Traumatic brain injury: A case-based review

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BACKGROUND: Traumatic brain injuries are common and costly to hospital systems. Most of the guidelines on management of traumatic brain injuries are taken from the Brain Trauma Foundation Guidelines. This is a review of the current literature discussing the evolving practice of traumatic brain injury.

DATA SOURCES: A literature search using multiple databases was performed for articles published through September 2012 with concentration on meta-analyses, systematic reviews, and randomized controlled trials.

RESULTS: The focus of care should be to minimize secondary brain injury by surgically decompressing certain hematomas, maintain systolic blood pressure above 90 mmHg, oxygen saturations above 93%, euthermia, intracranial pressures below 20 mmHg, and cerebral perfusion pressure between 60–80 mmHg.

CONCLUSION: Much is still unknown about the management of traumatic brain injury. The current practice guidelines have not yet been sufficiently validated, however equipoise is a major issue when conducting randomized control trials among patients with traumatic brain injury.

KEY WORDS: Traumatic brain injury; Emergency departments; Glasgow Coma Scale

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injury can be minimized by preventing and correcting hypoxemia, hypotension, anemia, hypoglycemia, and hyperthermia, and by evacuating certain intracranial masses. Prehospital and inpatient hypoxemia, pyrexia, and hypotension are independent predictors of mortality and disability. One prospective trial found that a single episode of hypotension with a systolic blood pressure <90 mmHg was an independent risk factor for death and disability. Many medications have been used to target secondary injury, including as bradykinin beta-antagonists, magnesium, and calcium channel blockers, however, as of yet none have shown improved outcomes.

On initial presentation to the emergency department, the focus should be on stabilizing the patient with standard trauma protocols. In adults, hemodynamic instability is rarely due to brain injury, and other life-threatening injuries should be ruled out first. Goals of management should focus on preventing secondary injury by identifying treatable mass lesions, such as intracranial hematomas, maintaining a systolic blood pressure >90 mmHg, and preventing hypoxemia with a goal PaO₂ >60 mmHg or O₂ saturation >93%.

**Airway management**

Airway assessment and management is the first priority. While the current literature cites opposing arguments for whether the TBI patient requiring airway control should be intubated in the prehospital setting or in the hospital, some pre-hospital systems have moved away from prehospital intubation. This is not because of difficulty in securing the airway prehospital, but because of poor outcomes with over-ventilation.

Indications for intubating the TBI patient are similar to usual reasons for intubation and include inability to oxygenate, ventilate, and protect the airway or worsening status with expectations of needing airway support. While coma (i.e. GCS<8) is considered a definite indication, other findings such as significantly worsening neurologic examination or mental status, fixed and dilated pupils, posturing, or hemiparesis generally require intubation. Orotracheal intubation is preferred over nasotracheal intubation due to its increased likelihood of success, the risk of transiently increasing the ICP and the remote possibility of intracranial placement with basilar skull fractures.

In the ED Rapid Sequence Intubation is the mainstay for intubating the TBI patient to optimize first-pass success and minimize the transient hemodynamic changes peri-intubation. A quick and facile intubation is integral to maintaining perfusion, oxygenation and proper ventilation. As such, pre-planning your induction and post-intubation medications could have a real impact on your patient's long-term prognosis.

We recommend etomidate for induction, as sedative agents such as propofol and barbiturates are associated with hypotension and should be used with caution. Etomidate has a rapid onset and short half-life, and is one of the more hemodynamically stable medications, causing fewer decreases in blood pressure. Etomidate also exhibits neuroprotective effects by reducing intracranial pressure (ICP). However, etomidate can cause hypotension, especially in the critically-ill and under-resuscitated patient such as most emergent trauma patients. We recommend having vasopressor agents ready if needed to treat peri-intubation hypotension. Other agents to consider are fentanyl and benzodiazepines. Sedation requirements are significantly reduced in comatose patients.

While historically ketamine was associated with increased ICP, recent studies have found no harm when used in patients with TBI. Given its hemodynamic advantages, ketamine may be preferred in the hypotensive patients, although definitive recommendations are pending further research on long-term outcomes.

To maximize first-pass success, neuromuscular paralysis is essential. The best agent is debatable, but generally is still considered succinylcholine. In animal and brain tumor studies, succinylcholine had been demonstrated to increase ICP that could be blunted by defasciculating doses of neuromuscular agents (level 2 evidence). However, in case reports of human studies, no significant rise in ICP was seen after succinylcholine administration. Nondepolarizing agents such as rocuronium and vecuronium have been shown to attenuate increases in intracranial pressure during suctioning which may be related to the transient increase in ICP during RSI but long-term outcomes have not been studied.

Once intubated, sedation is helpful in controlling agitation and undesired increases in ICP. It may also prevent unwanted self-extubation.

**Additional airway considerations**

Pretreatment with lidocaine, a defasciculating dose of a paralytic, and fentanyl can be considered for blunting the initial rise in ICP that occurs with intubation, though the benefit of these medications, either alone or in combination remains unproven. While they most likely
have little downside, intubation should not be delayed to administer them for pretreatment.\(^{[19,26]}\)

Ideal positioning is important for optimizing first-pass success. Unfortunately, most TBI patients also have concomitant spinal cord injury. The fear of worsening an unstable cervical spine fracture is always a concern. Though in-line cervical immobilization is standard to prevent worsening of existing c-spine fractures, recent studies have questioned its efficacy while showing that it increases failure rates and may even increase movement of unstable segments.\(^{[21]}\) Our current practice is to use in-line stabilization until definitive evidence shows otherwise.

The use of direct laryngoscopy versus video assisted laryngoscopy also continues to evolve; most studies\(^{[22–25]}\) show that glidescope provides improved visualization and increases first pass success. However, it does not decrease cervical spine motion.\(^{[22]}\) Our practice is to have both direct laryngoscopy and glidescope available depending on the situation and the comfort of the operator.

**Intracranial pressure and cerebral perfusion pressure**

As the hematoma expands or cerebral edema worsens, ICP increases. This decreases the cerebral perfusion pressure (CPP), the difference between the mean arterial pressure and the intracranial pressure. After injury, brain's normal autoregulatory mechanisms to maintain perfusion are lost and the brain is more susceptible to changes in blood pressure and ischemia. Even a single episode of hypotension can worsen prognosis. There are no class I recommendations for target CPP, but it likely should be maintained between 60–80 mmHg.

ICP has been shown to be an independent marker for mortality and worse neurological outcomes especially in the first 48 hours.\(^{[2,26]}\) In the ED, determination of elevated ICP is a clinical diagnosis and can be facilitated by the placement of an ICP monitoring device (Table 1).

Treatment should be initiated when the ICP is sustained over 20 mmHg for more than five minutes.\(^{[3]}\) The treatment includes first adequately sedating the patient, elevating the head of the bed, and straightening the jugular veins by positioning the head midline to promote venous drainage from the brain. If the ICP remains elevated, consideration should be given to osmotic therapy and more aggressive therapy, such as surgical decompression.

Mannitol and hypertonic saline are common osmotic agents for acute reduction of ICP. Mannitol and hypertonic saline have been shown to be equally effective in lowering ICP and additionally increasing cerebral blood flow.\(^{[27]}\) For both agents, osmolarity needs to be closely monitored for it can precipitate acute renal failure. The goal serum osmolality should be 15–20 mOsm/kg above the upper limit of normality, with a ceiling around 320–340 mOsm/kg. With the use of hypertonic saline, sodium as high as 180 mEq/L has been observed clinically without significant neurologic, cardiac or renal injury.\(^{[28]}\) Generally, for hypertonic saline, intermittent boluses are given for acute rises in ICP and continuous drips to specific sodium targets to maintain a higher sodium target in the first few days after injury, and at times longer depending on the extent of the injury. An initial target for the sodium of 145–150 mEq/L would suffice for most situations and can be changed according to the clinical situation.

Sustained prophylactic hyperventilation is contraindicated for acute ICP reduction given its minimal efficacy and significant reduction in cerebral blood flow during a time when it is already decreased from mass effect (level II).\(^{[29]}\) Hyperventilation should be avoided during the first 24 hours given the increased risk of cerebral ischemia (level III evidence).\(^{[29]}\) To accomplish this, arterial blood gas should be checked and PaCO\(_2\) should be maintained in a normal range of 35–40 mmHg. In emergent circumstances, e.g. clinical signs of herniation, short-term mild hyperventilation can be considered to prevent herniation. In these cases, a PaCO\(_2\) of 30 mmHg should be targeted as the lowest limit.

**Fluid management, blood pressure, and oxygenation management**

Generally, patients should be kept euvoletic. Hypotensive patients should receive isotonic fluids. It is necessary to avoid the use of hypotonic intravenous fluids, which can increase the risk of cerebral edema, including those that are slightly hypotonic and sometimes labeled "isotonic" such as lactated ringer's solution. Normal saline and hypertonic saline are the fluids of choice in the treatment of patients with TBI.\(^{[30]}\) Albumin is not indicated. In the SAFE trial, subgroup analysis found an increased mortality among TBI patients

<table>
<thead>
<tr>
<th>Table 1. Indications for placement of an ICP monitoring device(^{[3]})</th>
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<tbody>
<tr>
<td>1. Patients with severe TBI with a GCS of 3–8 and an abnormal head CT</td>
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<td>2. Patients with severe TBI and a normal head CT with two or more of the following:</td>
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<td>Age &gt;40</td>
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<tr>
<td>Unilateral or bilateral motor posturing</td>
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<td>Systolic blood pressure &lt;90 mmHg</td>
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receiving albumin for resuscitation. Further studies are underway to explore this subgroup finding.

It is critical to avoid hypotension, whenever preventable, among patients with TBI. Retrospective studies revealed that even one episode of hypotension (systolic BP <90 mmHg) was associated with increased morbidity and doubling of mortality. Further studies have shown that among patients with two or greater episodes of hypotension, the relative risk of death increases to 8.1. Our recommendation is to aggressively monitor and treat hypotension with isotonic fluids and vasopressors in TBI patients.

Similarly, hypoxemia should be avoided. It is associated with a 50% mortality and severe disability among all patients with O₂ saturations <60%. Furthermore, the duration of hypoxemia with O₂ saturations <90% was an independent predictor of mortality. Our recommendation is to maintain the O₂ saturation >93% or PaO₂ >60 mmHg.

Imaging

Noncontrast computed tomography (CT) is the initial diagnostic imaging study of choice. Many decision aids exist to determine the need for CT scan in the trauma patient. In a large study comparing several protocols in patients with mild TBI, all decision aids (NEXUS II, Canadian Head CT, NCWFNS, NICE, New Orleans, Scandinavian Neurotrauma Committee guideline) were found to have similar sensitivities (98%–100%), with specificities of 44%–50% for Canadian Head CT rule and NEXUS-II guidelines. Despite decision aids, compliance among EDs is highly variable, and often quite low. This can lead to unnecessary radiation exposure, increased length of ED stay, and increased healthcare costs.

Of note, however, in patients with moderate to major head injuries, most guidelines would recommend imaging, as the likelihood of a treatable lesion is significantly increased as the GCS decreases. For example, in one study, a GCS of 13 as opposed to 15 increased the likelihood of requiring surgery by threefold.

Poor prognostic indicators on CT include brainstem involvement, hemorrhagic injuries, and maximal thickness of traumatic SAH of 7±3 mm. Additionally, routine serial head CTs in the absence of a change in neurological status are not recommended. Commonly, TBI patients present with confounding variables such as drug and alcohol intoxication. Earlier studies have described GCS calculated at 6 hours to be more reliable in necessitating further intervention. However, in a large retrospective study with blood alcohol level ranging from 80–482 mg/dL, alcohol intoxication was found to reduce the patient’s GCS score by at most one point. Additionally, another study described a low incidence of head CT findings among patients presenting to the emergency department with alcohol intoxication. These studies suggest that GCS is only one data point and that imaging should be considered on a case-by-case basis.

Antiplatelet and anticoagulation concerns

The effects of aspirin and clopidogrel are associated with progression of intracranial bleeding, increased rate of mortality, and longer hospital and ICU stay among patients with TBI. Platelet transfusions are used frequently because of lack of other treatments for chronic anti-platelet users, but have not been shown to improve mortality.

Of warfarin users, therapeutic INR is associated with more extensive bleeding and up to a six-fold increase in mortality. Coagulation studies should be routinely performed in patients on chronic anticoagulation and in all patients older than 50 years. Corrective therapy should be administered accordingly and promptly. Retrospective evaluation of protocols to rapidly thaw and administer FFP as soon as possible to anticoagulated patients with head injury has shown a significant mortality. However, prophylactic fresh frozen plasma in TBI is associated with poor outcomes.

Other therapies include antifibrinolytic therapy, where the CRASH-2 trial showed that early administration decreased hematoma growth and mortality. Off-label use of recombinant factor VIIa in TBI is currently not recommended and is associated with increased risk of mesenteric and cerebral arterial thromboembolism with no appreciable reduction in mortality.

Seizure prophylaxis

Posttraumatic seizures are often complicated with TBI and can cause secondary injury by increasing metabolic demands and raising ICP, with an incidence varying from 4% to 25% within the first 7 days of injury. Prophylactic anticonvulsants decrease the incidence of early posttraumatic seizures (level II evidence), but have not been shown to decrease mortality, improve neurological dysfunction, or affect late seizures that occur after 7 days post-injury. Valproic acid and phenytoin have been shown to have similar efficacies. Emerging studies have shown that levetiracetam has similar efficacy as phenytoin, which is recommended as an agent for the first line
 prophylaxis because of its higher availability and lower cost. Antiepileptic medications include an IV loading dose administered as soon as possible after injury (level A evidence). Continued use after the acute setting may cause delayed neurologic recovery. Our practice is to give seizure prophylaxis in the first 7 days after the injury and only restart it if the patient develops new seizures after the 7 days.

**Glucocorticoids and insulin therapy**

There are theoretical benefits to administering glucocorticoids, but studies show that they might increase mortality and morbidity. Glucocorticoids should not be given to patients with TBI (level 1 evidence).

Randomized controlled trials examining high dose insulin therapy showed no improvement of neurological disability or mortality, but a large number of hypoglycemic events.

**Surgical decompression**

Indications for surgical decompression of traumatic intracranial lesions are listed in Table 2. Decompressive craniectomy can also be considered in patients with persistently elevated ICPs despite aggressive therapy. There are few studies on decompressive craniectomy in TBI. Most of the recommendations are borrowed from craniectomy among patients with malignant strokes. A few meta-analyses found lower mortalities and favorable outcomes with ICP monitoring and decompressive craniotomy. Even at advanced age >80 years, aggressive treatment was still more cost-effective though the impact was less. However, a recent randomized controlled trial found that early bifrontal decompressive craniectomy for refractory ICP elevations resulted in lower ICPs, and decreased the length of ICU stay but at the expense of more unfavorable neurologic outcomes.

**Therapeutic hypothermia**

Prophylactic hypothermia has been shown in animal studies and small retrospective human studies to improve outcomes, but has not shown benefit in large prospective human studies. The use of hypothermia remains controversial and is not currently supported by multiple meta-analysis showing potential harm. However, hypothermia has been used as salvage therapy for patients with persistently elevated ICPs resistant to all other treatments.

**Author’s recommendation**

Patients presenting to the ED with a history of head trauma should be assumed to have significant injury until otherwise determined, either by clinical examination or imaging. Initial work-up including history, physical examination, and diagnostic imaging as needed should be thorough and complete. We recommend that treatment of TBI be guided by the clinical situation utilizing the GCS to grade severity.

Management of moderate TBI patients is case-dependent but will likely be similar to that of severe TBI. Generally, the patient with a persistent GCS of 13 or less may require admission and observation. A small percentage may worsen from increasing ICP. What may present as a moderate TBI may quickly convert to a severe TBI even in the absence of risk factors.

Severe TBI patients should be stabilized and have rapid neurosurgical consultation. Diagnostic imaging with CT should be performed promptly to quantify the extent of injury and need for intervention. Aggressive therapy should be started immediately to reduce secondary injury (Table 3). Coagulation studies should be ordered in patients on chronic anticoagulation or who may be at risk for increased bleeding such as malignancy, hemophilia, von Willebrand's disease, or

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**Table 2. Indications for surgical decompression of traumatic intracranial lesions**

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<thead>
<tr>
<th>Traumatic lesions</th>
<th>Indications for surgical decompression</th>
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<tr>
<td>Epidural hematoma (EDH)</td>
<td>GCS score &lt;9, and anisocoria</td>
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<td></td>
<td>Midline shift &gt;5 mm</td>
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<td></td>
<td>Hematoma thickness &gt;15 mm</td>
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<td></td>
<td>Hematoma volume &gt;30 cm³ regardless of GCS</td>
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<tr>
<td>Subdural hematoma (SDH)</td>
<td>SDH larger than 5 mm on CT</td>
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<td></td>
<td>Hematoma thickness &gt;10 mm</td>
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<td></td>
<td>Midline shift &gt; 5 mm</td>
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<tr>
<td></td>
<td>GCS &lt;9 with decrease since presentation</td>
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<tr>
<td></td>
<td>ICP &gt;20 mmHg</td>
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<tr>
<td>Intraparenchymal lesions</td>
<td>Asymmetric or fixed and dilated pupils</td>
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<tr>
<td></td>
<td>Progressive neurologic deterioration</td>
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<td></td>
<td>Failed medical management with CT evidence of mass effect</td>
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<tr>
<td></td>
<td>GCS 6–8 with frontal or temporal contusions &gt;20 cm³ and midline shift of &gt;5 mm or cisternal compression on CT</td>
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<tr>
<td>Posterior fossa lesions</td>
<td>Mass effect on CT</td>
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<tr>
<td></td>
<td>Neurologic deterioration</td>
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<tr>
<td>Depressed skull fractures</td>
<td>Skull depression &gt;1 cm</td>
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<tr>
<td></td>
<td>Frontal sinus involvement</td>
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<tr>
<td></td>
<td>Dural penetration</td>
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<tr>
<td></td>
<td>Associated intracranial hematoma</td>
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<tr>
<td></td>
<td>Gross cosmetic deformity</td>
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<tr>
<td></td>
<td>Infection or obvious contamination</td>
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<td>Pneumocephalus</td>
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therapies, such as surgical decompression. If the ICP remains persistently elevated, we consider osmotic therapy and salvage surgical decompression of the jugular veins are straight. If the ICP remains persistently elevated, we consider osmotic therapy and salvage surgical decompression of the jugular veins. If the ICP remains persistently elevated, we consider osmotic therapy and salvage surgical decompression of the jugular veins.

Maintain ICP <20 mmHg and CPP between 60–80 mmHg
Aggressively maintain systolic blood pressure >90 mmHg
Avoid hypotonic fluids and albumin for resuscitation
Oxygen saturation above 93% or PaO₂ >60 mmHg
Euthermia
Maintain normal PaCO₂ (35–40 mmHg)
Seizure prophylaxis for first week post-injury

Emergency neurosurgical evaluation for surgical decompression of certain hematomas

Avoid hypotonic fluids and albumin for resuscitation
Oxygen saturation above 93% or PaO₂ >60 mmHg
Euthermia
Maintain normal PaCO₂ (35–40 mmHg)
Seizure prophylaxis for first week post-injury

Table 3. Authors recommendations

<table>
<thead>
<tr>
<th>Treatment Area</th>
<th>Recommendation</th>
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<tr>
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Figure 1. Epidural Hematoma (EDH): Lenticular-shaped hemorrhage that does not cross suture lines. The hemorrhage caused most commonly by injury to the middle meningeal artery. Collection of blood between the dura mater and cranium is classically associated with a lucid interval followed by unconsciousness. Subdural hematoma (SDH): Crescent-shaped hemorrhage that crosses suture lines secondary to shearing of bridging veins between the dura and arachnoid space. Classic presentation includes gradually increasing headache and confusion after head injury. Diffuse axonal injury (DAI): MRI preferred diagnostic modality given that over half of CT scans of patients with DAI are normal on presentation. When present on CT, it appears as multiple ovoid-shaped petechial hematomas at gray-white junction, typically bilateral, resulting from the breaking of axons from the neuronal body. Frequently, DAI involves the frontal and temporal lobes, corpus callosum, caudate nuclei, thalamus, tegmentum, and internal capsule. Intraparenchymal hemorrhage (IPH): Collection of blood in the cerebral parenchyma. Acute hemorrhage in traumatic brain injury appears hyperdense, whereas subacute and chronic appear isodense and hypodense respectively.

other congenital coagulation disorders. Anticoagulation should be reversed as soon as possible. All patients with severe TBI should receive seizure prophylaxis with phenytoin or levetiracetam for the first week post-injury (level II evidence). For elevated ICPs, we ensure that the patient is well sedated, the head of bed is elevated, and jugular veins are straight. If the ICP remains persistently elevated, we consider osmotic therapy and salvage therapies, such as surgical decompression.

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Contributors: Escobedo LVS proposed the study and wrote the paper. All authors contributed to the design and interpretation of the study and to further drafts.

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