Traumatic brain injury - global developments in research and treatment

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Medical Faculty of Pecs University,
Pecs, Hungary, H-7624
What are we talking about?

- definitions - epidemiology
- TBI research and discovery - clinical relevance
  - outcome prediction - predictive models
- personal notes
What are we talking about?
TBI Definition VA/DoD

- VA/DoD “Clinical Practice Guideline For Management of Concussion/ Mild Traumatic Brain Injury” (V1.0 2009) and Brain Trauma Foundation, AANS and ANC joint “Guidelines for the management of the Severe Traumatic Brain Injury” (3rd edition, 2007) has defined traumatic brain injury as a 

  traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force that is indicated by new onset or worsening of at least one of the following clinical signs, immediately following the event:
TBI Definition VA/DoD II

- loss of or a decreased level of consciousness (LOC)
- loss of memory for events immediately before or after the injury (post-traumatic amnesia [PTA])
- alteration in mental state (confusion, disorientation, slowed thinking etc.) (Alteration of consciousness/mental state [AOC])
- Neurological deficits (weakness, loss of balance, change in vision, praxis, paresis/plegia, sensory loss, aphasia, etc.) that may or may not be transient
- Intracranial lesion
- A computed tomography scan (CT or CAT scan) is the gold standard for the radiological assessment of a TBI patient.
The spectrum of traumatic brain injury

Self reported/minimal - **Mild** -  

**Moderate** -  

**Severe** -  

Non-salvageable
Traumatic brain injury...

- ...the silent epidemic
- ...the disease of unmet medical need
- ...leading cause of mortality in the active population
The significance of severe TBI

- 2.1 million TBI cases per year causing
  - 100,000 deaths and
  - 500,000 hospitalizations
- TBI-related death rate of the population under 35 years of age is 3.5 times as many as that of cancer and heart disease together
- 90,000 survivors will endure life-long debilitating loss of function
- 5,000 new cases of epilepsy
- 2,000 permanent vegetative state
- The cumulative societal cost per year for TBI is $48 billion

TBI in the Military

- penetrating brain injuries claim 25% of soldiers killed in battle
- 2/3 of casualties have brain injuries and concussion is growing military medical problem

Mild Traumatic Brain Injury (MTBI) in Sports

- 1.6 - 3.8 million sports related concussions occur each year
- N.F.L. found that dementia-related diseases are much higher in former players than the national population
- Sports incidence of TBI (5-18 yrs of age)
  - Cycling: 64,993
  - Football: 36,412
  - Baseball and Softball: 25,079
  - Basketball: 24,701
  - Powered RV: 24,090
  - Skateboards/Scooters w/power: 18,542
  - Soccer: 17,108
  - Skateboards/Scooters: 16,477

http://educationalissues.suite101.com/article.cfm/tbi_statistics

September 26, 2009 Florida vs Kentucky, Tim Tebow from Univ. of Florida suffered a mild concussion
Emerging (but debated...)

- **Mild traumatic brain injury**
  - CT negative, MRI positive
  - SWI negative, MRI positive
  - Post-concussive syndrome
Emerging (but debated...)

- **Mild traumatic brain injury**
  - CT negative, MRI positive
  - SWI negative, MRI positive
  - Post-concussive syndrome
The burden of traumatic brain injury

- Traumatic brain injury is the primary cause of death under 40

- WHO estimates that until 2020 TBI will be the third most frequent cause of death in the Earth

(Langlois et al., *J. Head Trauma Rehabil.* 2006, 21, 375-378
<table>
<thead>
<tr>
<th>Intervention</th>
<th>GBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Se cholesterol check-up (age 40-69)</td>
<td>220</td>
</tr>
<tr>
<td>Neurosurgical care for TBI</td>
<td>240</td>
</tr>
<tr>
<td>Neurosurgical care for SAH</td>
<td>490</td>
</tr>
<tr>
<td>Stroke prevention with anti-hypertensive medication (age 40-64)</td>
<td>940</td>
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<tr>
<td>pm implantation</td>
<td>1100</td>
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<tr>
<td>Kidney transplantation</td>
<td>4710</td>
</tr>
<tr>
<td>Neurosurgical care for brain tumors</td>
<td>107780</td>
</tr>
</tbody>
</table>
„global developments in research and treatment”

• Development ≠ achievement
TBI research and discovery

- Understanding the pathobiology
  - Stratification of the injury
- Clinically relevant models of TBI
  - Should resemble real-life trauma
  - Common endpoints to validate
- Pathobiology-based therapeutic targets
  - Should resemble real-life circumstances (dosage, therapeutic window, etc...)
  - Common endpoints to compare therapeutic efficacy
TBI research and discovery

• Understanding the pathobiology
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General classification

**PRIMARY BRAIN INJURY**

**SECONDARY BRAIN INJURY**
- hypoxia
- hypoperfusion

**ASSOCIATED CNS INJURY**
- associated C-spine (CO-II) injury
- tandem injury

**ASSOCIATED INJURY**
- associated multiorgan injury/failure (MOF)
PRIMARY BRAIN INJURY

- occurs at the time of impact
- almost immediate clinical effects
- refractory to most treatment
- can be influenced by preventive measures
MIND YOUR HEAD
SECONDARY BRAIN INJURY

- occurs at some time after the impact
- characterized by hypoperfusion/hypoxia
- propagates gradually
- preventable and treatable
Advanced Trauma Life Support®-ATLS®

- circumstances of injury + energy/forces + type of impact

- potential structural damage, pathobiological processes evoked
Potential forces

- STATIC

- DYNAMIC
  - impact
  - acceleration-deceleration
Patho-morphology

Focal
- contusion
  - coup - contrecoup
- epidural hemorrhage
- subdural hemorrhage

Diffuse
- Diffuse Axonal Injury (DAI)
- Hypoxic Brain Damage
- Brain Swelling
- Diffuse Vascular Injury
- Diffuse Neuronal Somatic Injury

IMPACT-TYPE, dynamic forces

Acceleration-deceleration-type, dynamic forces
• Traumatic brain injury is an extremely complex disease entity affecting the most complex organ of the most complex living creature...
TBI research and discovery

- Understanding the pathobiology
  - Stratification of the injury

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Triage

- pre-CT- classification
- classification upon the severity of brain injury
## Classification of TBI Severity adopted from 2009 VA/DOD Guideline

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural imaging</td>
<td>Normal</td>
<td>Normal or abnormal</td>
<td>Normal or abnormal</td>
</tr>
<tr>
<td>Loss of Consciousness (LOC)</td>
<td>0–30 min</td>
<td>&gt; 30 min and &lt; 24 hours</td>
<td>&gt; 24 hrs</td>
</tr>
<tr>
<td>Alteration of consciousness/mental state (AOC) *</td>
<td>a moment up to 24 hrs</td>
<td>&gt; 24 hours. Severity based on other criteria</td>
<td></td>
</tr>
<tr>
<td>Post-traumatic amnesia (PTA)</td>
<td>0–1 day</td>
<td>&gt; 1 and &lt; 7 days</td>
<td>&gt; 7 days</td>
</tr>
<tr>
<td>Glasgow Coma Scale (best available score in first 24 hours)</td>
<td>13-15</td>
<td>9-12</td>
<td>&lt; 9</td>
</tr>
</tbody>
</table>
Moderate head injury: GCS 9-12 is NOT a homogenous group

Neuroworsening, seizures, and medical complications as outcome predictors with a GCS of 11 to 13

Low motor GCS score is more outcome-related in patients with GCS of 9 and 10.
Factors contributing to outcome - GCS

- clinical utility of the GCS is limited by the application of therapeutic guidelines based on sedation

FIG. 1. Heterogeneity of severe traumatic brain injury (TBI). Computed tomography (CT) scans of six different patients with severe TBI, defined as a Glasgow Coma Scale score of <8, highlighting the significant heterogeneity of pathological findings. CT scans represent patients with epidural hematomas (EDH), contusions and parenchymal hematomas (Contusion/Hematoma), diffuse axonal injury (DAI), subdural hematoma (SDH), subarachnoid hemorrhage and intraventricular hemorrhage (SAH/IVH), and diffuse brain swelling (Diffuse Swelling).

"At 3 months after injury, 33% of the mTBI subjects were functionally impaired (Glasgow Outcome Scale-Extended score ≤6); 22.4% of the mTBI subjects available for follow-up were still below full functional status at 1 year after injury. The term "mild" continues to be a misnomer for this patient population and underscores the critical need for evolving classification strategies for TBI for targeted therapy."
The spectrum of traumatic brain injury...

Self reported/minimal - Mild - Moderate - Severe - Non-salvageable

...should be
- redefined
- recharacterized
TBI research and discovery

- Understanding the pathobiology
  - Stratification of the injury

- Clinically relevant models of TBI
  - Should resemble real-life trauma
  - Common endpoints to validate

- Pathobiology-based therapeutic targets
  - Should resemble real-life circumstances
    (dosage, therapeutic window, etc...)
  - Common endpoints to compare therapeutic efficacy
• Common endpoints also serve as cornerstones that can aid
  - monitoring of treatment efficacy
  - outcome prediction
  - quality of care measures

• Prognostic models/prognostic calculators
Outcome prediction: why do we bother with?

- support early clinical decision-making
- inform the relatives
- facilitate comparison of outcomes (patient series, results over time)
- audit of care
- provide endpoint and facilitate the selection of target population in RCTs
Historically, doctors have been helpless to prevent secondary cell death after a traumatic brain injury. But unintended results during a series of experiments in the early 1990s showed cyclosporine can mitigate cellular damage once the pharmaceutical crosses the blood-brain barrier.

Oftentimes called the silent epidemic, traumatic brain injury (TBI) affects approximately 1.7 million Americans annually. More than 52,000 are killed, and 275,000 are hospitalized. Most are left in various states of disability—from almost full recovery to mild symptoms but able to function with some or moderate disability to severe disability requiring around-the-clock intensive care and support. The annual costs of TBI, both direct and indirect, including such factors as lost work time or reduced productivity, have been estimated at more than $60 billion, and there may be more than six million TBI survivors in society.

Over the past decade, TBI has come to the fore as tens of thousands of wounded soldiers return home from the Middle East suffering both hidden and visible TBIs and trauma caused by blast injuries from improvised roadside explosions.

What is called post-traumatic stress disorder may actually be the long-term effects of TBI. Due to the economic and social costs of TBI, a significant ongoing effort is being made to develop and apply emerging new clinical and pre-clinical pharmaceuticals with the potential to mitigate the cascading additional brain damage that occurs during the critical secondary phase in TBI. Among these is an interesting pharmaceutical compound called cyclosporine (also known as cyclosporin-A, or CsA), which has been found to have significant neuroprotective capabilities and the ability to moderate the resulting damage and long-term disability in TBI.

First discovered by Sandoz (now Novartis) scientists in Norway in 1969, cyclosporine is isolated from the fungus Tolypocladum inflatum.
Building Blocks for prognosis

courtesy of A. Maas

<table>
<thead>
<tr>
<th>Characteristics of the individual</th>
<th>Admission</th>
<th>Clinical Course</th>
<th>Early Endpoints</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biological constitution</td>
<td>Injury details</td>
<td>Biological response to injury</td>
<td>Early mortality (day 14)</td>
<td>Mortality</td>
</tr>
<tr>
<td>- genotype</td>
<td>type (closed, penetrating etc.)</td>
<td>- metabonomics</td>
<td>Neuroworsening</td>
<td>GOS (E)</td>
</tr>
<tr>
<td>Demographic factors</td>
<td>cause</td>
<td></td>
<td></td>
<td>HRQoL</td>
</tr>
<tr>
<td>- age</td>
<td>Clinical severity</td>
<td>Clinical severity</td>
<td></td>
<td>Neuro-imaging</td>
</tr>
<tr>
<td>- race</td>
<td></td>
<td>- intracranial (GCS/pupils)</td>
<td></td>
<td>Neuro-psychological assessment</td>
</tr>
<tr>
<td>Socioeconomic status and education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical History</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injuries</td>
<td>Second insults</td>
<td>Change in adm. parameters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- type (closed, penetrating etc.)</td>
<td>- systemic (hypoxia, hypotension, hypothermia)</td>
<td></td>
<td>Neuroworsening</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- intracranial (GCS/pupils)</td>
<td>- clin. severity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- extracranial (AIS/ISS)</td>
<td>- change in CT</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Second insults</td>
<td>- biomarkers, lab values</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- systemic (hypoxia, hypotension, hypothermia)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- intracranial (neuroworsening, seizures)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Biomarkers/lab values</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

courtesy of A. Maas
Factors contributing to outcome -

AGE

- studies identified age as the strongest independent predictive factor
- Cut off for survival: 50y
- Cut off for good outcome 30y
Factors contributing to outcome - GCS

- clinical utility of the GCS is limited by the application of therapeutic guidelines based on sedation

# Marshall CT classification

<table>
<thead>
<tr>
<th>Category</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse Injury I.</td>
<td>No visible pathology seen on CT scan</td>
</tr>
<tr>
<td>/No visible pathology/</td>
<td></td>
</tr>
<tr>
<td>Diffuse Injury II.</td>
<td>Cisterns are present with midline shift 0-5 mm and/or:</td>
</tr>
<tr>
<td></td>
<td>lesion densities present</td>
</tr>
<tr>
<td></td>
<td>no high- or mixed-density lesion &gt; 25 cc may include bone fragments and foreign bodies</td>
</tr>
<tr>
<td>Diffuse Injury III.</td>
<td>Cisterns compressed or absent with midline shift 0-5 mm, no high- or mixed-density lesion &gt; 25 cc</td>
</tr>
<tr>
<td>/Swelling/</td>
<td></td>
</tr>
<tr>
<td>Diffuse Injury IV.</td>
<td>Midline shift &gt; 5 mm, no high- or mixed-density lesion &gt; 25 cc</td>
</tr>
<tr>
<td>/Shift/</td>
<td></td>
</tr>
<tr>
<td>Evacuated mass lesion</td>
<td>Any lesion surgically evacuated</td>
</tr>
<tr>
<td>Nonevacuated mass lesion</td>
<td>High- or mixed-density lesion &gt; 25 cc, not surgically evacuated</td>
</tr>
</tbody>
</table>
Rotterdam CT Score

- Basal cisterns
  - Normal: 0
  - Compressed: 1
  - Absent: 2

- Midline shift
  - No shift or shift ≤ 5mm: 0
  - Shift > 5mm: 1

- Epidural mass lesion
  - Present: 0
  - Absent: 1

- Intraventricular blood or tSAH
  - Absent: 0
  - Present: 1

- Add plus 1 to make the grading numerically consistent with the grading of the motor score of the GCS and with the Marshall CT classification.

- Based on: Maas et al.: Neurosurgery 57:1173-1182, 2005
Overall Mortality

Mortality at D 0-3

Mortality at D 0-10
Factors contributing to outcome – CT, MR

- CT misses diffuse lesions,
- Predictive value of diffuse lesions identified on CT is relatively low
- MR: problems with:
  - Availability
  - Cost efficiency

• The significance of MRI-only lesions is not yet established
Factors contributing to outcome – Monitoring

- Multiparametric ICU monitoring primarily reflects secondary insults;
- Initial results do not necessarily harbour predictive value;
- Conflicting data on the significance of Pbr02-monitoring.


ICP MONITORING

- INDICATION: GCS < 8, Traumatic Brain Injury
- TYPE: Ventricular catheter connected to external strain gauge or indwelling fiberoptic/strain gauge
- INFECTION: < 10%. Not usually clinically significant
- HEMORRHAGE: < 1%. Not usually clinically significant
A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury

Randall M. Chesnut, M.D., Nancy Temkin, Ph.D., Nancy Carney, Ph.D., Sureyya Dikmen, Ph.D., Carlos Rondina, M.D., Walter Videtta, M.D., Gustavo Petroni, M.D., Silvia Lujan, M.D., Jim Pridgeon, M.H.A., Jason Barber, M.S., Joan Machamer, M.A., Kelley Chaddock, B.A., Juanita M. Celix, M.D., Marianna Cherner, Ph.D., and Terence Hendrix, B.A.

ABSTRACT
Intracranial pressure monitoring in severe traumatic brain injury
Should not be abandoned on the basis of recent evidence

Peter J Hutchinson reader in neurosurgery¹, Angelos G Kolas National Institute for Health Research academic clinical fellow in neurosurgery¹, Marek Czosnyka reader in brain physics¹, Peter J Kirkpatrick consultant neurosurgeon¹, John D Pickard professor of neurosurgery¹, David K Menon professor of anaesthesia²

¹Division of Neurosurgery, Addenbrooke’s Hospital and University of Cambridge, Cambridge CB2 0QQ, UK; ²Division of Anaesthesia, Addenbrooke’s Hospital and University of Cambridge, Cambridge, UK
Combined predictive models
Predicting Outcome after Traumatic Brain Injury: Development and International Validation of Prognostic Scores Based on Admission Characteristics

Ewout W. Steyerberg1,∗, Nino Mushkudiani2, Pablo Perez2, Isabella Butcher3, Juan Lu4, Gillian S. McHugh2, Gordon D. Murray5, Anthony Mamarilou4, Ian Roberts2, J. Dirk F. Habbema1, Andrew I. R. Raaz5

1 Center for Medical Decision Sciences, Department of Public Health, Erasmus MC, Rotterdam, The Netherlands; 2 London School of Hygiene and Tropical Medicine, Nutrition and Public Health Intervention Research Unit, London, United Kingdom; 2 Division of Community Health Sciences, University of Edinburgh, Scotland; 4 Department of Neurosurgery, Virginia Commonwealth University, Richmond, Virginia, United States of America; 5 Department of Neurosurgery, Erasmus MC, Rotterdam, The Netherlands

ABSTRACT

Background

Traumatic brain injury (TBI) is a leading cause of death and disability. A reliable prediction of outcome on admission is of great clinical relevance. We aimed to develop prognostic models with readily available traditional and novel predictors.

Methods and Findings

Prospectively collected individual patient data were analyzed from 11 studies. We considered predictors available at admission in logistic regression models to predict mortality and unfavorable outcome according to the Glasgow Outcome Scale at 5 mo after injury. Prognostic models were developed in 8,509 patients with severe or moderate TBI with cross-validation by omission of each of the 11 studies in turn. External validation was on 6,681 patients from the recent Medical Research Council (MRC) CRASH trial and found that the strongest predictors of outcome were age, motor score, pupillary reactivity, and CT characteristics, including the presence of traumatic subarachnoid hemorrhage. A prognostic model that combined age, motor score, and pupillary reactivity had an area under the receiver operating characteristic curve (AUC) between 0.66 and 0.64 at cross-validation. This performance could be improved (AUC increased by approximately 0.05) by considering CT characteristics, secondary insults (hypotension and hypoxia), and laboratory parameters (glucose and hemoglobin). External validation confirmed that the discriminatory ability of the model was adequate (AUC 0.80). Outcomes were systematically worse than predicted, but less so in 1,588 patients who were from high-income countries in the CRASH trial.

Conclusions

Prognostic models using baseline characteristics provide adequate discrimination between patients with good and poor 6 mo outcomes after TBI, especially if CT and laboratory findings are considered in addition to traditional predictors. The model predictions may support clinical practice and research, including the design and analysis of randomized controlled trials.

The authors’ summary of this article follows the references.
IMPACT (International Mission for Prognosis And Clinical Trial Design)
Outcome calculator

- core prognostic model: based on three clinical predictors: age, motor component of Glasgow coma score (GCS), and pupillary reactivity

- extended model: core + secondary insults and CT characteristics

- laboratory model: also includes haemoglobin and glucose
<table>
<thead>
<tr>
<th>Trial</th>
<th>Model subset</th>
<th>Validation exercise</th>
<th>AU ROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRASH</td>
<td>L/MIC</td>
<td>Internal validation</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>HIC</td>
<td>Internal validation</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td>L/MIC CT</td>
<td>Internal validation</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>HIC CT</td>
<td>Internal validation</td>
<td>0.83</td>
</tr>
<tr>
<td></td>
<td>HIC CT</td>
<td>External validation (IMPACT)</td>
<td>0.77</td>
</tr>
<tr>
<td>IMPACT</td>
<td>Core</td>
<td>Internal validation</td>
<td>0.72–0.82</td>
</tr>
<tr>
<td></td>
<td>Core + CT</td>
<td>Internal validation</td>
<td>0.73–0.84</td>
</tr>
<tr>
<td></td>
<td>Core + CT + Laboratory</td>
<td>Internal validation</td>
<td>0.775–0.82</td>
</tr>
<tr>
<td></td>
<td>Core + CT</td>
<td>CRASH CT; GCS &lt;12</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>Core + CT</td>
<td>CRASH CT; GCS &lt;12 [P]</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td>Core + CT</td>
<td>CRASH CT; GCS &lt;12; HIC only</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Figures are AUROC/‘c’ statistic. L/MIC, low/middle income countries; HIC, high-income countries; [P], placebo patients only.
Probability of unfavorable outcome: IMPACT-calculator

![Graph showing the relationship between probability of unfavorable outcome and observed mortality. The graph includes a scatter plot with error bars and a trend line.]
• **Concerns:**
  - **Statistics:** decision tree analysis vs. Logistic regression analysis
  - **Content:** limitations due to initial data-collection:
    - **Lack of:**
      - data on coagulopathy
      - Rotterdam score
      - detailed data on surgery
      - some physiological parameters

• **Work is needed to establish the accuracy of these models prospectively in patients not enrolled in clinical trials.**
What measures should help?

- Coagulopathy
- Rotterdam score
- Biomarkers
Patients with SDH above 60

- Gender: 2,289
- Age: 0,930
- GCS on admission: 0,850
- Alcohol: 0,946
- Primary coagulopathy: 6.955*
- Secondary coagulopathy: 2,173
Patients with SDH below 60

- Gender: 4,105
- Age: 1.160*
- GCS on admission: 0.788
- Alcohol: 0.435
- Primary coagulopathy: 55.513*
- Secondary coagulopathy: 23.846*
BIOMARKERS

Prediction of outcome in severe traumatic brain injury

David K. Menon and Cameron Zahed

The purpose of this review is to assess the current status of risk prediction models for predicting outcome after severe traumatic brain injury (TBI), based on the development in recent years. The review focuses on the development of new risk prediction models for TBI and on the factors that may influence the outcome of patients with TBI. The review concludes with a discussion of the future directions for research in this area.

Keywords: CRASH, IMPACT, outcome, prediction, traumatic brain injury

Update on protein biomarkers in traumatic brain injury with emphasis on clinical use in adults and pediatrics

Ezzebet Kövesdi, János Lőcsei, Péter Bukavics, Orsolya Farkas, József Pál, Endre Creter, Dára Szellár, Tamás Jancsó, Samuel Komsy, András Bikó

The article reviews the current knowledge on protein biomarkers in traumatic brain injury (TBI) and their potential clinical applications. The review covers the development of new biomarkers and their applicability in different clinical settings, including adults and pediatrics. The review concludes with a discussion on the future directions for research in this area.
Brain Injury Biomarkers May Improve the Predictive Power of the IMPACT Outcome Calculator
Conclusion

- **Outcome prediction is important:**
  - Continuous validation and revision of institutional protocols
- **Outcome calculators should take into consideration additional issues primarily biomarkers**
- **At least some components of outcome models can serve as common endpoints for preclinical and clinical studies**
the way “from bench to bedside”
• epidemiology
• classification – injury
• classification – injured: triage
• treatment – general considerations
• sequelae of traumatic brain injury
• personal notes - what dreams may come...
Neurotrauma... the poor relative in the family...

- patient population: hard to admit one who is not intoxicated
- typically not a white collar disease
- recovery is usually slow, outcome is not favorable
- not rewarding to the care givers
- major psychological load to the team
- malpractice issues...
Emergency surgery for post-traumatic intracranial hematomas may be among the most difficult procedures...because of heavy bleeding and brain swelling, yet because these operations frequently occur at night ... the less experienced surgeons are delegated to do them”

(Jones, Bullock, Reilly, Head Injury 2nd ed., publ.:Hodder Arnold, 2005)
no way to abandon or give up!

- residents learn and excercise their skills:
  - surgical
  - triage/decision making
  - patient management, consenting the relatives

- almost all fields from vascular to spine, oncology to functional are attacked by other professions, while trauma still stays in our hands

- the primary link to emergency care, positions us to the field of multidisciplinary care and enables to provide extremely cost efficient acute care
Contemporary clinical care for TBI should be characterized by:

- scientific evidence based treatment protocols including prehospital care
- actual decisions influenced by multimodal physiological monitoring and imaging
- audit/quality control
- gradual, continuous decrease in mortality and improvement in outcome
MOTTO

- no injury to the skull can be as trivial or so severe to deny treatment

Hippocrates of Kos (460–377 BC)
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Thank You!