OPEN

The management of severe traumatic brain injury in the initial postinjury hours – current evidence and controversies

Iftakher Hossain[a,b,*], *Elham Rostami*[c,d,*] *and Niklas Marklund*[e]

Purpose of review
To provide an overview of recent studies discussing novel strategies, controversies, and challenges in the management of severe traumatic brain injury (sTBI) in the initial postinjury hours.

Recent findings
Prehospital management of sTBI should adhere to Advanced Trauma Life Support (ATLS) principles. Maintaining oxygen saturation and blood pressure within target ranges on-scene by anesthetist, emergency physician or trained paramedics has resulted in improved outcomes. Emergency department (ED) management prioritizes airway control, stable blood pressure, spinal immobilization, and correction of impaired coagulation. Noninvasive techniques such as optic nerve sheath diameter measurement, pupillometry, and transcranial Doppler may aid in detecting intracranial hypertension. Osmotherapy and hyperventilation are effective as temporary measures to reduce intracranial pressure (ICP). Emergent computed tomography (CT) findings guide surgical interventions such as decompressive craniectomy, or evacuation of mass lesions. There are no neuroprotective drugs with proven clinical benefit, and steroids and hypothermia cannot be recommended due to adverse effects in randomized controlled trials.

Summary
Advancement of the prehospital and ED care that include stabilization of physiological parameters, rapid correction of impaired coagulation, noninvasive techniques to identify raised ICP, emergent surgical evacuation of mass lesions and/or decompressive craniectomy, and temporary measures to counteract increased ICP play pivotal roles in the initial management of sTBI. Individualized approaches considering the underlying pathology are crucial for accurate outcome prediction.

Keywords
coagulopathy, emergency department, intracranial pressure, prehospital management, surgical treatment, traumatic brain injury

INTRODUCTION

Traumatic brain injury (TBI) affects approximately 70 million people globally [1]. With ageing populations, the epidemiology of TBI is changing worldwide, especially in high-income countries [2▪▪]. Thus, more patients with TBI have comorbid medical conditions making their management more challenging. The survivors of severe TBI (sTBI) are often left with debilitating deficits in motor, sensory, and cognitive functions with marked impact on their quality of life [3]. After the introduction of international treatment guidelines [3–5], the acute mortality decreased significantly. Disappointingly, however, during the last two decades TBI outcomes or acute mortality have not improved further [6].

The initial impact may result in immediate death to neuronal and nonneural cells and may

[a]Neurocenter, Department of Neurosurgery, Turku University Hospital, Turku, Finland, [b]Department of Clinical Neurosciences, Neurosurgery Unit, University of Cambridge, Addenbrooke's Hospital, Cambridge, UK, [c]Department of Medical Sciences, Section of Neurosurgery, Uppsala University, Uppsala, [d]Department of Neuroscience, Karolinska institute, Stockholm and [e]Department of Clinical Sciences Lund, Neurosurgery, Lund University, Department of Neurosurgery, Skåne University Hospital, Lund, Sweden

Correspondence to Niklas Marklund, MD, PhD, Department of Clinical Sciences Lund, Neurosurgery, Lund University, Department of Neurosurgery, Skåne University Hospital, Lund, Sweden.
Tel: +46 72 595 0261; e-mail: niklas.marklund@med.lu.se

*These authors contributed equally to this work.

Curr Opin Crit Care 2023, 29:650–658

DOI:10.1097/MCC.0000000000001094

KEY POINTS

- The primary goal of prehospital management of severe traumatic brain injury (sTBI) is to minimize the secondary insults.
- Prehospital and emergency department (ED) managements of sTBI should adhere to Advanced Trauma Life Support (ATLS) principles and to prioritize airway control, stable blood pressure, spinal immobilization, and correction of impaired coagulation, respectively.
- Noninvasive techniques could help to identify raised intracranial pressure (ICP) and osmotherapy as well as hyperventilation could be applied as temporary measures to reduce ICP.
- Surgical evacuation of mass lesions and/or decompressive craniectomy are the key measures to counteract increased ICP in the acute management of sTBI.
- Treatment of sTBI patients with very low Glasgow Coma Scale (GCS) and poor pupillary reactivity remains a matter of debate, not least in the elderly population.

injure blood vessel causing extra- or intraparenchymal hemorrhages. This primary injury is exacerbated by early pathophysiological changes in the brain that include a complex cascade of secondary injury mechanisms. Since the injured brain is highly vulnerable to systemic insults such as hypoxia, hypotension, and coagulopathy, a primary goal of prehospital management of sTBI is to minimize these secondary insults. Upon arrival to the emergency department (ED), stabilization of vital parameters must be continued, and many potential treatment opportunities be considered simultaneously. Further refinement of the acute management of sTBI focusing on the early identification and minimization of the secondary insults is needed to reduce the acute mortality.

The aim of this narrative review is to provide a summary of recent studies reflecting the novel strategies, controversies, and challenges of the acute management in the critical initial postinjury hours of sTBI.

SEARCH CRITERIA

A literature search was performed in PubMed, Scopus, Google Scholar and ISI Web of Knowledge for articles in English with the words ''traumatic brain injury'' together with one or a combination of the words ''prehospital management'', ''emergency department management'', ''secondary injury'', ''coagulopathy'' and ''intracranial pressure''. The search included recent guidelines, meta-analyses, randomized controlled trials (RCTs) and systematic reviews. The search was restricted mainly to literature published in English during the last 18 months.

PRE-HOSPITAL MANAGEMENT

The initial management of patients with TBI should be performed according to the Advanced Trauma Life Support (ATLS) principles of managing airway, breathing, and circulation, followed by a rapid neurologic exam [7]. All patients with a Glasgow Coma Scale (GCS) of ≤ 8 should liberally be intubated [8], although the use of a strict threshold GCS to dictate intubation remains controversial [9]. Major systemic, extracranial injuries often mandate intubation in the prehospital setting [2▪▪]. Time to hospital should be minimized although in unstable patients with hypotension and/or hypoxia, stabilization and rapid sequence intubation (RSI) at the scene of the accident may be preferable. Plausibly, the chances of survival can be influenced by the expertise and experiences of, for example, paramedics or emergency doctors [10]. While the presence of an on-scene physician experienced in airway, fluid, and blood pressure management, for example, decreased mortality rates, the benefits of physician-staffed prehospital management on sTBI outcomes have not been firmly established [11–13].

After prehospital stabilization, the sTBI patients must promptly be transferred to definitive care while maintaining adequate oxygen saturation (SpO_2; treatment goal >90%). Presumably even more important, the systolic blood pressure must be maintained at $\geq$100–110 mmHg at all times. An isolated TBI does not result in hypotension, and if present other differential causes must be considered. Permissive hypotension, a treatment option during the initial resuscitation of polytrauma patients with significant bleeding [14], aims at minimizing further blood loss and tissue damage by reducing the pressure exerted on injured blood vessels. However, this strategy may be detrimental for sTBI patients, as hypotension with systolic blood pressure <90 mmHg significantly impairs the outcome [15].

The incidence of dual diagnosis of brain and spinal cord injuries (SCIs) can range from 25% to more than 60% in sTBI, particularly in cases involving motor vehicle collisions or falls, emphasizing the significance of spinal motion restriction (SMR) in prehospital care [16]. Although the use of spinal immobilization by a rigid neck collar is still common, there is little evidence showing its benefit [17,18]. In fact, cervical fixation with a stiff collar is suboptimal and it could, for example, occlude

venous return and thus increase intracranial pressure (ICP). Cushion blocks on either side of head or vacuum mattress are preferable prehospital options. There should be a suspicion of an associated SCI in all sTBI patients [4]. Assessment of the GCS score, pupillary reactivity, and focal neurological deficits is performed at the scene of the accident, and preferably on arrival at the hospital (the postresuscitation GCS). Patients presenting with low GCS scores, including extensor posturing and/or dilated pupil (s), have a high likelihood of increased ICP and/or cerebral herniation, requiring temporary ICP-reducing measures. Hyperosmolar solutions such as mannitol or hypertonic saline (HTS) [2▪▪], and mild-to-moderate hyperventilation to, but not less than, a p_aCO_2 of 4.0–4.5 kPa due to a risk of cerebral vasoconstriction exacerbating ischemic injuries, are ICP-lowering options [19].

Based on the findings of the largest randomized trial in TBI to date, CRASH-3 [20], and subsequent studies [21,22], early administration of tranexamic acid (TXA) within 3 h postinjury is safe and recommended for moderate head injuries, as well as mild injuries with bleeding observed on acute CT scans [23]. Although recent systematic reviews found no significant impact on mortality or disability, early TXA administration is still considered in sTBI patients due to its favorable adverse side effect profile and potential benefits. This recommendation takes into account the challenges of accurately classifying TBI in the prehospital setting, as well as its use in polytrauma [22,24].

EMERGENCY DEPARTMENT MANAGEMENT

Upon arrival to the emergency department (ED) the ATLS is reassessed with a focus on airway management, maintaining mean arterial pressure (MAP) at 80 mmHg or higher, immobilization of the spine (time on spine board should be minimized, and must be <2 h), and securing venous access as well as placement of an arterial line and an indwelling urinary catheter (see Table 1 for thresholds of target goals for key physiological parameters). The airway is secured according to local institutional protocols, although endotracheal intubation is mandatory in any sTBI patient. Induction agents such as propofol should be cautiously used, possibly only in conjunction with induction inotropes, in view of the risk of systemic hypotension resulting in an impaired cerebral blood flow (CBF) [19]. Ketamine is a commonly used option, although early studies using ketamine in sTBI patients implied that it could increase ICP and decrease cerebral perfusion pressure (CPP) [25▪]. To date, an ICP-reducing effect of ketamine is suggested and in hypotensive sTBI patients ketamine may be preferred due to less risk of hypotension compared with other induction agents [26]. Barbiturates can cause hypotension and are not recommended for intubating sTBI patients [27▪].

Table 1. Thresholds for avoiding secondary insults

ICP < 20–22 mmHg
CPP ≥ 60 mmHg[a]
Systolic BT >100 mmHg
pO_2 >10 kPa
O_2 saturation >95%
pCO_2 4.5–5.5 kPa
Temperature < 38°C
β-Glucose 5–10 mmol/l
S-Na 140–150

ICP, intracranial pressure.
[a]The recommended target cerebral perfusion pressure (CPP) for favorable outcomes is between 60 and 70 mmHg. The optimal minimum threshold, whether it is 60 or 70 mmHg, depends on the patient's autoregulatory status [15,79].

While intraparenchymal or intraventricular ICP monitoring is gold standard, those techniques require surgical insertion. In the ED, noninvasive techniques for the estimation of raised ICP such as optic nerve sheath diameter (ONSD) measurement, pupillometry and transcranial Doppler (TCD) are emerging. These tools may be useful in the detection of intracranial hypertension and may be applied as triage tools in the ED [28].

Intracranial pressure lowering therapies

When signs of increased ICP and/or cerebral herniation are present, temporary ICP-reducing measures must be considered (Table 2). Any coagulation disorder must promptly be corrected (*vide infra)*. Obviously, head-and whole-body imaging by multislice CT scanning, also evaluating the entire spine, is acquired immediately following stabilization. Depending on the CT findings, prompt surgical evacuation of mass lesions or a primary decompressive craniectomy (DC) may be needed (e.g., see Fig. 1) [29▪▪]. A CT-angiogram should be performed in suspicion of traumatic cerebrovascular injuries such as skull base fractures involving the carotid canal [15]. In sTBI patients, ICP and CPP monitoring is also needed - either following initial surgical treatment, or as a primary measure [2▪▪]. Extensive surgeries on other organ system should be avoided. or minimized to the extent possible, in the emergent phase [30].

Table 2. ICP lowering options

Always consider – is there a mass lesion in need of evacuation?
1. Head in neutral position, avoid neck extension – optimize jugular vein effluent
2. Elevated head of bed (HOB) at 15–30°, treat fever
3. Optimize pain relief and sedation
4. Normal or negative fluid balance
5. Osmotherapy (3% NaCl or mannitol; 0.25–0.5 g/kg of 20% solution over 10–15 min)
6. Optimize S-Na 145–150 mmol/l
7. High suspicion of seizures, consider continuous EEG monitoring
8. Increase analgesia and sedation
9. Increase S-Na to 150–155 mmol/l, consider moderate hyperventilation pCO_2 4.0–4.5 kPa
10. Consider adding ketamine
11. Barbiturates
12. Mild hypothermia 34–35°C
13. Decompressive hemicraniectomy

ICP, intracranial pressure.

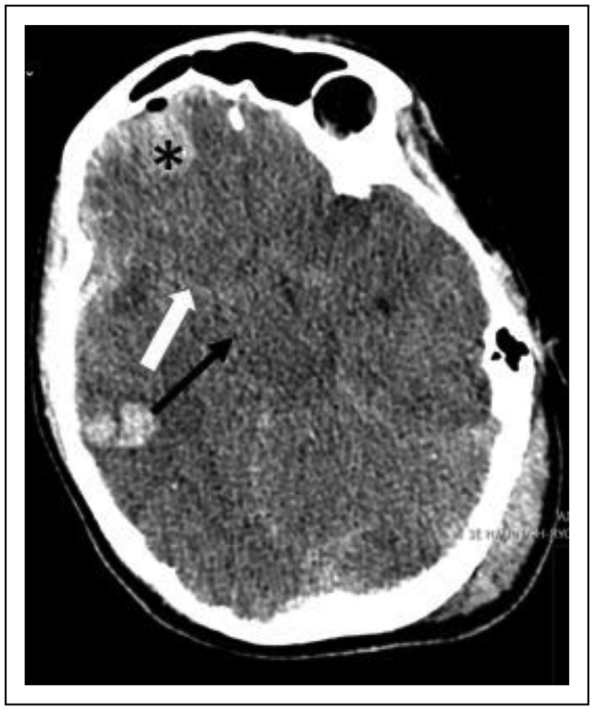

FIGURE 1. CT Image of a patient with severe traumatic brain injury. A young patient with life-threatening TBI presenting with unilaterally dilated pupils on the right side, and a GCS score of 5. The CT image shows diffuse brain swelling in addition to brain contusions (marked with ∗), effaced basal cisterns (indicted with a black arrow) and a pseudosubarachnoid hemorrhage sign (indicated with a white arrow) typically seen in patients with markedly increased intracranial pressure. This patient received emergent intubation, hyperosmolar therapy, mild hyperventilation and was subjected to an acute decompressive craniectomy. After prolonged neurocritical care therapy, the patient had an excellent outcome at 6 months postinjury. GCS, Glasgow Coma Scale; TBI, traumatic brain injury.

Since CPP is a surrogate marker for cerebral blood flow (CBF), it should be maintained by optimizing MAP using fluids, inotropes, and vasopressors, and/or by decreasing ICP. To decrease ICP, bedside manoeuvres such as sedation, cerebrospinal fluid (CSF) drainage, and, in refractory cases, barbiturate coma or DC can be used (Table 2) [15,31,32]. Of note, while several potentially neuroprotective agents that have been investigated in clinical trials, all failed to show benefit for sTBI [33,34▪].

Hyperosmolar therapy by 3% to 30% of HTS or mannitol for ICP lowering has been extensively studied. While reduced ICP can be achieved with hyperosmolar therapy, there is no firm evidence about the most effective agent, its administration, or timing. Whether HTS or mannitol is more effective for reducing ICP has been debated for over 20 years and despite several systematic reviews, including two Cochrane reviews and five meta-analyses, the optimal choice remains unsettled [35▪]. Lately, the COBI RCT showed that in moderate to severe TBI patients, continuous infusion of 20% HTS compared with standard care did not improve neurological outcome at 6 months postinjury [36]. An RCT in the UK entitled ''Sugar or Salt'' comparing the use of bolus HTS and mannitol for the management of elevated ICP in the neurointensive care unit (NICU) setting is currently underway [37▪▪]. However, there are no RCTs targeting the prehospital and ED settings. At present, osmotherapy should only be used as an interim measure for emergent ICP-lowering, by bolus administration and not as a continuous therapy [38▪].

RED BLOOD CELL TRANSFUSION AND ERYTHROPOIETIN

The optimal hemoglobin (Hb) level triggering transfusion for sTBI patients is controversial. A recent RCT showed that sTBI patients transfused ''liberally'' (at Hb 9 g/dl) had less posttraumatic vasospasm, lower hospital mortality and better neurological status at 6 months postinjury compared to patients transfused ''restrictively'' (at Hb 7 g/dl) [39]. While current recommendations argues against a liberal transfusion strategy at Hb 10 g/dL, a recent meta-analysis found no difference in mortality between restrictive (Hb <7 g/dl) and liberal (Hb <10 g/dl)

thresholds ($P = 0.79$). At present, best available evidence suggest a Hb threshold for transfusion between 7 and 9 g/dl [40▪▪].

Erythropoietin (EPO) is a potential neuroprotectant with effects on many organ systems and has thoroughly been investigated in clinical and experimental TBI. A recent meta-analysis of 10 RCTs of 2402 TBI patients suggested a reduced mortality with EPO [41▪▪]. However, EPO has a poor blood-brain barrier penetration and rather mixed efficacy in available RCTs. At present, EPO cannot be recommended in the routine management of sTBI patients [42].

CORRECTION OF IMPAIRED COAGULATION

Impaired coagulation is a crucial yet potentially treatable secondary insult in sTBI [43]. The proportion of sTBI patients on drugs targeting coagulation is increasing due to their increasing age. TBI *per se* also induces a coagulopathy, and 2/3 of patients in the ED have abnormal coagulation with risk factors being GCS $\leq$8, base excess (BE) ≤ -6, hypothermia and hypotension. Moreover, low fibrinogen levels should be corrected.

Management of low platelet count and platelet dysfunction

A platelet count $\leq 100 \times 10^9$/l is associated with increased mortality. Moreover, platelet dysfunction is common regardless of the use of platelet inhibitors. However, while platelet transfusion attenuates hematoma expansion there is no clear benefit on outcome [44,45], and the potential harms and risks of platelet transfusion of must be considered. Platelet transfusion, desmopressin, and tranexamic acid remain options for sTBI patients requiring surgery.

Anticoagulants (warfarin/direct oral anticoagulant)

In most studies, mortality and hemorrhage expansion are worse with warfarin when compared to direct oral anticoagulants (DOACs). In sTBI patients on warfarin, rapid reversal using Prothrombin complex concentrate (PCC) with the addition of Vitamin K1 (Vit K) is mandatory. Note that Vit K in itself is too slow, and that fresh-frozen plasma may not be well tolerated in elderly patients due to the volume load.

Due to the short half-lives of DOACs [46], up to 80% of the therapeutic effects will be gone with normal renal function, if the last dose taken at least 24 h prior to urgent surgery [47]. The antidote Idarucizumab should be administered to sTBI patients on Dabigatran. The antidote andexanet alpha, a modified recombinant inactive human factor Xa (FXa) was designed to reverse FXa inhibitors available for patients on apixaban or rivaroxaban [48]. To date, PCC administration is recommended for sTBI patients since the indications of andexanet alpha in sTBI have not been defined [49]. It should be noted, however, that it was recently found superior to standard care in FXa inhibitor- treated patients with spontaneous intracerebral hemorrhage, and its role in sTBI patients may be revisited in the near future (Fig. 2) [46,50].

STEROIDS

There is level 1 evidence that dexamethasone is ineffective in improving outcomes and is associated with significantly increased complication rates and mortality, and should thus be avoided in the acute management of sTBI [15].

SEIZURE MANAGEMENT

There is no evidence that the prophylactic use of any antiepileptic drug prevents late post traumatic

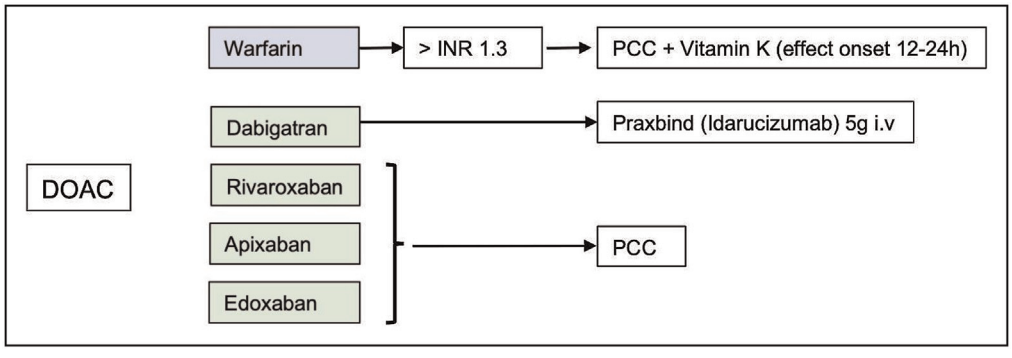

FIGURE 2. Reversal strategy for TBI patients on anticoagulant therapy. Recommended reversal strategy of oral anticoagulants using multifactor prothrombin complex concentrates (PCC) and antidotes in patients with severe TBI. DOAC, direct oral anticoagulant; INR, international normalized ratio; TBI, traumatic brain injury.

seizures (PTS) or improve outcome. Phenytoin is recommended in the recent Brain Trauma Foundation guideline since it is effective in decreasing early PTS, although early PTS is not correlated to worse outcome [11]. Levetiracetam is an alternative with a lower incidence of adverse effects [38▪]. The ongoing MAST trial aims to define best practice in the use of antiepileptic drugs following TBI [51].

TEMPERATURE MANAGEMENT

Temperature management in TBI addresses three main issues: the use of therapeutic hypothermia as a neuroprotectant, use of hypothermia to reduce ICP, and the avoidance of hyperthermia [19]. When summarizing several RCTs on hypothermia for sTBI, including the POLAR [52] and EUROTHERM [53] studies, ICP is reduced. However, the outcome is not improved, in fact in the EUROTHERM study the mortality was higher and the functional outcomes were worse. Current practice, based on limited evidence, focuses on reducing significant elevations in temperature while active hypothermia should only be evaluated in the setting of RCTs [15].

INITIAL NEUROCRITICAL CARE MONITORING

One of the cornerstones of acute sTBI management is the monitoring of ICP, which has been shown to reduce in-hospital and 2-week postinjury mortality [15]. Advanced neuromonitoring including, for example, brain tissue oxygen ($PbtO_2$) and microdialysis can be used in ICP reducing treatment algorithms [32,54]. A comprehensive discussion on NICU multimodality neuromonitoring is beyond the scope of this review and has been extensively covered in previous literature [55▪,56,57▪▪,58▪,59].

SURGICAL PERSPECTIVES

Immediate removal of mass lesions and/or decompressive craniectomy (DC) is often lifesaving, and may be the most crucial treatment in the early management of sTBI patients. Mass lesions consists of epidural (EDH), acute subdural hematoma (ASDH) and cortical contusions (CCx). At time of initial surgery, ICP monitoring may be initiated. Both intraparenchymal devices and external ventricular drain (EVD) can be used for ICP monitoring, however, the EVD offers the benefit of draining CSF. In patients with effaced basal cisterns and/or marked brain swelling presenting in a poor neurological state, a primary DC is considered. A large frontotemporoparietal DC (15 cm in diameter) is recommended, as it reduces mortality and improves neurological outcomes [60].

Surgical evacuation is the primary treatment for EDHs. They are often associated with skull fractures, occur in young individuals and should be surgically evacuated regardless of GCS if exceeding 30 cm^3, or if they present with coma and/or anisocoria. Nonoperative management may be considered for smaller hematomas in alert patients monitored by serial CT scans and close neurological surveillance.

Surgical intervention is generally recommended for ASDHs with a thickness $\geq$10 mm or a midline shift $\geq$5 mm. However, smaller ASDHs may still require surgery if certain conditions are met: a drop of two or more points in the GCS, presence of asymmetric or fixed and dilated pupils, or ICP exceeding 20 mmHg. A recent CENTER-TBI study found no evidence that an aggressive surgical approach in ASDH yielded better functional outcomes. However, treatment for patients with ASDH varied across different centers and the group that underwent acute surgery had a lower initial GCS score, larger volumes of ASDHs, and more often large contusions. The observational CENTER-TBI project has provided a unique increase in TBI knowledge. However, it was not designed to firmly evaluate treatment efficacy and changed management routines cannot be based solely on this ASDH study [61▪▪].

The Randomised Evaluation of Surgery with Craniectomy for patients Undergoing Evacuation of Acute SubDural Haematoma (RESCUE-ASDH) trial comparing DC versus craniotomy showed that patients with traumatic ASDH who underwent craniotomy or primary DC (as a primary operation), disability and quality-of-life outcomes were similar with the two approaches with no added benefit of performing DC [29▪▪].

Cerebral contusions (Ccx) are common in sTBI and usually coexist with traumatic subarachnoid hemorrhage (tSAH) and ASDH. Many progress – ''blossom'' - within the first 24 h [62▪]. In localized Ccx, immediate craniotomy and hematoma removal is indicated in sTBI patients showing progressive neurological deterioration and significant mass effect on CT, with significant midline deviation and compressed basal cisterns. As an alternative, a primary DC can be performed, particularly in Ccx accompanied by diffuse swelling [63]. It should be noted that DC significantly increases the risk of contusion expansion [64].

Penetrating head injury are mainly caused by gunshot and stab wounds. Gunshot wounds (GSWs) have higher mortality than stab wounds and have a higher incidence of intracerebral hemorrhage (ICH), and raised ICP [65,66]. Stab wounds and GSWs are also commonly associated with vascular injuries [67] that need to be evaluated by digital subtraction angiography (DSA), which is superior to

CT-angiography [68]. Coagulopathy combined with cerebrovascular injury forms a distinct endophenotype [69]. Patients with penetrating head injuries are prone to significant brain swelling where primary DC is a treatment option. Debridement of necrotic brain tissue, and wound revisions, are surgical options where excessive removal of foreign material should be avoided. There is a significant risk of posttraumatic epilepsy and infectious complications in sTBI patients with penetrating injuries and prophylactic anticonvulsants and antibiotics are recommended [69,70].

Recently, cisternostomy has emerged as a potential surgical approach for treating sTBI. This neurosurgical method includes, for example, extradural anterior and posterior clinoidectomy along with basal cisternostomy with opening of membrane Liliequist and lamina terminalis [71]. A recent, criticized, RCT compared DC with cisternostomy and found similar outcomes [72▪▪]. Importantly, this technique requires the expertise of highly skilled and trained neurosurgeons, surpassing the level typically available during on-call shifts handled by trainees [72▪▪,73,74▪].

Finally, hinge craniotomy could offer an intermediate intervention between treatment-refractive medical therapy and traditional DC, however, no RCT currently exists for this surgical technique [75].

PROGNOSTIC FACTORS

Outcome is difficult to predict since sTBI is a markedly heterogeneous disease. A limitation of classification based on GCS is that the underlying pathology is not considered. However, severity of TBI is one the most robust negative predictive factors followed by advanced age, absence of pupillary reaction, and initial hypotension [76]. The timing of GCS assessment is crucial since rapid alterations are common in the initial postinjury hours. Patients with low GCS persisting from the scene with bilaterally fixed dilated pupils (BFDP) have a dismal chance of survival [77]. The mortality in sTBI patients with a GCS of 3 and BFDP in the field is 90–95%, with merely 2–3% achieving a good functional recovery [78]. Patients with GCS $\leq$8 after resuscitation also face high mortality rates although many survivors reach a favorable recovery. Currently, there are no national guidelines recommending prognostic models for individual patient care decisions in sTBI and existing prognostic models, such as International Mission on Prognosis and Analysis of Clinical Trials (IMPACT), are primarily designed for research purposes and not widely implemented in clinical practice. Each patient should be approached individually, considering all the above-mentioned factors in addition to the underlying TBI pathology. In sTBI patients with a low GCS caused by an EDH, evacuation is more likely to result in a favorable outcome than if the cause is, for example, multifocal contusion and/or diffuse injuries. Furthermore, additional factors such as comorbidities and additional systemic injuries should be considered in the decision-making for advanced neuromonitoring and further treatment. These factors play a significant role in determining the appropriate approach to treatment and the potential outcomes for sTBI patients. Additionally, while the sTBI population is aging, the biological age is also shifting and patients $\geq$65 years old today may be healthier than in the recent past. Many older adults with TBI respond positively to aggressive management and rehabilitation, arguing that chronological age and TBI severity alone are insufficient prognostic markers. Making decision of palliative care or end-of-life decisions for this population is ethically complex and there are no specific guidelines for managing TBI in the geriatric population. Recent developments of frailty indexes may aid in prognostication in the elderly population.

Overall, balancing the goal of maximizing functional independence with the patient's wishes and quality of life becomes critical in decision-making processes. Additionally, the local or regional availability of rehabilitation services can significantly impact the functional outcome of sTBI patients.

There are many controversies surrounding prognostication and end-of-life decisions in sTBI. Legal and cultural variations may influence the decision-making process, including the acceptance of palliative care and withdrawal of life-sustaining treatments. Understanding and respecting these variations is crucial when making decisions for sTBI patients.

CONCLUSION AND FUTURE DIRECTION

The acute managements in the critical initial postinjury hours of sTBI is focused on preventing any possible secondary insults. Advancement of the prehospital and the ED care include rapid correction of impaired coagulation, noninvasive techniques to identify raised ICP in addition to the neurological exam, and rapid management of presumed or established increases in ICP and/or cerebral swelling. Upcoming clinical trials and large observational studies might provide stronger evidence for the use of osmotherapy, antiepileptic medications, and temperature management. Awaiting the emergence of neuroprotective therapies, multimodal monitoring, and treatment of secondary injury factors during the initial postinjury hours remain the

best treatment of patients with sTBI. A comprehensive approach tailored to each individual is recommended for the decision-making process of older patients with sTBI.

Acknowledgements

None.

Financial support and sponsorship

Funding: The Finnish Medical Foundation (IH), The Päivikki and Sakari Sohlberg Foundation (IH), The Paulo Foundation (IH), The Finnish Cultural Foundation (IH), SciLifeLab/KAW (ER), Wallenberg Clinical Fellow (ER), Swedish government and the County Councils (ER), The ALF agreement (ER), Kjell and Märta Beijer Foundation (ER), Skåne University Hospital ALF funds (NM), Hans-Gabriel af Trolle Wachtmeister Foundation (NM) and Swedish Brain Foundation (NM).

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

1. Dewan MC, Rattani A, Gupta S, *et al.* Estimating the global incidence of traumatic brain injury. J Neurosurg 2019; 130:1080–1097.
2. ■■ Maas AIR, Menon DK, Manley GT, *et al.* Traumatic brain injury: progress and challenges in prevention, clinical care, and research. Lancet Neurol 2022; 21:1004–1060.

This latest update of the Lancet Neurology Commission presents new insights and challenges across a range of TBI topics.

3. Masel BE, DeWitt DS. Traumatic brain injury: a disease process, not an event. J Neurotrauma 2010; 27:1529–1540.
4. Overview. Head injury: assessment and early management. Guidance. NICE. Available at: https://www.nice.org.uk/guidance/ng232.
5. Undén J, Ingebrigtsen T, Romner B. Scandinavian guidelines for initial management of minimal, mild and moderate head injuries in adults: an evidence and consensus-based update. BMC Med 2013; 11:50.
6. Lenell S, Nyholm L, Lewén A, Enblad P. Updated periodic evaluation of standardized neurointensive care shows that it is possible to maintain a high level of favorable outcome even with increasing mean age. Acta Neurochir 2015; 157:417–425.
7. Cooper DJ, Nichol AD, Bailey M, *et al.* Effect of early sustained prophylactic hypothermia on neurologic outcomes among patients with severe traumatic brain injury. J Am Med Assoc 2018; 320:2211–2220.
8. Mayglothling J, Duane TM, Gibbs M, *et al.* Emergency tracheal intubation immediately following traumatic injury: an eastern association for the surgery of trauma practice management guideline. J Trauma Acute Care Surg 2012; 73(Suppl 4):S333–S340.
9. Hatchimonji JS, Dumas RP, Kaufman EJ, *et al.* Questioning dogma: does a GCS of 8 require intubation? Eur J Trauma Emerg Surg 2021; 47:2073–2079.
10. Wilson MH, Habig K, Wright C, *et al.* Prehospital emergency medicine. Lancet 2015; 386:2526–2534.
11. Popal Z, Bossers SM, Terra M, *et al.* Effect of Physician-Staffed Emergency Medical Services (P-EMS) on the outcome of patients with severe traumatic brain injury: a review of the literature. Prehosp Emerg Care 2019; 23:730–739.
12. Pakkanen T, Nurmi J, Huhtala H, Silfvast T. Prehospital on-scene anaesthetist treating severe traumatic brain injury patients is associated with lower mortality and better neurological outcome. Scand J Trauma Resusc Emerg Med 2019; 27:9.
13. Bernard SA, Nguyen V, Cameron P, *et al.* Prehospital rapid sequence intubation improves functional outcome for patients with severe traumatic brain injury: a randomized controlled trial. Ann Surg 2010; 252:959–965.
14. Kudo D, Yoshida Y, Kushimoto S. Permissive hypotension/hypotensive resuscitation and restricted/controlled resuscitation in patients with severe trauma. J Intensive Care 2017; 5:11.
15. Carney N, Totten AM, O'Reilly C, *et al.* Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery 2017; 80:6–15.
16. Kushner DS, Alvarez G. Dual diagnosis: traumatic brain injury with spinal cord injury. Phys Med Rehabil Clin North Am 2014; 25:681–696; ix–x.
17. Bazaie N, Alghamdi I, Alqurashi N, Ahmed Z. The impact of a cervical collar on intracranial pressure in traumatic brain injury patients: a systematic review and meta-analysis. Trauma Care 2021; 2:1–10.
18. Zileli M, Osorio-Fonseca E, Konovalov N, *et al.* Early management of cervical spine trauma: WFNS spine committee recommendations. Neurospine 2020; 17:710–722.
19. Menon DK, Ercole A. Critical care management of traumatic brain injury. Handb Clin Neurol 2017; 140:239–274.
20. Williams J, Roberts I, Shakur-Still H, *et al.* Cost-effectiveness analysis of tranexamic acid for the treatment of traumatic brain injury, based on the results of the CRASH-3 randomised trial: a decision modelling approach. BMJ Global Health 2020; 5:e002716.
21. Acar N, Canakci ME, Bilge U. Early and ultraearly administration of tranexamic acid in traumatic brain injury: our 8-year-long clinical experience. Emerg Med Int 2020; 2020:6593172.
22. Yokobori S, Yatabe T, Kondo Y, *et al.* Efficacy and safety of tranexamic acid administration in traumatic brain injury patients: a systematic review and meta-analysis. J Intensive Care 2020; 8:46.
23. Rostami E, Kongstad P, Marklund N. Should all patients with traumatic brain injury receive tranexamic acid? Lakartidningen 2020; 117:117.
24. Lawati K Al, Sharif S, Maqbali S Al, *et al.* Efficacy and safety of tranexamic acid in acute traumatic brain injury: a systematic review and meta-analysis of randomized-controlled trials. Intensive Care Med 2021; 47:14–27.
25. ■ Dengler BA, Karam O, Barthol CA, *et al.* Ketamine boluses are associated with a reduction in intracranial pressure and an increase in cerebral perfusion pressure: a retrospective observational study of patients with severe traumatic brain injury. Crit Care Res Pract 2022; 2022:3834165.

This single center study suggests that ketamine boluses may lead to reduced ICP and increased CPP, findings that need support from multicenter studies or randomized control trials.

26. Bar-Joseph G, Guilburd Y, Tamir A, Guilburd JN. Effectiveness of ketamine in decreasing intracranial pressure in children with intracranial hypertension: clinical article. J Neurosurg Pediatr 2009; 4:40–46.
27. ■ Léger M, Frasca D, Roquilly A, *et al.* Early use of barbiturates is associated with increased mortality in traumatic brain injury patients from a propensity score-based analysis of a prospective cohort. PLoS One 2022; 17:e0268013.

This study suggests that each early barbiturate administration requires a careful assessment of the risk/benefit ratio.

28. Singer KE, Wallen TE, Jalbert T, *et al.* Efficacy of noninvasive technologies in triaging TBI and correlating with ICP: a prospective study. J Surg Res 2021; 262:27–37.
29. ■■ Hutchinson PJ, Adams H, Mohan M, *et al.* Decompressive craniectomy versus craniotomy for acute subdural hematoma. N Engl J Med 2023; 388:2219–2229.

This is established that decompressive craniectomy (DC) may reduce intracranial hypertension, but whether it is associated with better outcome in acute subdural hematomas (ASDHs) is not clear. This RCT concluded that among patients with traumatic ASDH who underwent craniotomy or DC, disability and quality-of-outcomes were similar with the two approaches arguing against added benefit of DC in the management of ASDH.

30. Picetti E, Rossi S, Abu-Zidan FM, *et al.* WSES consensus conference guidelines: Monitoring and management of severe adult traumatic brain injury patients with polytrauma in the first 24 h. World J Emerg Surg 2019; 14:53.
31. Hutchinson PJ, Kolias AG, Timofeev IS, *et al.* Trial of decompressive craniectomy for traumatic intracranial hypertension. N Engl J Med 2016; 375:1119–1130.
32. Chesnut R, Aguilera S, Buki A, *et al.* A management algorithm for adult patients with both brain oxygen and intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). Intensive Care Med 2020; 46:919–929.
33. Strickland BA, Bakhsheshian J, Emmanuel B, *et al.* Neuroprotective effect of minocycline against acute brain injury in clinical practice: a systematic review. J Clin Neurosci 2021; 86:50–57.
34. ■ Mansour NO, Elnaem MH, Abdelaziz DH, *et al.* Effects of early adjunctive pharmacotherapy on serum levels of brain injury biomarkers in patients with traumatic brain injury: a systematic review of randomized controlled studies. Front Pharmacol 2023; 14:1185277.

This review highlights s the current evidence of adjuvant neuroprotective treatments for TBI patients.

35. ■ Raman V, Bright M, Mitchell G. A brief review of bolus osmotherapy use for managing severe traumatic brain injuries in the pre-hospital and emergency department settings. Trauma Care 2022; 2:427–433.

This latest review suggests that local policies and individual patient characteristics will continue to guide the use of osmotherapy.

36. Roquilly A, Moyer JD, Huet O, *et al.* Effect of continuous infusion of hypertonic saline vs standard care on 6-month neurological outcomes in patients with traumatic brain injury: the COBI Randomized Clinical Trial. JAMA 2021; 325:2056–2066.

37. Rowland MJ, Veenith T, Scomparin C, *et al.* Sugar or salt (''SOS''): a protocol ■■ for a UK multicentre randomised trial ofmannitol and hypertonic saline in severe traumatic brain injury and intracranialhypertension. J Intensive Care Soc 2022; 23:222–232.

The results of this RCT will inform current clinical practice in the routine use of hyperosmolar therapy as well as assesses the impact of potential side effects.

38. Wiles MD. Management of traumatic brain injury: a narrative review of current ■ evidence. Anaesthesia 2022; 77(Suppl 1):102–112.

This narrative review summarizes the current advances of TBI management.

39. Gobatto ALN, Link MA, Solla DJ, *et al.* Transfusion requirements after head trauma: a randomized feasibility controlled trial. Crit Care 2019; 23:89.

40. Montgomery EY, Barrie U, Kenfack YJ, *et al.* Transfusion guidelines in ■■ traumatic brain injury: a systematic review and meta-analysis of the currently available evidence. Neurotrauma Rep 2022; 3:554–568.

This important article suggests that an intermediate threshold between 7 and 9 g/dl of Hgb, reflects the physiological oxygen needs of cerebral tissue in adult TBI.

41. Li Y, Zhang J, Wang H, *et al.* Does erythropoietin affect the outcome and ■■ complication rates of patient with traumatic brain injury? A pooled-analysis. Neurol Sci 2023; 44:355–356.

This meta-analysis suggests that the use of EPO could reduce mortality rate for TBI patients.

42. Liu M, Wang AJ, Chen Y, *et al.* Efficacy and safety of erythropoietin for traumatic brain injury. BMC Neurol 2020; 20:399.

43. Adatia K, Newcombe VFJ, Menon DK. Contusion progression following traumatic brain injury: a review of clinical and radiological predictors, and influence on outcome. Neurocrit Care 2021; 34:312–324.

44. Brogi E, Corbella D, Coccolini F, *et al.* The role of platelet transfusions after intracranial hemorrhage in patients on antiplatelet agents: a systematic review and meta-analysis. World Neurosurg 2020; 141:455–466; e13.

45. Thorn S, Güting H, Mathes T, *et al.* The effect of platelet transfusion in patients with traumatic brain injury and concomitant antiplatelet use: a systematic review and meta-analysis. Transfusion 2019; 59:3536–3544.

46. Prior A, Fiaschi P, Iaccarino C, *et al.* How do you manage ANTICOagulant therapy in neurosurgery? The ANTICO survey of the Italian Society of Neurosurgery (SINCH). BMC Neurol 2021; 21:98.

47. Verma A, Ha ACT, Rutka JT, Verma S. What surgeons should know about non-vitamin K oral anticoagulants a review. JAMA Surg 2018; 153:577–585.

48. Connolly SJ, Crowther M, Eikelboom JW, *et al.* Full study report of andexanet alfa for bleeding associated with factor Xa inhibitors. N Engl J Med 2019; 380:1326–1335.

49. Maragkos GA, Nelton EB, Richter S, Stippler M. Low risk of traumatic intracranial hematoma expansion with factor xa inhibitors without andexanet reversal. World Neurosurg 2020; 142:e95–e100.

50. Fiaschi P, Iaccarino C, Stefini R, *et al.* Clinical practice for antiplatelet and anticoagulant therapy in neurosurgery: data from an Italian survey and summary of current recommendations – part I, antiplatelet therapy. Neurosurg Rev 2021; 44:485–493.

51. MAnagement of Seizures post-TBI. [Protocol, 2021]. Available at: https://masttrial.org/.

52. Cooper DJMD, Nichol ADMBP. Bailey MP, *et al.* Effect of early sustained prophylactic hypothermia on neurologic outcomes among patients with severe traumatic brain injury: the POLAR Randomized Clinical Trial. JAMA 2018; 320:2211–2220.

53. Andrews PJD, Sinclair HL, Rodríguez A, *et al.* Therapeutic hypothermia to reduce intracranial pressure after traumatic brain injury: the Eurotherm3235 RCT. Health Technol Assess 2018; 22:1–134.

54. Hutchinson PJ, Jalloh I, Helmy A, *et al.* Consensus statement from the 2014 International Microdialysis Forum. Intensive Care Med 2015; 41:1517–1528.

55. Meyfroidt G, Bouzat P, Casaer MP, *et al.* Management of moderate to severe ■ traumatic brain injury: an update for the intensivist. Intensive Care Med 2022; 48:649–666.

This review provides and update of the management of TBI patients from the first few hours to the intensive care unit (ICU) treatment.

56. Young AMH, Guilfoyle MR, Donnelly J, *et al.* Multimodality neuromonitoring in severe pediatric traumatic brain injury. Pediatr Res 2018; 83:41–49.

57. Tas J, Czosnyka M, van der Horst ICC, *et al.* Cerebral multimodality monitoring ■■ in adult neurocritical care patients with acute brain injury: a narrative review. Front Physiol 2022; 13:1071161.

This narrative review discusses the recent advance on multimodality monitoring of TBI patients in a neuroICU setting.

58. Lindblad C, Raj R, Zeiler FA, Thelin EP. Current state of high-fidelity multi- ■ modal monitoring in traumatic brain injury. Acta Neurochirur 2022; 164:3091–3100.

This review critically discusses the neuroICU management modalities for TBI patients.

59. Zeiler FA, Ercole A, Czosnyka M, *et al.* Continuous cerebrovascular reactivity monitoring in moderate/severe traumatic brain injury: a narrative review of advances in neurocritical care. Br J Anaesth 2020; 124:440–453.

60. Hawryluk GWJ, Rubiano AM, Totten AM, *et al.* Guidelines for the management of severe traumatic brain injury: 2020 update of the decompressive craniectomy recommendations. Neurosurgery 2020; 87:427–434.

61. van Essen TA, Lingsma HF, Pisică D, *et al.* Surgery versus conservative ■■ treatment for traumatic acute subdural haematoma: a prospective, multicentre, observational, comparative effectiveness study. Lancet Neurol 2022; 21:620–631.

This recent CENTER-TBI study found that treatment for patients with ASDH with similar characteristics differed depending on the treatment center, and in patients without radiological and clinical features mandating acute surgery could initial conservative treatment be considered.

62. Fletcher-Sandersjöö A, Tatter C, Tjerkaski J, *et al.* Time course and clinical ■ significance of hematoma expansion in moderate-to-severe traumatic brain injury: an observational cohort study. Neurocrit Care 2023; 38:60–70.

This article concluded that expansion of a traumatic intracranial hematoma is a driver of unfavorable outcome in TBI and that small changes in hematoma volume also impacts functional outcome.

63. Bullock MR, Chesnut R, Ghajar J, *et al.* Surgical management of traumatic parenchymal lesions. Neurosurgery 2006; 58(3 Suppl):S25–46; discussion Si–iv.

64. Cepeda S, Castaño-León AM, Munarriz PM, *et al.* Effect of decompressive craniectomy in the postoperative expansion of traumatic intracerebral hemorrhage: a propensity score–based analysis. J Neurosurg 2019; 132:1623–1635.

65. Günther M, Dahlberg M, Rostami A, *et al.* Incidence, demographics, and outcomes of penetrating trauma in sweden during the past decade. Front Neurol 2021; 12:730405.

66. Bieler D, Kollig E, Hackenberg L, *et al.* Penetrating injuries in Germany – epidemiology, management and outcome an analysis based on the TraumaRegister DGU®. Scand J Trauma Resusc Emerg Med 2021; 29:80.

67. Harrington BM, Gretschel A, Lombard C, *et al.* Complications, outcomes, and management strategies of nonmissile penetrating head injuries. J Neurosurg 2020; 134:1658–1666.

68. Ares WJ, Jankowitz BT, Tonetti DA, *et al.* A comparison of digital subtraction angiography and computed tomography angiography for the diagnosis of penetrating cerebrovascular injury. Neurosurg Focus 2019; 47:E16.

69. Lazaridis C, Mansour A, Alvarado-Dyer R, *et al.* Civilian firearm-inflicted brain injury: coagulopathy, vascular injuries, and triage. Curr Neurol Neurosci Rep 2021; 21:47.

70. Ragel BT, Klimo P, Martin JE, *et al.* Wartime decompressive craniectomy: technique and lessons learned. Neurosurg Focus 2010; 28:E2.

71. Cherian I, Bernardo A, Grasso G. Cisternostomy for traumatic brain injury: pathophysiologic mechanisms and surgical technical notes. World Neurosurg 2016; 89:51–57.

72. Chandra VVR, Mowliswara Prasad BC, Banavath HN, Chandrasekhar Reddy ■■ K. Cisternostomy versus decompressive craniectomy for the management of traumatic brain injury: a randomized controlled trial. World Neurosurg 2022; 162:e58–e64.

This criticized RCT suggests that cisternostomy was effective in reducing ICP.

73. Giammattei L, Messerer M, Oddo M, *et al.* Cisternostomy for refractory posttraumatic intracranial hypertension. World Neurosurg 2018; 109:460–463.

74. Giammattei L, Starnoni D, Messerer M, Daniel RT. Basal cisternostomy for ■ severe TBI: surgical technique and cadaveric dissection. Front Surg 2022; 9:915818.

This article discusses the surgical techniques of basal cisternostomy and emphasizes the training of young neurosurgeons for the procedure.

75. Mohan M, Layard Horsfall H, Solla DJF, *et al.* Decompressive craniotomy: an international survey of practice. Acta Neurochir 2021; 163:1415–1422.

76. Roozenbeek B, Lingsma HF, Lecky FE, *et al.* 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 2012; 40:1609–1617.

77. Chaudhuri K, Malham GM, Rosenfeld JV. Survival of trauma patients with coma and bilateral fixed dilated pupils. Injury 2009; 40:28–32.

78. Mauritz W, Leitgeb J, Wilbacher I, *et al.* Outcome of brain trauma patients who have a Glasgow Coma Scale score of 3 and bilateral fixed and dilated pupils in the field. Eur J Emerg Med 2009; 16:153–158.

79. Howells T, Elf K, Jones PA, *et al.* Pressure reactivity as a guide in the treatment of cerebral perfusion pressure in patients with brain trauma. J Neurosurg 2005; 102:311–317.