Acute Management of Traumatic Brain Injury

Michael A. Vella, MD, MBA\textsuperscript{a,b}, Marie L. Crandall, MD, MPH\textsuperscript{c}, Mayur B. Patel, MD, MPH\textsuperscript{d,e,*}

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\textsuperscript{a} Department of Surgery, Section of Surgical Sciences, Vanderbilt University Medical Center, Medical Center North, CCC-4312, 1161 21st Avenue South, Nashville, TN 37232-2730, USA; \textsuperscript{b} Division of Traumatology, Surgical Critical Care, and Emergency Surgery, Department of Surgery, University of Pennsylvania, Philadelphia, PA 19104, USA; \textsuperscript{c} Division of Acute Care Surgery, Department of Surgery, University of Florida, Jacksonville, 655 West 8th Street, Jacksonville, FL 32209, USA; \textsuperscript{d} Division of Trauma, Surgical Critical Care, and Emergency General Surgery, Department of Surgery, Section of Surgical Sciences, Center for Health Services Research, Vanderbilt Brain Institute, Vanderbilt University Medical Center, 1211 21st Avenue South, Medical Arts Building, Suite 404, Nashville, TN 37212, USA; \textsuperscript{e} Surgical Services, Nashville Veterans Affairs Medical Center, Tennessee Valley Healthcare System, 1310 24th Avenue South, Nashville, TN 37212, USA

* Corresponding author. Division of Trauma, Surgical Critical Care, and Emergency General Surgery, Department of Surgery, Section of Surgical Sciences, Center for Health Services Research, Vanderbilt Brain Institute, Vanderbilt University Medical Center, 1211 21st Avenue South, Medical Arts Building, Suite 404, Nashville, TN 37212.

E-mail address: mayur.b.patel@vanderbilt.edu

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- Decompressive craniectomy

KEY POINTS

- Traumatic brain injury (TBI) is a leading cause of death and disability in patients with trauma with a significant economic impact.
- The acute management of TBI focuses on the prevention of secondary injury through the avoidance of hypotension and hypoxia and maintenance of appropriate cerebral perfusion pressure and, by extension, cerebral blood flow.
- Mass lesions may require operative intervention based on imaging characteristic, examination findings, and measurements of intracranial pressure (ICP).
- Increased ICP can be managed in an algorithmic fashion using a combination of simple bedside maneuvers, hyperosmolar therapy, cerebrospinal fluid drainage, pentobarbital coma, and decompressive craniectomy.
- Other important considerations in patients with TBI include venous thromboembolism, stress ulcer, and seizure prophylaxis, as well as nutrition and metabolic optimization.
EPIDEMIOLOGY

Trauma is the leading cause of death in individuals aged 1 to 45 years, with traumatic brain injury (TBI) responsible for most these deaths; more than 50,000 deaths per year in the United States.1–3 TBI can be clinically stratified into mild, moderate, and severe based on the Glasgow Coma Scale (GCS) score, with associated permanent disability rates of 10%, 60%, and 100%, respectively, and overall mortalities of 20% to 30%.3,4 The economic impact is more than $80 billion in the United States alone according to the most recent US Centers for Disease Control and Prevention data.3,5 This article focuses on the prehospital, emergency department, and intensive care unit (ICU) management of TBI.

MECHANISM AND PATHOPHYSIOLOGY

Traumatic brain injuries can result from both blunt and penetrating mechanisms. Falls (35%) and motor vehicle collisions (17%) are the most common, with motor vehicle collisions leading most fatalities. Gunshot wounds to the head are the most lethal injuries, but, because of overall incidence, result in fewer total deaths.3,4

The primary insult to the brain cannot be undone and results in brain tissue damage, impaired cerebral blood flow (CBF) regulation, and alterations in brain metabolism with upregulation of inflammatory mediators, oxidative stress, and vasospasm. These processes ultimately lead to cell death and generalized brain edema.6

The Monro-Kellie hypothesis holds that the total intracranial volume is made up of brain tissue, cerebral spinal fluid (CSF), venous blood, and arterial blood. CBF remains constant under normal conditions via cerebral autoregulatory mechanisms over a range of blood pressures. When one compartment is increased, by a hematoma for example, there must be a compensatory decrease in another compartment in order to prevent intracranial hypertension. Cerebral perfusion pressure (CPP) is a surrogate for CBF. CPP is defined as mean arterial pressure (MAP) minus intracranial pressure (ICP). A decrease in CPP implies a decrease in CBF, although this association is not perfect. Decreased CBF ultimately leads to ischemia and hypoxia and worsening of the initial brain insult.2,5 The goal of TBI management is to prevent this secondary insult.

AVOIDANCE OF SECONDARY INJURY

At present, the initial insult causing a TBI cannot be reversed, and this is referred to as the primary injury. Hypotension, previously defined as systolic blood pressure (SBP) less than 90 mm Hg, and hypoxia, defined as a PaO2 less than or equal to 60 mm Hg, have been associated with doubling of mortality in patients with head injuries.7,8 Early studies from the 1970s showed an association between systemic insults (mainly hypotension, hypoxia, and hypercarbia) and increased mortality, suggesting an important role for trauma center transfer in patients with severe TBI.9 Management strategies must therefore focus on the prevention of secondary injury (ie, hypoxia, hypotension) through maintenance of adequate CBF and prevention of hypoxia.

PREHOSPITAL MANAGEMENT

Consistent with all phases of TBI management, prehospital strategies should focus on preventing secondary brain injury. In one study, patients with moderate to severe TBI transferred to level I trauma centers via helicopter and who had secondary insults (either SBP<90 mm Hg or SpO2<92%) had a 28% mortality, compared with 20% of patients without such insults. Prehospital hypoxia in these same patients was associated with a significant increase in mortality, and there was no difference in hypoxic episodes between patients intubated versus those not intubated in the field.10 Similarly, prehospital
rapid-sequence intubation performed by paramedics in patients with head injuries with GCS less than 9 was associated with an increase in mortality. This result may be associated with the transient hypoxia during the prehospital procedures, excessive overventilation causing hypocarbia, vasoconstriction, impaired CBF, and longer scene times.\textsuperscript{11} This body of work implies a need for rapid transfer to definitive care and a focus on more basic airway strategies to maintain oxygenation in patients with head injuries.

Several studies have also evaluated the use of hypertonic saline in the prehospital arena as a means to improve CPP by decreasing ICP and increasing MAP. In a 2004 study by Cooper and colleagues,\textsuperscript{12} patients with severe TBI (GCS<9) and hypotension (SBP<100 mm Hg) were assigned to either rapid administration of 7.5% saline or a similar bolus of Ringer lactate by paramedics. Neurologic function at 6 months did not differ between the two groups, although mean sodium level in the treatment group was only 149 mEq/L. A multicenter randomized clinical trial in 2010 by Bulger and colleagues\textsuperscript{13} studied patients with severe TBI (GCS<9) not in hypovolemic shock. Patients were administered either 7.5% saline/6% dextran 70, 7.5% saline alone, or 0.9% saline. Neurologic outcome at 6 months and survival did not differ among groups. At this time, prehospital use of hypertonic saline cannot be recommended.

**EMERGENCY DEPARTMENT MANAGEMENT**

The initial management of patients with TBI is identical to that of all patients with trauma, focusing on the Advanced Trauma Life Support (ATLS) principles of management of airway, breathing, and circulation, followed by a rapid neurologic examination and exposure of the patient with prevention of hypothermia.\textsuperscript{14}

The airway should be secured according to local protocols. Induction agents such as propofol should be carefully used, possibly in conjunction with induction inotropes, given the risk of systemic hypotension with impaired CBF. Ketamine is an attractive agent in patients with trauma, given its favorable hemodynamic profile. Despite theoretic risks, a systematic review of ketamine use in TBI suggests that ketamine does not increase ICP\textsuperscript{15}

Breathing should be optimized to maintain oxygenation and prevent ventilatory dysfunction, because extremes in CO\textsubscript{2} levels can lead to cerebral vasoconstriction and vasodilatation, and have been shown to be predictors of morbidity and mortality.\textsuperscript{8} Hyperventilation is used by some providers to acutely decrease ICP through hypocarbic vasoconstriction, despite evidence showing an association between even brief periods of hyperventilation and increased levels of mediators of secondary brain injury in areas adjacent to injured brain tissue as well as local reductions in cerebral perfusion.\textsuperscript{16–18} This strategy should be used with caution, and perhaps only to acutely combat signs of active herniation while initiating more definitive treatment.

Circulation should be maintained to prevent hypotension and maintain CBF. There is a known coagulopathy related to head injury likely related to tissue factor release coupled with hypoperfusion, which may be exacerbated by a pure crystalloid resuscitation. A balanced blood product resuscitation has been shown to be beneficial in patients with trauma,\textsuperscript{19–21} and may be extended to patients with TBI. Non–cross-matched packed red blood cells are an initial resuscitative fluid choice that is often used in hypotensive patients with trauma, with a goal to maintain SBP at greater than or equal to 90 mm Hg in patients suspected of having a TBI. The concept of permissive hypotension does not apply to patients with known or suspected TBI, and normal physiologic blood pressure parameters should be targeted in this population.

During the disability component of the primary survey, a rapid neurologic evaluation is performed. The evaluation focuses on the pupillary examination, assesses for
lateralizing signs suggesting a mass lesion with increased ICP, and calculates a GCS score to stratify the TBI severity. The patient should then be exposed to evaluate for injury and rapidly covered to prevent hypothermia. A more detailed examination is performed during the secondary survey. Agents such as hypertonic saline and/or mannitol (discussed in more detail later) can be given during this initial resuscitation if physical examination findings suggest a neurologic decline, significant head injury, or lateralizing neurologic examination.

Following the initial resuscitation, patients suspected of having a TBI usually undergo a noncontrasted head computed tomography (CT) scan, depending on the presence of other injuries that require more urgent attention. Recent level II recommendations from the Eastern Association for the Surgery of Trauma (EAST) suggest obtaining a head CT scan in patients who present with suspected brain injury in the acute setting if it is available. If rapid CT scanning is not available, providers can consider using one of the various criteria for determining need for additional imaging, such as the Canadian CT Head Rule and the New Orleans Criteria.

OPERATIVE MANAGEMENT OF MASS LESIONS

Recent guidelines recommend surgical evacuation for epidural hematomas (EDHs) larger than 30 cm³ regardless of GCS. Surgical evacuation should be considered for patients with EDH and GCS less than 9, clot thickness greater than 15 mm, midline shift greater than 5 mm, or focal neurologic deficits. EDHs less than 30 cm³, less than 15 mm thick, with less than 5 mm shift in patients with GCS greater than 8 and no focal deficits can be watched with close observation and serial imaging (with repeat scan 6–8 hours after the previous scan). Evacuation should be considered for subdural hematomas (SDHs) larger than 1 cm or those associated with midline shift greater than 5 mm, a GCS less than 8 with rapid decline, or ICP less than 20 mm Hg. Patients with parenchymal lesions and progressive neurologic decline, mass effect, refractory intracranial hemorrhage (ICH), GCS scores of 6 to 8 with frontal or temporal contusions greater than 20 cm³, midline shift of at least 5 mm and/or compression of cisterns, or lesion volume greater than 50 cm³ should be considered for decompression. Early studies found a significant mortality benefit if evacuation was performed within 4 hours from injury. The STITCH (Trauma) trial (Surgical Trial in Traumatic Intracerebral Hemorrhage), which compared 6-month outcomes in patients with trauma with intraparenchymal hemorrhage randomized to early operative evacuation (<12 hours) with conservative management, was stopped early at 170 patients because of recruitment issues but showed a mortality benefit in patients who underwent early operative intervention.

INTENSIVE CARE UNIT CIRCULATORY CONSIDERATIONS

SBP should be maintained a greater than or equal to 90 mm Hg through use of fluids and pressors, although the Brain Trauma Foundation (BTF) provides level III recommendations for higher thresholds, depending on age. The ideal fluid for patients with TBI is unknown, although fluids should be administered judiciously and hypotonic fluids avoided to prevent volume overload and potential worsening of cerebral edema. In a post-hoc analysis of patients with head injuries in the SAFE (Saline vs Albumin Fluid Evaluation) study, those who received albumin had higher mortalities compared with those who received saline. Although packed red blood cells are often used as the initial fluid in traumatically injured patients, transfusing to a hemoglobin level greater than 10 g/dL has been associated with more adverse events and no
improvement in 6-month neurologic outcome in patients with TBI compared with those transfused to a restrictive threshold of 7 g/dL.\textsuperscript{33}

Brain-injured patients may require reversal of anticoagulant and antiplatelet agents, because the prehospital use of these medications may increase mortality after TBI.\textsuperscript{34–36} The most recent EAST guideline suggests that all elderly patients on prehospital systemic anticoagulation who are suspected of having a head injury should undergo rapid head CT evaluation.\textsuperscript{37} It is also recommended that patients with head injuries on warfarin should undergo rapid (within 2 hours of presentation) reversal of warfarin with fresh frozen plasma (FFP) and vitamin K.\textsuperscript{37,38} McMillian and Rogers\textsuperscript{39} propose a simple algorithm for management of patients on aspirin, clopidogrel, and warfarin who are suspected of having a head injury. If intracranial hemorrhage is identified on an immediate head CT scan in a patient on warfarin, 4 units of type-specific FFP and 10 mg of intravenous (IV) vitamin K are administered with a goal International Normalized Ratio (INR) of less than 1.6. If the patient is on an antiplatelet agent, a 10 pack of type-specific platelets is administered. Prothrombin complex concentration (PCC) and desmopressin can also be considered to reverse warfarin anticoagulation and antiplatelet agents, respectively.\textsuperscript{40–42} Novel anticoagulants, both direct thrombin inhibitors (dabigatran) and factor Xa inhibitors (rivaroxaban, apixaban, edoxaban), pose a unique challenge given a lack of reversal options. Readers are referred to a review article from 2013 that suggests an approach to the management of bleeding patients on novel anticoagulants, which may be extrapolated to patients with head injuries. In addition to treating coagulopathies with FFP and platelets when appropriate, 4-factor or activated PCC can be administered, and dialysis can be considered for patients on dabigatran if feasible.\textsuperscript{43} Idarucizumab, a monoclonal antibody fragment, has been found to rapidly reverse the effects of dabigatran in patients with serious bleeding and may have a role in patients with trauma.\textsuperscript{44} Early administration of tranexamic acid (TXA), an antifibrinolytic agent, has been shown to reduce all-cause mortality and death caused by bleeding in patients with trauma with significant bleeding.\textsuperscript{45} The CRASH-2 (Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage 2) intracranial bleeding study showed that neither moderate benefits nor moderate harmful effects of TXA can be excluded in bleeding patients with trauma with TBI.\textsuperscript{46} The CRASH-3 trial is designed to quantify the effects of early administration of TXA on death and disability in patients with TBI and is currently underway.\textsuperscript{47}

INTENSIVE CARE UNIT MANAGEMENT OF INTRACRANIAL HYPERTENSION

Fig. 1 presents a simple algorithm for the management of patients with severe TBI used at the authors’ institution and focuses mainly on the management of increased ICP. The neurosurgical service is consulted on identification of a TBI, and mass lesions are evacuated if indicated. Basic laboratory tests are ordered to evaluate for coagulopathy and seizure prophylaxis is started (discussed later). Patients with moderate to severe TBI are admitted to the ICU for ongoing resuscitation and prevention of secondary brain injury. A 2013 study found that acute care surgeons can effectively manage patients with mild TBI without neurosurgical evaluation, although this cannot be firmly extrapolated to patients with moderate or severe TBI, and the authors suggest neurosurgical consultation for any ICH, irrespective of neurologic function.\textsuperscript{48}

As noted in Fig. 1, patients admitted to the ICU should have optimization of oxygen, ventilation, and SBP. Simple maneuvers like loosening of the cervical collar, raising the head of bed to greater than 30° or maintaining a reverse Trendelenburg position (if no contraindication), and optimizing sedation and analgesia can decrease ICP, although some of these may not improve CBF or CPP.\textsuperscript{49} Blood products can be given to keep
INR less than 1.5 and platelets greater than or equal to 100,000/μL to prevent further intracranial bleeding, although these are arbitrary hemostatic thresholds and may be influenced by preinjury antiplatelet/anticoagulants, availability of thromboelastography, neurologic changes, imaging changes, and/or institutional culture.

**INTRACRANIAL PRESSURE MONITORING**

Consideration should be given to placement of an ICP monitor in patients with severe TBI. External ventricular drains (EVDs), which are placed in the lateral ventricle and connected to a pressure monitor, can also be used for continuous or intermittent drainage of CSF as a means to decrease ICP. Open or continuous EVDs have been...
associated with better ICP reduction than intermittent or closed EVDs, although EVD monitors have not been shown to be superior to intraparenchymal ICP monitors. Intraparenchymal monitors are placed directly into brain tissue but may not accurately measure pressure in the CSF because of pressure gradients that occur after TBI. Both device types measure ICP, and the calculated CPP is used as a surrogate for CBF, and, by extension, brain oxygenation and metabolic supply.

The BTF recommends (level IIB) ICP monitoring in patients with severe TBI (GCS<9) and abnormal CT scan to reduce 2-week and in-hospital mortality. It is also recommended that CSF drainage be considered to reduce ICP in patients with a GCS less than 6 within the first 12 hours of injury. General goals are to maintain an ICP less than 20 mm Hg and CPP between 50 and 70 mm Hg, depending on autoregulatory status. Values higher have been associated with respiratory complications and poor outcomes.

In a study evaluating compliance with the third edition of the BTF ICP monitoring guidelines, patients who underwent ICP monitoring had less in-hospital mortality and less herniation-related mortality but longer ICU and hospital lengths of stay compared with patients who did not undergo ICP monitoring. In 2134 patients with severe TBI, those treated with a protocol-based ICP monitoring algorithm had significantly less mortality compared with patients treated without an ICP monitor (19% vs 33%), although no mention is made regarding goal ICP/CPP or the treatment modalities used to reduce ICP. In contrast, the Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure (BEST:TRIP) multicenter randomized clinical trial from 6 hospitals and 324 ICU patients with severe TBI, ICP monitoring was not superior to care based on imaging and physical examination.

CPP and ICP are inexact surrogates for CBF given the heterogeneity of TBI and an unknown optimal CPP for a given patient, suggesting a role for more multimodal monitoring. Transcranial Doppler ultrasonography is a noninvasive technique that measures CBF velocity, and uses differences in CBF velocity to estimate differences in CBF. Jugular bulb monitoring of arteriovenous oxygen content difference (AVDo2) uses a central line placed in the jugular bulb and a peripheral arterial line. The difference in oxygen content between blood entering and leaving the brain can be calculated to provide a global picture of supply and demand. Cerebral microdialysis is a technique in which a catheter is placed in the penumbra, or area adjacent to the traumatized brain, and used to evaluate the local biochemical environment. Brain tissue oxygen tension can be measured with a parenchymal probe but is highly dependent on placement, provides a very focal measurement of oxygenation, and may not be an appropriate surrogate for global perfusion. Given lack of sufficient data, routine use of novel neuromonitoring strategies is not common at this time. In its most recent guidelines, the BTF provides level III recommendations for measurement of AVDo2, the optimization of which has been associated with favorable outcomes 6 months after injury. It is recommended to avoid AVDo2 less than 50%.

As noted in Fig. 1, patients undergo EVD placement if criteria are met and the procedure is technically feasible. If ICP remains increased, continuous CSF drainage is used. If the CPP remains low, MAP is increased using a combination of volume expansion and pressors, as discussed later.

HYPEROSMOLAR THERAPY

Intracranial hypertension can be managed with hyperosmolar therapy, although there is no strong evidence about the appropriate agent, administration (ie, continuous vs bolus), or timing. Hypertonic saline (HTS) of various concentrations and mannitol are
the primary pharmacologic agents used to reduce ICP, perhaps through reduction in blood viscosity, improved microcirculatory flow, and decreased cerebral blood volume.

A BTF class II retrospective study using data from the BTF’s Database evaluated patients treated with a single agent for ICP reduction. HTS administrations were typically 3% concentrations, and mannitol administrations were 20% concentrations. Bolus HTS therapy was more effective at reducing ICP and ICU length of stay. There was no statistically significant difference in 2-week mortality.62

The 2016 BTF guidelines indicate that there is insufficient evidence on clinical outcomes to support recommendations on the use or type of hyperosmolar therapy.30 Our protocol as noted in Fig. 1 is to use 3% saline at 30 to 50 mL/h and 250-mL to 500-mL intermittent boluses every 4 to 6 hours with laboratory draws to maintain serum sodium level at 145 to 160 mEq/L and osmolality less than 320 mOsm/L. Mannitol is used as a second-line agent and/or considered when hypervolemia is present. If CPP remains less than 60 mm Hg, MAP can be increased with a combination of fluid resuscitation and pressors, with phenylephrine often used.31

**BARBITURATE COMA**

Patients without mass lesions amenable to intervention and refractory ICP greater than 20 mm Hg can be treated with barbiturates. In one multicenter study, patients with severe TBI refractory to basic maneuvers, hyperosmolar therapy, and intraventricular catheter drainage were treated with a continuous pentobarbital drip with electroencephalogram (EEG) monitoring. Pentobarbital coma effectively improved CPP. Forty percent of patients survived to discharge and 68% of patients had good functional outcomes in 1 year or more after injury.53 Other investigators question the benefit of pentobarbital therapy, especially in light of systemic effects like hypotension.64 Ultimately, the 2016 BTF guidelines do not advocate barbiturate therapy as prophylaxis against intracranial hypertension. However, when treating refractory intracranial hypertension with barbiturates, avoiding hemodynamic instability is recommended.30

The authors suggest that patients with ICP 21 to 29 mm Hg for at least 30 minutes, 30 to 39 mm Hg for at least 15 minutes, or 40 mm Hg or more for 1 minute who have met sodium and osmolality thresholds (ie, on maximal hyperosmolar therapy) are candidates for pentobarbital coma. Pentobarbital is bolused at 10 mg/kg over 30 minutes, followed by a 5 mg/kg/h infusion for 3 hours, after which time it is titrated to 1 mg/kg/h and adjusted as needed with an EEG burst suppression goal of 2 to 5 bursts per minute while monitoring for significant side effects (ie, hypotension).65

**DECOMPRESSIVE CRANIECTOMY**

Decompressive craniectomy (DC) has been shown to reduce ICP and can be considered if ICP is refractory to other measures, although some clinicians consider it earlier in the treatment algorithm.24,26,66,67 In the DECRA (Decompressive Craniectomy in Diffuse Traumatic Brain Injury) randomized clinical trial, bifrontotemporoparietal DC in patients with diffuse TBI and refractory ICH resulted in lower ICP and shorter ICU length of stay. However, DC was associated with unfavorable long-term neurologic function, as measured by the Extended Glasgow Outcome Scale (GOSE), and similar mortality at 6 months compared with patients receiving standard treatment.68

The most recent 2016 guidelines from the BTF do not recommend bifrontal DC as a means to improve neurologic outcomes based on these results, although they do
recommend a large frontoparietal DC rather than a smaller one.\textsuperscript{30} This BTF recommendation was released before the results of the more recently published RESCUEicp study (Randomized Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of Intracranial Pressure). In the RESCUEicp randomized clinical trial, patients with refractory ICP greater than 25 mm Hg for 1 to 12 hours despite multimodal therapy were assigned to either DC or standard management. The primary outcome was the 6-month GOSE. Patients undergoing DC had higher rates of vegetative state but lower rates of mortality, severe disability, and upper severe disability. Compared with the DECRA trial, patients in this most recent study underwent DC as the last tier in the algorithm for management of refractory ICH. Patients with mass lesions were included as well as those who underwent unilateral decompression. Similar to the DECRA RCT, the RESCUEicp showed increased disability among survivors.\textsuperscript{69}

**ABDOMINAL DECOMPRESSION**

The differential for intracranial hypertension should also include intra-abdominal hypertension or abdominal compartment syndrome, in particular in patients subject to large volume resuscitations and/or patients with polytrauma.\textsuperscript{70} Monitoring serial bladder pressures with possible paralysis may assist with the diagnosis. Abdominal decompression in patients with increased ICP refractory to medical management with concomitant intra-abdominal hypertension has been shown to be efficacious in reducing ICP and should be considered in this patient group.\textsuperscript{71,72}

**HYPOTHERMIA**

Hypothermia has been investigated as a means of neuroprotection following TBI. A systemic review of randomized controlled trials of hypothermia in TBI found that hypothermia was associated with reduced mortality and improvements in neurologic function.\textsuperscript{73} Other investigators question the benefits of hypothermia in TBI, citing poor-quality trials.\textsuperscript{74} The BTF currently recommends against the routine use of early, short-term prophylactic hypothermia in patients with diffuse TBI.\textsuperscript{30}

**INTENSIVE CARE UNIT MANAGEMENT: VENOUS THROMBOEMBOLISM PROPHYLAXIS**

Patients with TBI are at risk for venous thromboembolic disease given venous stasis, venous injury, and potential coagulopathy associated with TBI. Pharmacologic agents are often withheld in the initial postinjury period because of concerns for worsening of an intracranial bleed. A study from 2011 by Scudday and colleagues\textsuperscript{75} investigated 812 patients with head injuries, about half of whom received pharmacologic prophylaxis (most with heparin). Forty percent of patients received prophylaxis within 48 hours, with an average start time of 96 hours after hospital arrival. Patients who received pharmacologic prophylaxis had a lower incidence of venous thromboembolism (VTE) compared with those who did not (1% vs 3%). There was also a trend toward lower incidence of worsening hemorrhage in the treatment group, although VTE diagnosis in that study was based on clinical symptoms and asymptomatic VTE may have been more prevalent.

A review by Phelan\textsuperscript{76} in 2012 presents a protocol whereby patients with low-risk TBI can be started on enoxaparin within 24 hours postinjury, those with moderate-risk TBI based on specified imaging characteristics can be started after 72 hours, and those with high-risk TBI should undergo inferior vena cava (IVC) filter placement. The BTF recommends pharmacologic deep vein thrombosis prophylaxis if the injury is stable and the benefits of prophylaxis outweigh the risks of hemorrhage progression. There
are no recommendations regarding timing, dose, or agent.30 Local culture along with input from neurosurgery colleagues may help to dictate the approach to anticoagulation in these patients as well.

**INTENSIVE CARE UNIT MANAGEMENT: STRESS ULCER PROPHYLAXIS**

Head injury has been associated with increased gastric acid secretion. Both proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2) have been shown to reduce the incidence of upper gastrointestinal bleeding in patients with trauma and receiving neurocritical care.77–79 In a review of the literature involving neurologic and neurosurgical ICU patients, H2 blockers were found to be associated with increased rates of pneumonia, drug interactions, and coagulopathy, calling into question the role of these agents in patients with TBI.78 In one recent study of mechanically ventilated critical care patients, including a small number of patients with ICH, PPIs were associated with increased rates of pneumonia, *Clostridium difficile* infection, and gastrointestinal hemorrhage.80 These data suggest a role for future prospective studies evaluating the ideal prophylaxis in patients with severe TBI.

**INTENSIVE CARE UNIT MANAGEMENT: SEIZURE PROPHYLAXIS**

Early studies showed the benefit of phenytoin in the prevention of early posttraumatic seizures (ie, seizures within the first week after injury). However, early prophylaxis with antiepileptics has not been showed to improve late posttraumatic seizures (ie, >7 days postinjury), mortality, or neurologic function.81 The 2016 BTF guidelines recommend phenytoin to decrease early posttraumatic seizures when the risk/benefit ratio favors treatment.30

Studies comparing levetiracetam and phenytoin have shown that levetiracetam is as effective at reducing early seizures and is an attractive alternative given that it does not require serum monitoring, is less expensive, and has fewer drug-drug interactions.82–84 Although the BTF currently outlines insufficient evidence to recommend levetiracetam rather than phenytoin, our practice is to use levetiracetam (1000mg IV bolus followed by 500 mg IV/by mouth twice a day for 7 days with renal adjustment if needed) for patients with any structural intracranial injury on cross-sectional imaging. We also consider omission of seizure prophylaxis if patients are older than 65 years with good neurologic function.

**NUTRITION**

Early enteral nutrition (EN) has been shown to have a beneficial effect in many patient populations, including those with TBI. A study by Hartle and colleagues85 found that patients who were not fed within the first week after TBI had significant increases in mortality, even when controlled for other factors known to affect outcome. Early enhanced EN, in which goal feeds are reached on day 1 of injury, has also showed benefit compared with more traditional EN in terms of infectious and overall complications and possibly even longer term outcomes out to 3 months postinjury.86 Other studies have shown that EN within 48 hours is associated with improved survival and neurologic outcome in patients with severe head injuries.87 There is some evidence that transpyloric feeding is associated with a decreased incidence of pneumonia and is more efficacious than the gastric route in patients with TBI.88 Achieving adequate caloric intake by day 7 and transgastric jejunal feeding is currently supported by the BTF guidelines.
INTENSIVE CARE UNIT MANAGEMENT: OTHER THERAPIES

Results of the CRASH trial do not support use of corticosteroids in patients with head injuries.89,90 Intensive insulin therapy (80–120 mg/dL) in patients with TBI has been associated with fewer infectious complications and shorter ICU length of stay compared with a less aggressive strategy (<220 mg/dL), but was associated with more hypoglycemia and similar outcomes and infectious complications and has not generated strong clinical enthusiasm.91 In 2 large multicenter randomized clinical trials, administration of IV progesterone also failed to show a clinical benefit in humans.92,93 Previous work has shown an association between beta-blockade and improvement in mortality after TBI in humans and improvement in CBF in mice.94,95 There are currently trials underway to assess the effect of adrenergic and sympathetic blockade on outcomes after TBI (NCT01322048 and NCT02957331).96,97

SUMMARY

TBI is a leading cause of death and disability in patients with trauma. The rapid transfer of patients with TBI to trauma centers and the avoidance of secondary insults such as hypotension and hypoxia are paramount. Increased ICP should be managed in an algorithmic fashion using simple beside maneuvers, hyperosmolar agents, ventricular drainage, barbiturates, and operative intervention when appropriate. Nutritional status should be optimized and clinicians should focus on prophylaxis against stress ulceration, early seizures, and VTEs. The role of novel techniques to measure CBF and oxygenation is still being elucidated.

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