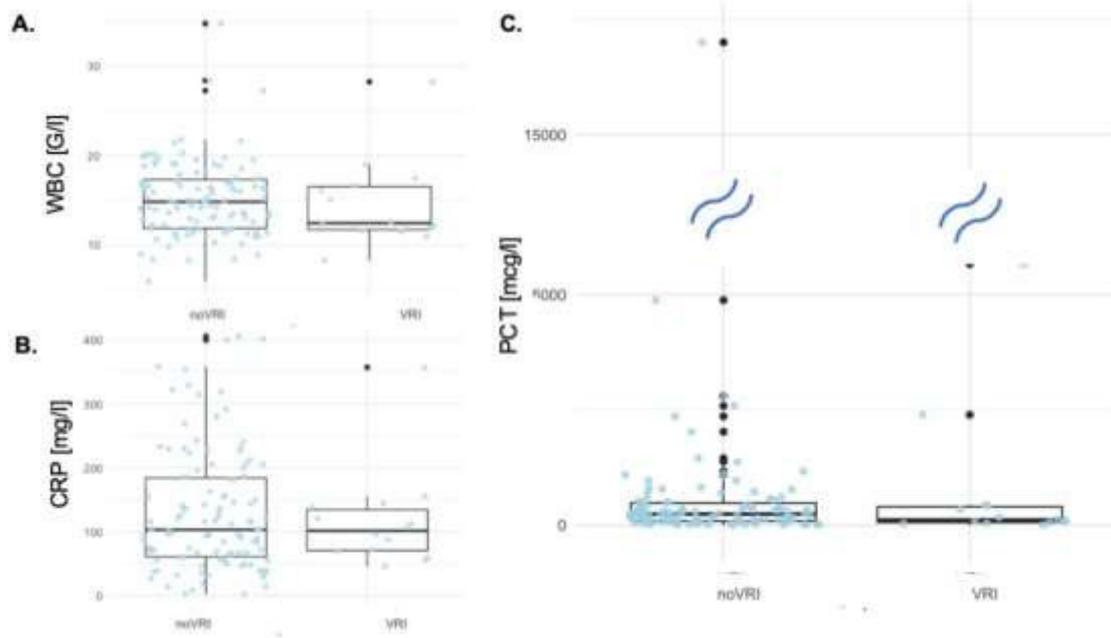
Results

Between both groups, WBC and CRP were similar (WBC: 15.13 G/L and 14.55 G/L, $p=0.68$ and CRP: 115.93 mg/l and 129.44 mg/l, $p=0.56$ in the group VRI and no-VRI, respectively) (Figure 1, panel A and B). In the group VRI, PCT was low and significantly lower than in the group no-VRI (0.16 ug/l and 2.61ug/l, $p=0.03$ in the group VRI and no-VRI, respectively) (panel C). WBC in CSF were similar between groups (710.14/ul and 675.16/ul $p=0.93$ in the group VRI and no-VRI, respectively).

Conclusion

We are able to show in our study population that serum PCR and PCT were not significantly different in patients with true VRIs (microbiologically confirmed) compared our control group ("no-VRI"). Therefore, the routine determination of those parameters for screening ventriculostomy-related infections caused by EVD in neurosurgical ICU patients with hemorrhagic stroke should be carefully evaluated.

Fig 1



Schädelhirntrauma und Kranioplastie/*Traumatic brain injury and cranioplasty*

V258

Sterblichkeitsrate – Qualitätsindikator in der Neurointensivmedizin? *Mortality rate – indicator of quality in the neurological intensive care?*

U. Planitzer¹, K. Gaber¹, S. Rasche², D. Lindner¹, J. Meixensberger¹

¹Universitätsklinikum Leipzig, Klinik und Poliklinik für Neurochirurgie, Leipzig, Germany

²Universitätsklinikum Leipzig, Klinik und Poliklinik für Anästhesiologie und Intensivtherapie, Leipzig, Germany

Objective

In the quality analysis of acute brain diseases such as stroke, subarachnoid hemorrhage or traumatic brain injury mortality often is given as an indicator of treatment quality.

Against the background of a constantly growing self-determination, the number of patients with living wills is increasing and subsequently, a decision to withdraw life-sustaining treatment is made in cooperation with the relatives.

In this context, the question arises to what extent death can be evaluated as a suitable quality parameter for possible therapeutic success.

The aim of this retrospective monocentric study was to investigate the number of deaths as a result of treatment de-escalation with regard to neurosurgical diseases.

Methods

The cases of death in neurosurgical patients in the intensive care unit (ICU) were analysed in the period between January 2017 to June 2019.

The first step was to investigate how many patients died during the study period and how large their share was in relation to the total disease specific number of neurosurgical patients treated in the ICU.

In a further step an analysis was performed with regard to the main diagnoses intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH) and traumatic brain injury (TBI) over the same period. The individual course of treatment was worked out with regard to a possible therapy de-escalation. Finally, an investigation was carried out to determine when a therapy de-escalation occurred.

Results

A total of 1531 ICU patients (608 patients with ICH, 220 patients with SAH, 703 patients with TBI) were included in our analysis. Overall 176 patients (11,5 %) died during time course. Mortality rates were 14,3 % for ICH, 13,2 % for SAH and 8,5 % for TBI.

The individual course of treatment was worked through for the patients who had passed away and finally a division into five different groups or decision paths was made with regard to a possible therapy de-escalation.

In 88 cases (50 %), the treatment was de-escalated during the course, with the time of de-escalation varying from day 0 to day 71.

60 % of patients with ICH, 34 % with SAH and 42 % with TBI had their treatment de-escalated.

In almost one fifth of these cases, death could have been prevented from a medical point of view.

Conclusion

Mortality as an indicator of treatment quality only appears to be appropriate if the proportion of patients with therapy de-escalation is taken into account.

Wirbelsäule mixed topics/*Spine mixed topics*

V259

Intrakranielle Komplikationen nach wirbelsäulenchirurgischen Eingriffen *Intracranial complications after spinal surgery*

H. Allouch, K. Abu Nahleh, K. Mursch, M. Shousha, M. Alhashash, H. Boehm

Zentralklinik Bad Berka, Wirbelsäulenchirurgie/Neurochirurgie, Bad Berka, Germany

Objective

Intracranial complications after spinal surgery are rare but potentially life-threatening. Beside intracranial haemorrhage (ICH) and subdural effusion, both due to a significant loss of cerebrospinal fluid (CSF), cerebral ischemia may complicate the postoperative course after spinal surgery

Methods

Retrospective study of cases with intracranial complications after spinal surgery treated in our institution between January 2012 and December 2018 with analysis of demographic, clinical, radiographic, treatment and outcome data

Results

Our investigation revealed 23 patients with cerebral ischemia, 10 patients with ICH and 2 with subdural effusion. Incidence of stroke and ICH after spinal surgery was 0.26% and 0.0657% respectively. The mean age of the 21 female and 14 male patients was 69 years. A CSF-loss was evident in all cases of ICH or subdural effusion and 17% of cerebral ischemia. 80% of patients with bleeding and 78% with ischemia suffered from arterial hypertension. In 6 patients out of the ischemic population a history of stroke or TIA was described while 5 had a history of cancer. 74% of the strokes were located in the territory of the middle cerebral artery. In the ICH-group, 6 patients were treated conservatively while 3 required CSF-diversion measure and in 3 cases lumbar revision was necessary. In the ischemia-group rT-PA was used in one case locally and in one patient systemically, a thrombectomy was performed in another. Out of the ICH-group 8 patients could be discharged with mild or no neurologic symptoms, 3 patients suffered from significant deterioration while one patient died due to symptoms of brain stem compression. In the ischemia-group 14 patients showed complete recovery, in 5 cases significant deficits persisted whereas 4 patients died

Conclusion

Despite a very low complication rate, due to the large number of operated cases, we were able to present one of the largest series in the literature. It can be supposed that intracranial hypovolemia due to a significant CSF-loss may induce brain sagging which may promote ICH due to stretching of cortical bridging veins. After intentionally or inadvertently opening of the dura a watertight closure should be attempted. Patients with intraoperative CSF-loss should be under closely supervision in the postoperative course. ICH or cerebral ischemia must be considered in every patient with neurological deterioration after spinal surgery. A high index of suspicion is mandatory for early recognition and to prevent fatal outcome.

Wirbelsäule mixed topics/*Spine mixed topics*

JM–JNS05

Gesundheitsbezogene Lebensqualität nach mikroskopischer Totalentfernung von spinalen intramedullären Ependymomen mit sicherer und präziser Strategie in einer 3-jährigen prospektiven Studie mit einem einzigen Institut

Health-related quality of life after microscopically total removal of spinal intramedullary ependymomas with safe and precise strategy in a single-institute 3-year prospective study

Y. Nakanishi¹, K. Naito¹, T. Yamagata², K. Ohata¹, T. Takami¹

¹Osaka City University, Department of Neurosurgery, Osaka, Japan

²Osaka City General Hospital, Department of Neurosurgery, Osaka, Japan

Objective

A single-institute, 3-year, prospective study was conducted to examine HRQOL after microscopically total removal of spinal intramedullary ependymomas with a safe and precise strategy.

Methods

A cohort of 20 patients with a possible diagnosis of spinal intramedullary benign ependymomas was recruited. This study included those patients who underwent microscopically total removal of the tumor and for whom the pathological diagnosis was verified as benign ependymoma of World Health Organization grade 2. A final total of 16 patients (average age 48.7 years) was eligible for study analysis. Careful assessment was performed for all patients before and 6–12 months after surgery. The short-form 36 Health Survey (SF-36) was used to assess HRQOL, with the surveyor recording answers as reported by the individual patient.

Results

Functional outcomes appeared satisfactory or acceptable with minimal surgery-related complications. Average total HRQOL score was 431.1 before surgery and was maintained at 434.2 at 6–12 months postoperatively. Patients with mild functional symptoms preoperatively tended to demonstrate a higher total HRQOL score preoperatively compared with patients showing moderate to severe functional symptoms preoperatively. A strong correlation was noted between postoperative functional conditions and preservation of HRQOL.

Conclusion

Microscopically total removal of spinal intramedullary ependymoma under a safe and precise strategy appears justifiable in preventing progressive aggravation of HRQOL.

Fig 1

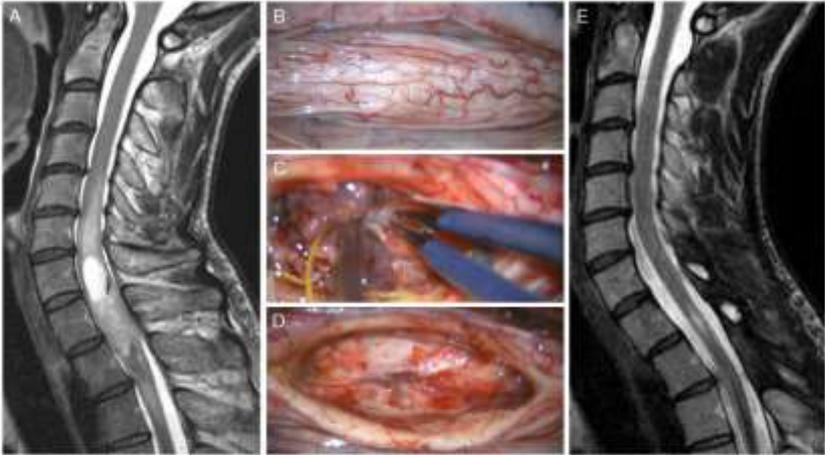
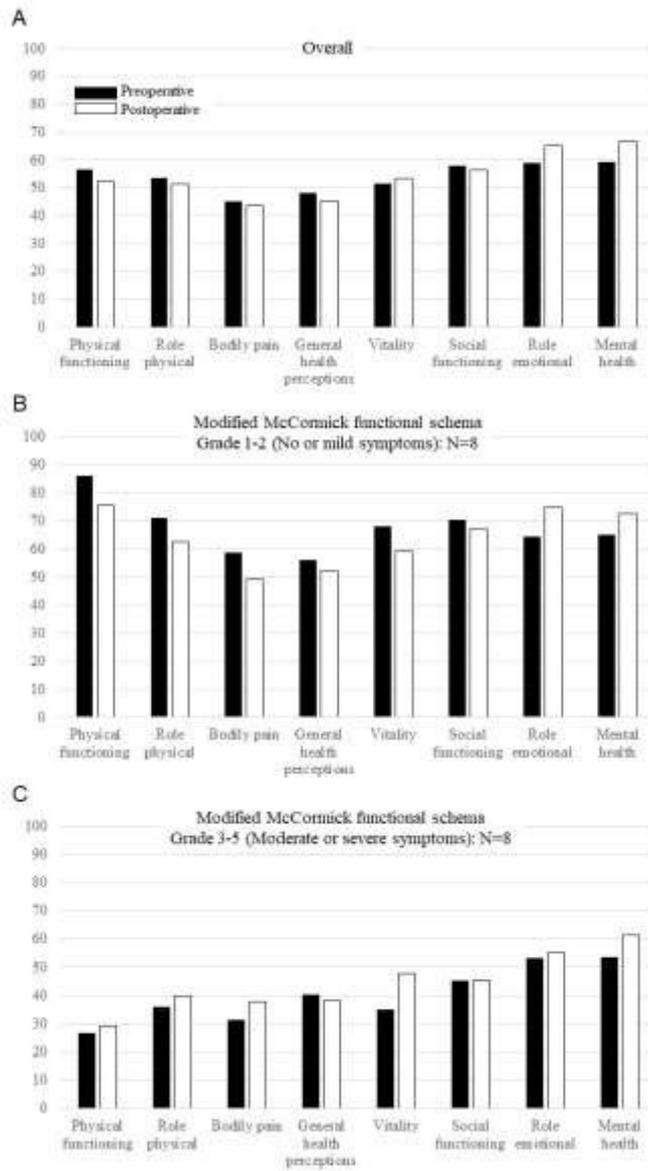


Fig 2



Wirbelsäule mixed topics/*Spine mixed topics*

V260

Primäre Knochentumore der Wirbelsäule – Behandlungsempfehlung basierend auf einer Kohortenstudie *Primary bone tumours of the spine – proposal for treatment based on a single-centre experience*

N. Lange¹, A. K. Jörger¹, A. Wagner¹, Y. M. Ryang¹, F. Liesche², B. Meyer¹, J. Gempt¹

¹Technische Universität München, Neurochirurgie, München, Germany

²Technische Universität München, Neuropathologie, München, Germany

Objective

Primary bone tumours (PBTs) of the spine are considered to be a rare disease. They represent less than 0.2% of all newly diagnosed tumours. The aim of this study was to report a large contemporary single-center series of PBTs of the spine and review the concepts of management.

Methods

We identified 92 patients (59 male, 33 female) receiving surgery for PBTs from January 2007 to August 2019. We analysed the patients' clinical characteristics, comorbidities, surgical management, and adjuvant/neoadjuvant strategies. Overall survival and outcome were measured using the Karnofsky performance index (KPI) at intervals of three months and six months, and then one-, three-, and five years postoperatively.

Results

The median patient age was 46 (ranging from 7 to 80). About 14.6% were younger than 18 years. A total of 50 patients suffered from benign lesions (18 haemangiomas, 14 osteoidosteomas, 9 aneurysmatic bone cysts, 4 osteoblastomas, 3 fibrous bone cell dysplasias, 1 enchondroma, 1 fibroma), 40 had malignant lesions (15 chordomas, 8 chondrosarcomas, 8 osteosarcomas, 7 ewing-sarcomas, 2 fibrosarcomas), and two were semi-malignant lesions (giant cell tumours).

The following symptoms were observed: local pain (97%), pareses (19%), dysesthesia (25%), and myelopathy (13%). Overall 73% showed improvement of symptoms directly after surgery. We performed 145 surgical procedures (50 in the cervical spine, 46 thoracic, 28 lumbar, and 21 sacral). In 65%, complete resection of the tumour was achieved. Of these, 22% suffered a recurrence of the tumour during the follow-up period (mean 417 days, 10–3172 days" range). The five-year mortality rate was 12% (3% after complete resection vs 25% after subtotal resection). Instrumented spinal fusion was needed in 51%.

Conclusion

PBTs mostly lead to local pain, dysesthesia, and pareses. Complete resections are often possible and result in better survival rates. Nevertheless, overall recurrence and mortality rates are high. Decision making strategies based on 92 cases were reported.

Wirbelsäule mixed topics/*Spine mixed topics*

V261

Operative Therapie bei Spondylodiszitis des älteren Menschen *Surgical treatment of spondylodiscitis in the elderly*

I. Janssen^{1,2}, E. Shiban³, J. Gempt¹, A. K. Jörger¹, B. Meyer¹

¹Klinikum rechts der Isar München, Abteilung für Neurochirurgie, München, Germany

²Genfer Universitätsspitaler, Abteilung für Neurochirurgie, Genf, Switzerland

³Universitätsklinikum Augsburg, Abteilung für Neurochirurgie, Augsburg, Germany

Objective

Due to ageing society the incidence of pyogenic spondylodiscitis is still rising. Whereas surgical treatment for spondylodiscitis in general is more and more accepted as treatment of choice, there is not much known about the prognosis of spondylodiscitis in the elderly. Aim of the study was to assess the incidence, clinical course and outcome after surgical treatment of elderly patients.

Methods

We performed a retrospective analysis of our clinical database. All patients suffering from spondylodiscitis between January 2006 and January 2018 were included. We assessed clinical findings, laboratory tests, treatment and outcome comparing patients of an of 70 years or older with patients younger than 70 years.

Results

In the defined period 454 patients were operated for pyogenic spondylodiscitis (male n= 289, female n= 165). We identified 213 patients aged 70 years or older (group 1) with a mean age of 76.78 +/- 5.56 years (range 70-94yrs). 241 patients were younger than 70 years (group 2) with a mean age of 58.35 +/- 10.44 years (range 17-69 yrs). Distribution of localization of discitis was similar in both groups. There was also no significant difference between the duration of hospitalization (group 1: 28.9 +/- 19.27 days; group 2: 24.83 days +/- 17.64 days). The majority of patients was cured, respectively 8 patients sustained a recurrence of infection.

Conclusion

Surgical treatment of the elderly population suffering from spondylodiscitis is safe and not associated with a significantly worse outcome compared to the younger patient group.

Wirbelsäule mixed topics/*Spine mixed topics*

V262

Erhöhte Detektion des FAS-Ligand im Liquor bei Patienten mit degenerativer zervikaler Myelopathie – ein Hinweis auf Apoptose als Teil der Pathophysiologie

Increased detection of FAS ligand in cerebrospinal fluid in patients with degenerative cervical myelopathy – an indication of apoptosis as part of pathophysiology

C. Blume¹, L. O. Brandenburg², H. R. Clusmann³, V. Mainz⁴, A. Riabikin⁵, K. Jütten³, C. A. Mueller³

¹Rheinisch-Westfälische Technische Hochschule Aachen, Neurochirurgie, Aachen, Germany

²Rheinisch-Westfälische Technische Hochschule Aachen, Institut für Anatomie und Zellbiologie, Aachen, Germany

³Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neurochirurgie, Aachen, Germany

⁴Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Psychiatrie, Aachen, Germany

⁵Rheinisch-Westfälische Technische Hochschule Aachen, Klinik für Neuroradiologie, Aachen, Germany

Objective

Apoptosis plays an important role in determining neurological outcome in degenerative cervical myelopathy (DCM) based on clinically relevant animal models and cadaver studies. These show that FAS mediated apoptosis plays a role in demyelination and axonal dysfunction, leading to the development of neurological deterioration in DCM. The aim was to detect FAS ligand (FASL) in CSF, in vivo in patients with DCM

Methods

Patients with DCM and indication for surgery were included. Patients were monitored for neurological symptoms (NDI/mJOA). CSF samples were taken pre- and 3 months postoperatively. A control group of patients with thoracic abdominal aortic aneurysm surgery (TAAA-group), who needed a lumbar drain for intraoperative CSF pressure monitoring was established. The control group was monitored to exclude neurological signs of DCM (NDI/mJOA). CSF samples were taken preoperatively. The samples were evaluated via ELISA. Protein-concentrations of FAS ligands (FASL) were measured in CSF pg/ml

Results

Overall 21 patients (mean age 63y) and 32 controls (mean age 60 years; $p=0.411$) were included. In 21 cases FASL was preoperatively examined, in 8 patients postoperatively. Preoperative clinical scores: mJOA DCM group 10.15 ± 2.9 , TAAA group 17.3 ± 1.2 ($p<0.001$); NDI DCM group 45.2 ± 21.7 , TAAA group 5.6 ± 9.0 ($p<0.001$). Significant differences of preoperative concentrations of FASL were detected in CSF: DCM group 179.5 ± 73.9 pg/ml, TAAA group 138.5 ± 35.1 pg/ml ($p=0.009$). In DCM patients, the preoperative FASL concentrations were reduced in each patient (179.5 ± 73.9 pg/ml) versus postoperative values (73.5 ± 30.5) but did not reveal statistically significant differences ($p=0.074$)

Conclusion

FASL initiates cytokine production by binding to FAS on microglia or astrocytes, which also lead to cell death in the lesion zone in animal model and cadaver study. This is the first time that FASL could be detected in DCM patients. We hypothesize, that blockade of FASL could be a therapeutic target in DCM to prevent apoptotic cell death. A larger postoperative cohort is necessary to determinate how far surgery in DCM is beneficial concerning FASL mediated cell death.

Wirbelsäule mixed topics/*Spine mixed topics*

V263

Verbesserung der Stammzelltherapie nach thorakaler Rückenmarksverletzung durch die Gabe von Sonic Hedgehog

Enhancement of stem cell therapy after thoracic spinal cord injury by the administration of sonic hedgehog

A. Younsi¹, H. Zhang¹, M. Tail¹, G. Zheng¹, A. Harms¹, J. Roth¹, M. Hatami², T. Skutella², A. W. Unterberg¹, K. Zweckberger¹

¹Universitätsklinikum Heidelberg, Neurochirurgie, Heidelberg, Germany

²Ruprecht-Karls-Universität Heidelberg, Institut für Anatomie und Zellbiologie, Heidelberg, Germany

Objective

Traumatic spinal cord injury (SCI) is a devastating event with limited functional recovery. As a potential treatment approach, neural precursor cell (NPC) transplantation has shown beneficial effects on neuroregeneration. However, survival and differentiation of transplanted NPCs and thus functional recovery remain limited. The Sonic Hedgehog (SHH) pathway might play a protective role after CNS injury. We, therefore, investigated the effects of intrathecal SHH administration on transplanted NPCs as well as the impact of a combined treatment approach on neuroregeneration after thoracic SCI in rats.

Methods

37 Wistar rats were subjected to thoracic clip-contusion/compression SCI at Th10. Animals were randomized into five treatment groups (SHH only, NPC only, SHH+NPC, Vehicle, Sham). NPCs were injected into the spinal cord of immunosuppressed rats seven days after SCI. During the same surgery, an osmotic pump was implanted and the intrathecal administration of SHH was initiated and continued for seven days. To assess functional recovery, the BBB score, the Gridwalk test as well as the CatWalk gait analysis were performed weekly. Animals were sacrificed 38 days after SCI and immunohistological analyses were conducted. Results were compared between groups and statistical analysis was performed ($p < 0.05$ was considered significant).

Results

The administration of SHH alone led to significant improvements in neuroinflammation (less invasion of T-lymphocytes, M1-macrophages and microglia) as well as astrogliosis while the impact of NPC-transplantation alone on such postinjury changes was limited. However, in contrast to SHH only animals, NPC only animals showed improved functional recovery when compared to Vehicle animals. When SHH-administration and NPC-transplantation were combined, neuroinflammation as well as the rates of apoptosis, and preserved tissue were significantly improved compared to each individual treatment. Moreover, the addition of SHH-administration to NPC-transplantation led to higher survival of NPCs and increased NPC-differentiation into adult neurons and oligodendrocytes. Finally, with the combined treatment approach, animals showed the highest functional recovery 38 days after SCI.

Conclusion

In our study, a combined treatment approach with intrathecal SHH-administration and NPC-transplantation showed the highest improvements of neuroregeneration on the cellular as well as the functional level 38 days after thoracic SCI.

Lymphome und Akustikusneurinome/*Lymphomas and acoustic neurinomas*

JM–JNS06

Zirkulierender Biomarker für Glioblastome und primäre Lymphome des zentralen Nervensystems – next generation sequencing von kleinen nicht-kodierenden RNA

Circulating biomarker for glioblastoma and primary central nervous system lymphoma – next-generation sequencing of small noncoding RNA

S. Onishi^{1,2}, F. Yamasaki¹, Y. Nishiyama³, M. Takano¹, U. Yonezawa¹, A. Taguchi¹, H. Tahara³, K. Sugiyama⁴, K. Kurisu¹

¹Hiroshima University Hospital, Neurosurgery, Hiroshima, Japan

²National Hospital Organization Kure Medical Center and Chugoku Cancer Center, Neurosurgery, Hiroshima, Japan

³Hiroshima University Hospital, Cellular and Molecular Biology, Hiroshima, Japan

⁴Hiroshima University Hospital, Clinical Oncology and Neuro-oncology Program, Hiroshima, Japan

Objective

Glioblastoma (GBM) and Primary Central Nervous System Lymphoma (PCNSL) are common intracranial malignant tumors. The treatment of these tumors is quite different, accurate preoperative differentiation is the essential of clinical relevance. However, they sometimes present similar radiological findings and diagnoses could be difficult without surgical biopsy. For improving the current management, development of non-invasive biomarkers are desired. In this study, we explored the differently expressed circulating small noncoding RNA (sncRNA) in serum for specific diagnostic tool of GBM and PCNSL.

Methods

Serum samples were obtained from three groups: 1) GBM patients (N=26), 2) PCNSL patients (N=14), 3) healthy control (N=114). Written informed consent to participate in the study were obtained. The total small RNAs were extracted from serum by using the QIAGEN® kit. The whole expression profiles of serum sncRNAs were measured using Next-Generation Sequencing System (Thermo Fisher, Ion S5). We analyzed serum levels of sncRNAs (15-55 nt) in each serum samples. The difference of sncRNAs expression profile among three groups were compared. Data analysis was performed by logistic regression analysis followed by leave-one-out cross-validation (LOOCV). The accuracy of diagnostic models of sncRNAs combination were evaluated by receiver operating characteristic (ROC) analysis.

Results

We created the combination models using three sncRNA in each models based on the logistic regression analysis. The model 1 (based on sncRNA-X1, X2 and X3) enabled to differentiate GBM patients form healthy control with a sensitivity of 92.3% and a specificity of 99.2% (AUC : 0.993). The model 2 (based on sncRNA-Y1, Y2 and Y3) enabled to differentiate PCNSL patients form healthy control with a sensitivity of 100% and a specificity of 93.9% (AUC: 0.984). The model 3 (based on sncRNA-Z1, Z2 and Z3) enabled to differentiate GBM patients form PCNSL patients with a sensitivity of 92.3% and a specificity of 78.6% (AUC: 0.920).

Conclusion

We found three diagnostic models of serum sncRNAs as non-invasive biomarkers potentially useful for detection of GBM and PCNSL from healthy control, and for differentiation GBM from PCNSL.

Lymphome und Akustikusneurinome/*Lymphomas and acoustic neurinomas*

V264

Klinische Präsentation, Behandlung und Therapieergebnisse von primär duralen Lymphomen *Clinical presentation, management and outcome in primary dural lymphomas*

P. Karschnia^{1,2}, J. T. Jordan², T. T. Batchelor², B. Shaw², S. F. Winter², F. J. Barbiero³, L. D. Kaulen³, N. Thon¹, J. Tonn¹, A. J. Huttner⁴, R. K. Fulbright⁵, J. Loeffler⁶, J. Dietrich⁷, J. M. Baehring³

¹Klinikum der Ludwig-Maximilians-Universität München, Klinik für Neurochirurgie, München, Germany

²Massachusetts General Hospital, Klinik für Neurologie, Boston, MA, United States

³Yale School of Medicine, Clinic for Neurology, New Haven, CT, United States

⁴Yale School of Medicine, Department of Neuropathology, New Haven, CT, United States

⁵Yale School of Medicine, Department of Radiology, New Haven, CT, United States

⁶Massachusetts General Hospital, Clinic for Radiotherapy, Boston, MA, United States

⁷Massachusetts General Hospital, Clinic for Neurology, Boston, MA, United States

Objective

Primary dural lymphoma (PDL) represents a rare subtype of primary CNS lymphomas arising from the dura mater. Population-based incidence data is scarce and clinical experience is limited. We aimed to determine relative incidence, therapeutic approaches, and survival in primary dural lymphomas.

Methods

We retrospectively searched the institutional databases of the Divisions of Neuro-Oncology at two large academic cancer centres for patients with primary CNS lymphoma (n=316). In cases with pathologically confirmed dural lymphoma and no evidence of parenchymal cerebral or systemic involvement, we collected demographic and histological information; diagnostic findings; therapeutic approaches; and outcome.

Results

We identified twenty patients treated for PDL, representing 6.3% among all patients with primary CNS lymphomas. PDL mostly arose from the cranial dura mater. The following histologies were encountered: diffuse large B-cell lymphoma (10/20 patients); marginal zone lymphoma (6/20); follicular lymphoma (2/20); undefined B-cell non-Hodgkin lymphoma (1/20); and T-cell non-Hodgkin lymphoma (1/20). On imaging studies, all patients had dural-based tumors with vivid contrast enhancement. Lesions displayed high signal on diffusion-weighted imaging (DWI)-MRI and median diffusion coefficient (ADC)-ratio was $667 \pm 26 \text{ mm}^2/\text{s}$. CSF analysis and symptoms were unspecific, and diagnosis rested upon tissue analysis. Localized (surgery; stereotactic or involved-field radiation therapy) or systemic therapeutic approaches (steroids; chemotherapy) were provided. Median overall survival was not reached after five years. Three patients were deceased at database closure due to tumor progression. Tumor resection other than biopsy positively correlated with improved overall survival ($p = 0.044$).

Conclusion

PDL is a rare variant of primary CNS lymphomas. Outcome may be excellent with multimodal therapeutic approaches. Aggressive surgery may form the basis for a favourable outcome in selected cases.

Lymphome und Akustikusneurinome/*Lymphomas and acoustic neurinomas*

V265

Einfluss von präoperativem Kortison auf die Diagnoserate bei primären ZNS Lymphomen *Diagnostic yield of biopsy in corticosteroid pretreated patients with primary central nervous system lymphoma*

F. Scheichel¹, D. Pinggera², B. Kiesel³, T. Rossmann⁴, B. Popadic¹, M. Weber⁵, M. Kitzwögerer⁶, K. Geissler⁷, A. Dopita⁸, S. Oberndorfer⁹, C. F. Freyschlag², G. Widhalm³, K. Ungersböck¹, F. Marhold¹

¹Universitätsklinikum Sankt Pölten, Neurochirurgie, St. Pölten, Austria

²Medizinische Universität Innsbruck, Neurochirurgie, Innsbruck, Austria

³Medizinische Universität Innsbruck, Neurochirurgie, Wien, Austria

⁴Sozialmedizinisches Zentrum Ost - Donauspital, Neurochirurgie, Wien, Austria

⁵Karl Landsteiner Privatuniversität für Gesundheitswissenschaften, Forschungsmanagement, Krems, Austria

⁶Universitätsklinikum Sankt Pölten, Pathologie, St. Pölten, Austria

⁷Sigmund Freud Privatuniversität, Wien, Austria

⁸Sozialmedizinisches Zentrum Ost - Donauspital, Pathologie und Mikrobiologie, Wien, Austria

⁹Universitätsklinikum Sankt Pölten, Neurologie, St. Pölten, Austria

Objective

Corticosteroid treatment (CST) prior to biopsy may hinder histopathological diagnosis in primary central nervous system lymphoma (PCNSL). Therefore, preoperative CST in patients with suspected PCNSL should be strictly avoided if clinically possible. The aim of this study was to analyze the difference in the diagnostic yield of PCNSL patients with and without preoperative CST.

Methods

A retrospective study including all immunocompetent patients diagnosed with an intracranial PCNSL between 1/2004 and 9/2018 at four specialized neurosurgical centers in Austria, was conducted. Diagnostic yield was defined as successful diagnosis of PCNSL without the need for repeat biopsy.

Results

A total of 143 patients could be included in this study. There was no statistically significant difference in the diagnostic yield of biopsy in patients with and without preoperative CST with 95.7% (67/70) and 97.3% (71/73) respectively ($p=0.676$). Preoperative tapering and pause of CST led to significant delay of the median timespan from first consultation to surgery with 18 days in patients without CST or ongoing CST to 24 days in patients with paused CST ($p=0.023$). Time to surgery over 45 days showed significant decrease of overall survival in multivariate regression.

Conclusion

No statistically significant difference in the diagnostic yield of biopsy in PCNSL patients with and without preoperative CST was found. Tapering and pause of preoperative CST led to significant delay of surgery and subsequently diagnosis and therapy which might result in worse outcome. In our opinion, surgeons therefore should try to keep the diagnostic delay to a minimum as the diagnostic yield still seems to be sufficiently high in patients with preoperative CST.

Lymphome und Akustikusneurinome/*Lymphomas and acoustic neurinomas*

V266

Klinisches und radiographisches Outcome nach radiochirurgischer Einzeit-Bestrahlung von Akustikusneurinomen am CyberKnife

Clinical and radiographic outcome in a large cohort of acoustic neuromas treated with single-fraction CyberKnife radiosurgery

F. Loebel¹, C. Senger², J. Garduno-Jaenz², G. Acker¹, M. Kufeld^{1,2}, V. Budach², P. Vajkoczy¹, A. Conti^{1,3}

¹Charité – Universitätsmedizin Berlin, Neurochirurgie, Berlin, Germany

²Charité – Universitätsmedizin Berlin, Radioonkologie, Berlin, Germany

³University of Messina, Abteilung für Neurochirurgie, Messina, Italy

Objective

Stereotactic radiosurgery of acoustic neuromas (ACN) is supposed to present a non-invasive treatment alternative to microsurgical resection with a low risk profile. However, longterm tumor control and the risk of decrease in auditory function or new-onset facial paresis still need to be evaluated. We here present the clinical and radiographic outcome in a large series of ACN treated with Cyberknife stereotactic radiosurgery.

Methods

We retrospectively analyzed 232 patients treated for ACN of all KOOS grades with single-fraction CyberKnife stereotactic radiosurgery in a single institution between 2011 and 2018. All patients underwent multislice computed tomography and 3D contrast enhanced and CISS MR imaging, followed by treatment planning using the Accuray software Clinical as well as treatment associated parameters were collected together with radiographic follow up.

Results

Median age of the population was 61.9 yrs (range 18.7 – 93.9 yrs). Median follow-up was 45.8 months (range 12.3 – 88.7 months). The population included 44 Koos grade T1 (18.9%), 95 T2 (40.9%), 82 T3 (35.3) and 11 T4 (4.7%) tumors. Single-fraction doses between 12.5 and 13.5 Gy (median 13 Gy) were applied to the 70% isodose line. Median GTV irradiated was 0.58 (range 0.03 – 6.77) cm³. Mean dose applied was 15.7 Gy (range 14.05- 16.75 Gy). Median conformality was 1.2 (range 1.06 – 3.56). Auditory function was impaired pre-interventional in 203 cases (87.5%). Post-CK, hearing improved in 6 cases (2.6%), remained stable in 208 cases (89.6%) and decreased slightly in 18 patients (7.8%). No case of complete loss of auditory function was seen in patients with residual hearing pre-interventionally. 20 patients (8.6%) presented with facial paresis (FP) prior to radiation therapy. New-onset-FP was seen in an additional 7 patients (3.0%), with only 2 cases of severe FP (0.1%), requiring surgical intervention. Tumor control was achieved in 219 cases (94.4%) with substantial or partial response in 32 (13.7%) and 107 (46.1%) patients respectively and stable disease (no change) in 79 patients (34.0%). Adverse effects remained rare. Symptoms of trigeminal neuralgia occurred in 5 cases (2.2%). Focal edema was seen in 13 cases (5.6%), with only three cases (1.3%) requiring steroid treatment.

Conclusion

In our large cohort of ACN of all KOOS grades, CyberKnife radiosurgery provides satisfying tumor control and preserves hearing function with low rates of new-onset FP or other adverse effects.

Lymphome und Akustikusneurinome/*Lymphomas and acoustic neurinomas*

V267

Vergleichende Outcomeanalyse zwischen halb-sitzender und lateraler Position bei einer großen Serie von 544 Vestibularisschwannomen

Comparative outcome analysis between semi-sitting and lateral decubitus positions in a large series of 544 vestibular schwannomas

G. Schackert, M. Kowalski, G. Reiss, S. B. Sobottka, D. Martin, T. Juratli

Universitätsklinikum Carl Gustav Carus Dresden, Klinik für Neurochirurgie, Dresden, Germany

Objective

Vestibular schwannomas (VS) are surgically challenging tumors. Due to the tumor adherence to the cochlear and the facial nerves, gross total resection is difficult. As the debate regarding the best position used for tumor resection – lateral decubitus vs semi-sitting position – continues, the goal of our study is to compare the outcome results of VS patients with lateral decubitus vs semi-sitting position.

Methods

Data were analyzed from 544 patients with VS who underwent surgical resection in our institution. The majority of patients (77%) had T3 and T4 tumors. The patient cohorts were divided in three decades: 1991-1999 (n=103), 2000-2009 (n=210) and 2010-2019 (n=231). Before 2010, all patients were treated in the lateral decubitus position. After 2010, patients with a patent foramen ovale (n=68) underwent resection in the lateral decubitus, while the semi-sitting position was performed in patients without a patent foramen ovale (n=163). The majority of the latter had a T3 or T4 tumor (n=143). We utilized data analysis with regard to the duration of surgery, intraoperative blood loss and functional outcome of the facial and the cochlear nerves, based on the House-Brackmann Grading System and the Gardner Robertson Scale.

Results

The functional outcome of the facial nerve improved significantly over the three decades (HB 1-2: 59.8%, 78.9%, 81.7%; $p < .001$; HB 1-3: 81.4% 90.4%, 92.7%). Also, a higher percentage of hearing preservation was achieved (23.3%, 46.8%, 50.5%). For large T3 and T4 tumors, the semi-sitting position was superior to the lateral (HB 1-2: 81.2 vs 74.5%). The same was found for hearing preservation for the whole group (43.3% vs 53.4%). Again for T3 and T4 tumors, the duration of the surgical procedure and blood loss were significantly different (lateral decubitus vs. semi-sitting: 328 vs 286 min ($p = .001$), 200 vs 150 ml) ($p < .001$), but not for T1 and T2 tumors. The rates of CSF leakage and wound infections were higher in the semi-sitting position (8.6% vs 2.9%, resp. 4.9% vs 2.9%). Pulmonary embolisms as a major risk for the semi-sitting position occurred in 4.3%. The postop mortality rate was 0.6% (1 patient).

Conclusion

There is a learning curve in VS surgery. The semi-sitting position facilitates surgery since it provides a clean surgical field and allows the preparation with both hands. Operative time and blood loss are significantly reduced; the functional outcome has been further improved. The risk of complications is slightly higher.

Lymphome und Akustikusneurinome/*Lymphomas and acoustic neurinomas*

V268

Evaluation eines spezifisch entwickelten EMG-Biofeedback Systems für die heimbasierte Therapie von Facialisparesen bei Patienten mit Vestibularisschwannomen

Evaluation of a custom-made EMG-biofeedback system for home-based treatment of postoperative facial palsy in vestibular schwannoma patients

K. Machetanz, J. Sandritter, M. Tatagiba, G. Naros

Universitätsklinikum Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

Objective

Maintaining facial nerve function is a major concern in vestibular schwannoma surgery. Despite the routine application of continuous intraoperative neuromonitoring, there is still a risk for a postoperative facial palsy limiting patient's postoperative quality of life dramatically. So far, facial rehabilitation depends on repetitive voluntary movements accompanied by physiotherapy. However, in the early rehabilitation state active movements are often restricted and, thus, restricting patient's motivation. In these situations, biofeedback of the facial electromyographic (EMG) signals enables the visual representation of the rehabilitation progress, even without visual movements of the facial muscles. In the present study, we evaluate a custom made EMG biofeedback system enabling cost-effective, home-based rehabilitation of postoperative facial palsy.

Methods

This prospective study enrolled 30 patients with and without a postoperative facial palsy within the first 5 days after surgery. The EMG biofeedback system consisted of Arduino®-based muscle sensors which were used to record, process and visualize the EMG activity of the affected and unaffected facial muscles on a screen. Finally, recorded EMG activity was correlated to the facial outcome as measured by the House and Brackman (H&B), Facial nerve grading scale 2.0 (FNG2) and the Sunnybrook scale (SUNNY).

Results

Detection of EMG activity was possible in all patients with sufficient quality to operate the biofeedback system. There was a good correlation between EMG activity of the zygomatic muscle and the H&B ($r= 0.56$; $p<0.01$) as well as the FNG2 ($r= 0.54$; $p<0.01$), respectively. However, there was no significant correlation between the EMG activity of the frontal muscle and these clinical measures.

Conclusion

The present study proves the feasibility of our EMG biofeedback device to detect facial muscle EMG activity in patients with facial palsy after vestibular schwannoma surgery. There is a good correlation between the electrophysiological measurements and the clinical outcome. This EMG activity can be used for home-based facial EMG biofeedback.

KI und Ethik in der Medizin/*AI and ethics in medicine*

V269

Automatische Detektion und Segmentierung von zerebralen Lymphomen mit einem Deep Learning Model auf der Basis von multiparametrischen MRT

Performance of an advanced deep learning model in fully automated detection and segmentation of primary cerebral lymphoma using multiparametric MRI

L. Goertz, J. Borggreffe, L. L. Caldeira, C. Hoyer, R. H. Goldbrunner, B. Krischek, K. R. Laukamp, L. Pennig

Universitätsklinikum Köln, Köln, Germany

Objective

Magnetic resonance imaging (MRI) is the imaging modality of choice for detection of primary cerebral lymphoma. After initiating therapy, follow-up MRI scans are necessary to evaluate treatment response. An automated detection and segmentation of the (residual) lymphoma would provide additional information for the clinician, in particular regarding an increasing workload and physician fatigue. The objective of this study was to evaluate a deep learning model (DLM) based on convolutional neuronal networks for automated detection and segmentation of primary cerebral lymphoma on multiparametric MRI.

Methods

Seventy-nine MRI scans (T1-/T2-weighted, T1-weighted contrast-enhanced (T1CE), T2-weighted FLAIR) from 51 patients with histologically proven primary cerebral lymphomas were selected for this study. Of these scans, six datasets of three patients were excluded due to MR artifacts and three datasets of three patients due to pronounced leukoencephalopathy (Fazekas III). Independent manual segmentations of the tumor core (on T1CE) and peritumoral edema (on FLAIR) by a neurosurgeon and a radiologist served as the ground truth. For this study, a three-dimensional convolutional neural network architecture based on DeepMedic (Biomedica, Singapore) was employed, which was originally established and trained for detection and segmentation of glioblastoma using five-fold cross validation (5-FCV). The DLM did not receive dedicated training for this study. Dice similarity coefficients were calculated to determine segmentation accuracy.

Results

The final data set consisted of 70 MRI scans (45 patients, mean age: 62.5 ± 13.6 years, 22 females). The detection sensitivity of the glioblastoma-trained DLM was 0.89. Compared to the ground truth, the DLM achieved a median dice coefficient of 0.71 for segmentation of tumor core (average size: 11.61 ± 12.87 cm³) and a dice coefficient of 0.74 for peritumoral edema (average size 76.32 ± 63.22 cm³), hence representing a high segmentation accuracy. There were no significant differences of detection and segmentation accuracies between initial and follow-up scans ($p > 0.05$).

Conclusion

Even though primary cerebral lymphoma is a complex and irregular tumor entity, the glioblastoma-trained DLM detects and segments primary cerebral lymphoma with acceptable accuracy on a heterogeneous data set without dedicated training.

KI und Ethik in der Medizin/*AI and ethics in medicine*

V270

Automatische Detektion und Segmentierung von intrakraniellen Aneurysmen in Patienten mit Subarachnoidalblutung durch ein Deep Learning Model

Performance of an advanced deep learning model in fully automated detection and segmentation of intracranial aneurysms in patients with subarachnoid haemorrhage

L. Goertz, J. Borggreffe, R. Shahzad, R. H. Goldbrunner, L. Pennig, B. Krischek

Universitätsklinikum Köln, Köln, Germany

Objective

Aneurysmal subarachnoid haemorrhage (aSAH) is a potentially life-threatening condition that requires early aneurysm embolization in order to prevent rebleeding. Initial diagnosis of the aneurysm is usually made by computed tomography angiography (CTA), however, misdiagnosis may occur, particularly in association with physician fatigue and lacking experience. Convolutional neural networks have proven great potential in performing diagnostic and analyzing tasks as assistance for clinicians. The objective was to develop a deep learning model (DLM) that detects and segments intracranial aneurysms fully automatically on CTA in patients with aSAH.

Methods

All patients received digital subtraction angiography to confirm the aneurysms. Sixty-eight patients with 79 aneurysms (2016-2017) served as the training cohort. Three DLMs with different architecture were trained using 5-fold cross-validation and their respective outputs were merged via an ensemble strategy (DLM-Ens). The DLM-Ens was evaluated on two independent validation cohorts (2010-2015): Cohort 1: 101 patients, 112 aneurysms, Cohort 2: 84 patients, 104 aneurysms. Independent manual segmentations of the aneurysms was performed in a voxel-wise manner by an experienced radiologist and a neurosurgeon and served as the ground truth.

Results

In the combined validation cohort, the detection sensitivity of the DLM-Ens for intracranial aneurysms was 0.82 (Cohort 1: 0.84, Cohort 2: 0.81) and the average number of false-positives per scan was 0.81 (Cohort 1: 0.78, Cohort 2: 0.82). The overall median dice coefficient was 0.75 (Cohort 1: 0.75, Cohort 2: 0.73), representing the segmentation accuracy. Detection sensitivity was 0.90 for aneurysms > 50 mm³ and 0.96 for aneurysms > 100 mm³. Aneurysm location (anterior/posterior circulation, $p=0.07$) and Fisher grade (grade ≤ 3 vs. grade 4; $p=0.33$) had no impact on diagnostic accuracy. There was a strong correlation between automated aneurysm segmentation and the ground truth, with a Pearson's correlation coefficient of 0.95 for volume and 0.78 for maximum aneurysm diameter.

Conclusion

The created DLM detects aneurysms with sufficient sensitivity and independent of aneurysm location and bleeding severity, hence, convolutional neuronal networks may provide a valuable adjunct for radiologists during emergency imaging of patients with SAH.

KI und Ethik in der Medizin/*AI and ethics in medicine*

V271

TMS-Rekrutierungskurve und Analyse der kortikalen Innervationsstille – sensitive Parameter zur Erkennung bevorstehender motorischer Defizite bei Hirntumorpatienten

TMS recruitment curve and cortical silent period analysis – a sensitive tool to detect imminent motor deficits in brain tumour patients

I. Bährend¹, M. Engelhardt², T. Rosenstock², H. Schneider², U. Grittner³, O. Schweizerhof³, R. Khakhar³, A. Zdunczyk², V. Schwarzer², P. Vajkoczy², T. Picht²

¹Charité Vivantes GmbH, Neurochirurgie, Berlin, Germany

²Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

³Charité – Universitätsmedizin Berlin, Biostatistik und Klinische Epidemiologie, Berlin, Germany

Objective

One of the challenges of tumor resection in motor eloquent areas is the individual risk assessment for a postoperative motor disorder. Previously, a predictive model was developed that permits objective evaluation of the risk prior to surgery based on topographical and neurophysiological data, derived from an investigation with navigated transcranial magnetic stimulation (nTMS). The aim of this study is the improvement of the prognostic power of the aforementioned model by inclusion of additional neurophysiological parameters.

Methods

Prospective data from 170 patients with malignant glioma in motor eloquent areas was collected and further investigated by topographical and neurophysiological nTMS parameters: Resting Motor Threshold (RMT), Recruitment Curve (RC) and Cortical Silent Period (CSP) bi-hemispherically prior to surgery. Motor function was quantified according to the British Medical Research Council Scale preoperatively as well as seven days and three months postoperatively.

Results

The univariate analysis confirmed the RMT ratio's predictive value ($p=0.008$) for the postoperative motor outcome after seven days with an increased number of patients. An association between a pathological CSP ratio and development of a new postoperative motor deficits after seven days was observed ($p=0.025$). A pathological RC Ratio was significantly associated with the preoperative motor status ($p=0.019$) as well as the postoperative deterioration of motor function after three months ($p=0.003$). Multiple regression analysis concluded that an abnormal RMT ratio was significantly associated with motor worsening in high risk patients after seven days.

Conclusion

To conclude, the present study was able to confirm an existing risk-stratification model for patients with motor eloquent brain tumors. RMT ratio is the most important distinguished predictor in the tractography based "high-risk group" for the postoperative motor outcome. Further, we identified a disturbed RC ratio as specific predictor for long-term motor impairments after surgery, compared to the RMT and CSP indexing short-term deficits.

KI und Ethik in der Medizin/*AI and ethics in medicine*

V272

Die Vorhersagegenauigkeit des Patientenoutcomes der aneurysmatischen Subarachnoidalblutung wird durch die Anwendung von modernen machine learning-Techniken mit traditionellen klinischen und radiologischen Kriterien nicht verbessert

Outcome prediction in aneurysmal subarachnoid haemorrhage is not improved by modern machine learning applications using traditional clinico-radiological features

M. Unteroberdörster¹, V. I. Madai², E. Zini^{3,2}, S. C. Brune¹, S. Wolf¹, P. Vajkoczy¹, D. Frey^{1,2}, N. F. Dengler¹

¹Charité – Universitätsmedizin Berlin, Klinik für Neurochirurgie, Berlin, Germany

²Charité – Universitätsmedizin Berlin, CLAIM - Charité Lab for AI in Medicine, Berlin, Germany

³Technical University Dublin, Dublin, Ireland

Objective

Numerous clinical, radiological and combined grading scales exist to describe the severity of aSAH and predict outcome. However, prognostic accuracy of scales is limited. We aimed to test whether the application of modern machine learning techniques by using traditional clinical and radiological features improves the predictive performance.

Methods

The single-institution database of 378 patients with aneurysmal subarachnoid hemorrhage was analyzed by inclusion of traditional clinico-radiological parameters: age, sex, pupillary state, presence of intracerebral hemorrhage (ICH), intraventricular hemorrhage (IVH), and / or subdural hemorrhage (SDH), aneurysm location (dichotomized anterior / posterior circulation) with respect to outcome prediction using the modified Rankin scale (mRS). Three different machine learning models were trained: ElasticNet logistic regression, Catboost boosted tree model and multilayer perceptron (MLP) as a neuronal layer example. Data was randomly assigned to training and test purposes in a 4:1 relation. Models were tuned with 5 cross-validations, and the analysis was repeated in 50 shuffles. Variable ranking was calculated by weights for ElasticNets, by shap values for Catboost and by Taylor-decomposition for MLP.

Results

Prognostic ability of poor patient outcome (mRS 3-6) was similar between traditional ElasticNets logistic regression (mean area-under-the-curve 0.74) and modern machine learning methods (Catboost: 0.77 und MLP=0.76). All three models identified GCS (AUC 0.7) as the most important predictor. Other variables of importance were age, ICH, and aneurysm location.

Conclusion

Modern methods like boosted tree and neuronal networks do not inevitably lead to better performances in outcome prediction using traditional clinico-radiological features. This may imply that new biomarkers are needed to reach clinically relevant performance values.

Fig 1

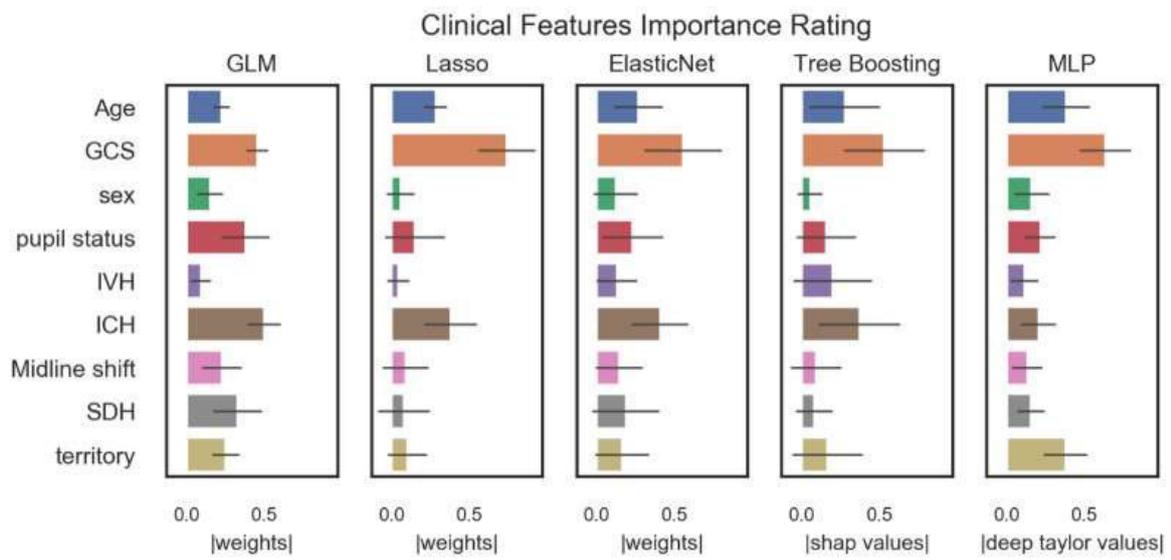
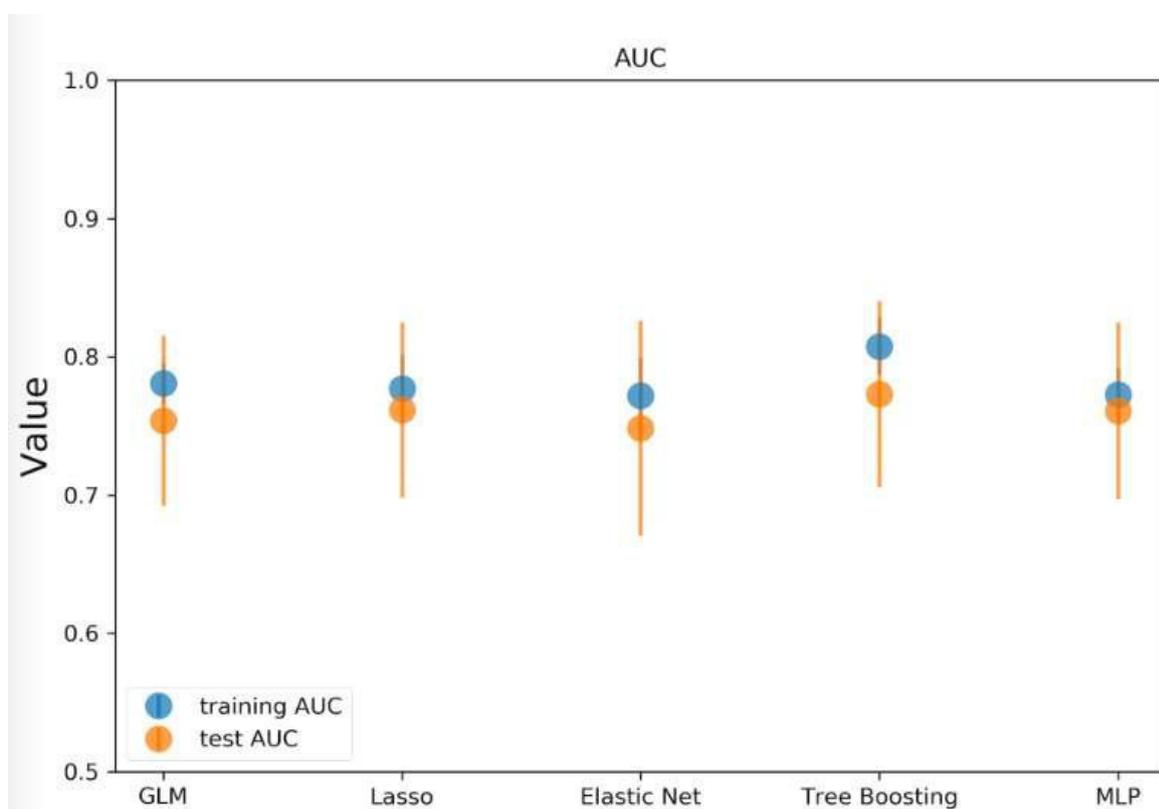


Fig 2



KI und Ethik in der Medizin/*AI and ethics in medicine*

V273

Die Entscheidungsfindung des Patienten im Rahmen der elektiven zerebralen Aneurysmaversorgung – Befangenheit durch die Erstberatung (z. B. "Anker-Effekt")?

Patients' decision-making in elective intracranial aneurysma treatment – bias of initial counselling (e.g. "anchoring effect")?

S. Siller¹, M. Kunz¹, J. Thorsteinsdottir¹, F. Dorn², T. Liebig², J. Tonn¹, C. Schichor¹

¹Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, Institut für Neuroradiologie, München, Germany

Objective

Interdisciplinary neurovascular boards (INVB) are deemed to find the optimum treatment modality in elective intracranial aneurysma repair (EIAR) for each individual patient. However, if risk estimation and prospect of therapeutic success are judged similar for microsurgical or interventional EIAR, the treatment decision is made by the patient after secondary counselling by both disciplines. A highly reputed determinant in this context is the so-called "anchoring effect" which describes the phenomenon that initial counselling drives the decision in favour of the first specialist who was contacted before INVB.

Methods

We analysed all patients with EIAR after INVB discussion at our interdisciplinary neurovascular center between 2007–2017 and investigated the patients' characteristics, imaging/procedural parameters and outcomes and determined if the mode of initial counselling prior to INVB influenced the patients' choice of EIAR in the above mentioned context.

Results

Altogether 572 patients with EIAR were discussed in our INVB. While in 473 (83%) patients the INVB recommended one superior treatment of choice, in a subset of 99 patients (17%) the INVB recommendation estimated similar treatment risks for both modalities. All these patients received subsequent secondary counselling by specialists of both disciplines. Mean age in this subset was 58.2yrs with a predominance of the female sex (m:f=1:2); the most frequent aneurysm location was ICA (48%) and AcomA (35%) and the median diameter was 5.5mm. 66 patients underwent microsurgical and 33 patients interventional EIAR with no significant differences in baseline characteristics or outcome parameters at last follow-up (median 18mos). Initial patients' counselling prior to INVB presentation took place at the neurosurgical department in 80 cases of that 53 (66%) decided for microsurgical EIAR after INVB, while initial patients' counselling at the neuroradiological department in 19 cases was followed by interventional EIAR in 8 patients (42%). There was no statistical significance indicating a bias in patients' treatment decision-making due to "anchoring effects".

Conclusion

Initial patients' counselling in different neurovascular disciplines seems not to influence the final patients' decision-making for a distinct mode of EIAR. However, we found a preference towards surgical repair after secondary counselling. Outcome measures of both treatment modalities suggest that equal risk estimation by INVB was correct.

KI und Ethik in der Medizin/*AI and ethics in medicine*

V274

Retinotopie bei Patienten mit raumfordernden Läsionen im okzipitalen Kortex

Retinotopic mapping in patients with space-occupying lesions in the occipital cortex

K. Rosengarth¹, K. Hense², C. Ott¹, C. Doenitz¹, A. Brawanski¹, T. Plank³, M. Greenlee³, C. Wendl², N. O. Schmidt¹, M. Proescholdt¹

¹Universitätsklinikum Regensburg, Klinik und Poliklinik für Neurochirurgie, Regensburg, Germany

²Universitätsklinikum Regensburg, Radiologie, Regensburg, Germany

³Universität Regensburg, Experimentelle Psychologie, Regensburg, Germany

Objective

The areas surrounding the calcarine sulcus of the occipital cortex exhibit a retinotopic organization by representing a spatial map of the retinal surface. Therefore, lesions in the occipital cortex may lead to visual field deficits. To avoid those in patients with space-occupying lesions of the occipital cortex we applied retinotopic mapping in presurgical functional imaging. We looked for feasibility of retinotopic mapping in presence of a lesion. Additionally, we compared brain activation of patients with occipital lesions with healthy subjects.

Methods

15 patients with lesions on the occipital cortex (8 brain tumors, 2 metastatic lesions, 5 vascular malformations) and 15 healthy subjects matched for age and sex were included. To assess retinotopic organization of the visual field a visual eccentricity paradigm was applied during functional MRI. Patients were instructed to strictly fixate a blue spot in the center of a gray screen while a flickering checker board spreads from the inner to the outer visual field. To achieve an exact cortical retinotopy representation data analysis was done using *Freesurfer* version 6.0 including motion correction, skull stripping, normalization, white matter segmentation and smoothing. Statistical analysis on single a group level as well as group differences were conducted on the basis of the general linear model. To address lesion size effects the patient group was stratified using a median split according to lesion size.

Results

Retinotopic organization of visual eccentricity in presence of a space occupying lesion in the occipital cortex could be reconstructed in all patients of this study sample independently of lesion entity. The retinotopic organization of the inner, middle and outer visual field could be shown in patients and healthy subjects. However, patients showed lower activation in primary visual areas belonging to those retinotopic association areas compared to healthy controls. Additionally, patients with smaller lesions exhibited more activation associated with stimulation of the visual field in the precuneus and the inferior parietal and temporal cortex.

Conclusion

These results show the feasibility of retinotopy mapping in patients with occipital lesions. But, those patients showed similar reduced activation of the visual cortex due to retinotopic stimulation which negatively correlates with lesion size.

Neuroonkologie experimentell/*Neurooncology experimental*

V275

Bedeutung von Typ-III-Rezeptortyrosinkinasen für Viabilität, Proliferation, Metabolismus und Therapiesensitivität von stammzellähnlichen Gliomzellen

Impact of type III receptor tyrosine kinases on viability, proliferation, metabolism and therapy-sensitivity of stem-like glioma cells

L. M. Boldt, T. Lueg, V. Willeke, J. Ellsner, J. J. Ostermaier, F. Däumer, V. M. Tronnier, C. Zechel

Universitätsklinikum Schleswig-Holstein, Experimentelle Neuroonkologie, Lübeck, Germany

Objective

The glioblastoma multiforme (GBM) and the gliosarcoma (GSarc) are primary brain tumors with a high morbidity and mortality, offering only palliation. Stem-like glioma cells (SLGCs) are considered as one major cause of treatment failure and relapse. It has been shown that alterations in receptor tyrosine kinase PDGFRA (platelet-derived growth factor receptor), a member of the type III receptor tyrosine kinase (RTK) family, may contribute to GBM initiation and progression. The potential roles of the close relative PDGFRb or the type III RTK cKit remain elusive.

Methods

We have isolated and characterized SLGCs from patients with WHO grade II, III and IV neuroepithelial primary brain tumors. Nine GBM- and two GSarc-derived SLGCs lines underwent a detailed cellular and molecular characterization and were treated with increasing doses of the type III RTK inhibitor Imatinib (Ib; Glivec®). In order to elucidate whether the two PDGF receptors and/or cKit would be responsive for the Ib-mediated effects, we generated functional knock-outs of the PDGFRA- and b-genes, as well as of the cKit-gene by CRISPR-Cas9-mediated genome editing.

Results

We observed that increasing doses of Ib affected proliferation, viability and migration of SLGCs. Responsiveness was distinct for SLGCs from different patients and additionally varied between clones derived from the same SLGC mother cell lines, supporting previous suggestions that SLGCs display a high degree of cellular and molecular heterogeneity. We edited the genes coding for the PDGFRA or b, or cKit in six distinct SLGC-lines, which differed with respect to their Tp53- and PTEN-status. It turned out that bi-allelic editing of both PDGF receptor genes in the same cell was possible, but with very low efficacy. Notably, the respective clones did not display full inactivation of all *pdgfr* alleles, but small in frame deletions in at least one of the four alleles. This indicated the requirement of functional PDGF-signaling and suggested that PDGFRA might replace PDGFRb and *vice versa* in vitro. It appeared that Ib-responsiveness of the edited clones was distinct.

Conclusion

The edited SLGC clones will serve as very precious tools for future in vitro and in vivo experiments, addressing the function of the type III RTKs in glioma progression, metabolism and invasiveness.

Neuroonkologie experimentell/*Neurooncology experimental*

V276

Auswirkungen der CRISPR/Cas9-vermittelten Editierung des Prom-1/CD133-Gens auf Viabilität, Stammzellcharakter und Therapiesensitivität von stammzellähnlichen Gliomzellen
Impact of the CRISPR/Cas9-mediated editing of the Prom1/CD133 gene on viability, stemness and therapy-sensitivity of stem-like glioma cells

T. J. Kahl, J. Kruse, E. Riebel, E. Pawlak, V. M. Tronnier, C. Zechel

Universitätsklinikum Schleswig-Holstein, Experimentelle Neuroonkologie, Lübeck, Germany

Objective

The glioblastoma multiforme (GBM) and the gliosarcoma (GSarc) are the most aggressive and lethal primary brain tumors in adults. Therapy options which include chemotherapy with temozolomide (TMZ), radiotherapy and surgery are basically palliative. Even under optimized chemotherapy complete tumor regression is not achievable. To a large extent therapy resistance is caused by so-called stem-like glioma cells (SLGCs). SLGCs display characteristics of neural stem cell cells like self-renewal, indefinite proliferation and the expression of neural markers. Moreover, SLGCs tolerate irradiation and TMZ treatment much better than non-SLGCs. Controversy exists about the significance and function of the cell surface protein Prominin-1 (Prom1)/CD133.

Methods

We generated functional Prom1/CD133 knock-outs in genetically distinct GBM- and GSarc-derived human SLGCs in order to investigate the impact of this protein on stemness, viability and therapy resistance. We infected nine GBM-derived and two GSarc-derived SLGC lines with a replication-deficient lentiviral vector containing the genetic information for targeting exon 4 of the Prom1/CD133 gene with the prokaryotic endonuclease Cas9. In this, the CRISPR-Cas9 system targeted the sequence which essentially encodes the transmembrane domain 1 of the protein.

Results

Infected cells, which survived a 7-day Puromycin selection were subjected to limited dilution assays followed by further expansion. The proof of successful editing was obtained by Sanger sequencing, as well as analyses of protein expression by Western blotting, immunocytochemistry and flow-cytometry (FACS). SLGCs harboring large deletions and/or truncations of the Prom1/CD133 protein showed self-renewal and expressed high levels of the pluripotency factor Sox2 (sex determining region Y (SRY)-box 2). Clones carrying functional Prom1/CD133 inactivation displayed a similar differentiation capacity as their wildtype counterparts. Ongoing experiments compare the TMZ and radiation sensitivity of the Prom1/CD133-edited clones with that of their wildtype counterparts.

Conclusion

Overall it appeared that the functional biallelic knock-out of the Prom-1/CD133 gene does not impair viability and stemness of stem-like glioma cells.

Neuroonkologie experimentell/*Neurooncology experimental*

V277

RNA-Sequenzierung und bioinformatische Analysen zur Vorbeurteilung der Chemotherapie-Sensitivität beim GBM

RNA-sequencing and bioinformatic analysis to pre-assess sensitivity to chemotherapeutics in GBM

S. R. Kantelhardt¹, D. Kalasauskas¹, B. Sprang¹, F. Ringel¹, S. E. Bikar², N. Naumann², M. Sorokin³, A. Buzdin³, A. Giese⁴, E. Kim¹

¹Universitätsmedizin Mainz, Neurochirurgie, Mainz, Germany

²StarSEQ GmbH, Mainz, Germany

³Sechenov First Moscow State Medical University, Laboratory of Clinical and Genomic Bioinformatics, Moskau, Russian Federation

⁴OrthoCentrum, Hamburg, Germany

Objective

Development of a molecular guided approach for individualized selection of chemotherapeutics in (recurrent) GBM. In this EU-funded project high-throughput RNA sequencing and bioinformatics were utilized to quantitatively analyze activities of oncopathways involved in response to FDA-approved chemotherapeutics.

Methods

Biopsy material from primary and recurrent GBM was used for RNA sequencing (RNA-seq) and establishing primary cultures of glioma stem cells (GSCs), which were then examined in the same way. RNA-seq data were subjected to analyses of differential gene expression (DE) and quantitative pathway activation analysis using Oncobox – an original bioinformatic tool developed at Oncobox (www.oncobox.com). Results for primary and recurrent GBM were compared. Oncobox analysis was further used to model the efficacy of 130 FDA-approved anti-cancer drugs.

Results

128 tissue samples and 42 GSC cultures from 44 GBMs were analyzed. 23 primary GBM, 19 recurrent cases and 2 secondary recurrent GBMs were included. In 14 cases matching pairs of primary and recurrent GBM could be obtained. DE analysis revealed a high degree of concordance between tumor tissues and GSCs in the longitudinal transcriptomic changes associated with tumor recurrence. Oncobox analysis showed downregulation of key pathways involved in the regulation of DNA repair and upregulation of immune pathways in recurrent GBM compared to the corresponding primary tumors. When specifically looking at pathways involved in response to chemotherapeutics we found a downregulation of pathways targeted by Temozolomide and Lomustine in recurrent GBM. In contrast, several pathways showed a significant ($p < 0.05$) increase in their activities in the setting of recurrence. Interestingly, among the upregulated pathways those targeted by chemotherapeutics currently investigated in phase II or III trials on GBM (Durvalumab or Pomalidomide) were also found upregulated in recurrent tumors.

Conclusion

Our study suggests that the spectrum of potentially effective drugs may differ between newly diagnosed and recurrent glioblastomas and provides a transcriptional rationale for the lack of significant therapeutic benefit from temozolomide in patients with recurrent glioblastoma. The approach carries the potential of predicting sensitivity to specific chemotherapeutics and might be used for individual optimization of treatment regimes.

Neuroonkologie experimentell/*Neurooncology experimental*

V278

Abgrenzung und Identifizierung von primären und sekundären Hirntumoren durch multiple Analyse Raman-spektroskopischer Datensätze

Delineation and identification of primary and secondary brain tumours by multiple analyses of Raman spectroscopic datasets

O. Uckermann¹, R. Galli², E. Koch², G. Schackert¹, G. Steiner², M. Kirsch¹

¹Universitätsklinikum Carl Gustav Carus Dresden, Klinik und Poliklinik für Neurochirurgie, Dresden, Germany

²Technische Universität Dresden, Klinisches Sensoring und Monitoring, Dresden, Germany

Objective

Raman spectroscopy provides a comprehensive molecular signature of the tissue and has been suggested as innovative tool for intraoperative brain tumor analysis. Here, we performed multiple analysis of the Raman spectroscopic dataset with the aim to extract different diagnostic tumor parameters.

Methods

Fresh, unprocessed biopsies of 202 tumor patients were investigated. Non-neoplastic brain tissue was obtained during surgical treatment of drug-resistant epilepsy (n=7). Within 30 min from tissue resection, five Raman spectra were acquired on each sample using a standard Raman microscope and 785 nm laser excitation. After baseline correction and normalization, principal component analysis (PCA) of Raman spectra was applied. Quadratic discriminant analysis of PCA scores was performed in reference to the diagnostic information retrieved by standard histopathology.

Results

Raman bands of lipids at 1090, 1297, 1438, 2708 and 2847 cm^{-1} were significantly reduced in primary and secondary brain tumors compared to non-tumor brain. In contrast, Raman bands assigned to proteins at 1003, 1240, 1660, 2945 cm^{-1} were increased. Spectral changes were more pronounced in high grade glioma than in low grade glioma which is in line with previous studies. Classification led to the correct recognition of all non-neoplastic biopsies and of 95% of the investigated tumor biopsies, confirming the potential of Raman spectroscopy for tumor delineation. Further analysis of the Raman signatures of the tumor samples allowed the characterization of the tumor type: Differentiation of glioma and brain metastases was obtained with an accuracy of 90%. Moreover, oligodendroglioma and *IDH1*-mutant astrocytoma, which differ in the presence of 1p/19q codeletion, were discerned with a correct rate of 81%.

Conclusion

These results demonstrate the feasibility of i) general brain tumor recognition and ii) extraction of diagnostic information by means of one analytical method. This opens the possibility to perform intraoperative optical biopsies using Raman spectroscopy for *in situ* delineation and diagnosis of brain tumors.

Neuroonkologie experimentell/*Neurooncology experimental*

V279

4Gy-Bestrahlung induziert die Expression von Stammzellmarkern in nicht-pathologischen Dura mater-Zellen *4Gy irradiation induces expression of stem cell markers in non-pathological dura mater cells*

L. Hain¹, D. Freitag¹, N. Abbasi-Senger², T. Wiezorek², A. Wittig², R. Kalff¹, J. Walter^{1,3}

¹Universitätsklinikum Jena, Klinik für Neurochirurgie, Jena, Germany

²Universitätsklinikum Jena, Klinik für Strahlentherapie und Radioonkologie, Jena, Germany

³Klinikum Saarbrücken, Klinik für Neurochirurgie, Saarbrücken, Germany

Objective

Ionizing radiation is a known risk factor for the possible transition of dura mater into a meningeal neoplasia. However, the effects of diagnostic and therapeutic radiation on this mechanism are still largely unknown. Nonetheless, the stem cell hypothesis is often used to explain tumorigenesis. The aim of this study was to investigate the effect of ionizing radiation on a possible reprogramming to the stem cell phenotype in primary dura mater cell cultures (DMC).

Methods

Three DMCs were exposed to a single photon radiation dose (1, 2, 4, 8, 12, 16, 20 Gy) and cultured under standard conditions until they reached the primary (10 passes) or secondary (84 days after irradiation) endpoint. Generation times, passenger ability and morphological abnormalities were analyzed. For the analysis of possible reprogramming effects, the expression of the transcription factor NANOG and its regulators SOX2 and OCT4 was determined by immunocytochemistry and qPCR compared to non-irradiated healthy cells.

Results

The analysis showed that especially in the irradiation groups 4 to 8 Gy higher generation times were observed compared to the control group not irradiated and thus slower or stagnating growth. Clear signs of necrotic processes were not detected. In parallel, the non-pathological cells irradiated with 4Gy showed increased expression levels for NANOG ($r=2.04$) as well as OCT4 ($r=2.14$) and SOX2 ($r= 1.17$) and CD44 ($r=1.68$). The DMCs treated with 8Gy did not increase the expression levels of NANOG ($r=0.55$), SOX2 ($r=0.25$) and OCT4 ($r=0.50$) as well as CD44 ($r=0.50$).

Conclusion

The high expression values of the transcription factors NANOG, SOX2 and OCT4 as well as the stem cell marker CD44 clearly show that an induction of stem cell properties in non-pathological dura mater cells is possible, even after a single irradiation with a 4 Gy dose. Thus, it seems likely that ionizing radiation has long-term effects on reprogramming and thus on possible tumor initiating processes.

Neuroonkologie experimentell/*Neurooncology experimental*

V280

Lokale Vorläuferzellen formen die Tumor-Angiogenese im Gehirn *Local progenitors shape tumour-angiogenesis in the brain*

R. E. Kälin, L. Cai, G. Cheng, S. Siller, J. Tonn, R. Glaß

Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik, München, Germany

Objective

Glioblastoma (GBM) depend on support by their local environment. Vascular cells as well as tumour-associated myeloid cells (TAM) constitute the major components of the GBM-parenchyma. TAM, which consist of microglia and peripheral macrophages, accelerate GBM cell-invasion and the rich vascular network of GBM has important tumour-trophic functions. In this study, we identified a previously unacknowledged population of a local myeloid progenitor cell that transiently appeared during glioblastoma growth.

Methods

Using a glioma mouse model for lineage-tracing of tumor-parenchymal cells (*nestin-creER2*, R26-tdTomato; abbreviated as nestin-reporter mice), we observed (by single cell transcriptomics and immunofluorescence analysis) a subset of tumor-associated avascular cells over a time-course. In different transgenic mouse strains and in bone-marrow chimeric models we investigated the point-of-origin as well as the lineage-identity of these traced cells. These cells were further characterized by immunofluorescence in mouse models and patient samples of GBM. In a functional experiment, we induced a knockout of the transcription factor SOX2 in the traced tumor-associated cells and effects on tumor-progression were compared to SOX2 wild-type controls.

Results

The population of tumor-associated lineage-traced cells in the nestin-reporter model had remarkable similarity with microglia. However, they were distinct from TAM as they have no microglial origin and do not derive from the bone marrow. Strikingly, these traced cells derived from a local progenitor cell that is dormant in brain homeostasis. Induction of orthotopic glioma in nestin-reporter activated this SOX2-dependent progenitor cell population (as assessed in $n > 15$). Abrogation of this progenitor cell-population by conditional *Sox2*-knockout ablated the entire subset of these traced cells with a myeloid expression profile (TAMEP; $n = 9$ vs. 8 for control vs. ablated). Histopathological inspection showed that the small subset of TAMEP has large impact on disease-progression by reducing glioblastoma-vascularization by over 40% (with statistical significance of $P < 0,005$ by T-test) and -size by more than 60% (with $P < 0,05$ by T-test).

Conclusion

Our data suggest that dormant progenitors generate TAMEP (which are cells expressing myeloid markers but lacking a myeloid origin) that have profound neurooncological impact and point towards a new and promising therapeutic target in order to support anti-angiogenic regimen in GBM.

Hirnmetastasen/*Brain metastases*

V281

Intraoperative Radiotherapie nach der Resektion von Gehirnmetastasen (INTRAMET) – Ergebnisse einer Interims-Sicherheits- und Wirksamkeitsanalyse einer prospektiven Phase II Studie *Intraoperative radiotherapy after resection of brain metastases (INTRAMET) – interim analysis on safety/efficacy of a prospective phase II study*

S. Brehmer¹, A. Förster², M. Seiz-Rosenhagen¹, S. Clausen³, F. Schneider³, D. Hänggi¹, N. Etminan¹, F. A. Giordano³

¹Universitätsklinikum Mannheim, Klinik für Neurochirurgie, Mannheim, Germany

²Universitätsklinikum Mannheim, Institut für Neuroradiologie, Mannheim, Germany

³Universitätsklinikum Mannheim, Klinik für Strahlentherapie und Radioonkologie, Mannheim, Germany

Objective

Brain metastases occur in roughly 40% of patients diagnosed with systemic cancer. External beam radiotherapy (to the cavity or whole brain) lowers local recurrence rates but also prolongs the time to (systemic) salvage therapies after surgical treatment of metastases. We here present the interim data on INTRAMET, a phase II trial that evaluates safety and efficacy intraoperative radiotherapy (IORT) of the resection cavity.

Methods

INTRAMET is an investigator-initiated, monocentric, open-label, one-arm, prospective, phase II study that includes patients aged 18 years and older with newly diagnosed, resectable brain metastases with a KPS of 50 or better. Following resection of the macroscopic tumor, all patients receive IORT with 30 Gy prescribed to the margin of the resection cavity. The primary endpoint is local progression-free survival (L-PFS), secondary endpoints are time to salvage cancer therapy (TTST), overall survival (OS), global (cancer-specific) PFS, cognitive performance, quality of life and dose-limiting toxicities (DLT) defined as wound healing disorders, cerebral hemorrhage, ischemia or radionecrosis requiring surgical intervention. Radiological analyses are conducted by an external/independent neuroradiologist. We here report (i) safety and efficacy results of a planned safety/interim analysis after inclusion of 22 patients and (ii) on a pre-planned comparison of TTSTs of IORT-treated patients, compared to a control cohort of 108 patients treated with surgery and conventional radiotherapy within the same time period.

Results

The median follow-up in the IORT-group was 10.5 months [0.9-28.9]. Although 2 cases of radionecrosis at the surgical site occurred - both in combination with systemic immunotherapy treatment - no DLT were observed. 1 Patient had a confirmed local recurrence which occurred concomitant with multiple other new out-of-field metastases 41 days after treatment. At follow-up. 5 additional patients developed new out-of-field brain metastases [mean 215d], which were treated with rescue radiotherapy. The mean TTST after IORT was 41 days compared to 56 days in the control group ($p=0.037$), with a mean time to cerebral radiotherapy after surgery of 25 days.

Conclusion

IORT for cerebral brain metastases appears to be safe and effective. In addition, the time to systemic therapy is significantly reduced with less hospitalization, which is of high impact for patients' quality of life.

Hirnmetastasen/*Brain metastases*

V282

Chemotherapie-induzierte Dormanz und NKG2D-Liganden-Überexpression führen zu kleineren Hirnmetastasen in Mäusen

Chemotherapy-induced dormancy and overexpression of NKG2DL lead to smaller brain metastases in mice

R. Hufnagel, M. Synowitz, J. Held-Feindt, [C. Flüh](#)

Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Kiel, Germany

Objective

Cerebral breast and lung cancer metastases are the most common secondary malignancies in the brain and are often associated with a devastating prognosis. Dormancy is a mechanism of therapy resistance, in which tumor cells transverse into a non-proliferating, immunologically silent phenotype, which easily survive chemotherapy and are considered a source of recurrence. The NKG2D system consists of NKG2D ligands (NKG2DL), which are expressed on tumor cells, and NKG2D receptors, which are expressed on immune effector cells like NK cells and cytotoxic T cells. These usually can detect and eliminate NKG2D carrying tumor cells. We investigated, how dormancy marker and NKG2DL expression changes in brain metastases after chemotherapeutic treatment and if dormant cells have the ability to form a tumor in a cerebral microenvironment.

Methods

We analyzed the dormancy marker (DM) and NKG2DL expression in the murine breast cancer cell line E0771 and the lung cancer cell line LLC by qrtPCR and immunocytochemistry in vitro. Cells received a chemotherapeutic treatment with Cyclophosphamid or Cisplatin, were analyzed concerning their DM and NKG2DL expression again and were then stereotactically implanted into the brains of naïve C57BL6 mice. As a control, we implanted non-treated cells. Next, size, invasiveness and marker expression were analyzed using immunohistochemistry.

Results

In-vitro chemotherapeutic treatment with Cyclophosphamid and Cisplatin led to an upregulation of DM and NKG2DL in a dose and time dependent fashion. When implanting equal amounts of treated (dormant) and non-treated (non dormant) cells into the right striatum of naïve mice, non-dormant tumors grew significantly bigger and more invasive compared to dormant tumors.

Conclusion

Although chemotherapy induced a potentially more tumorigenic cell phenotype with overexpression of DM, dormant tumors were smaller and less invasive than non-dormant tumors. We therefore conclude, that dormant cells, although being chemo resistant, do not have the ability to sufficiently form tumors in a cerebral microenvironment. A possible reason could be the overexpression of NKG2DL, which also was induced by chemotherapeutic treatment. For future therapeutic approaches against brain metastases, addressing the NKG2D system might be promising, whereas dormancy as a mechanism of tumor surveillance might not be as relevant in brain metastases.

Hirnmetastasen/*Brain metastases*

V283

Klonalität RGB-markierter Tumorzellen offenbart Auswirkungen der lokalen Immunantwort auf die Heterogenität metastatischer Tumore
Clonality of RGB-labelled metastatic cells reveals effects of local immunoediting on tumour heterogeneity

A. Piffko

Universitätsklinikum Hamburg-Eppendorf, Klinik für Neurochirurgie, Hamburg, Germany

Objective

The aim of this study is to evaluate the effects of cancer immunoediting on the clonality of metastatic tumors in distinctive locations. Our hypothesis is that the peripheral immune system favors the proliferation of some specific metastasis subclones, however such subpopulations have not yet been identified.

Methods

Murine melanoma (B16), NSCLC (LLC) and breast cancer (EO771) cell lines were transduced with lentivirus carrying either mCherry (Red) Venus (Green) or Cerulean (Blue) fluorescent proteins (RGB) and selected until a stable expression was achieved. Syngeneic tumor cells were injected subcutaneously, intracardially or stereotactically implanted in the striatum of C57Bl/6 immunocompetent mice. Four specific organs (lung, liver, brain, adrenal glands) and any additional macroscopic metastases were analyzed by flow-cytometry and immunohistochemistry to investigate tumor heterogeneity and clonal selection patterns of metastatic tumor cells. The degree of clonal restriction was assessed by quantification of the chromaticity of RGB labeled tumor cells analyzed by flow cytometry.

Results

Overall 64 mice were analyzed (B16 n=21; LLC n=21; EO 771 n=22). Survival was significantly altered by type of tumor cell as well as type of injection method utilized, with intracerebrally injected EO771-RGB breast cancer cells yielding the shortest survival (median 10 d, $p < 0.0001$, Log-rank test). Metastasis spread also differs based on cell line and injection location with the intracardiac B16 injection leading to the highest number of affected organs (12/12 organs). Interestingly, intracranial injection of these non-glioma tumor cell lines also led to metastatic spread, although to a lesser extent. In the primary site of injections we did not observe any restriction in our color barcode, meaning that most cells injected were able to grow without selection from the microenvironment. However, in the metastases, particularly in the adrenal gland, an important clonal selection occurred leading us to conclude that only very specific clones were able to escape the primary site and proliferate into a new environment. Interestingly, these clones seem to differ between mice.

Conclusion

The confirmation that different clones can emerge from the primary site to colonize specific organs raised the idea that immunoediting on tumor cells is a major driver of tumor heterogeneity that requires a deeper understanding and multiple site sampling to enable new therapeutic options.

Hirnmetastasen/*Brain metastases*

V284

F-18-FET-PET Bildgebung bei Hirnmetastasen zeigt Tumorstabilität und Tumorstabilität *F-18-FET-PET imaging in brain metastases is indicative of tumour vitality and proliferation*

H. S. Meyer¹, F. Liesche², S. Motov¹, B. Meyer¹, B. Wiestler², J. Gempt¹

¹Klinikum der Ludwig-Maximilians-Universität München, Neurochirurgische Klinik und Poliklinik, München, Germany

²Klinikum der Ludwig-Maximilians-Universität München, München, Germany

Objective

FET PET has been proposed to provide diagnostic information on brain metastases in addition to MRI imaging. For example, the selection of biopsy targets most likely yielding a valid diagnosis could be supported by pre-biopsy FET PET imaging. Moreover, the differentiation of post-radiation or post-resection tissue changes from tumor recurrence could be improved by FET PET. We aimed at better understanding the relation between FET PET imaging (as measured by standardized uptake values, SUV) and potential (i.e., MRI contrast enhancing) tumour tissue properties determined histologically.

Methods

Patients underwent FET PET and MRI (T1 ± Gd-DTPA) ahead of surgery for brain metastasis. Imaging data were fused (iPlan cranial / Brainlab). FET uptake was quantified as SUV, and a tumour-to-background-ratio of 1.6 or more was defined as PET-positive. Tissue samples were obtained during surgery and assigned to three groups (1. PET- and MRI-positive; 2. PET-positive and MRI-negative; 3. PET-negative and MRI-positive). Tissue samples were processed immunohistochemically and labelled for Ki-67 / Mib-1 to determine proliferation (Ki-67 labelling indices). In addition, necrosis, vital tumour and brain parenchyma ratios were quantified for each tissue sample based on histology.

Results

15 patients were enrolled (origin of neoplasm: four melanoma; four upper/lower GI; four NSCLC, one SCLC; one breast; one renal). 27 samples were obtained. For five samples, histology revealed parenchyma only (including all three groups). One sample was completely necrotic. The tumour ratio within the specimen increased with PET positivity, as did the tumour proliferation (Fig. 1, left and right). The necrosis ratio within the specimen decreased with PET positivity (Fig. 2). Samples from PET- and MRI-positive locations (group 1) had the highest tumour ratio and proliferation index (57.1 and 65.8%, respectively), which were lower in group 3 (50.2 and 63.7%) and lowest in group 2 (34.7 and 57.5%).

Conclusion

In this preliminary study, FET PET provided diagnostic information on brain metastases. There is a trend towards tissue containing more vital, proliferating tumour and less necrotic material with increasing SUV TBR. This confirms that in brain metastasis treatment, FET PET can be helpful in guiding selection of biopsy targets and in differentiation of actual tumor progression from treatment-associated (necrotic) tissue changes, i.e., pseudoprogression.

Fig 1

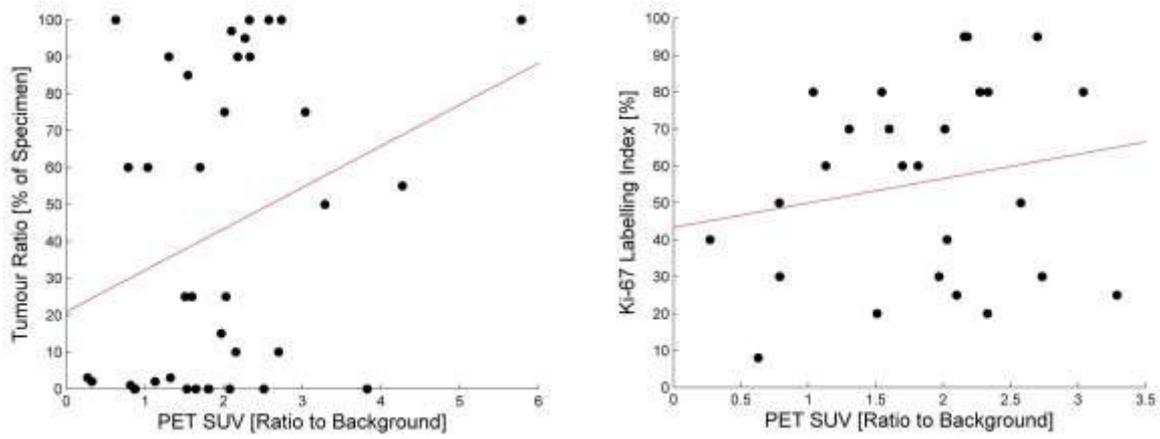
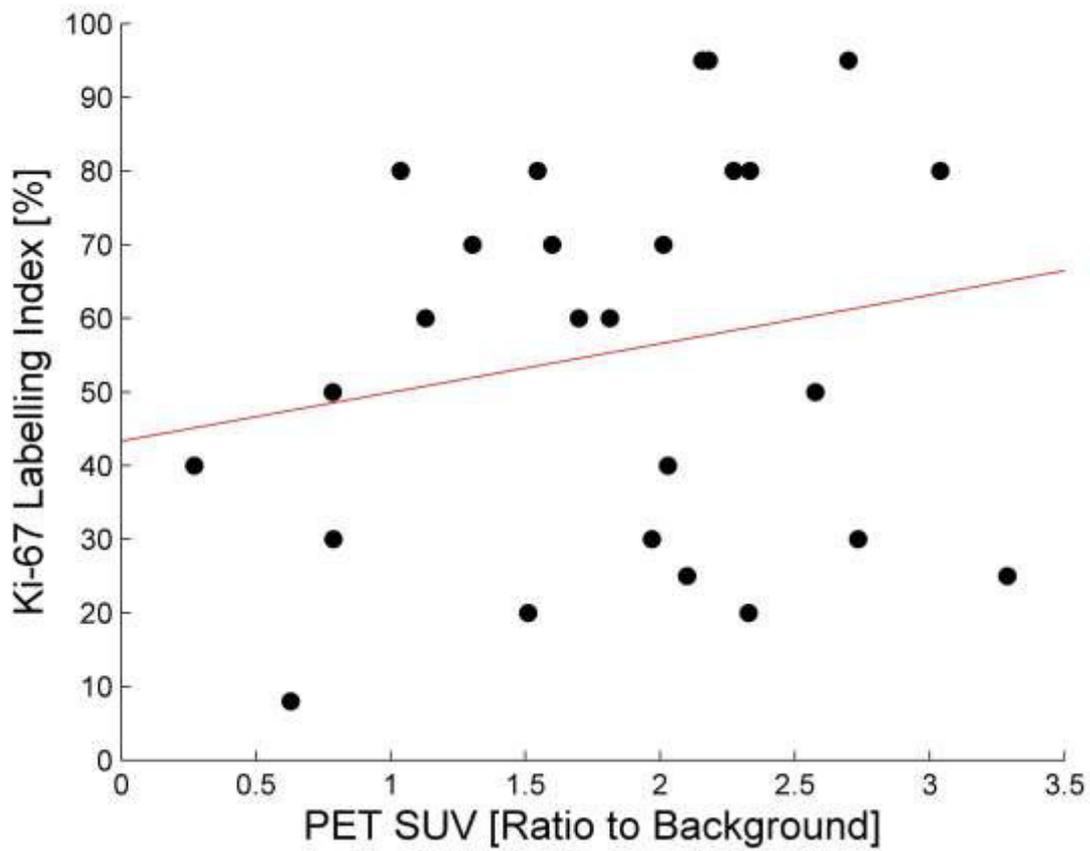


Fig 2



Hirnmetastasen/*Brain metastases*

V285

Chirurgie bei Hirnmetastasen – Einfluss auf klinischen Zustand, adjuvante Therapie und Überleben *Surgical resection of symptomatic brain metastases – impact on clinical status, adjuvant treatment and survival*

S. T. Jünger¹, M. Proescholdt², K. M. Schebesch², C. Doenitz², L. Rams², A. Brawanski², C. Reinhardt³, L. Plambeck¹, M. Wittersheim⁴, P. Schödel², S. Grau¹, R. H. Goldbrunner¹

¹Universitätsklinikum Köln, Neurochirurgie, Köln, Germany

²Universitätsklinikum Regensburg, Neurochirurgie, Regensburg, Germany

³Universitätsklinikum Köln, Onkologie, Köln, Germany

⁴Universitätsklinikum Köln, Pathologie, Köln, Germany

Objective

Novel systemic targeted treatment strategies for various cancers have led to both an improved overall survival and increased incidence of brain metastases. We analyzed structure and quality of the interdisciplinary treatment and outcome of patients undergoing resection of symptomatic brain metastases in the context of these molecular treatment regimens.

Methods

We retrospectively analyzed patients receiving resection of at least one symptomatic BM between 2012 and 2019 at two large academic hospitals. Baseline clinical and treatment-related parameters were retrieved.

Post-treatment survival was calculated using Kaplan-Meier analysis. Prognostic factors were identified using multivariate Cox-regression.

Results

806 patients were included. Primary tumors comprised lung cancer (n=333), breast cancer (n=126), melanoma (n=119), gastrointestinal (n= 77), kidney cancer (n=29) and others (n=122). Solitary BM occurred in 372 (46.15%), singular in 238 (29.53%) and multiple in 196 (24.32%) patients. Systemic disease status was controlled in 367 (45.53%). Postoperative radiotherapy was applied in 624 (77.42%) patients and systemic treatment was initiated in 372 (46.15%) patients. Treatment decision correlated with postoperative clinical status ($p = 0.0001$), which was improved significantly by surgery; median preoperative KPS of 80 (range: 20-100) increasing to 90 (range: 50-100) after surgery ($p = 0.00001$). Resulting in an alteration of RPA class allocation in 114 (14.14%) patients, 89 (11.04%) of which were improvements. Pre- and postoperative RPA allocation reliably predicted survival ($p=0.0065$). In multivariate regression analysis, poor clinical status, absence of systemic treatment and multiple metastases were strong negative predictors for survival (0.00001).

Conclusion

Resection of symptomatic BM improves clinical status and increases the likelihood of adjuvant systemic treatment leading to prolonged survival.

Hirnmetastasen/*Brain metastases*

V286

Symptomatische Hirnmetastasen bei alten Patienten – Nutzen und Risiko der Neurochirurgie im Kontext onkologischer Systemtherapie

Symptomatic brain metastases in the elderly population – the risk and benefit of surgery in the context of systemic oncological treatment

S. T. Jünger¹, P. Schödel², M. Proescholdt², S. Grau¹, K. M. Schebesch², C. Doenitz², L. Rams², A. Brawanski², M. Kocher³, H. Schulz⁴, K. König¹, R. H. Goldbrunner¹

¹Universitätsklinikum Köln, Neurochirurgie, Köln, Germany

²Universitätsklinikum Regensburg, Neurochirurgie, Regensburg, Germany

³Universitätsklinikum Köln, Stereotaxie, Köln, Germany

⁴Praxis internistischer Onkologie und Hämatologie, Onkologie und Hämatologie, Frechen, Germany

Objective

For patients with brain metastases (BM) advanced age is considered a negative prognostic factor, especially since general condition frequently limited systemic treatment options. Due to lower toxicity, novel molecular agents comprise a suitable alternative for these patients. Therefore, we analyzed the postoperative clinical course of elderly patients operated on symptomatic BM in this context.

Methods

We retrospectively analyzed patients receiving resection of mostly symptomatic BM at two institutions between 2012 and 2018. Primary tumor, number of lesions, pre- and postoperative KPS, co-morbidity and postoperative treatment were analyzed. Post-treatment survival was calculated using Kaplan-Meier analysis. Prognostic factors were identified using multivariate Cox-regression.

Results

We included 313 patients aged at least 65 years (group A) and compared them to 493 patients below 65 years (group B). Primary tumor, systemic status and number of metastases did not differ significantly between the groups. Surgical complication rate was similar in both groups and clinical status significantly improved despite patients age ($p=0.0001$).

Induction of systemic treatment was administered less frequently to elderly patients ($p=0.000$), induction of such therapies correlated with the clinical status ($p = 0.037$) though. Median survival after resection of BM differed significantly between groups ($p = 0.0049$), however, survival curves separated only in the long-term course. Postoperative systemic treatment increased further survival significantly in both groups ($p = 0.00001$). Considering those patients who received systemic treatment, age itself was no longer a negative prognostic factor ($p = 0.865$). In the multivariate regression analysis, clinical status and systemic treatment remained the strongest predictors for survival ($p = 0.0001$).

Conclusion

Resection reduces neurological deficits in patients with brain metastasis, disregarding age, and leads to a higher frequency of systemic treatment induction, which in turn increases further survival

Bildgebung/Imaging

V287

Der Einfluss eines CT-Perfusions Protokoll auf das funktionelle Langzeit-Outcome von Patienten mit aneurysmatischer Subarachnoidalblutung und assoziierten ischämischen Komplikationen
The impact of an elaborated CT-perfusion protocol for acute management of patients with aneurysmal subarachnoid haemorrhage (aSAH) on ischemic complication and functional long-term outcome

K. Döring, D. Mielke, V. Rohde, V. Malinova

Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

Objective

The long-term functional outcome of patients with aneurysmal subarachnoid hemorrhage (aSAH) depends mainly on the aSAH-severity and the occurrence of early and late ischemic complications in the acute phase after the ictus. Computer tomography perfusion (CTP) has been increasingly implemented in the acute management of aSAH. Despite of increasing evidence supporting the usefulness of CTP in aSAH-patients, its effective impact on functional outcome is still insufficiently evaluated. The aim of this study was to assess the functional outcome in aSAH-patients treated according to an elaborated CTP-protocol compared to patients treated for aSAH before the implementation of the CTP-protocol.

Methods

We performed a retrospective analysis of aSAH-patients treated between 2008 and 2018 (2008-2011 without CTP-protocol and 2012-2018 with CTP-protocol) . Demographic and clinical data were extracted from the medical records. The CTP-protocol included a routine CTP on day 3 and day 7 in sedated/comatose patients and in case of clinical deterioration or blood flow acceleration measured by transcranial Doppler sonography over 120 cm/s. The functional outcome was assessed according to the modified Rankin scale (mRS) at least 3 months after ictus, whereas a mRS \leq 3 was considered as good outcome.

Results

A total of 375 patients were included in the analysis of this study. 95 patients were treated without a CTP-protocol (group 1) and 279 patients with a CTP-protocol (group 2). A good aSAH-grade (Hunt&Hess I-III) was found in 60.6% in group 1 compared to 67.1% in group 2. A good mRS was found in 47.6% in group 1 vs 63.3% in group 2. The mean cumulative radiation exposure (RE) in group 1 was 36.7 mSV compared to 55.4 mSv in group 2.

Conclusion

Patients with aSAH managed according to an elaborated CTP-protocol have better functional outcome compared to patients who were treated without CTP protocol. Due to a higher radiation exposure of a CTP-based protocol the evaluation of equivalent alternative imaging protocols without radiation exposure is necessary in order to reduce the RE in aSAH-patients during the acute phase after the ictus.

Bildgebung/Imaging

V288

Die routinemäßige Anwendung der CT Perfusionsbildgebung in der Behandlung der schweren spontanen Subarachnoidalblutung

The routine use of CT perfusion to detect cerebral vasospasm in the setting of severe spontaneous subarachnoid haemorrhage

J. Oltmann¹, C. Ditz¹, M. Hartlieb¹, J. F. Wojak¹, J. Leppert¹, A. Neumann², V. M. Tronnier¹, J. Küchler¹

¹Universitätsklinikum Schleswig-Holstein, Neurochirurgie, Lübeck, Germany

²Universitätsklinikum Schleswig-Holstein, Neuroradiologie, Lübeck, Germany

Objective

The occurrence of cerebral vasospasm (CVS) constitutes a major complication after spontaneous subarachnoid haemorrhage (sSAH) and is associated with unfavourable outcome. CT perfusion imaging (CTP) is known to verify suspected CVS in SAH patients, while causing considerable radiation exposure. Literature regarding routine use of CTP in the setting of SAH is still limited. This study analyses the value of routinely performed CTP to improve early identification of CVS and to prevent CVS related cerebral infarction.

Methods

We performed a 3-year retrospective analysis of sSAH patients who underwent CTP imaging. All patients received invasive monitoring for intracranial pressure and cerebral oxygenation (PBrO₂). Transcranial Doppler sonography (TCD) was executed daily. According to our own treatment protocol for unconscious patients with SAH, CTP was performed routinely every 4 days and in case of suspected CVS, when a sudden decrease of PBrO₂ (<15mmHg) or increase of the mean flow velocity (>150cm/s) was detected. CTPs were classified as routine (rCTP) or symptomatic (sCTP). If cerebral malperfusion was observed in CTP imaging, a diagnostic angiography was performed. Angiographically confirmed CVS was treated by endovascular rescue therapy. Clinical, radiographic and demographic data were collected.

Results

During the study period, 213 CTPs (136 rCTPs and 77 sCTPs) were carried out in 65 patients. The rate of new onset of cerebral malperfusion was significantly higher in sCTPs (49%) than in rCTPs (20%), while the rate of angiographic confirmation of CVS was similar in both groups (84% vs. 74%). In 27 cases (20%), rCTP led to a clinical response. Endovascular rescue therapy was performed after 30 sCTPs and 21 rCTPs. A 48h follow-up CT revealed CVS related cerebral infarction after 19 sCTPs (25%) and 14 rCTPs (10%). Multivariate logistic regression analysis revealed a higher probability for new onset of malperfusion in rCTP in those patients who already developed cerebral infarction during the previous clinical course.

Conclusion

Routine CTP in sSAH patients is able to identify cerebral malperfusion, which is not assessable by established clinical diagnostics. However, despite routinely performed CTP and endovascular rescue therapy, CVS related infarction is still present in some patients. Concerning the effectiveness of rCTP, prospective trials are necessary to evaluate both its potential benefits and possible adverse effects.

Bildgebung/Imaging

V289

Breite Indikationsstellung der CT-Angiographie zur Identifizierung traumatischer Läsionen zerebrovaskulärer Gefäße – eine gute Strategie?

A liberal CT angiography screening protocol to detect blunt cerebrovascular injuries in trauma patients – a good strategy?

P. Nagel¹, K. Michalas¹, C. Ditz¹, H. Schacht², A. Neumann², V. M. Tronnier¹, J. Küchler¹

¹Universitätsklinikum Schleswig-Holstein, Klinik für Neurochirurgie, Lübeck, Germany

²Universitätsklinikum Schleswig-Holstein, Klinik für Neuroradiologie, Lübeck, Germany

Objective

High energy trauma may cause blunt cerebrovascular injuries (BCVIs). There is a consensus about the use of CT angiography (CTA) to detect BCVIs but no agreement exist concerning the exact indication for CTA in trauma patients. On the one hand an early identification of BCVIs may prevent serious complications like cerebral ischemic stroke. Otherwise a CTA also consists of relevant radiation to the patient and a risk of contrast agent associated nephrotoxicity. Thus, we aimed to evaluate the effectiveness of a liberal CTA screening strategy for the detection of BCVIs in trauma patients.

Methods

We screened all patients, who were admitted to our Level I trauma center during a 2-year period. Inclusion criteria: i. admission to the hospital's trauma room and ii. a traumatic injury. Following the hospital's guideline, all patients with a high energy trauma or a suspected BCVI underwent CTA imaging.

Results

We identified 1317 patients, fulfilling the inclusion criteria. Traffic accidents (n=739, 56%) were the leading trauma mechanism, followed by falls (n=446, 34%). A CTA imaging was conducted in 588 patients (45%), consisting of 12 patients (1%) with BCVIs. The BCVIs were classified as Denver Grading Scale Grade II (n=6) and Grade IV (n=6). Blunt injury of the internal carotid artery was more frequent (n=8, 67%) than injuries of the vertebral artery (n=4, 33%). Bilateral BCVIs were present in 2 patients (17%). 2 patients underwent an endovascular stenting and antiplatelet therapy (APT), 4 received only APT and 6 did not receive a specific therapy. BCVIs were associated with a high risk for intrahospital stroke (n=2, 17%) and mortality (n=3, 25%). Logistic regression analysis identified the Glasgow coma scale, intracranial lesions, C-spine fractures and visceral injuries as risk factors for BCVIs.

Conclusion

BCVI is a rare condition in trauma patients and its occurrence is associated with high morbidity and mortality, even in case of an early detection using CTA. A liberal CTA-indication strategy efficiently identifies BCVIs but contains many negative findings as well.

There is a need for further prospective studies comparing this strategy with evidence-based decision rules to improve the decision making in trauma patients.

Bildgebung/Imaging

V290

Nachweis von Komplikationen nach Kranioplastie durch Ultraschall *Imaging of complications after cranioplasty using transcranioplasty ultrasound*

D. I. Lungu, H. Qassim, J. Behnke-Mursch, K. Mursch

Zentralklinik Bad Berka, Neurochirurgie, Bad Berka, Germany

Objective

Recently, we were able to demonstrate that cranioplasty material (in our case Polyether-Ether-Ketone (PEEK)) is lucent for diagnostic ultrasound and enables the investigator to obtain images of the underlying brain. The value of this technique in daily practice has to be proven.

Methods

Eight patients requiring a PEEK-cranioplasty were examined with transcranioplasty ultrasound (TCU) in the postoperative course. High-resolution near-field imaging with frequencies up to 15 MHz was combined with larger views of the whole cranial cavity, using lower frequencies. Images were compared with CT or MRI images acquired on the same day

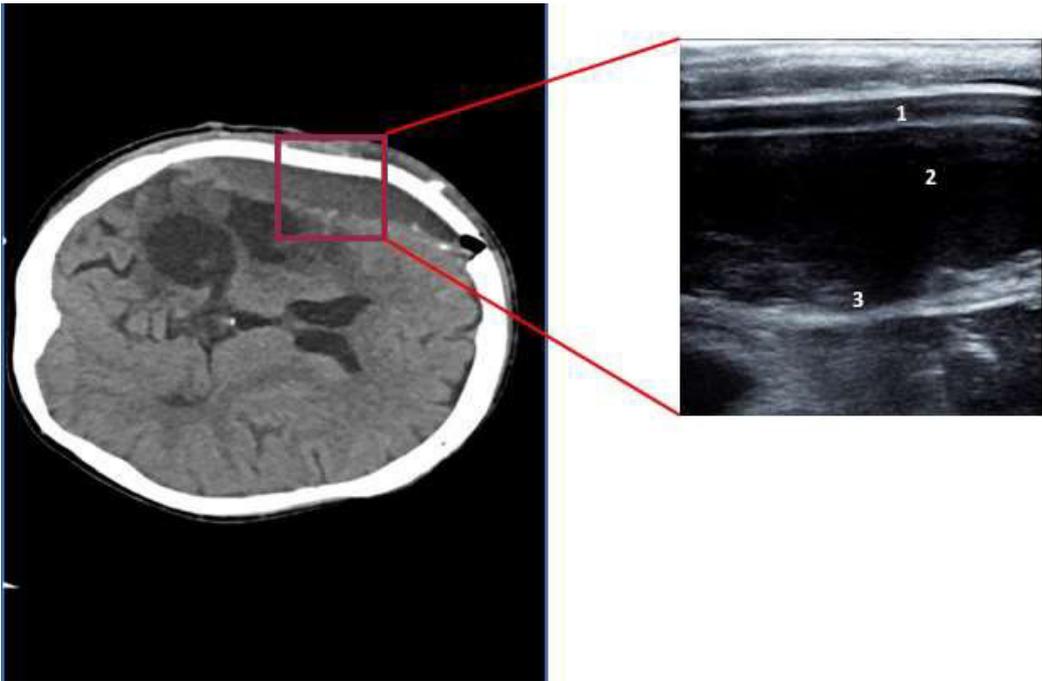
Results

In three patients, postoperative complications were observed by TCU. Two patients had extracerebral fluid collections, one patient developed a hydrocephalus. CT imaging confirmed the results. Moreover, a transcranioplasty navigation procedure could be performed via the burr-hole.

Conclusion

Knowledge about the properties of TCU may be useful for the management of patients after cranioplasty.

Fig 1



Bildgebung/Imaging

V291

Die Entwicklung und Evaluation eines Aneurysmaclips ohne Artefaktbildung im Kernspintomographen *Development and evaluation of an MRI artifact free aneurysm clip*

S. Senger¹, R. Mühl-Benninghaus², S. Urbschat¹, J. R. Reisel¹, W. Reith², J. Oertel¹, G. Fischer¹

¹Universitätsklinikum des Saarlandes, Klinik für Neurochirurgie, Homburg, Germany

²Universitätsklinikum des Saarlandes, Klinik für Neuroradiologie, Homburg, Germany

Objective

The digital subtraction angiography is still the gold standard in the follow-up for patients, who have undergone a clipping of an intracranial aneurysm. This is still a recurrent invasive method with accumulating x-ray exposure. MRI angiography could be an alternative. However, it has the drawback, that the metal clip causes artifacts around the intracranial vessels and impairs the clinical assessment. A metal-free aneurysm clip could overcome this problem. Recent advances in manufacturing technologies of fiber-reinforced plastics made it possible to produce a prototype of a metal-free clip.

Methods

The prototype was formed out of carbon-fiber-reinforced PEEK (CF-PEEK) in accordance with the standard clip design. The prototype was tested in a phantom in a 3-Tesla MRI scanner and in a microtomography scanner. *In vivo* experiments followed. The left renal artery of Sprague Dawley rats was either ligated with a suture, clipped with a regular titanium clip or with the CF-PEEK prototype. Sham operated animals served as control. The animals underwent standard MRI sequences and MRI angiography. The size of the artifacts as well as the quality of the vessel imaging was analyzed. *In vivo* and *in vitro* studies were performed to analyze the CNS biocompatibility of CF-PEEK compared to titanium and PEEK.

Results

The results of the phantom studies with the prototype showed no signs of artifacts. The *in vivo* studies showed a clear reduction of the artifacts size of the prototype compared to the titanium clip ($0.07 \pm 0.0 \times 0.06 \pm 0.06$ cm vs. $2.8 \pm 0.16 \times 1.09 \pm 0.1$ cm). In the MRI angiography, the vessels adjacent to the clipped vessel could be identified clearly in the suture group and the CF-PEEK clip group. The renal artery was successfully occluded in all treatment groups. Samples of CF-PEEK showed no signs of impaired biocompatibility compared to the titanium samples *in vitro* and *in vivo*. The clamping force of the prototype was markedly reduced compared to the standard titanium clip.

Conclusion

Former attempts of metal-free aneurysm clips did not meet the criteria of the standard clip design. In this study the practicability of this new artifact-free aneurysm clip based on CF-PEEK has been proven. The further development in the fabrication techniques should overcome the problem of a reduced clamping force in the future. This might help to reduce the amount of DSA in the follow up of patients suffering from aneurysm.

Bildgebung/Imaging

V292

Quantitative Erfassung vaskulärer Veränderungen in traumatisch geschädigten peripheren Nerven mit Hochfrequenz-Neurosonographie

Quantitative assessment of intraneural vascular alterations in peripheral nerve trauma using high-resolution neurosonography – technical note

C. Heinen¹, T. Kretschmer², U. Janssen-Bienhold³, J. Woitzik¹, B. Kewitz³, P. Dömer³

¹Evangelisches Krankenhaus Oldenburg, Universitätsklinik für Neurochirurgie, Oldenburg, Germany

²Klinikum Klagenfurt am Wörthersee, Neurochirurgie, Klagenfurt, Austria

³Carl von Ossietzky Universität Oldenburg, Visuelle Neurowissenschaft, Oldenburg, Germany

Objective

High-resolution neurosonography (HRNS) has become a major imaging modality in assessment of peripheral nerve trauma in the recent years. However, only little attention was given to the assessment of vascular changes of such lesions in HRNS. Here, we describe the quantitative assessment of intraneural vascular alterations in patients.

Methods

N=9 patients suffering from peripheral nerve trauma were examined clinically, electrophysiologically and with HRNS (SonoSite Exporte, Fuji). Image analyses using Fiji included determination of the established fascicular ratio (FR), the cross-section ratio (CSR), and as an extension, the calculation of a vascular ratio (VR) of healthy versus damaged nerve and a muscle perfusion ratio (MPR) in comparison to a healthy control group.

Results

The mean VR in the healthy part of the affected nerve (14.14%) differed significantly ($p < 0.0001$) from the damaged part (VR of 43.26%). This coincides with significant differences in the FR and CSR calculated for the damaged part versus the healthy part and the controls. In comparison, there was no difference between VRs determined for the healthy part of the affected nerve and the healthy controls (14.14% / 17.72%). However, the MPR of denervated muscles was significantly decreased compared to the non-affected contralateral controls.

Conclusion

VR and MPR serve as additional tools in assessing peripheral nerve trauma. Image analysis and calculation are feasible. Combined with the more morphologic FR and CSR the VR and MPR provide a more detailed insight into alterations accompanying nerve trauma.

Freie Themen/*Free topics*

V293

Qualitätsindikatoren in der Neurochirurgie – 30-tägige ungeplante Reoperationsrate bei 3760 Patienten – Erfahrung einer neurochirurgischen Klinik

The rise of quality indicators in neurosurgery – 30-day unplanned reoperation rate evaluated in 3760 patients – a single-centre experience

E. Suero Molina¹, C. Schildmacher¹, J. Doods², M. Freistühler³, S. J. Hellwig¹, W. Stummer¹, S. Schipmann-Miletic¹

¹Universitätsklinikum Münster, Klinik für Neurochirurgie, Münster, Germany

²Westfälische Wilhelms-Universität Münster, Institut für Medizinische Informatik, Münster, Germany

³Universitätsklinikum Münster, Controlling Department, Münster, Germany

Objective

Quality indicators are emerging as tools to evaluate health care outcomes. Few studies have evaluated indicators suitable for neurosurgery so far. Among others, reoperation rate has been suggested as a possible indicator. We aimed to evaluate the reoperation rate in a large neurosurgery adult collective.

Methods

In this exploratory post-hoc analysis we evaluated all patients operated in our service for elective and emergency surgery between January 2014 and May 2016. Planned and unplanned reoperations were filtered and a quantitative analysis, including uni- and multivariate analyses, was performed.

Results

A total of 3760 patients were included in this evaluation. From 378 reoperated patients within 30-days (10.1%), 51 underwent planned procedures (1.4%). 327 Patients (8.7%) represented the analyzed collective of patients having undergone unplanned surgical procedures, causing a total of 409 from 4268 additional procedures (9.6%). Early unplanned 7-days reoperation rate was 4.5% (n=193), occurring in 4.5% of patients (n=193). Postoperative hemorrhage (n=107, 26.2%) and external ventricle drainage-associated infections or dislocation (n=105, 25.7 %) were the most common indication for unplanned surgery.

Conclusion

Unplanned re-operation rate of a neurosurgical service can help to internally evaluate health care outcome and improve quality of care. Benchmarking with this indicator however is not recommendable as results can vary distinctly due to the heterogenic patient collective of each institution. We expect unplanned reoperation rates to be higher in large university hospitals and tertiary centers with complex cases, as compared to center with less complex cases treating patients with lower morbidity. In this study, we deliver an authentic portrait of a large neurosurgical center in Germany.

Freie Themen/*Free topics*

V294

Wie sicher sind elektive Kraniotomien bei älteren Patienten in der modernen Neurochirurgie? – eine prospektive Kohortenstudie über 1452 konsekutive Fälle

How safe are elective craniotomies for elderly patients in the modern era of neurosurgery? – a prospective cohort study of 1452 consecutive cases

R. Schär¹, C. Schwarz¹, S. Tashi¹, M. Branca², N. Söll¹, D. Cipriani³, C. Pollo¹, P. Schucht¹, C. Ulrich¹, J. Beck³, W. Z'Graggen¹, A. Raabe¹

¹Universitätsspital Bern, Neurochirurgie, Bern, Switzerland

²Universität Bern, Clinical Trials Unit Bern, Bern, Switzerland

³Universitätsklinikum Freiburg, Neurochirurgie, Freiburg, Germany

Objective

To assess the safety of elective craniotomy for elderly patients in modern neurosurgery.

Methods

This is a prospective cohort, single-centre study at a tertiary hospital over seven years. Adult patients who underwent elective craniotomy were allocated to three age groups (group 1 <65 years [n=1008], group 2 ≥65 to <75 [n=315], group 3 ≥75 [n=129]). The primary outcome was 30-day mortality after craniotomy. The secondary outcomes included rate of delayed extubation (>1 hour), need for emergency head CT scan and reoperation within 48 hours after surgery, length of postoperative intensive or intermediate care unit stay, length of hospital stay, and rate of discharge to home directly. Descriptive analysis was performed for baseline characteristics, surgical, postoperative care and patient transfer data. Binary outcomes measures were analysed by Fisher exact test or Chi-squared test, while the Kruskal-Wallis test was used to account for large values for continuous outcomes. Adjustment for ASA class, estimated blood loss and duration of surgery was also tested as a comparison using multiple logistic regression to account for potential selection bias. For significant differences a post-hoc analysis was performed.

Results

This study included 1452 patients (mean age 55.4 ± 14.7 years). Overall mortality was 0.55% (n=8) and there were no significant differences between the three groups. Patients with fatal outcome had a significantly higher ASA class (2.88 ± 0.35 vs. 2.42 ± 0.62, 95%CI 0.46 [0.03, 0.89], *P* = 0.036) and increased estimated blood loss (1444 ± 1973 ml vs. 436 ± 545 ml; difference of 1008 with 95%CI [618, 1398], *P* = <0.001). Significant differences were found in rate of emergency postoperative head CTs (group 1: 6.65% [n = 67], group 2: 7.30% [n = 23], group 3: 15.50% [n = 20]; *P* = 0.006), length of hospital stay (group 1: 6.35 ± 3.82 days, group 2: 6.59 ± 4.12, group 3: 7.21 ± 3.61; *P* = 0.019), and rate of discharge to home (group 1: 79.0% [n = 796], group 2: 72.0% [n = 227], group 3: 44.2% [n = 57]; *P* < 0.001). Remaining secondary outcomes were similar between the three groups.

Conclusion

Mortality after elective craniotomy was low in all age groups. Today, elective craniotomy for well-selected patients is safe, also for elderly patients. Elderly patients are more dependent on discharge to other hospitals and postacute care facilities after elective craniotomy.

Freie Themen/*Free topics*

V295

Gezielte multisegmentale epidurale Blutpflasterbehandlung bei spontaner intrakranieller Hypotonie in einer Schlaf-Wach-Technik

Targeted multisegmental epidural blood patch treatment for spontaneous intracranial hypotension in a sleep-awake technique

T. Abboud, I. Fiss, B. Schatlo, D. Mielke, V. Rohde, C. Von der Bröle

Universitätsmedizin Göttingen, Neurochirurgie, Göttingen, Germany

Objective

Spontaneous intracranial hypotension is increasingly recognized as a cause for refractory headache. Symptoms are variable but oftentimes limit quality of life especially in younger patients. High resolution imaging using CT and MR-modality are of paramount importance for the localization of the suspected leak of cerebrospinal fluid in order to create a tailored therapeutic approach. Treatment can range from blood patch injection to invasive closure of the CSF leak. Success rates of conventional blood patch injection range from 29% to 60%. We present our series to investigate the safety and efficacy of targeted multisegmental epidural blood patch injection in the therapy of intracranial hypotension.

Methods

We reviewed cases of seventeen patients who were treated for refractory spontaneous intracranial hypotension at our institute between 2005 and 2019. Head and spine MRI as well as whole spine myelography with contrast were performed as standard diagnostic procedures. All patients underwent a surgical implantation of two epidural drains above and beneath the site of suspected CSF leak through a minimally invasive interlaminar microsurgical approach under general anaesthesia. Afterward, blood was injected at multiple levels under clinical surveillance in awake patients. This procedure was repeated in patients with persistent symptoms.

Results

Patients presented with orthostatic headache, vertigo, sensory deficits and hypoacusis (94%, 18%, 18%, 12% of the cases, respectively). Subdural effusions were present in 65% of the cases, either unilaterally (12%) or bilaterally (53%). An epidural CSF leakage was identified in all cases, 76% on MRI and 82% on myelography. The exact site of CSF leak could be defined in 71% of the cases (18% in cervical spine and 53% in thoracic spine). Drainage of subdural hematoma was necessary in 6% of the cases. Targeted injection of blood patch was performed with an average blood amount of 34 ml. Significant improvement of symptoms was reported in 94% of the cases. Two patients (12%) had recurrent symptoms and underwent a second blood patch injection. No therapy related complications were reported.

Conclusion

Targeted multisegmental blood patch injection is a safe technique that showed a higher success rate than other blood patch techniques for treatment of spontaneous intracranial hypotension. It is performed in a minimally invasive procedure that can be repeated if necessary with a very low risk profile.

Freie Themen/*Free topics*

V296

Eine Störung der kortikalen β -Resonanz nach transkranieller Magnetstimulation als electrophysiologischer Marker einer motorischen Störung trotz erhaltener kortospinaler Integrität
Disturbed cortical network beta resonance to transcranial magnetic stimulation elucidates motor dysfunction despite intact cortico-spinal integrity

G. Naros, K. Mounts, L. Wiesinger, T. Leao, M. Tatagiba, A. Gharabaghi

Eberhard Karls Universität Tübingen, Klinik für Neurochirurgie, Tübingen, Germany

Objective

The synchronization of functionally related brain areas creates a channel for effective communication. In the motor system, these coherent oscillations occur within the beta-band frequency range. However, it is currently unknown what role the cortical beta resonance plays in the behavioral output of the motor system. By utilizing a noninvasive stimulation method, the functional significance of beta-band synchronization in large-scale interactions can be explored using the partly disrupted network state.

Methods

To investigate this, the present study characterizes the electroencephalographic (EEG) response to transcranial magnetic stimulation (TMS) applied to primary motor cortex (M1) at rest in twelve patients with tumors residing in motor eloquent areas. Electrophysiological results were compared to clinical motor performance measurements.

Results

Results indicate that lesions based in the cortical motor system areas disrupt the natural beta resonance response of M1 to a TMS pulse. Results further provided evidence that the motor system dysfunction occurs in spite of an undisturbed corticospinal tract, and instead relates to a weakened ability of the cortical motor network to synchronize.

Conclusion

These results demonstrate that a behavioral malfunction can relate to changes in the selective frequency of the brain network, as an altered cortical resonance accumulates in effect to impair the motor performance. Thus, TMS-EEG recordings could be used in neurosurgery to predict behavioral outcome after brain surgery.

Freie Themen/*Free topics*

V297

Die molekularen Marker, nicht aber die Tumorumfänge von niedriggradigeren Gliomen unterscheiden sich in der altersspezifischen Analyse

Lower-grade gliomas show different molecular markers but not different tumour volumes in an aged population

A. Krügers, J. Kerschbaumer, M. Demetz, C. Thomé, C. F. Freyschlag

Medizinische Universität Innsbruck, Universitätsklinik für Neurochirurgie, Innsbruck, Austria

Objective

The mean age of the population is rising, and the health care system is going to deal with this tendency. The aim of our study was to find specific age-related aspects and behavioural qualities of the lower-grade gliomas.

Methods

99 consecutive patients with histologically proven diffuse or anaplastic glioma, which underwent their first tumour resection in our institution, were retrospectively selected. The volume of MRI findings was measured in T1 CE and native, T2, Flair and DWI sequences using ITK-SNAP software. The casual neuropathological, epidemiological and clinical data was retrieved from patients' charts.

Results

The mean age of 55 males and 44 females in our series was 45 years (SD ± 16). The patients harboring more aggressive LGGs were older – 47 patients with diffuse glioma had the mean age of 38 years (SD ± 14) compared to 52 patients with anaplastic gliomas, which had mean age of 50 years (SD ± 16), $p < 0.001$.

Patients with wildtype IDH1 were also older – 53 years (SD ± 19) vs. 41 years (SD ± 14 , N=72), $p = 0.004$. Patients with ATRX expression were older as well – 49 years (SD ± 17) vs. 38 years (SD ± 11) or for 12 (SE ± 4) years, N=55, $p = 0.006$.

The CE volume in T1 sequence by the time of diagnosis higher increased with age: Spearman $r = 0.32$, N=54, $p = 0.015$. At the same time the native volumes in the older patient group were lower: in T1 – $r = -0.33$, $p = 0.013$; in T2 – $r = -0.29$, $p = 0.03$, DWI – $r = -0.35$, $p = 0.09$. They were significantly more often symptomatic at the time of first imaging, $p = 0.037$; and the first resection was performed earlier – $r = -0.2$, $p = 0.05$.

We did not find any significant differences in resection rate or volume with regard to age. However, the remnant absolute CE volume in T1 sequence stayed higher in older patients: $r = 0.22$, N=75, $p = 0.014$. The PFS in them was significantly lower, $p < 0.008$; but the OS did not differ in Cox models.

Conclusion

The higher age correlates to negative molecular marker expression and lower PFS compared to a younger cohort, however, this could not be translated into a shorter OS.

Freie Themen/*Free topics*

V298

Navigierte repetitive transkranielle Magnetstimulation verbessert das Outcome von postoperativen, ischämie-bedingten Paresen in Gliom-Patienten – eine randomisierte, sham-kontrollierte Doppel-Blind-Studie

Navigated repetitive transcranial magnetic stimulation improves the outcome of postsurgical ischemia-related paresis in glioma patients – a randomised, sham-controlled double-blinded trial

S. Ille¹, A. Kelm¹, A. Schröder¹, L. Albers¹, C. Negwer¹, V. Butenschön¹, N. Sollmann², T. Picht³, P. Vajkoczy³, B. Meyer¹, S. Krieg¹

¹Technische Universität München, München, Germany

²Technische Universität München, München, Germany

³Charité – Universitätsmedizin Berlin, Berlin, Germany

Objective

Navigated repetitive transcranial magnetic stimulation (nrTMS) is effective therapy for stroke patients. Neurorehabilitation could be supported by low-frequency stimulation of the non-damaged hemisphere to reduce transcallosal inhibition. The present study examines the effect of postoperative nrTMS therapy of the unaffected hemisphere in glioma patients suffering from acute surgery-related paresis of the upper extremity (UE) due to subcortical ischemia.

Methods

We performed a randomized, sham-controlled, double-blinded trial on patients suffering from acute surgery-related paresis of the UE after glioma resection. Patients were randomly assigned to receive either low-frequency nrTMS (1 Hz, 15 minutes) or sham stimulation directly before physical therapy for 7 consecutive days. We performed primary and secondary outcome measures on day 1, on day 7, and at a 3-month follow-up (FU). The primary endpoint was the change in Fugl-Meyer Assessment (FMA) at FU.

Results

Compared to the sham stimulation, nrTMS significantly improved outcomes between day 1 and FU based on the FMA (mean [95% CI] +31.9 [22.6, 41.3] vs. +4.2 [-4.1, 12.5]; P=0.001) and the National Institutes of Health Stroke Scale (NIHSS) (-5.6 [-7.5, -3.6] vs. -2.4 [-3.6, -1.2]; P=0.02). To achieve a minimal clinically important difference of 10 points on the FMA scale, the number needed to treat is 2.19.

Conclusion

The present results show that patients suffering from acute surgery-related paresis of the UE due to subcortical ischemia after glioma resection significantly benefit from low-frequency nrTMS stimulation therapy of the unaffected hemisphere.

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