How Do We Identify the Crashing Traumatic Brain Injury Patient – The Neurosurgeon's View

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Abstract

Purpose of the review: To provide an overview on recent advances in the field of assessment and monitoring of patients with severe traumatic brain injury (sTBI) in neurocritical care from a neurosurgical point of view.

Recent findings: In high-income countries, monitoring of patients with sTBI heavily relies on multimodal neurocritical parameters, nonetheless clinical assessment still has a solid role in decision-making. There are guidelines and consensus-based treatment algorithms that can be employed in both absence and presence of multimodal monitoring in the management of patients with sTBI. Additionally, novel dynamic monitoring options and machine learning-based prognostic models are introduced. Currently, the acute management and treatment of secondary injury/insults is focused on dealing with the objective evident pathology. An ongoing paradigm shift is emerging towards more proactive treatment of neuroworsening as soon as premonitory signs of deterioration are detected.

Summary: Based on the current evidence, serial clinical assessment, neuroimaging, intracranial and cerebral perfusion pressure, and brain tissue oxygen monitoring are key components of sTBI care. Clinical assessment has a crucial role in identifying the crashing patient with sTBI, especially from a neurosurgical standpoint. Multimodal monitoring and clinical assessment should be seen as complementary evaluation methods that support one another.

Keywords: traumatic brain injury, neurocritical care, intensive care, neurosurgery, monitoring, assessment

Introduction

Severe traumatic brain injury (sTBI) often has a complex, dynamic and unpredictable acute clinical course. Initially, patients with sTBI require continued care and monitoring in a neurointensive care unit (NICU). The goal of NICU care is to maintain systematic homeostasis. Thus, allowing the best possible physiological framework for limiting secondary brain damage by controlling intracranial pressure (ICP), cerebral perfusion pressure (CPP), and brain tissue oxygen ($P_{bt}O_2$). Neurointensivists and neurosurgeons work daily to achieve these theoretically simple but practically demanding goals.

Despite the long and well-established tradition of NICU care and an active field of interest, TBI-associated mortality remains high (20–30%). (1,2*) The lack of improvement in TBI-related mortality is at least partly due to epidemiological change, as patients with sTBI are getting increasingly older (1). Yet, it has been postulated that outcome-worsening secondary insults cannot be timely and sufficiently detected in current practice. Further, although there have been trials trying to prevent the progression of secondary brain injury (3), currently, the treatment of sTBI is inherently dealing with the consequences of pathology once it has already developed.

A main challenge in developing diagnostic and therapeutic tools for secondary insults in TBI is the heterogeneous and unpredictable nature of the disease. Active research in the field including high-resolution prospective datasets [such CENTER-TBI (4)] and guidelines [such Brain Trauma Foundation guidelines (BTF) (5)] provide neurosurgeons with a frame of reference, but many acute problems remain to be solved based on individually applied knowledge—either alone or with a neurointensivist. The aim of this review is to provide an expert distillation on how to identify a crashing adult patient with sTBI from a neurosurgical perspective.

Clinical Assessment

In the NICU, patient monitoring heavily relies on multimodal objective data, especially in high-income countries. Nonetheless, serial clinical assessment plays an important role in the management of patients with sTBI. (6)

Although some patients with a Glasgow Coma Scale (GCS) score of above 8, without painful extracerebral injuries can be monitored awake, most of the patients are sedated, intubated and mechanically ventilated. During the first two days in the NICU, up to 40% of patients develop neuroworsening (7,8), which emphasises the importance of early rigorous management strategies—with clinical assessment and multimodal NICU monitoring. The motor component of the GCS score and pupillary reactivity possess the best prognostic value of the clinical covariates. (9) According to current definitions, deterioration of the level of consciousness is defined as a drop of two or more points in the GCS motor score. (10) Any standardised definitions regarding changes in ICP, CPP, $P_{bt}O_2$ for recognising neuroworsening do not exist. Thus, is a neurological wake-up test required to identify the crashing sTBI patient?

There is no level I evidence for or against the neurological wake-up test (11) and it is not mentioned in the BTF guidelines. (5) However, some European and American centres advocate the use of this test, because it allows reliable detection of clinically relevant deterioration necessitating investigations and emergency interventions (12,13*). It is argued that multimodal monitoring does not diminish the value of the wake-up test, because herniation can sometimes take place in the absence of ICP elevation. (11,14) -there are also arguments against the use of the wake-up test. For instance, the test may induce stress responses and increase cerebral metabolism and concurrently oxygen demand. (12) Thus, some consider that the value of the information provided by the wake-up test does not overweigh its possible harm. The test is seen as even negligible when multimodal monitoring data is obtained. (15) Ultimately, in most Nordic centres, where the wake-up test is in active use, the policy is not choosing between multimodal monitoring and the wake-up test but combining these approaches. Moreover, when neuroworsening is identified, an urgent repeat head computed tomography (CT) scan should be considered in order to identify possible intervention targets. (16)

Although in high-income countries, patient monitoring is usually based on a multimodal approach in tertiary centres, the vast majority of patients with sTBI in the world are treated in low-resource centres without the possibility of even ICP monitoring. So far, the only tested TBI patient management protocol without ICP monitoring stems from the Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure (BEST:TRIP) trial. (6) The main finding of the study was that there were no differences in outcome between head CT imaging + clinical assessment and ICP monitoring groups. Although the clinical assessment protocol was equally effective to the ICP-based protocol, the clinical assessment protocol proved less efficient as the treatment duration was fixed and there was a lack of agreement in escalating or tapering therapy. (6)

The aforementioned premise and findings yielded the Consensus-Based Management Protocol (CREVICE) for the treatment of sTBI. (17**) The key points in this suspected intracranial hypertension protocol with regard to initiating therapy were radiological signs of increased intracranial pressure (midline shift >5mm, compressed basal cisterns, mass lesion), a GCS motor component <5, and pupillary asymmetry or abnormal reactivity. Importantly, pupillary asymmetry with normal reactivity and a negative head CT in “briskly localising patient” does not activate treatment. The protocol also recommends starting the treatment of elevated ICP with a single intervention: hyperosmolar therapy. In terms of escalating treatment, neurological worsening or lack of improvement on follow-up imaging in response to the initial intervention should explicitly prompt consideration of additional interventions. Furthermore, the minimum duration for hyperosmolar treatment was not set and the treatment length was rendered subject to the new escalation/tapering criteria. In this context, neurological worsening implies a high-probability of elevated ICP, so the consensus working-group increased its sensitivity by lowering the GCS motor drop to ≥1 and adding signs of herniation from the Cushing triad to the definition. To target an adequate CPP in the absence of ICP monitoring, a MAP threshold of 90 mmHg was chosen. (17**) The availability of multimodal monitoring is limited in many places around the world, thus the details of the CREVICE Protocol are important for all neurosurgeons treating patients with TBI.

Neuroimaging

In NICU management of sTBI, CT is the main imaging modality to assess the need of neurosurgical interventions. (18) Progressive haemorrhagic injury (19), where lesions evolve and increase in volume, can be reliably detected by CT scanning. Progressive haemorrhagic injury, in particular progressive traumatic contusions, is an important secondary injury, which contributes to subsequent clinical deterioration and requirement for surgical intervention (20*). Among the various subtypes of intracranial haemorrhage, contusions are most likely to progress (16–75%). In the majority of contusion patients, progression occurs within the first 24 hours. (20*) Contusion progression cannot be predicted from a single CT scan. However, some clinical and radiological risk factors for progression have been reported. These risk factors include initial GCS, history of hypertension, current smoking, coagulopathy, initial contusion size, contusion location (frontal, contrecoup, multiple), presence of concurrent subarachnoid or subdural haemorrhage, and absence of peri-contusional oedema. (20*) Clinicians treating sTBI should keep these risk factors in mind as warning features of neuroworsening.

Intracranial Pressure and Cerebral Blood Flow

The management of sTBI in the NICU is focused on reducing raised ICP and optimising impaired CPP in order to limit and reduce secondary insults. (1,21) The BTF (5), European guidelines (European Brain Injury Consortium, EBIC) (22), Addenbrooke's guidelines (21) and Rosner protocol (23) are CPP-targeted guidelines, while the Lund concept is based on physiological principles such as brain volume control, optimisation of brain perfusion and oxygenation of the penumbra zone. (24,25) The guidelines recommend initiation of ICP measurement in all patients with sTBI (Addenbrooke's, Rosner and Lund), in unconscious patients with abnormal CT (BTF), or when considered desirable (EBIC). ICP treatment is recommended to be initiated when ICP is >20–25 mmHg (EBIC and Addenbrooke's), >22 mmHg (BTF), or early and independent of ICP (Lund). The Rosner protocol does not define a limit for initiating ICP treatment. CPP targets are as follows: 60–70 mmHg (BTF and Lund), >60–70 mmHg with MAP >90 mmHg (EBIC), >70 mmHg (Addenbrooke's and Rosner).

During the last 25 years since the introduction of the Addenbrooke's guidelines (21), retrospective data shows that the ICP/CPP-directed therapy has resulted in increased CPP, decreased ICP and less time spent outside the ICP and CPP targets. However, this had no effect on the pressure reactivity index (PRx). Similarly, the introduction of cerebral microdialysis did not have any major effects on ICP, CPP or PRx. Noteworthy is that during this 25-year period, patient age increased, but the mortality remained at 22%. (2*)

The first two editions of the BTF guidelines (26,27) included various treatment algorithms. However, they were removed from the latest third edition (5,28) as the different treatments had not been studied in a

comparative or combinative setting. There was insufficient evidence of their effectiveness to establish an evidence-based protocol. This led to the development of a consensus-based management algorithm for patients with sTBI when ICP monitoring is available (level III evidence). Further, the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC) introduced a three-tier algorithm targeting to lower ICP (when $P_{bt}O_2$ is normal). The algorithm includes 18 preferable interventions and 10 avoidable treatments. The novelties of the algorithm consist of i) cerebrovascular autoregulation (CA)-based ICP management with the inclusion of MAP challenges, ii) consideration of the neurological wake-up tests, and iii) ICP monitoring termination. The SIBICC algorithm adopted the definition of neuroworsening from the BEST:TRIP trial (6), and relabelled it "critical neuroworsening". The concept of critical neuroworsening assists in the identification and treatment of crashing patients. (13**)

In a recent single-centre study, six different ICP trajectory groups were formed based on data from 446 patients. The different ICP trajectories were independent predictors of six-month outcome across multiple measures. The findings challenge the current conception that elevated ICP (20–25 mmHg) and the proportion of ICP spikes are associated with mortality but not morbidity in survivors. The trajectory-based classification identified two groups ("low, slow rise" and "persistent low") with unfavourable outcome despite low ICP. Conversely, groups exhibiting intermittent ICP spikes and frequent ICP spikes had a good outcome. (29)

In recent years, attention has been drawn to maintenance of CA in addition to ICP/CPP protocols as impairment in CA is known to have a detrimental effect on clinical outcome (30,31). CPP-targeted therapy with one fixed level has failed to improve outcome in patients with sTBI compared to ICP-targeted therapy. (32) NICU treatment can be individualised by identifying optimal CPP (CPP_{opt}) based on the PRx, which is calculated as a moving correlation co-efficient between slow waves of mean arterial blood pressure and ICP. The PRx may be seen as a surrogate marker for CA and has been shown to correlate with patient outcome. Negative PRx values reflect normal CA maintaining stable cerebral blood flow. Positive PRx values represent impaired CA, which leads to oxygen and energy mismatch in the brain. (33)

Although the CPP_{opt} and PRx have not yet been uniformly established to guide the maintenance of CA in patients with sTBI in the NICU setting, a large number of both descriptive and clinical results have been published in recent years—especially from the multi-centre high resolution ICU cohort of the CENTER-TBI. These reports show that CPP_{opt} and PRx are associated with 6–12-month outcome (34,35*,36), CA is associated with diffuse injury patterns (37) and PRx is associated with progression of pericontusional oedema and intraparenchymal hemorrhage but not with extra-axial hemorrhage (38). The results suggest that impaired CA as denoted by PRx can be used to risk-stratify patients with sTBI in the NICU setting (impaired CA=high risk for neuroworsening).

Brain Tissue Oxygen

Along with ICP and CPP, $P_{bt}O_2$ has become another important target in the management of sTBI although it can be considered even a more regional or local measurement than the aforementioned. There is currently

phase II data from a randomised controlled trial suggesting improved outcomes employing $P_{bt}O_2$ and ICP-targeted therapy with a $P_{bt}O_2$ threshold of 20 mmHg compared to ICP-targeted therapy alone. (39) The latest revision of the BTF guidelines suggest $P_{bt}O_2$ thresholds of 20 or 22 mmHg. (5)

Due to this, the SIBICC group developed an additional consensus-based algorithm adding $P_{bt}O_2$ monitoring as the first-choice secondary parameter (the first being ICP). The development process combined practice-based recommendations and resulted in level III evidence. The algorithm divides patients into four clinical conditions encountered in patients in whom both $P_{bt}O_2$ and ICP monitoring are utilised. The first condition reflects normal values for both variables (ICP <22 mmHg and $P_{bt}O_2$ >20 mmHg) and does not require treatment. The other three conditions are (i) elevated ICP + normal $P_{bt}O_2$, ii) normal ICP + lowered $P_{bt}O_2$, iii) elevated ICP + lowered $P_{bt}O_2$) have distinct sub-algorithms. (40**)

A recent study demonstrated that elevated ICP is correlated with impaired PRx and low $P_{bt}O_2$. (41*) However, the relationship between abnormal $P_{bt}O_2$ and PRx has remained nebulous. In a preliminary multicentre analysis, it was demonstrated that in BTF guideline-based therapeutic strategies, PRx does not respond to treatment, whereas ICP and $P_{bt}O_2$ remain responsive—impaired PRx dominated the impaired cerebral physiology metrics. The authors suggest that either the pathological state resulting in low $P_{bt}O_2$ is so severe that CA is also impaired—or vice versa: impaired PRx may cause low $P_{bt}O_2$ by limiting the brain's ability to compensate its perfusion leading to oxygen mismatch. (42**)

Surgical Perspectives

Treatment of patients with mass lesions should be centralised to centres providing 24-hour neurosurgical services. Intracranial mass lesions occur in 25–45% of patients with sTBI and they often lead to neurological deficits and compromised outcomes. (43) The surgical management of mass lesions causing neuroworsening and midline shift of >5 mm and/or have tendency to expand is well established by the expert opinion-based BTF guidelines (5) and Scandinavian Neurotrauma Committee recommendations (44). However, the management of multiple contusions, smaller convexity haematomas causing swelling over time and diffuse brain injury leading to intractable ICP represent more controversial challenges and deserve some remarks.

Intraparenchymal contusions are frequently associated with epidural and subdural haematomas. Multiple contusions often develop in frontobasal and temporopolar areas. Principally, patients with intraparenchymal contusions without neuroworsening and mass effect on CT scan can be followed with intensive monitoring. Categorically, patients who develop frontal or temporal contusions of >20 cm^3 with midline shift >5 mm and/or basal cisternal compression should undergo surgery. (5,44)

Epidural, subdural and intraparenchymal haematomas detected upon admission can expand and result in perifocal oedema. In patients with intraparenchymal ICP monitoring, these patients may be initially identified by increasing ICP levels and alterations in the ICP pulse curve. A follow-up CT scan is indicated, if malignant ICP characteristics are observed. Even if ICP trends seem normal, patients who develop neurological deficits

at follow-up should be re-CT scanned. In case of hematoma enlargement or symptomatic perifocal oedema, the surgical management follows the guideline principles. (5,44)

Diffuse brain injury with brain swelling may result in high refractory ICP despite tiered medical treatment. (45) Randomised controlled trials (46–48) show that decompressive craniectomy effectively lowers ICP and reduces mortality, but these benefits are translated into survival with disability as presented by the DECRA (47) and RESCUEicp (48) trials. Because patient age is one of the most important prognostic factors, decompression should be considered an option mainly in young patients who have a realistic possibility of recovery to an acceptable level of functionality and life-quality. Numerous themes related to decompressive craniectomy yet remain to be scientifically unanswered and no solid consensus among neurosurgeons consists. These areas of uncertainty include i.a.: i) surgical technique (anatomic area of decompression, hinge craniotomy, duraplasty etc.), ii) the role of primary decompressive craniectomy, and iii) patient selection in secondary decompressive craniectomy.

Future Aspects and Conclusion

Identification of the crashing patient with sTBI remains a daily task for a neurosurgeon and neurointensivist. However, as the monitoring possibilities increases, there always seems to be another flipside to the coin. The authors suggest a simple scheme for identification and management of neuroworsening depicted in Figure.

The published guidelines for the management of patients with sTBI have required revisions and accompanying consensus-based algorithms in order to reflect the constantly evolving research field. It has become clear that it is impossible for a clinician to combine information flow of several variables in an effective way and make objective, and increasingly individualised, treatment decisions. This realisation has led to development of machine learning-based prediction models that may in the future influence the way we work in the NICU. One example is a recent machine learning-based dynamic mortality prediction algorithm. (49**) This algorithm was based on NICU data from three centres including patients who were monitored for ICP for at least 24 hours. Specifically, two algorithms were created: ICP-MAP-CPP and ICP-MAP-CPP-GCS. The first yielded AUCs from 0.67 (Day 1) to 0.81 (Day 5), while the latter yielded AUCs from 0.72 (Day 1) to 0.84 (Day 5) in predicting mortality. (49**) As the models are based upon only ICP, MAP (and GCS), they can relatively easily be implemented outside high-resource neurosciences centres.

Blood-based biomarkers are promising tools to complement clinical variables and imaging findings in monitoring the injured brain and outcome prediction of TBI. In a recent study, glial fibrillary acidic protein (GFAP), ubiquitin carboxyl-terminal hydrolase L1, tau, neurofilament light chain (NF-L), neuron specific enolase and S100B were assessed from serial blood samples over two weeks after admission in patients with sTBI. All biomarkers were associated with injury severity and they outperformed other clinical variables in predicting unfavourable outcome in univariate analyses. Of all variables, GFAP and NF-L added most predictive value after adjusting for TBI outcome predictors included in the IMPACT model. (50,51) This is

consistent with the increasing body of evidence. Biomarkers most likely should be used in combination with clinical and imaging findings in the acute diagnostics and outcome prediction of TBI. (52,53)

In conclusion, serial clinical assessment is a key method to identify the crashing patient with sTBI in the NICU, but data streams from multimodal monitoring are also invaluable. Based on the current evidence—from the updated guidelines and consensus-based algorithms—ICP, CPP and $P_{bt}O_2$ are crucial components of the patient monitoring. Emerging evidence also suggests that sTBI care should also include also PRx-targeted treatment. We consider likely that in the near future, neurosurgeons and neurointensivists will be able to utilise dynamic prognostic models that include aforementioned objective measures and possibly serial biomarker sampling in monitoring patients with sTBI and also in assessing treatment effects. This change will facilitate the treatment to change from reactive to proactive in nature.

Key Points

- During the first two days in neurocritical care, up to 40% of patients with severe traumatic brain injury develop neurological worsening and early identification of these patients remains challenging
- There are guidelines and consensus-based treatment algorithms that can be employed in both absence and presence of multimodal monitoring in the management of patients with severe traumatic brain injury
- From the neurosurgical viewpoint, serial clinical assessment, intracranial pressure, cerebral perfusion pressure and brain tissue oxygen monitoring form the basis for modern severe traumatic brain injury care
- When neuroworsening is identified, an urgent repeat head CT scanning should be considered
- Pressure reactivity index is a promising monitoring tool that is significantly associated with clinical outcome, but it appears to be irrespective of intracranial pressure and brain tissue oxygen-targeted treatment
- In case of intractable ICP after failed maximal medical therapy, decompressive craniectomy should be considered an option mainly in young patients who have a realistic possibility of recovery to an acceptable level of functionality and life-quality
- Prognostic and dynamic models will facilitate the treatment of severe traumatic brain injury to change from reactive to proactive

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