[Frontiers in Bioscience, Landmark, 20, 763-771, January 1, 2015]

Prediction of clinical outcome in severe traumatic brain injury

Liang Gao[1], Xuehai Wu[2]

[1]Department of neurosurgery, shanghai tenth people hospital, tongji university, 301yanchang road shanghai P.R. China 200072, [2]Department of Neurosurgery, Huashan Hospital, Fudan University, Shanghai, China

TABLE OF CONTENTS

1. ABSTRACT

Traumatic brain injury (TBI) is the main cause of death and disability in adults worldwide. Early detection of TBI would be useful for evaluating and designing treatment strategies. Both single predictors from early clinical examination and multiple hospitalization variables/parameters can be used to determine the long-term prognosis of TBI. Predictive models like the IMPACT or CRASH prognosis calculator (based on large sample sizes) can predict mortality and unfavorable outcomes. Moreover, imaging techniques like MRI (Magnetic Resonance Imaging) can also predict consciousness recovery and mental recovery in severe TBI, while biomarkers associated with stress correlate with, and hence can be used to predict, severity and mortality. All predictors have limitations in clinical application. Further studies comparing different predictors and models are required to resolve limitations of current predictors.

2. INTRODUCTION

Traumatic brain injury (TBI) is a major health problem worldwide. It is estimated to affect approximately 10 million people every year and is the leading cause of death and disability among young adults in Western countries (1,2). It affects 1.5 million people each year in the United States alone, 52,000 of whom die in-hospital (3). Higher incidence and poorer outcomes have been recorded in racial minority groups than in non-Hispanic whites (4-6). African-Americans and Asians have a higher in-hospital mortality rate than non-Hispanic whites, following TBI (4). Many survivors of TBI have residual defects in cognitive, emotional and behavioral functioning. Behavioral changes are common in patients with moderate to severe TBI (7-9), which negatively affects everyday life, social and vocational reintegration, and the overall quality of life of these patients (10-12).

Hence, it is necessary to accurately predict the outcome of traumatic brain injury. A survey of Canadian intensivists, neurosurgeons and neurologists revealed that an accurate prognosis might be extremely helpful during the first 7 days following severe TBI (13). In another survey on the favorability of patient prognosis at 1 year following injury, approximately one-third respondents agreed, one-third were neutral, and the rest disagreed that it would be unfavorable (13). Hence, early prediction of TBI will be useful not only for designing currently available treatments, but also for assessing novel therapeutic strategies in future randomized controlled trials (RCTs) using outcome versus predicted outcome as end-points. In this review, we discuss recent findings on the clinical predictors of severe TBI prognosis.

3. CLINICAL MANIFESTATIONS OF SEVERE TBI AND THEIR UTILITY IN PREDICTING PATIENT OUTCOME

While determining the prognosis of TBI, some previous studies focused on the clinical

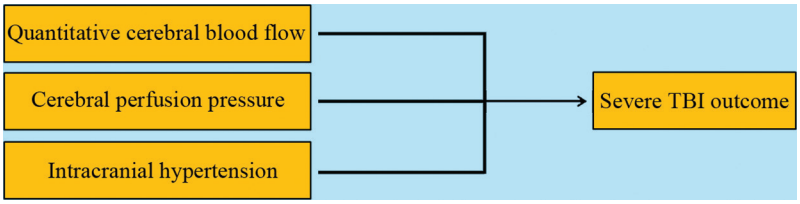

Figure 1. Quantitative cerebral blood flow within the first 6 and 12 hours after severe TBI, cerebral perfusion pressure (CPP) and intracranial hypertension predict outcome after severe TBI.

manifestations of injury. The somatosensory evoked potential (SEP), a parameter recorded and used for evaluating the abnormality of the somatosensory tract that extends from the peripheral nerve to the cerebral cortex, can be correlated with the outcome in severe TBI. Unilateral or bilateral absence of the cortical component of SEP is associated with a poor outcome (death or severe disability) (14). Early SEP grades at day three following TBI are indicators of information-processing speed, working memory and the ability to attend to tasks 1 year after TBI. These findings suggest early SEP has a predictive property in both short and long term outcome of TBI. Amongst patients diagnosed with severe TBI, SEP grades I and III can provide an accurate prognosis in more than 80% cases (15). In short and medium term prognosis, visual evoked potential, besides SEP, is also valuable for predicting survival of patients rendered comatose due to severe TBI (16).

In addition to SEP, the disability status and quantitative cerebral blood flow can also be used as single predictors. A greater disability is found to be associated with better psychological functioning, which although seems paradoxical, is observed among patients with anosognosia or poor awareness of psychological functioning 1 year after TBI (17). Early prediction within the first 6 to 12 h following severe TBI can be obtained from quantitative cerebral blood flow, a parameter which can predict the 6-month outcome (18), in accordance with previous findings that cerebral perfusion pressure (CPP) (<60 mm Hg) and intracranial hypertension (ICP) (>30 mm Hg) have great potential in the prognosis of neurological deterioration (19) (Figure 1). The association between ICP and mortality was confirmed in a study of 501 children under 16 years of age and diagnosed with TBI (20). This suggested that quantitative cerebral blood flow in the early stage of severe TBI, can be used as a single predictor to determine long-term survival outcome. Transcranial Doppler (TCD) ultrasonography, which is used to measure ICP and CPP, has been validated as a tool for predicting the 6-month outcome in patients. When performed within the first 24 h of severe TBI, it correlates significantly with ICP and CPP values (21).

Another outcome predictor at 3 and 6 months post-injury, is duration of the coma (22). Also, the duration of posttraumatic amnesia and time since injury can predict functional outcomes 1 year after moderate to severe TBI (23). When the intelligence coefficient of patients was examined using the Wechsler adult intelligence scale III, after severe TBI, cognitive deficits such as a slow processing speed were detected as the predominant symptom; this could be correlated with predictors such as the length of coma and posttraumatic amnesia (24).

Although single predictors are useful in the prognosis of severe TBI, performing a comprehensive analysis of multiple factors has been considered, since this may provide more information than a single predictor. In a retrospective study involving 846 cases of severe TBI (Glasgow coma scale (GCS) < or = 8), multiple parameters such as the GCS score, age, pupillary response and size, hypoxia, hyperthermia and high ICP were associated with outcome 1 year after severe TBI (25). The outcomes included good recovery, moderate disability, severe disability, vegetative status and death. A study involving 12 patients that underwent bilateral decompressive craniectomy predicted good outcomes in younger patients with better pupillary response and neurological status on admission, following similar categories as the former study (26). With regard to survival and functional recovery, factors such as a reduction in economic and social costs, prevention and early treatment of complications, and maintenance of homeostasis predict a good outcome (27). However, in predicting cognitive function, pupillary examination, Marshal CT Classification, GCS and serum glucose level were found to have limited capability in determining

outcome in severe TBI patients (GCS≤8) (28). Hence, multiple hospitalization variables may be valuable in predicting outcomes of long-term behavioral rehabilitation, but not cognitive function, in severe TBI patients. However, since studies comparing the predictive effects of single predictors versus multiple factors are rare, it is difficult to conclude which of the two is a better strategy in the prognosis of severe TBI.

4. STATISTICAL MODELS FOR OUTCOME PREDICTION IN SEVERE TBI PATIENTS

While multiple predictors may provide valuable information in the prognosis of severe TBI, predictive models based on a statistical model and large sample size, may be more accurate and practical. A comprehensive model that included multiple factors such as pre-injury behavioral problems, sex of the patient (male), post-injury cognitive and physical deficits and lack of access to transportation, predicted largely unfavorable occupational performance outcomes (29). Analysis of data from 513 severe closed head-injury patients using a hybrid model with baseline admission parameters could accurately predict the 6-month injury outcome (30). Another predictive model based on age, absence of light reflex, presence of extensive subarachnoid hemorrhage, intracranial pressure and midline shift, has a high predictive value in severe TBI (31).

The models mentioned above are limited by small sample size. The International Mission on Prognosis in Traumatic Brain Injury (IMPACT) project, which is focused on advancing knowledge in prognosis, trial-design and treatment of TBI, has been developed on a dataset obtained from 8509 patients from eleven studies on moderate and severe TBI (32). The IMPACT project developed three different models based on the dichotomized GOS (Glasgow outcome scale) at 6 months after injury: the Core Model, the Extended Model and the Lab Model, for the prediction of mortality and unfavorable outcome (including death, vegetative state and severe disability) (Figure 2). An external validation of the IMPACT models with a total of 9,036 moderate and severe TBI patients confirmed its generalizability in predicting mortality and unfavorable outcomes (33). Similar predictions were made using the Corticosteroid Randomisation after Significant Head Injury (CRASH) prognostic models (33). The IMPACT prognostic models were further validated in a study that included 508 patients diagnosed with moderate or severe TBI; the IMPACT models could reliably predict the probability of mortality and unfavorable outcome at 6 months after injury (34).

However, when the IMPACT and CRASH prognosis calculators were applied to severe TBI patients treated with an ICP-targeted therapy based on the Lund concept, both models led to an overestimation of mortality and unfavorable outcome (35,36). The Lund Concept is an approach used for treatment of severe brain trauma, and is mainly based on hypotheses originating from the physiology of brain volume and cerebral perfusion regulation (37,38). Moreover, a study including 9,578 patients with moderate and severe TBI enrolled in 10 RCTs and three observational studies showed that the outcome following TBI differs substantially between different examination centers, particularly in Europe (39). Overall, these studies suggest that the IMPACT models, based on a large sample size, can predict mortality and unfavorable outcome at 6 months after injury, reasonably well in patients not undergoing ICP-targeted therapy, and that regional differences should be considered while deciding their clinical application in TBI prognosis.

5. IMAGING STRATEGIES FOR OUTCOME PREDICTION IN SEVERE TBI PATIENTS

Predictive models consider multiple factors, which may be accurate but may not be simple and convenient in clinical application, especially in emergency cases where the therapeutic strategy needs to be decided quickly. It is known that lesions in the brainstem influence patient outcome after severe TBI (40). Hence, imaging techniques, especially magnetic resonance imaging, may be a quick and practical way to predict outcome following injury. Other studies showed that fractional anisotropy and MRI/magnetic resonance spectroscopy-based detection of N-acetyl aspartate/creatine localized in the thalamus, lenticular nucleus, insular cortex, occipital periventricular white matter and pons, have the potential to be used as quantitative outcome-prediction tools during the sub-acute phase of severe TBI (41). MRI has been shown to predict bad outcomes and the time before recovery of consciousness, in diffuse axonal injury patients (42). The amplitude and latency levels of N100, N200 and P300 components of acoustic evoked potentials together with data obtained from diffusion-tensor MRI, have the potential to reliably predict mental recovery in severe TBI (43).

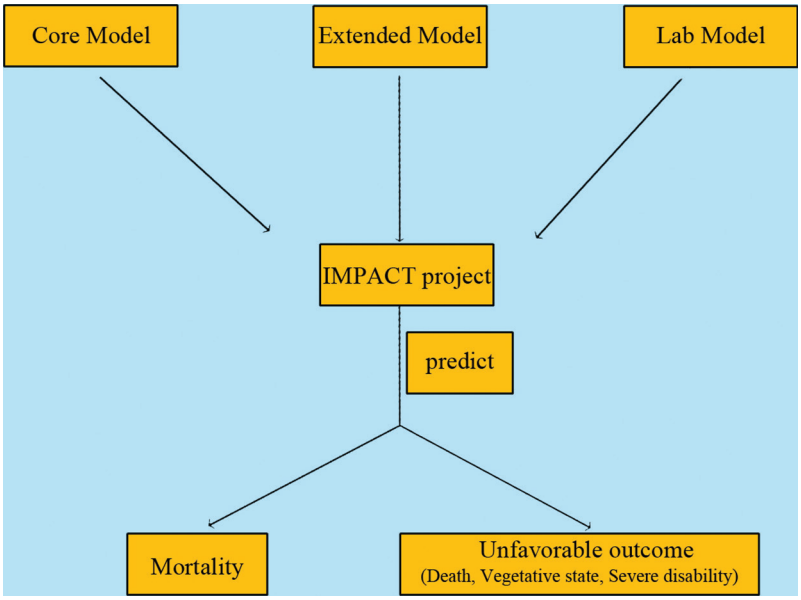

Figure 2. The IMPACT project predicts outcome after severe TBI. The IMPACT project developed three different models based on the dichotomized GOS (Glasgow outcome scale) at 6 months after injury: the Core Model, the Extended Model and the Lab Model, for the prediction of mortality and unfavorable outcome (including death, vegetative state and severe disability).

In addition to MRI, early head computed tomography (CT) scans have also been investigated as potential outcome predictors. It was found that CT scans cannot provide sufficient variables to predict disability in surviving patients, although CT characteristics could be correlated with the 6-month outcome in these patients (44). Thus, both MRI and CT techniques have predictive values in determining outcome in severe TBI, while MRI can also predict consciousness recovery and mental recovery.

6. BIOMARKERS FOR OUTCOME PREDICTION IN SEVERE TBI PATIENTS

Biomarkers are indicators of biological processes in normal or disease states. Endocrine abnormalities and inflammatory cytokines have been investigated as biomarkers in severe TBI. In patients (GCS >6), endocrine abnormalities resulted in decreased levels of T3, T4 and testosterone and increased levels of insulin (45). Further, in a study involving 117 adults (28 women and 89 men) with severe TBI, increased estradiol in men and increased testosterone in women seven days post-injury was associated with increased mortality and unfavorable global outcome (46). Hence, endocrine abnormalities may provide predictive information in the prognosis of severe TBI. In addition, the levels of the inflammatory cytokine IL-10 within 30 h following TBI was shown to be a useful independent biomarker in the prognosis of severe TBI, including prediction of GCS severity and hospital mortality (47). The endocrine abnormalities and elevation in inflammatory cytokines may be due to the stress resulting from severe TBI.

S100b, a calcium-binding cytosolic protein, is released into blood from astroglial cells in response to brain injury and disruption of the blood brain barrier. It regulates calcium flux and stimulates astrocyte proliferation (48,49). In severe TBI patients, the mean and peak levels of serum S100b within the first 6 days post-injury, may be an acute mortality predictor (50). However, the blood hemoglobin level had no significant influence on mortality (51).

7. CONCLUSIONS

In determining the prognosis of severe TBI, the utility of both single as well as a combination of multiple predictive factors has been investigated. Combining several clinical parameters may provide more information than single predictors, especially in certain statistical models. The IMPACT and CRASH prognosis calculators, which are based on large sample sizes, have predictive value in estimating long-term outcome. However, they have certain limitations in clinical application. On the other hand,

single predictors, such as the disability status, quantitative cerebral blood flow, ICP, CPP, and duration of coma, are simpler and more convenient to apply in emergency situations. Importantly, imaging techniques like MRI can also predict consciousness recovery and mental recovery in severe TBI, while biomarkers associated with stress can predict severity and mortality. All predictors have limitations when applied to clinical situations. Hence, further studies comparing different predictors and statistical models, is needed. Also, the prediction of clinical outcome in severe TBI patients should be individualized.

8. REFERENCES

1. Jennett B: Epidemiology of head injury. J Neurol Neurosurg Psychiatry 60(4):362-9 (1996)
DOI: 10.1136/jnnp.60.4.362
2. Steyerberg EW, Mushkudiani N, Perel P, Butcher I, Lu J, McHugh GS, Murray GD, Marmarou A, Roberts I, Habbema JD, Maas AI: Predicting outcome after traumatic brain injury: development and international validation of prognostic scores based on admission characteristics. PLoS Med 5(8):e165; discussion e165 (2008)
3. Faul M, Xu L, Wald M, Coronado V: Traumatic brain injury in the United States: emergency department visits, hospitalizations, and deaths. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. (2010)
4. Bowman SM, Martin DP, Sharar SR, Zimmerman FJ: Racial disparities in outcomes of persons with moderate to severe traumatic brain injury. Med Care 45(7):686–690 (2007)
DOI: 10.1097/MLR.0b013e31803dcdf3
5. Mushkudiani NA, Engel DC, Steyerberg EW, *et al*: Prognostic value of demographic characteristics in traumatic brain injury: results from the IMPACT study. J Neurotrauma 24(2):259–269 (2007)
DOI: 10.1089/neu.2006.0028
6. Staudenmayer KL, Diaz-Arrastia R, de Oliveira A, Gentilello LM, Shafi S: Ethnic disparities in long-term functional outcomes after traumatic brain injury. J Trauma 63(6):1364–1369 (2007)
DOI: 10.1097/TA.0b013e31815b897b
7. Benedictus MR, Spikman JM, van der Naalt J: Cognitive and behavioral impairment in traumatic brain injury related to outcome and return to work. Arch Phys Med Rehabil 91(9):1436-41 (2010)
DOI: 10.1016/j.apmr.2010.06.019
8. Brooks N, McKinlay W, Symington C, Beattie A, Campsie L: Return to work within the first seven years of severe head injury. Brain Inj 1(1):5-19 (1987)
DOI: 10.3109/02699058709034439
9. Zappalà G, Thiebaut de Schotten M, Eslinger PJ: Traumatic brain injury and the frontal lobes: what can we gain with diffusion tensor imaging? Cortex 48(2):156-65 (2012)
DOI: 10.1016/j.cortex.2011.06.020
10. Engberg AW, Teasdale TW: Psychosocial outcome following traumatic brain injury in adults: a long-term population-based follow-up. Brain Inj 18(6):533-45 (2004)
DOI: 10.1080/02699050310001645829
11. Hawthorne G, Gruen RL, Kaye AH: Traumatic brain injury and long-term quality of life: findings from an Australian study. J Neurotrauma 26(10):1623-33 (2009)
DOI: 10.1089/neu.2008.0735
12. Ponsford J, Draper K, Schönberger M: Functional outcome 10 years after traumatic brain injury: its relationship with demographic, injury severity, and cognitive and emotional status. J Int Neuropsychol Soc 14(2):233-42 (2008)
DOI: 10.1017/S1355617708080272
13. Turgeon AF, Lauzier F, Burns KE, Meade MO, Scales DC, Zarychanski R, Moore L, Zygun DA, McIntyre LA, Kanji S, Hébert PC, Murat V, Pagliarello G, Fergusson DA; Canadian Critical Care Trials Group:

Determination of neurologic prognosis and clinical decision making in adult patients with severe traumatic brain injury: a survey of Canadian intensivists, neurosurgeons, and neurologists. Crit Care Med 41(4):1086-93 (2013)
DOI: 10.1097/CCM.0b013e318275d046

14. Sleigh JW, Havill JH, Frith R, Kersel D, Marsh N, Ulyatt D: Somatosensory evoked potentials in severe traumatic brain injury: a blinded study. J Neurosurg 91(4):577-80 (1999)
DOI: 10.3171/jns.1999.91.4.0577

15. Amantini A, Grippo A, Fossi S, Cesaretti C, Piccioli A, Peris A, Ragazzoni A, Pinto F: Prediction of 'awakening' and outcome in prolonged acute coma from severe traumatic brain injury: evidence for validity of short latency SEPs. Clin Neurophysiol 116(1):229-35 (2005)
DOI: 10.1016/j.clinph.2004.07.008

16. González-García E, Vilela-Soler C, Romá-Ambrosio J, Fenollosa-Entrena B: The use of evoked potentials in the follow-up and prognosis of patients in coma following severe traumatic brain injury. Rev Neurol 44(7):404-10 (2007)

17. Demakis GJ, Hammond FM, Knotts A: Prediction of depression and anxiety 1 year after moderate-severe traumatic brain injury. Appl Neuropsychol 17(3):183-9 (2010)
DOI: 10.1080/09084282.2010.499752

18. Kaloostian P, Robertson C, Gopinath SP, Stippler M, King CC, Qualls C, Yonas H, Nemoto EM: Outcome prediction within twelve hours after severe traumatic brain injury by quantitative cerebral blood flow. J Neurotrauma 29(5):727-34 (2012)
DOI: 10.1089/neu.2011.2147

19. Feng H, Huang G, Gao L, Tan H, Liao X: Effect of intracranial pressure and cerebral perfusion pressure on outcome prediction of severe traumatic brain injury. Chin J Traumatol 3(4):226-230 (2000)

20. Forsyth RJ, Parslow RC, Tasker RC, Hawley CA, Morris KP; UK Paediatric Traumatic Brain Injury Study Group; Paediatric Intensive Care Society Study Group (PICSSG): Prediction of raised intracranial pressure complicating severe traumatic brain injury in children: implications for trial design. Pediatr Crit Care Med 9(1):8-14 (2008)
DOI: 10.1097/01.PCC.0000298759.78616.3A

21. Tan H, Feng H, Gao L, Huang G, Liao X: Outcome prediction in severe traumatic brain injury with transcranial Doppler ultrasonography. Chin J Traumatol 4(3):156-60 (2001)

22. Macpherson V, Sullivan SJ, Lambert J: Prediction of motor status 3 and 6 months post severe traumatic brain injury: a preliminary study. Brain Inj 6(6):489-98 (1992)
DOI: 10.3109/02699059209008146

23. Eastvold AD, Walker WC, Curtiss G, Schwab K, Vanderploeg RD: The differential contributions of posttraumatic amnesia duration and time since injury in prediction of functional outcomes following moderate-to-severe traumatic brain injury. J Head Trauma Rehabil 28(1):48-58 (2013)
DOI: 10.1097/HTR.0b013e31823c9317

24. Ferri J, Chirivella J, Caballero MC, Simó M, Ramírez RM, Noé E: Intelligence and prognosis in severe traumatic brain injury: a neuropsychological study with the Wechsler adult intelligence scale (WAIS-III) Neurologia 19(6):285-91 (2004)

25. Jiang JY, Gao GY, Li WP, Yu MK, Zhu C: Early indicators of prognosis in 846 cases of severe traumatic brain injury. J Neurotrauma 19(7):869-74 (2002)
DOI: 10.1089/08977150260190456

26. Yatsushige H, Takasato Y, Masaoka H, Hayakawa T, Otani N, Yoshino Y, Sumiyoshi K, Sugawara T, Miyawaki H, Aoyagi C, Takeuchi S, Suzuki G: Prognosis for severe traumatic brain injury patients treated with bilateral decompressive craniectomy. Acta Neurochir Suppl

106:265-70 (2010)
DOI: 10.1007/978-3-211-98811-4_50

27. Pace MC, Cicciarella G, Barbato E, Maisto M, Passavanti MB, Gazzerro G, Barbarisi M, Aurilio C: Severe traumatic brain injury: management and prognosis. Minerva Anestesiol 72(4):235-42 (2006)
28. de Oliveira Thais ME, Cavallazzi G, Formolo DA, de Castro LD, Schmoeller R, Guarnieri R, Schwarzbold ML, Diaz AP, Hohl A, Prediger RD, Mader MJ, Linhares MN, Staniloiu A, Markowitsch HJ, Walz R: Limited predictive power of hospitalization variables for long-term cognitive prognosis in adult patients with severe traumatic brain injury. J Neuropsychol. (2012) [Epub ahead of print]
DOI: 10.1111/jnp.12000
29. Devitt R, Colantonio A, Dawson D, Teare G, Ratcliff G, Chase S: Prediction of long-term occupational performance outcomes for adults after moderate to severe traumatic brain injury. Disabil Rehabil 28(9):547-59 (2006)
DOI: 10.1080/00222930500219258
30. Pang BC, Kuralmani V, Joshi R, Hongli Y, Lee KK, Ang BT, Li J, Leong TY, Ng I: Hybrid outcome prediction model for severe traumatic brain injury. J Neurotrauma 24(1):136-46 (2007)
DOI: 10.1089/neu.2006.0113
31. Tasaki O, Shiozaki T, Hamasaki T, Kajino K, Nakae H, Tanaka H, Shimazu T, Sugimoto H: Prognostic indicators and outcome prediction model for severe traumatic brain injury. J Trauma 66(2):304-8 (2009)
DOI: 10.1097/TA.0b013e31815d9d3f
32. Marmarou A, Lu J, Butcher I, et al: IMPACT database of traumatic brain injury: Design and description. J Neurotrauma 24:239–250 (2007)
DOI: 10.1089/neu.2006.0036
33. Roozenbeek B, Lingsma HF, Lecky FE, Lu J, Weir J, Butcher I, McHugh GS, Murray GD, Perel P, Maas AI, Steyerberg EW; International Mission on Prognosis Analysis of Clinical Trials in Traumatic Brain Injury (IMPACT) Study Group; Corticosteroid Randomisation After Significant Head Injury (CRASH) Trial Collaborators; Trauma Audit and Research Network (TARN): Prediction of outcome after moderate and severe traumatic brain injury: external validation of the International Mission on Prognosis and Analysis of Clinical Trials (IMPACT) and Corticoid Randomisation After Significant Head injury (CRASH) prognostic models. Crit Care Med 40(5):1609-17 (2012)
DOI: 10.1097/CCM.0b013e31824519ce
34. Lingsma H, Andriessen TM, Haitsema I, Horn J, van der Naalt J, Franschman G, Maas AI, Vos PE, Steyerberg EW: Prognosis in moderate and severe traumatic brain injury: external validation of the IMPACT models and the role of extracranial injuries. J Trauma Acute Care Surg 74(2):639-46 (2013)
DOI: 10.1097/TA.0b013e31827d602e
35. Olivecrona M, Koskinen LO: The IMPACT prognosis calculator used in patients with severe traumatic brain injury treated with an ICP-targeted therapy. Acta Neurochir (Wien) 154(9):1567-73 (2012)
DOI: 10.1007/s00701-012-1351-z
36. Olivecrona M, Olivecrona Z: Use of the CRASH study prognosis calculator in patients with severe traumatic brain injury treated with an intracranial pressure-targeted therapy. J Clin Neurosci 20(7):996-1001 (2013)
DOI: 10.1016/j.jocn.2012.09.015
37. Grände PO: New haemodynamic aspects on treatment of posttraumatic brain oedema. Swedish Society of Anaesthesia and Intensive Care 6: 41-46 (1992)
38. Asgeirsson B, Grände PO, Nordström CH: A new therapy of post-trauma brain oedema based on haemodynamic principles for brain volume regulation. Intensive Care Med 20: 260-267 (1994)
DOI: 10.1007/BF01708961
39. Lingsma HF, Roozenbeek B, Li B, Lu J,

Weir J, Butcher I, Marmarou A, Murray GD, Maas AI, Steyerberg EW: Large between-center differences in outcome after moderate and severe traumatic brain injury in the international mission on prognosis and clinical trial design in traumatic brain injury (IMPACT) study. Neurosurgery 68(3):601-7; discussion 607-8 (2011)
DOI: 10.1227/NEU.0b013e318209333b

40. Wedekind C, Hesselmann V, Lippert-Grüner M, Ebel M: Trauma to the pontomesencephalic brainstem-a major clue to the prognosis of severe traumatic brain injury. Br J Neurosurg 16(3):256-60 (2002)
DOI: 10.1080/02688690220148842

41. Tollard E, Galanaud D, Perlbarg V, Sanchez-Pena P, Le Fur Y, Abdennour L, Cozzone P, Lehericy S, Chiras J, Puybasset L: Experience of diffusion tensor imaging and 1H spectroscopy for outcome prediction in severe traumatic brain injury: Preliminary results. Crit Care Med 37(4):1448-55 (2009)
DOI: 10.1097/CCM.0b013e31819cf050

42. Calvi MR, Beretta L, Dell'Acqua A, Anzalone N, Licini G, Gemma M: Early prognosis after severe traumatic brain injury with minor or absent computed tomography scan lesions. J Trauma 70(2):447-51 (2011)
DOI: 10.1097/TA.0b013e3182095e14

43. Oknina LB, Sharova EV, Zaĭtsev OS, Zakharova NE, Masherov EL, Shekut'ev GA, Kornienko VN, Potapov AA: Long-latency components (N100, N200 and P300) of acoustic evoked potentials in prediction of mental recovery in severe traumatic brain injury. Zh Vopr Neirokhir Im N N Burdenko 75(3):19-30; discussion 30 (2011)

44. Jacobs B, Beems T, van der Vliet TM, van Vugt AB, Hoedemaekers C, Horn J, Franschman G, Haitsma I, van der Naalt J, Andriessen TM, Borm GF, Vos PE: Outcome prediction in moderate and severe traumatic brain injury: a focus on computed tomography variables. Neurocrit Care 19(1):79-89 (2013)
DOI: 10.1007/s12028-012-9795-9

45. Hackl JM, Gottardis M, Wieser C, Rumpl E, Stadler C, Schwarz S, Monkayo R: Endocrine abnormalities in severe traumatic brain injury--a cue to prognosis in severe craniocerebral trauma? Intensive Care Med 17(1):25-9 (1991)
DOI: 10.1007/BF01708405

46. Wagner AK, McCullough EH, Niyonkuru C, Ozawa H, Loucks TL, Dobos JA, Brett CA, Santarsieri M, Dixon CE, Berga SL, Fabio A: Acute serum hormone levels: characterization and prognosis after severe traumatic brain injury. J Neurotrauma 28(6):871-88 (2011)
DOI: 10.1089/neu.2010.1586

47. Schneider Soares FM, Menezes de Souza N, Libório Schwarzbold M, Paim Diaz A, Costa Nunes J, Hohl A, Nunes Abreu da Silva P, Vieira J, Lisboa de Souza R, Moré Bertotti M, Schoder Prediger RD, Neves Linhares M, Bafica A, Walz R: Interleukin-10 is an independent biomarker of severe traumatic brain injury prognosis. Neuroimmunomodulation 19(6):377-85 (2012)
DOI: 10.1159/000342141

48. Chen Y, Swanson RA: Astrocytes and Brain injury. J Cereb Blood Flow Metab 23:137-139 (2003)
DOI: 10.1097/00004647-200302000-00001

49. Donato R, Heizmann CW: S100B Protein in the Nervous System and Cardiovascular Apparatus in Normal and Pathological Conditions. Cardiovasc. Psychiatry Neurol 92:87-92 (2010)

50. Goyal A, Failla MD, Niyonkuru C, Amin K, Fabio A, Berger RP, Wagner AK: S100b as a prognostic biomarker in outcome prediction for patients with severe traumatic brain injury. J Neurotrauma 30(11):946-57 (2013)
DOI: 10.1089/neu.2012.2579

51. Yang TJ, Fei MM, Ye W, Pan AJ, Liu B: Effect of albumin and hemoglobin level on

prognosis of patients with uncomplicated severe traumatic brain injury: a retrospective cohort study. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 25(5):301-5 (2013)

Abbreviations: TBI, Traumatic brain injury; MRI, Magnetic Resonance Imaging; RCTs, randomized controlled trials; SEP, somatosensory evoked potential; CPP, cerebral perfusion pressure; ICP, intracranial hypertension; GCS, Glasgow coma scale; IMPACT, Traumatic Brain Injury; CRASH, Corticosteroid Randomisation after Significant Head Injury; CT, computed tomography

Key Words: Traumatic brain injury; Magnetic Resonance Imaging; Traumatic Brain Injury, somatosensory evoked potential, Review

Send correspondence to: Liang Gao, Department of Neurosurgery, Huashan Hospital, Fudan University, Shanghai, China; Tel:86-13601606098, Fax:86-021-52889999; E-mail: lianggaoh@yeah.net