EVIDENCED BASED TREATMENT FOR TBI:
2014 UPDATE

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Online TBI Guidelines

Print Version 2007
Online Version (Displayed Here) 2010
Case Study

A 42-year-old man presents to your intensive core unit (ICU) with acute brain trauma. He reportedly has fallen from a ladder at home while trying to fix the roof. There has been a loss of consciousness immediately after the fall, and he remains in obtunded mental status. In the emergency department (ED), his eyes open to painful stimulation, makes incomprehensible sounds, localizes to pain on the left side but is paretic on the right side (Glasgow Coma Scale [GCS] of 9: eye 2, verbal 2, motor 5). Pupils were reactive to light, and other brainstem reflexes were intact.

Patient was intubated with an endotracheal tube. Initial vital signs: heart rate 130 bpm, blood pressure 160/90 mm Hg, oxygen saturation 100% on assist control volume control mechanical ventilation with FIO2 of 0.4, tidal volume of 480 ml, at a rate of 12 times per minute. Body temperature is 37.5°C.

A computed tomographic image of the brain without contrast is obtained.
Case Study
Noncontrast Head CT
## Table: Criteria for immediate request for CT scan of the head in adults

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Details</th>
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<tbody>
<tr>
<td>GCS &lt; 13 on initial assessment in the emergency department</td>
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<tr>
<td>GCS &lt; 15 at 2 h after injury on assessment in the emergency department</td>
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<tr>
<td>Suspected open or depressed skull fracture</td>
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<td>Any sign of basal skull fracture (haemotympanum, ‘panda’ eyes, cerebrospinal fluid leakage from the ear or nose, Battle’s sign)</td>
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<td>Post-traumatic seizure</td>
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<td>Focal neurological deficit</td>
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<tr>
<td>More than one episode of vomiting</td>
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<tr>
<td>Amnesia for events &gt;30 min before impact</td>
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<tr>
<td>In addition, adult patients who have experienced some loss of consciousness or amnesia since the injury and:</td>
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<tr>
<td>Age &gt; 65 yr</td>
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<tr>
<td>Coagulopathy (history of bleeding, clotting disorder, current treatment with warfarin)</td>
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<tr>
<td>Dangerous mechanism of injury (a pedestrian or cyclist struck by a motor vehicle, an occupant ejected from a motor vehicle or a fall from a height of &gt;1 m or five stairs)</td>
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</table>
Noncontrast Head CT

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. [33,34]

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 indictors 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.

What are the initial steps in the management of this patient?

This is a typical case of severe TBI with **bilateral hemorrhagic contusions in the temporal lobes**. Its proximity to the bony structures makes it a frequent location in the brain to be contused in trauma.

Resuscitation of TBI patients varies widely, however, due to the heterogeneity of the disease itself.

The aim of all good early resuscitation efforts is to begin as early as possible, with many efforts beginning in the prehospital setting, with an attention to **airway, breathing, and circulation**.
What are the initial steps in the management of this patient?

Three specific end points have been found to be independent predictors of poor outcome in the prehospital/emergency department setting:\(^1\):

- **Hypothermia**
- **Hypoxia**
- **Hypotension**

What are the initial steps in the management of this patient?

**Hypothermia** is likely a marker of poor resuscitation, and most sources agree that core body temperature should be *passively* supported during the resuscitation phase rather than actively warmed with a device.
What are the initial steps in the management of this patient?

Clinical trials in the area of prophylactic hypothermia in patients with traumatic brain injury have yielded variable results. Overall, there was no clear demonstration of a reduction in all-cause mortality with multiple potential confounders being identified including baseline temperature [1a].

The 2011 National Acute Brain Injury Study: Hypothermia II (NABIS: HII) trial randomized 232 severe brain injury patients within 2.5 h after injury to hypothermia or normothermia. Ninety-seven patients were included for the primary analysis. No significant difference in outcome was found in the hypothermia group compared to the normothermia group.

In subgroup analyses, patients with surgically evacuated hematomas had an improved outcome with hypothermia compared to normothermia. This effect was not seen in the diffuse brain injury group. These authors conclude that further testing of the role of early hypothermia in patients with evacuated hematomas is warranted [1b].


What are the initial steps in the management of this patient?

Aggressive volume resuscitation for hypotension and adequate ventilation are the primary focus of initial resuscitation efforts.

Prehospital resuscitation with hypertonic saline in TBI has failed to demonstrate a long-term benefit,² and in a post-hoc analysis of the Saline versus Albumin Fluid Evaluation trial,³ fluid resuscitation with albumin was associated with higher mortality rates than was resuscitation with saline.


What are the initial steps in the management of this patient?

Therefore, the administration of isotonic crystalloids is the preferred method by which to volume resuscitate.

There is some evidence that hypertonic saline may be useful as a resuscitation fluid, with one study showing increased survival in a subgroup of patients with TBI and GCS <8.

What are the initial steps in the management of this patient?

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.\[3a\]

Further studies have shown that among patients with two or greater episodes of hypotension, the relative risk of death increases to 8.1.\[3a\]

Our recommendation is to aggressively monitor and treat hypotension with isotonic fluids and vasopressors in TBI patients.

What are the initial steps in the management of this patient?

All TBI patients should be **ventilated** to a goal of normal $\text{PaCO}_2$ and be given supplemental oxygen to achieve $\text{SpO}_2$ greater than 90%.

Similar to hypotension, **hypoxia is a strong predictor of poor outcome after TBI**. McHugh and colleagues analyzed secondary insults (hypotension, hypoxia, and hypothermia) occurring prior to or on admission and their relation to outcome. They reported an overall prevalence of 20% for hypoxia on admission and identified it as a significant predictor for adverse outcome [3b].

What are the initial steps in the management of this patient?

Hypoxemia should be avoided. It is associated with a 50% mortality and severe disability among all patients with O2 saturations <60%. [3]

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.

What are the initial steps in the management of this patient?

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.

<table>
<thead>
<tr>
<th>Table: Indications for intubation and ventilation for transfer after brain injury</th>
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<tbody>
<tr>
<td>GCS ≤ 8</td>
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<td>Significantly deteriorating conscious level (i.e. decrease in motor score ≥ 2 points)</td>
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<td>Loss of protective laryngeal reflexes</td>
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<td>Hypoxaemia ((P_{A\text{O}_2} \leq 13) kPa on oxygen) &lt; 97.5 mm Hg</td>
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<td>Hypercarbia ((P_{A\text{CO}_2} \geq 6) kPa) &gt; 45 mm Hg</td>
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<td>Spontaneous hyperventilation causing (P_{A\text{CO}_2} &lt; 4.0) kPa &lt; 30 mm Hg</td>
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<tr>
<td>Bilateral fractured mandible</td>
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<td>Copious bleeding into the mouth (e.g. from skull base fracture)</td>
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<tr>
<td>Seizures</td>
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What are the initial steps in the management of this patient?

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.

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).[3b]

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What are the initial steps in the management of this patient?

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.[3c]

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.[3d]


What are the initial steps in the management of this patient?

During the early resuscitation phase, it is important to realize that simple measures such as:

- Elevation of the head of the bed (30 degrees)
- Midline positioning of the head (relieving any blockage of jugular venous drainage), and
- Adequate pain control and sedation

are very simple and effective methods to reduce intracranial pressure (ICP).
The patient is now admitted to an ICU, and the repeat computed tomography (CT) of the brain 6 hours later confirms no expansion of the hemorrhagic contusion. His neurologic examination remains poor, being only partially responsive to painful stimulation. Remembering that the literature reports the combination of severe TBI plus status epilepticus (SE) carries a high mortality rate, you wonder whether he could have any non convulsive seizures.
How long should prophylactic antiepileptic drug (AED) be administered?

Reported risk factors for seizures include:
- GCS score less than 10
- Cortical contusions
- Depressed skull fractures
- Wounds with dural penetration
- Prolonged length (longer than 24 hours) of coma
- Posttraumatic amnesia

The majority of early posttraumatic seizures occur within the initial 48 hours of injury.¹⁴

How long should prophylactic antiepileptic drug (AED) be administered?

However, some seizures may escape clinical detection, and may be unnoticed in intubated sedated patients in the absence of electroencephalographic (EEG) monitoring.

The presence of convulsive SE is associated with high mortality rate.

Effective prophylaxis of early posttraumatic seizures reduces brain metabolic demands, thereby reducing intracranial pressure and neurotransmitter release.

This in turn minimizes secondary brain injury. Furthermore, anticonvulsant treatment can minimize cognitive and behavioral sequelae.
How long should prophylactic antiepileptic drug (AED) be administered?

Phenytoin is an established standard antiepileptic drug (AED) in the setting of acute TBI. The American Academy of Neurology suggests using phenytoin for seizure prevention only in the first 7 days after TBI⁵.

Temkin and colleagues reported 404 patients with severe head trauma randomized to phenytoin or placebo for 1 year with follow-up continued until 2 years.

Seizures occurred significantly more frequently on the first 7 days in the placebo group compared to the phenytoin group (14.2 % vs. 3.6 %, respectively), and the seizure frequency was not significantly different between day 8 and the end of the first year or at the end of year two⁵a.


How long should prophylactic antiepileptic drug (AED) be administered?

Levetiracetam (Keppra) has gained favor in acute brain injury setting due to its tolerability, ease of use without the need to follow a drug level, and minimal drug-to-drug interactions.

Newer anticonvulsants such as levetiracetam have also been studied for seizure prophylaxis after severe TBI. Jones and coworkers compared 32 severe TBI cases who received levetiracetam for the first 7 days after injury to 41 historical controls who received phenytoin. Seizure activity was not significantly different between the two groups [5c].

Similarly, no difference in seizure occurrence was reported in a prospective, randomized trial of severe TBI and SAH patients randomized to seizure prophylaxis for 7 days with phenytoin or levetiracetam [5d].

High doses of steroids are greatly beneficial in experimental models, reducing lipid peroxidation and improving tissue recovery. Clinical studies with glucocorticoids have not shown similar benefit.

The results from the large Corticosteroid Randomization After Significant Head injury (CRASH) trial demonstrated no benefit and increased mortality rate in TBI patients randomized to 3 g of methylprednisolone in the first 72 hours after injury. (The trial randomized 10,008 head injury patients within 8 h of injury to a 48-h methylprednisolone infusion or placebo).

Currently, no data exist to support the use of glucocorticoid steroids acutely, and given the increased mortality rates seen in the CRASH trial, they are contraindicated acutely after brain injury.\(^7,8\)

What type of intracranial monitoring is indicated after TBI? – ICP (Intacranial Pressure) Monitoring

The Brain Trauma Foundation guidelines state that ICP should be monitored in those with a postresuscitation GCS of 3 to 8 and an abnormal CT scan, and further for those with a similar severity and a normal CT scan if two of the following are present: age older than 40 years, posturing, or hypotension.

The first choice for monitoring should always be an external ventricular drain because it can be recalibrated after placement and also offers therapy in the form of cerebrospinal fluid (CSF) diversion.
What type of intracranial monitoring is indicated after TBI? – ICP (Intacranial Pressure) Monitoring

In a recent study:

_Intracranial Pressure Monitoring in Severe Traumatic Brain Injury: Results from the American College of Surgeons Trauma Quality Improvement Program_ - Aziz S. Alali, Robert A. Fowler, Todd G. Mainprize, Damon C. Scales, Alexander Kiss, Charles de Mestral, Joel G. Ray, and Avery B. Nathens

JOURNAL OF NEUROTRAUMA 30:1737–1746 (October 15, 2013)

Mary Ann Liebert, Inc. DOI: 10.1089/neu.2012.2802

Although existing guidelines support the utilization of intracranial pressure (ICP) monitoring in patients with traumatic brain injury (TBI), the evidence suggesting benefit is limited. To evaluate the impact on outcome, they determined the relationship between ICP monitoring and mortality in centers participating in the American College of Surgeons Trauma Quality Improvement Program (TQIP). Data on 10,628 adults with severe TBI were derived from 155 TQIP centers over 2009–2011. Results were comparable irrespective of the method of case-mix adjustment.

In this observational study, **ICP monitoring utilization was associated with lower mortality.**
What type of intracranial monitoring is indicated after TBI? – ICP (Intacranial Pressure) Monitoring

Table 1. Indications for placement of an ICP monitoring device[3]

1. Patients with severe TBI with a GCS of 3–8 and an abnormal head CT
2. Patients with severe TBI and a normal head CT with two or more of the following:
   - Age >40
   - Unilateral or bilateral motor posturing
   - Systolic blood pressure <90 mmHg

What type of intracranial monitoring is indicated after TBI? – CPP (Cerebral Perfusion Pressure)

The BTF guidelines suggest that the CPP value to target lies at the 50-70 mmHg range with a general CPP threshold in the realm of 60 mmHg [9]. They note that the parameters used to calculate CPP (blood pressure and ICP) have been shown to individually correlate to outcome after TBI since both hypotension and elevated ICP have been associated to poor outcome.

They also state that there is no defined critical lower threshold of CPP that is associated to cerebral ischemia or poor outcome, but they suggest that a CPP of 50-60 mmHg appears to be a critical lower threshold range for ischemia [9].

This threshold is based upon data that support CPP values lower than 50 mm Hg are associated with more cerebral insults, while achieving CPP more than 70 mm Hg on every TBI patient results in a fourfold increase in lung injury likely due to aggressive volume resuscitation and excessive use of pressors. [9a] The use of PbtO2 monitoring may help guide targeted CPP management so as to avoid tissue hypoxia while minimizing the risk of complications related to pressure augmentation.

What type of intracranial monitoring is indicated after TBI? – PRx (Cerebrovascular Pressure Reactivity)

PRx (CEREBROVASCULAR PRESSURE REACTIVITY) was continuously monitored as a moving, linear correlation coefficient between low frequency waves of intracranial and arterial blood pressures. Positive values of PRx approaching 1 indicate impaired cerebrovascular pressure reactivity, whereas negative PRx values or values close to 0 indicate preserved cerebrovascular pressure reactivity.

Intact cerebrovascular pressure reactivity quantified with the PRx is associated with survival after severe head trauma.
What type of intracranial monitoring is indicated after TBI? – PRx (Cerebrovascular Pressure Reactivity)
What type of intracranial monitoring is indicated after TBI? – PRx (Cerebrovascular Pressure Reactivity)

**Optimal CPP-oriented therapy**

Both PRx and Mx show the U-shape relationship with mean CPP (200 patients!). This indicates that for low CPP and CPP above 90 mm Hg both autoregulation and pressure reactivity are defective. **There is an ‘optimal’ CPP from 70 to 90 mm Hg which helps to restore vascular functions after head injury.**

What type of intracranial monitoring is indicated after TBI? – PRx (Cerebrovascular Pressure Reactivity)

Deterioration of PRx precedes refractory intracranial hypertension?
What type of intracranial monitoring is indicated after TBI? – PRx (Cerebrovascular Pressure Reactivity)

The target CPP in a given patient may ultimately vary depending on the individual's autoregulatory status. A study by Jaeger and colleagues supports the concept of determining individual optimal cerebral perfusion pressure based on measures of cerebrovascular pressure reactivity [10]. Howells and colleagues analyzed a group of patients treated with ICP-oriented vs. CPP-oriented protocols in two different centers. They concluded that the pressure reactivity index can identify the most appropriate treatment strategy in a given patient. They found that in pressure-passive patients (PRx>0), ICP-oriented therapy resulted in better outcomes, and in pressure-active and pressure-stable TBI patients (PRX<0), the CPP-oriented therapy was more beneficial [11]. In a study by Johnson and colleagues, patients with impaired cerebral pressure autoregulation with lower CPP had a more favorable outcome compared to patients with higher CPP. No difference in outcome was seen with different CPP levels in patients with intact autoregulation [12].

What type of intracranial monitoring is indicated after TBI? – PbtO2

The ability to monitor brain tissue oxygen tension (PbtO2) has added a dimension of monitoring that provides insight to cerebral metabolism. The preponderance of case series data indicate that a Pbto2 level less than 15 mm Hg is associated with poor outcome, and may respond to either augmentation of mean arterial blood pressure (MAP), alteration in ventilation strategy, or transfusion of red blood cells.

However, many questions regarding the utility of this monitoring technique have yet to be answered, such as timing, location, and pertinent treatment thresholds. Until such data become available, it is important to remember that the Pbto2 value is a composite of various components of the content of oxygen in the arteries as well as an unknown quantity of passive diffusion. This value is also a very focal/regional measure and should be put into context of the entire clinical picture prior to embarking on therapeutic interventions. 

What type of intracranial monitoring is indicated after TBI? – PbtO2

Effect of Brain Tissue Hypoxia on Outcome
Subarachnoid Hemorrhage

Kett-White R et al. Neurosurgery 2001;50; 1213-21
What type of intracranial monitoring is indicated after TBI? – PbtO2

Fig. 5. Real-time relationship of the physiological parameters brain oxygen tension (PbO₂), cerebral perfusion pressure (CPP), and intracranial pressure (ICP) over 2 hours in a patient with intracerebral hemorrhage complicated by intracranial hypertension. Note the striking parallel relationship between PbO₂ and CPP, indicative of autoregulatory failure. (From Wartenberg KE, Schmidt JM, Krieger DW. The future of the brain support: Multimodality monitoring. Future Neurology 2006;1(4):473; with permission.)
What type of intracranial monitoring is indicated after TBI? – PbtO2

<table>
<thead>
<tr>
<th>PbtO₂ &lt;15 mmHg</th>
<th>PbtO₂ &gt;20 mmHg</th>
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<tbody>
<tr>
<td>ICP &lt;20 mmHg</td>
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<tr>
<td>Administer FiO₂ 100% × 15 min to test probe</td>
<td>ICP &gt;20 mmHg</td>
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<tr>
<td>▲PaCO₂ to 40–45 mmHg range as tolerated; carefully monitor both ICP and PbtO₂</td>
<td>Drain CSF</td>
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<tr>
<td>Optimize CPP</td>
<td>Optimize CPP</td>
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<tr>
<td>Administer fluids to euvolemia; watch for signs and symptoms of fluid overload</td>
<td>Administer fluids to euvolemia</td>
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<tr>
<td>Give blood products for anemia</td>
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<tr>
<td>Cooling measures for brain; temperature &gt;37°C</td>
<td>Administer mannitol, 0.25–0.5 m/kg</td>
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<tr>
<td>Optimize sedation/analgesia; consider paralytics</td>
<td>Administer hypertonic saline for ICP</td>
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<tr>
<td></td>
<td>Optimize sedation/analgesia; consider paralytics</td>
</tr>
<tr>
<td></td>
<td>Cooling measures for brain temperature of &gt;37°C</td>
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</table>
What type of intracranial monitoring is indicated after TBI? – PbtO2

Used in ICU and OR to identify potential ischemia
Safety of use has been clearly established.

For the Licox catheter, PbtO₂ values below 15-20 mm Hg are concerning. Disparity exists between findings of different studies and catheters

What type of intracranial monitoring is indicated after TBI? – PbtO2

Several studies demonstrated that PbtO2-based therapy may be associated with reduced patient mortality and improved patient outcome after severe TBI.


In a recent systematic review, available medical literature was reviewed to examine whether PbtO2-based therapy is associated with improved patient outcome after severe TBI.

What type of intracranial monitoring is indicated after TBI? – PbtO2

Among patients who received PbtO2-based therapy, 38.8% had unfavorable and 61.2% had a favorable outcome. Among the patients who received ICP/CPP-based therapy 58.1% had unfavorable and 41.9% had a favorable outcome. Overall PbtO2-based therapy was associated with favorable outcome (OR = 2.1; 95% CI = 1.4-3.1). These results suggested that combined ICP/CPP- and PbtO2-based therapy is associated with better outcome after severe TBI than ICP/CPP-based therapy alone.

What type of intracranial monitoring is indicated after TBI? – PbtO2

Oddo et al. reported that brain hypoxia or reduced PbtO2 is an independent outcome predictor and is associated with poor short-term outcome after severe TBI independently of elevated ICP, low CPP, and injury severity.

PbtO2 may be an important therapeutic target after severe TBI.


PbtO2 has been documented to be superior to SjvO2, near infrared spectroscopy and regional transcranial oxygen saturation in detecting cerebral ischemia.


PbtO2 monitoring is a promising, safe and clinically applicable method in severe TBI patients; however, it is neither widely used nor available. The combinations of ICP/PbtO2 intraparenchymal monitoring are important and helpful modalities in the management of severe TBI.
What type of intracranial monitoring is indicated after TBI? – PbtO₂

Common Procedures if ICP > 20 mmHg X > 2 min: (in order)
1. Elevate HOB 30 degrees (as tolerated by MAP, ICP, PbtO₂)
2. Drain CSF* (if available)
3. Meds: Continuous
   a. Analgesic – Fentanyl or Morphine
   b. Sedation – Propofol x 24 to 48 hours, then Lorazepam
   c. Paralytics only if shivering or bucking ventilator
4. Control body temperature; avoid fever. Consider Normothermia Protocol
5. Follow Osmotherapy Guideline Administration Algorithm: Determine eligibility for Mannitol, 5% HTS or 3% HTS

**If PbtO₂ < 20 mmHg, 1st test response to 100% FiO₂ – O₂ challenge; If no change, confirm Licox position by CT

**PbtO₂ < 20 mmHg or SjvO₂ < 55%

- Increase FiO₂ & alter ventilator keeping PaO₂ > 150 mmHg & SaO₂ > 90; PbtO₂ goal = 20
- Hyperventilate to decrease PaCO₂ as tolerated by PbtO₂ & SjvO₂

ICP still > 20 mmHg?

- Yes
  - *Drain CSF*: Open drainage until:
    1. ICP drops below 20 mmHg, or
    2. 5 mL CSF drains, or
    3. Drainage Stops
    Repeat prn; don’t actively withdraw CSF
- No

For intractable ICP (options):
Discuss with Neurosurgical attending
1. Extend Propofol for an additional 24 hours
2. Decompressive Craniectomy
3. Pentobarbital bolus then continuous infusion
4. After 7 days, begin weaning therapy and assess neurologic exam

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Continued Monitoring / Re-evaluation as needed

Fig. 1 ICP management algorithm
What type of intracranial monitoring is indicated after TBI? – Jugular Venous O2 Monitoring

- Jugular venous oximetry is a method of analyzing the balance between oxygen supply and demand to the brain.
- The oxygen saturation of blood draining from the brain into the jugular bulb is continuously measured providing an indirect measure of oxygen extraction by the brain.
CEREBRAL OXYGENATION

Cerebral oxygenation can be done using jugular bulb oximetry. This involves retrograde placement of a catheter in the jugular vein, which allows intermittent or (preferably) continuous measurement of oxygen saturation of the blood leaving the brain (SjvO2):

\[
SjvO2 = SaO2 - \left( \frac{\text{Cerebral Oxygen Consumption}}{\text{Cerebral Oxygen Delivery}} \right)
\]

75% = 100% - 25% (i.e. Delivery is usually 4 x Consumption)

where CBF = cerebral blood flow and CMRO2 = cerebral metabolic rate for O2, SaO2 = systemic arterial oxygen saturation. If CMRO2 is constant then jugular saturation is dependent on cerebral blood flow.

- SjvO2 >90% Hyperemia, shunting of blood away from neurons or impending cell death (decreased CMRO2)
- SjvO2 60–80% Normal
- SjvO2 <50% Ischemia [Fall in CBF or rise in utilization (incr. CMRO2)]
What type of intracranial monitoring is indicated after TBI? – Jugular Venous O2 Monitoring

• SjvO2 is an indicator of **global oxygen extraction** of the brain.

• Jugular venous **desaturation** suggests an **increase in cerebral oxygen extraction** which indirectly implies that there has been a **decrease in cerebral oxygen delivery**, and hence **perfusion**.

The internal jugular vein drains the majority of blood from the brain, and in most patients the **right lateral sinus is larger**. Despite the fact that **flow is different on the two sides, oxygen saturations are normally very similar**. This also appears to be the case in diffuse brain injury, while in **focal injuries** there tends to be a **greater difference** in the saturations of the two veins.

• Jugular venous saturations can be measured using the principle of infrared refractometry via a specially designed catheter (Gopinath et al.1994).
What type of intracranial monitoring is indicated after TBI? – Jugular Venous O2 Monitoring

**SjvO2 values**

- 55–75% – normal
- >75% – luxury perfusion
- <54% hypoperfusion
- <40% suggests global ischemia and is associated with increased cerebral lactate production.
What type of intracranial monitoring is indicated after TBI? – Jugular Venous O2 Monitoring

- Lateral cervical spine radiograph demonstrating position of the jugular bulb catheter (arrow).

Figure 19.1. Jugular venous tip placement.
What type of intracranial monitoring is indicated after TBI? – Jugular Venous O2 Monitoring

\( \downarrow S_{jvO2} \) This implies inadequate cerebral oxygen delivery that may be due to *decreased oxygen delivery* (systemic hypoxia, anemia), *decreased CBF* (hypotension, raised ICP, excessive hypocapnia or vasospasm), or *increased cerebral oxygen consumption* (seizures, hyperthermia, pain)

\( \uparrow S_{jvO2} \): This is somewhat more difficult to interpret, and may represent either *hyperemia* (e.g., when the autoregulation mechanisms are lost) or *reduced oxygen consumption* (e.g., hypothermia, deep sedation, or cerebral infarction).
What type of intracranial monitoring is indicated after TBI? – Jugular Venous O2 Monitoring

SjvO₂ monitoring
What type of intracranial monitoring is indicated after TBI? – Jugular Venous O2 Monitoring

Arterio-venous oxygen difference (AVDO$_2$) = CaO$_2$ - CvO$_2$
Cerebral oxygen extraction of oxygen (CEO$_2$) = SaO$_2$ - SvO$_2$

A continuous global assessment of oxygen utilization can be derived from jugular bulb saturations and systemic pulse oximetry.

Normal jugular saturations = 55-80%

What type of intracranial monitoring is indicated after TBI? – Jugular Venous O2 Monitoring

In a prospective study of patients with severe acute brain trauma and intracranial hypertension, Cruz concluded that continuous monitoring of SjvO2 was associated with improved outcome. A sustained jugular venous desaturation of < 50% is the threshold of cerebral ischemia and for treatment.

SjvO2 monitoring can detect clinically occult episodes of cerebral ischemia, allowing the prevention of these episodes by simple adjustment of treatment. In TBI, jugular venous desaturation is mostly related to CBF reduction secondary to decreased CPP (hypotension, intracranial hypertension, and vasospasm) or hypocapnia-associated cerebral vasoconstriction.

Studies showed that a sustained reduction of the SjvO2 < 50% was associated with poor outcome, and an independent risk factor for poor prognosis. Consequently, SjvO2 monitoring is essential for adjustment of ventilation during the medical treatment of an established intracranial hypertension. However, the benefit of SjvO2 monitoring on severe TBI patients’ outcomes has not been confirmed in a RCT.

What type of intracranial monitoring is indicated after TBI? – PbtO2/Jugular Venous O2 Monitoring

The guidelines give a level III recommendation for the use of jugular venous saturation and brain tissue oxygen monitoring in addition to ICP monitoring in the management of severe TBI. They propose a jugular venous saturation (SjO2) <50 % and brain tissue oxygen tension (PbrO2) <15 mmHg as treatment thresholds [14].

In a study by Bohman and coworkers [50], patients with severe TBI with at least one episode of compromised brain oxygen (defined as PbtO2 <25 mmHg for >10 min) were identified retrospectively. They received medical therapies with goal to maintain PbtO2 >25 mmHg including manipulation of pulmonary function, CPP augmentation, sedation, and elevated ICP control. The response rate to medical treatment of compromised PbtO2 was associated to decreased mortality [15].

Ongoing studies, such as the brain oxygen and outcome in severe traumatic brain injury (BOOST II) phase II trial, are comparing an ICP/CPP-directed therapy to a PbrO2-directed therapy. Patients are randomized within 12 h after TBI to ICP/CPP care or ICP/CPP and brain oxygen care. All patients receive care according to BTF guidelines [16].

Cerebral microdialysis involves placement of a small catheter with a semipermeable membrane in the parenchyma of the brain, so that a dialysate fluid can be instilled into the catheter, allowed to equilibrate and withdrawn for analysis (Figure 20-1).

Neurochemical levels such as lactate, pyruvate, glucose, and glutamate can then be measured to determine metabolic and neurotransmitter activity in the area of interest.
Cerebral microdialysis

- Semi-permeable membrane
  - Perfuse with e.g. Ringer’s solution
  - Molecular transfer dependant on relative concentrations
- Regular sampling or continuous online analysis

Fig 2. Microdialysis catheter (CMA 70, CMA Microdialysis, Sweden). (1) Connection for pump; (2) inlet tube; (3) shaft (tunnelated); (4) microdialysis membrane; (5) outlet tube; (6) microvial holder; (7) microvial for collection of dialysis samples.
CEREBRAL MICODIALYSIS

• Microdialysis: A technique used to determine the chemical composition of extracellular fluid in a tissue/organ of interest.

• ■ Lactate: Chemical by-product of anaerobic metabolism.
• ■ Glutamate: Amino acid and excitatory neurotransmitter.
• ■ Glycerol: A marker of cell membrane breakdown.
CEREBRAL MICODIALYSIS

Glucose, lactate, and pyruvate concentrations provide information regarding the metabolic state of the brain.

Glycerol concentrations parallel cell wall disruption and neuronal damage.

Glutamate elevations correlate with excitotoxicity and occasionally ischemic damage.

### Normal values for commonly monitored brain parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial Pressure</td>
<td>2-10 mm Hg (6)</td>
</tr>
<tr>
<td>Brain Oxygen Content PbtO₂</td>
<td>&gt; 15-20 mm Hg (34)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Microdialysis Analytes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>2 mM (35)</td>
</tr>
<tr>
<td>Lactate</td>
<td>2 mM (35)</td>
</tr>
<tr>
<td>Pyruvate</td>
<td>120 mM (35)</td>
</tr>
<tr>
<td>Lactate / Pyruvate</td>
<td>15-20 (35)</td>
</tr>
<tr>
<td>Glycerol</td>
<td>20-50 mM (35)</td>
</tr>
<tr>
<td>Glutamate</td>
<td>10 mM (35)</td>
</tr>
<tr>
<td>AVDO₂</td>
<td>6.5 ml O₂ / 100 ml blood (36)</td>
</tr>
<tr>
<td>CMRO₂</td>
<td>3.2 ml O₂ / 100 g / min (36)</td>
</tr>
<tr>
<td>Xe133 Cerebral Blood Flow</td>
<td>50 ml / 100 g / min (37)</td>
</tr>
<tr>
<td>Jugular Bulb Saturation SJO₂</td>
<td>55-80% (13)</td>
</tr>
</tbody>
</table>
Figure 14-16. Lactate and lactate-to-pyruvate ratios rise and glucose drops with Pbto$_2$ levels < 10. (From Hillered L, Vespa PM, Hovda DA. Translational neurochemical research in acute human brain injury: The current status and potential future for cerebral microdialysis. J Neurotrauma, 2005;22:3-41.)
Brain Chemistry (Microdialysis)

Assessment of brain chemistry parameters by microdialysis has the potential to aid in the management of severe TBI patients in conjunction with the other physiological variables discussed previously.

In one of the largest TBI studies to date on microdialysis monitoring, Timofeev and coworkers studied 223 patients (75 % with severe TBI) and found on multivariate analysis that lactate/pyruvate ratio (>25) had a significant association with increased mortality. Also, higher cerebral glucose was associated with increased mortality, and higher pyruvate was associated with reduced mortality.


Definitive data are currently lacking regarding the potential impact that targeting the different derangements in the measured brain chemistry parameters would have on patients with TBI, but ongoing research will likely shed light on the subject.
What type of intracranial monitoring is indicated after TBI? – Transcranial Doppler US

Transcranial Doppler (TCD) is a non-invasive method to measure CBF velocity. It is increasingly utilized in neurocritical care including TBI. It is a clinically useful tool in the diagnosis of complications that may occur in patients with TBI such as vasospasm, critical elevations of ICP and decreases in CPP, carotid dissection, and cerebral circulatory arrest (brain death). TCD can predict post-traumatic vasospasm prior to its clinical manifestations.

Since ICP monitoring is an invasive procedure with potential risk of associated complications, TCD has been suggested as a non-invasive alternative technique for assessment of ICP and CPP.


The overall sensitivity of TCD for confirming brain death is 75% to 88%, and the overall specificity is 98%. Although, TCD is an established monitoring modality in neurocritical care, evidence to support its regular use for ICP/CPP management in severe TBI patients is lacking.


Severe TBI CPP Management Flow Sheet

**Fluid Therapy, Vasopressors**
- Early: Intravenous fluids (crystalloids or colloids)
- Later: Vasopressors (dopamine, norepinephrine, epinephrine)

**Sedation and Analgesia**
- Sedate to sedation score 4: The meaning of a BIS score is unclear in TBI
- Meperidine 0.1 to 0.4 mg/kg/hr infusion
- Fentanyl 0.5 to 3 mcg/kg/hr infusion
- Propofol 6 to 80 mcg/kg/min
- Consider remifentanil (REM)

**Hyperosmolar Therapies**
- Mannitol 0.25 to 0.5 g/kg bolus OR
- Mannitol 0.5 to 1.5 mg/kg every 4 to 6 hours OR
- Hypertonic saline (3%) 100 to 200 mL over 20 to 30 minutes
- Measured serum osmolality and serum Na+ levels every 4 to 6 hours

**2nd Tier Therapy**
- Check perfusion indices: Is there evidence of hypoperfusion? (PaO2 < 50 mm Hg)
- If hypoperfusion, consider deepening sedation, including low dose barbiturates

**Paco2 Management**
- Goal Paco2 is 30 to 45 mm Hg
- Avoid hypercapnia: let PaCO2 be 30 to 35 mm Hg may be considered for up to 2 hours with associated ICP
- Specify PaCO2 monitoring preferable in this situation
Severe TBI CPP Management Flow Sheet

1st Tier Therapy

**CHECK**
- Patient position (head neutral, elevated HOB 30° to 45° - Check Bed Indicator)
- Equipment functioning properly (good waveform)
- No recent interventions (respiratory, nursing)
- Exclude seizure activity
- Antiseizure prophylaxis (load with Dilantin)

**FLUID THERAPY, VASOPRESSORS**
- Basic monitors include Arterial pressure monitoring, End-Tidal CO2 monitoring, ECG, Bladder Temperature, SpO2, and CVP / PAC
- Arterial line zeroed at level of tragus
- Maintain CVP 5 to 10 mmHg, or PCWP 10 to 15 mmHg or EDVI 100 to 150mL / m²
- Use 0.9% Saline Solution or Plasmalyte solution
- Maintain Hct ~ 30% (Use packed RBC's)
- Once volume loaded, assess SsvcO2 or SvO2 before use of vasopressors
- If SsvcO2 or SvO2 ≥ 65% to 70%, use
  - Phenytoin 0.1 to 5 mcg / kg / min
  - Norepinephrine 0.01 to 1 mcg / kg / min
  - For vasopressor resistant hypotension, may use
    Vaspressin 0.01 to 0.04 Units / min
- If SsvcO2 or SvO2 < 65% to 70%, consider
  - Epinephrine 0.01 to 1 mcg / kg / min or

**SEDATION AND ANALGESIA**

Goals of management:
1. Maintain CPP > 60 to 65 (CPP = MAP – ICP)
2. Fluids therapy as noted
3. Osmolality ≤ 320 mOsm / L, Na+ 145 to 155 mEq / L
4. Hct 25% to 30%
5. Sedation / Analgesia / NMB as noted
6. Brain / core temperature 37 ± 0.5 °C
7. O2 sat > 93%, PaCO2 35 to 40 mmHg
8. Brain PO2 (PbtO2) ≥ 20 mm Hg
9. Blood sugar 80 to 110 mg / dL with insulin infusion
Severe TBI CPP Management Flow Sheet

**SEDATION AND ANALGESIA**
- Sedate to sedation score 4. The meaning of a BIS score is unclear in TBI
- Midazolam 0.1 to 0.4 mg/kg/hr iv infusion
- Fentanyl 0.5 to 3 mcg/kg/hr iv infusion
- Propofol 5 to 50 mcg/kg/min iv infusion
- Consider neuromuscular blockade

**CSF DRAINAGE OPTIONS**
- Ventriculostomy if GCS ≤ 8 unless contraindicated or unfeasible
- If contraindicated / unfeasible subdural bolt acceptable
- Consider SjvO2 monitoring
- Consider PbtO2 & Brain Temperature monitor by 3-way bolt
- Set to drain at 10 cm above external auditory canal
- To set at lower level call Neurosurgery
- Elevate ventriculostomy by 5 cm per day if ICP < 20 and drainage < 4 mL/hr

**HYPEROSMOLAR THERAPIES**
- Mannitol 0.25 to 0.5 gm/kg bolus OR
- Mannitol 0.25 to 0.5 mg/kg every 6 hours OR
- Hypertonic saline (3%) 100 to 200 mL over 30 minutes
- Measured serum osmolarity and serum Na⁺ levels every 4 to 6 hours

**Check perfusion indices**

- **PbtO2 < 20 OR SjvO2 < 50%**
  - Consider repeat CT
  - Administer FiO₂ 100% x 15 minutes
  - Check MAP & PaCO₂
  - Increase MAP until CPP > 70 mmHg
  - If perfusion indices normalize accept ICP up to 30 mmHg

- **PbtO2 > 20 OR SjvO2 > 50%**
  - Check MAP & PaCO₂
  - Is MAP appropriate?
  - Ensure adequate sedation
  - Titrate PCO₂ to 30 to 35 mmHg

**2nd TIER THERAPY**

- Persisting CPP deficit ICP > 30 mmHg
- Drain CSF if ventriculostomy present

- Persisting CPP deficit ICP > 30 mmHg
- Hyperosmolar therapies
Severe TBI CPP Management Flow Sheet

2nd TIER THERAPY

- Check perfusion indices - is there evidence of hyperemia? (PbtO₂ > 50 mm Hg)
- If hyperemic consider deepening sedation, including low dose barbiturates
- Not hyperemic - is the patient salvageable?
- Assess: Mechanism of injury, best GCS, age, pupil reactivity, CT scan
- Focal frontal contusions with initial good GCS – consider decompressive craniectomy
- Barbiturate therapy – pentobarbital infusion to EEG 90% burst suppression
- PAC in place
- Dose is 1 to 5 mg / kg IBW bolus over 15 to 30 minutes
- Infusion 1 to 5 mg / kg IBW / hr

PaCO₂ MANAGEMENT

- Goal PaCO₂ is 35 to 40 mm Hg
- Acute Hyperventilation to PaCO₂ to 30 mm Hg may be considered for up to 2 hours with uncontrollable ICP
- SjvO₂ or PbtO₂ monitoring preferable in this situation

APPENDIX

*PA catheter may be used at physician’s discretion
**ICP threshold of 30 may be tolerated if perfusion indices are within the normal range and CPP is maintained > 70 mmHg except if temporal lobe contusions are present on CT scan

What is the role for antibiotics with intracranial monitoring?

There are sufficient data to support the use of periprocedural antibiotics, but the infusion must begin prior to the skin incision. The choice of antibiotic should be either cefazolin (1 g IV) or nafcillin (1 g IV).

Vancomycin (1 g IV) can be utilized for those patients with a known penicillin allergy. The continued use of antibiotics for prophylaxis is controversial and has not been proven to reduce the rate of ventriculitis and may increase the incidence of drug-resistant bacterial infections.17

When should hypothermia be utilized after TBI?

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.
In the middle of a night, the ICU resident calls to notify you that the patient's left-side pupil has become enlarged (6 mm compared to 3 mm on the right) and is still reactive to light. Patient is right hemiplegic and the left side is not localizing to pain any longer. The overall mental status has been depressed further, and now painful stimulation does not lead to eye openings. Only minimal flexion to painful stimulation is seen in the left arm. Repeat CT reveals increased swelling and mass effect on the left temporal hemorrhagic lesion. ICP is 25 mm Hg, which is down from 40 mm Hg after 30 mL of 23.4% hypertonic saline injection given 4 hours ago. Patient is autohyperventilating himself with end-tidal CO2 of 28 mm Hg. Licox monitoring shows Pbto2 of 16 mm Hg in the left hemisphere frontal subcortical region where the probe is positioned.
Which patients should be considered for decompressive craniectomy?

Surgical decompression limits the damage caused by secondary injury (delayed brain injury) by reducing increased ICP with subsequent improvement in brain oxygenation.

As with any surgical procedure, there are inherent risks. The decision to perform decompressive techniques is primarily based on the evacuation of a mass lesion, with temporal and frontal lesions more likely to result in decompression. There are no standard clinical criteria, although many institutions reserve this procedure for younger patients in coma who have failed at least one ICP-lowering measure. The key is not to delay the procedure since the primary benefit is as a result of reducing sequelae from secondary injury. Once decompression is decided upon, resection of a larger bone fragment is performed to allow for greater dural expansion with less risk of herniation. All clinical studies of decompression have demonstrated immediate reductions in ICP; however, there is conflicting evidence regarding the effects of craniectomy on long-term outcomes. As a result, this technique is not as widely utilized as medical interventions for lowering ICP.


Which patients should be considered for decompressive craniectomy?


<table>
<thead>
<tr>
<th>Traumatic lesions</th>
<th>Indications for surgical decompression</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epidural hematoma (EDH)</strong></td>
<td>30.12±8.18, GCS score &lt;9, and anisocoria, midline shift &gt;5 mm, hematoma thickness &gt;15 mm, hematoma volume &gt;30 cm³ regardless of GCS</td>
</tr>
<tr>
<td><strong>Subdural hematoma (SDH)</strong></td>
<td>SDH larger than 5 mm on CT, hematoma thickness &gt;10 mm, midline shift &gt;5 mm, GCS &lt;9 with decrease since presentation of ≥2, ICP &gt;20 mmHg, asymmetric or fixed and dilated pupils</td>
</tr>
<tr>
<td><strong>Intraparenchymal lesions</strong></td>
<td>Progressive neurologic deterioration, failed medical management with CT evidence of mass effect</td>
</tr>
<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>
</tr>
<tr>
<td><strong>Posterior fossa lesions</strong></td>
<td>Hematoma volume &gt;50 cm³</td>
</tr>
<tr>
<td><strong>Depressed skull fractures</strong></td>
<td>Mass effect on CT, neurologic deterioration</td>
</tr>
<tr>
<td></td>
<td>Skull depression &gt;1 cm, frontal sinus involvement, dural penetration, associated intracranial hematoma, gross cosmetic deformity, infection or obvious contamination, pneumocephalus</td>
</tr>
</tbody>
</table>
Which patients should be considered for decompressive craniectomy?

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.

Barbiturates

Although the existing literature does not support a mortality benefit with the use of barbiturates in patients with traumatic brain injury, the BTF guidelines provide a level II Recommendation for the use of high-dose barbiturates for control of ICP refractory to maximum medical and surgical treatment.


It is noted though that there is no clear benefit on outcome and the potential complications and need for monitoring are stressed as well as the need for hemodynamic stability prior to therapy. Dosage is titrated to produce burst suppression on EEG.

Barbiturates

Pentobarbital is recommended for the induction of barbiturate coma as follows:
Pentobarbital: 10 mg/kg over 30 min, then
5 mg/kg/h for 3 hours, then
1 mg/kg/h

As alternative, sodium thiopental might be used as follows:
2.5-10 mg/kg IV, slow bolus, then
0.5-2 mg/kg/h
How does one clear the cervical spine in the setting of altered mental status?

The identification of any cervical spine injuries is part of the standard evaluation after the patient has been hemodynamically stabilized. The algorithm is straightforward in patients who are awake and alert.

In this population, the need for additional radiographic evaluations is based upon the bedside examination.

Those without pain (distracting, midline neck), no neurologic deficits localizing to the cervical spine, and not intoxicated are very unlikely to have significant cervical spinal injury and can be cleared without radiographs.

If any of these signs or symptoms is present, then patients should undergo full C-T1 spine radiographs (including anteroposterior, lateral, and odontoid films) in addition to CT images from the occiput to T1.
How does one clear the cervical spine in the setting of altered mental status?

In patients with an alteration in mental status with a negative CT and gross motor function of the extremities, flexion/extension radiography should not be performed. Many institutions have begun relying upon magnetic resonance (MR) images to look for ligamentous injury; however, the risk-to-benefit ratio of obtaining MR images in addition to CT is not clear, and its use must be individualized in each institution.

If a decision is made to perform MRI, it must be done within 72 hours of injury in order to have reliable results.

Most modern CT scanners in addition to plain radiographs likely identify nearly all significant cervical spine instabilities; however, there are no evidenced-based guidelines to support the practice of clearing cervical spines with only CT images in obtunded patients.

When should anti-thrombotic therapy be initiated for the prevention of deep venous thrombosis (DVT)?

- **There is a high rate of DVT after TBI**, indicating that this patient population should have prophylactic therapy. However, there is considerable concern that administering heparin and low-molecular-weight heparin will increase the risk for hematoma expansion.20


- In the absence of acquired coagulopathy, the risk for hematoma expansion decreases significantly after 48 hours. In addition, there is a very low risk for hematoma expansion with prophylactic doses of heparin or low-molecular-weight heparin resulting in hematoma expansion in this patient population. For these reasons, a reasonable, safe approach toward this patient population is to **begin prophylaxis 24 hours after radiographic demonstration of hematoma stability.**

- Others have advocated surveillance with weekly venous duplex ultrasound in addition to prophylaxis, although there is no evidence that this practice reduces the complications related to DVT after TBI.

When should anti-thrombotic therapy be initiated for the prevention of deep venous thrombosis (DVT)?

There are instances, such as the need for repeated surgeries or ongoing bleeding, where the use of DVT prophylaxis is not initiated for a prolonged period of time.

In these cases, the use of temporary inferior vena cava (IVC) filters should be considered. However, it must be recognized that an IVC filter only provides incomplete prevention for only lower-extremity DVT and can pose a risk for future complications related to filter thrombosis, migration, and/or fracturing. Therefore, removing IVC filters once a patient is able to receive pharmacologic prophylaxis is an important step in the prevention of future complications.

In cases where a DVT has been diagnosed, the general recommendation is to wait for 7 days after intracranial surgery, although there are no clinical trial data to support any specific timeline. Decisions regarding timing should balance the risk for intracranial as well as systemic bleeding with the urgency for therapy.
What is the preferred osmotic therapy, mannitol or hypertonic saline?

• Unfortunately, there is no level 1 evidence to support one therapy over another. In fact, owing to a paucity of prospective clinical trial data, there is a lack of level 1 data to support the use of any osmotic therapy after TBI.

• However, each therapy does have a slightly different physiologic impact, which may lead to a preferential use of one therapy over another.

• In general, serum osmolality and sodium should be measured every 4 h to guide osmotic therapy.

What is the preferred osmotic therapy, mannitol or hypertonic saline?

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. 


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.

Fink ME. Osmotherapy for intracranial hypertension: mannitol versus hypertonic saline. Continuum (Minneap Minn) 2012; 18: 640–654. the clinical situation

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 145–155 mEq/L would suffice for most situations and can be changed according to the clinical situation.
What is the preferred osmotic therapy, mannitol or hypertonic saline?

**Mannitol**

Mannitol is an osmotic agent that draws excess fluid from the cranial cavity, thereby decreasing ICP, and has also been associated with significant diuresis, acute renal failure, hyperkalemia, hypotension, and rebound increments in ICP. For these reasons, it has been recommended that mannitol only be used when signs of elevated ICP or deteriorating neurologic status suggest the benefits of mannitol outweigh potential complications or adverse effects.

There remains considerable uncertainty regarding how and when it should be used but the recommended dose is 0.25 to 1.0 g/kg of body weight, with a goal to avoid hypotension due to intravascular volume depletion. Some clinicians have advocated replacement of urinary losses to avoid intravascular volume depletion. (0.5 – 1.0 ml NSS replacement for every 1 ml of Urine Output, replaced ~hourly).

While improved outcomes may be obtained with higher doses, decisions regarding higher doses (higher than 1 g/kg) of mannitol administration should be made on a case-by-case basis.

Mannitol should not be administered if the serum osmolality exceeds 320 mOsm. If hypertonic saline is being administered concomitantly, the osmolar gap can be calculated to monitor renal clearance of mannitol. Mannitol doses should be held if the osmolar gap exceeds 10 mmol/L.
What is the preferred osmotic therapy, mannitol or hypertonic saline?

**Hypertonic Saline**

Hypertonic saline is an osmotic agent that has traditionally been used as an adjunct to mannitol or in individuals who have become tolerant to mannitol. However, recent studies have examined hypertonic saline as a primary measure for ICP control.

Hypertonic saline exerts its effect primarily by increasing serum sodium and osmolarity, thereby establishing an osmotic gradient. Water diffuses passively from cerebral intracellular and interstitial spaces into capillaries resulting in a reduction in ICP. Although mannitol works similarly, sodium chloride has a better reflection coefficient (1.0) than mannitol (0.9), making it a better osmotic agent.

Hypertonic saline may also normalize resting membrane potential and cell volume by restoring normal intracellular electrolyte balance in injured cells.

The dose and administration varies greatly, with boluses ranging between 30 mL of 23.4% NaCl and 150 mL of 3% NaCl, whereas others have advocated the use of a continuous infusion of either 2% or 3% NaCl to reach a goal Na of 150 mmol/L.

Regardless of the choice of administration, therapy should be targeted to a specific ICP/CPP goal.
What is the preferred osmotic therapy, mannitol or hypertonic saline?

Based on this evidence, some general clinical guidelines regarding the use of mannitol and hypertonic saline:

1. **Mannitol** may be of added benefit when there is intravascular volume overload, but careful attention should be paid to urine output so that patients do not become intravascular volume depleted. The goal is euvoletic intravascular volume status.

2. Mannitol dosing should be done as a weight-based schedule ranging between 0.25 and 1.0 g/kg.

3. While there is no ceiling as to when osmotic therapies should be discontinued, the likelihood of developing renal insufficiency does increase with supranormal serum sodium levels.

4. **Hypertonic saline** should be administered with caution in patients with renal insufficiency or congestive heart failure.

5. Hypertonic saline may have an additional benefit of raising the MAP and therefore have a dual impact on improving CPP.
What is the preferred osmotic therapy, mannitol or hypertonic saline?

Oddo and coworkers compared hypertonic saline to mannitol for refractory ICP elevation. They found that hypertonic saline reduced ICP as well as improved brain oxygen, CPP, and cardiac output when given as a second tier therapy for refractory ICP in patients with severe TBI. They analyzed 12 patients who had severe TBI, ICP, and Pbt02 monitoring and were treated with mannitol (25 %, 0.75 g/kg) for ICP >20 mmHg or hypertonic saline (7.5 %, 250 ml) if mannitol did not control ICP.


Hypertonic saline was associated with an improvement in Pbt02, whereas mannitol was not. They also observed lower ICP and higher CPP and cardiac output with hypertonic saline. The impact of HTS on Pbt02 was thought to be possibly due to its effects on CBF or due to cardiac output augmentation with subsequent increase in oxygen delivery or improvement of flow in the cerebral microcirculation.

The authors acknowledge that the question of the superiority of HTS vs. mannitol cannot be drawn from their study given limitations that include small numbers and the treatments not being compared in parallel (HTS was administered after mannitol in all patients); also, there may have been a cumulative effect and the fact that the treatments were not given in equi-osmolar doses.

What is the preferred osmotic therapy, mannitol or hypertonic saline?

Other studies have also shown the effects of HTS on CPP, brain oxygenation, and ICP. Pascual and coworkers reported a study of 12 hypotensive patients with severe TBI who had CPP and Pbt02 monitoring and received HTS infusions (250 cc of 7.5 % saline over 30 min). HTS administration resulted in ICP reductions by more than 45 % and elevation of CPP and brain oxygen.


In another study examining the role of 23.4 % hypertonic saline in patients with severe TBI, Rockswold and colleagues reported 25 patients who received 30 ml of 23.4% hypertonic saline boluses for ICP >20 mmHg after having failed mild hyperventilation, CSF drainage, and sedation. There was a decrease in ICP with increase in CPP levels and Pbt02 values, with a more significant response in patients with higher baseline ICP and lower CPP [33].

What is the preferred osmotic therapy, mannitol or hypertonic saline?

There are currently no definitive data to support the use of one osmotic agent over another (mannitol vs. HTS) for the treatment of elevated ICP.

Given the different potential benefits and complication profiles for each therapy, the patient's renal, cardiac, electrolyte, and hemodynamic status may play a role in the determination of which therapy to use in a given patient, e.g., HTS in the setting of hypotension and renal failure vs. mannitol in the setting of hypernatremia or volume overload.

Neuro-intensivists should be aware of the potential for cumulative nephrotoxicity in septic patients, those on aminoglycoside antibiotics, the elderly, and those with a history of renal disease, and avoid high osmolarity (>320 mOsm) in those cases in particular.
What is the optimal method by which to ventilate a patient with a TBI?

Regulation of blood carbon dioxide levels has a significant impact on cerebral blood flow and therefore intracranial volume and intracranial pressure.

During mild hyperventilation, increased oxygen extraction can compensate for decreased blood flow and volume, allowing normal cellular metabolism to continue; however, prolonged hyperventilation may increase metabolic acidosis.

In the short term, hyperventilation decreases cerebral blood CO2, leading to an increase in pH, which may diminish the detrimental effects of acidosis. However, this process depends on the availability of bicarbonate in the cerebrospinal fluid. Prolonged hyperventilation may deplete bicarbonate levels, which may in turn result in ischemia and poorer outcomes. There have been four studies examining hyperventilation after TBI.

The only RCT examining prolonged hyperventilation demonstrated poorer clinical outcomes, which were likely due to a depletion of cerebral bicarbonate supplies.

As a result, ventilation goals should be used to maintain arterial CO2 within the range of normal (35 to 45 mm Hg). The use of hyperventilation should be reserved for rescue therapy (sudden surges in ICP), temporary reduction of ICP during procedures, and/or as an intermediate intervention until a more durable therapy can be initiated.
What is the optimal method by which to ventilate a patient with a TBI?

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).

Hyperventilation should be avoided during the first 24 hours given the increased risk of cerebral ischemia (level III evidence).


Paralysis
In a retrospective review of 514 patients from the traumatic coma data bank, Hsiang and colleagues compared patients that had pharmacological paralysis early in the ICU course and lasting for at least 12 h to patients that did not receive paralytics. They suggested that early routine use of paralytics for ICP management does not improve overall outcome and can lead to greater ICU stay and higher rate of complications such as pneumonia.


The use of paralytics in the management of elevated intracranial pressure should be reserved to refractory cases despite the use of first-line therapies.
What are transfusion thresholds for brain injuries?

Among patients with severe TBI, the proportion of those who experience anemia and who receive a blood transfusion during the acute postinjury phase have not been carefully described, but recent series have described 40% to 50% of patients with moderate to severe TBI having at least one hematocrit less than 30%.


Clinical guidelines have recommended that anemia not be the sole consideration in decisions regarding transfusion. Instead, the decision to transfuse should be based upon reducing tissue ischemia. The TBI patient population is generally young and includes otherwise healthy people, and the Transfusion Requirements in Critical Care (TRICC) trial suggests that this particular subgroup of critically ill patients is at risk for harm from liberal transfusion. However, there is genuine disagreement and clinical equipoise as to whether brain-injured patients would benefit from more liberal (to maintain hemoglobin level greater than 10 g/dL) or more restrictive transfusion (to maintain hemoglobin level greater than 7 g/dL).

• On ICU day 13, the same patient who recently received a tracheostomy and a percutaneous endoscopic gastrostomy is now having paroxysmal sympathetic hyperactivity episodes; sudden onset of periodic autonomic instability with sympathetic surge and dystonia. The patient is reported to have dilated pupils, hypertension, tachycardia, tachypnea, high fever, and increased body tones with periodic self-extensor posturing during these episodes. These are occurring in the absence of agitation or painful stimulation.
How do you address sympathetic storming after TBI?

Periodic sympathetic hyperactivity occurs up to 33% after severe TBI, although it has been reported with less frequency in other injury types as well. Rabinstein AA. Paroxysmal sympathetic hyperactivity in the neurological intensive care unit. Neural Res. 2007;29:680-682.

These episodes are typically characterized as sudden onset of exaggerated sympathetic responses including hypertension, tachycardia, tachypnea, high fever, sweating, and papillary dilation, along with occasional dystonic posturing.

Clinicians should be aware of this syndrome and understand that the first step of managing these episodes is to investigate and rule out other underlying medical conditions. DVT, pulmonary embolism, myocardial infarction, pneumothorax, and sepsis with a hyperdynamic phase can all lead to a syndrome at least partially similar to sympathetic storming.
How do you address sympathetic storming after TBI?

People with TBI are prone to infection such as aspiration pneumonia as well as volume overload, which often leads to total-body water overload. Pleural effusion and pulmonary congestion are not uncommon, and these conditions can mimic the syndrome as well.

Bromocriptine, β blockers such as propranolol, morphine sulfate, dantrolene, and clonidine may be helpful. For severe refractory cases, continuous IV sedation and anesthetic medications are occasionally needed too.

Central nervous system (CNS) storming can be challenging to manage and long-lasting. It is not uncommon to observe prolonged phases of sporadically occurring storming events even weeks after the initial injury.
Continuing management

Early nutritional support is associated with better outcomes and **enteral** administration is preferable. Severe TBI patients are usually in hypermetabolic, hypercatabolic and hyperglycemic state, with altered G.I. functions. There is evidence suggesting that malnutrition increases mortality rate in TBI patients.


Studies documented the superiority of enteral feeding over parenteral nutrition (PN). Use of PN should be limited to contraindications of enteral feeding, as it is associated with complications and an increased mortality.

Continuing management

Although, the BTF recommended 140% of resting metabolic expenditure in non-paralyzed patients and 100% in paralyzed patients to be replaced, there is growing body of evidence suggesting the benefit of a lower caloric intake.


Continuing management

Early nutritional support is associated with better outcomes and **enteral** administration is preferable. Appropriate metabolic monitoring is essential, as hyperglycemia is associated with secondary ischemic injury. Studies showed that hyperglycemia has repeatedly been associated with poor neurological outcome after TBI. Blood glucose should be monitored, but optimal targets for glycemic control are yet to be defined. However, as with perioperative management, intermediate glucose levels in the range of 108-180 mg/dl (6–10.0 mmol⁻¹) are usually targeted. Hypoglycemia must be avoided.
GLUCOSE AND OUTCOMES IN TBI


CRITICAL CONSIDERATIONS

The purpose of continuing care is to provide optimum opportunity for brain recovery.

Maintenance of oxygenation, normocapnia, and hemodynamic stability is essential.

Adequate sedation and analgesia reduces pain, anxiety, and agitation and facilitates mechanical ventilation.

Multimodality monitoring of the injured brain is useful to tailor individual patient care. Advanced monitoring may include cerebral oxygenation, measurement of CBF, microdialysis, and electrophysiological monitoring.

Three specific endpoints have been found to be independent predictors of poor outcome in the prehospital/emergency department setting: hypothermia, hypoxia, and hypotension.

- During the early resuscitation phase, it is important to realize that simple measures such as elevation of the head of the bed (30 degrees), midline positioning of the head (relieving any blockage of jugular venous drainage), and adequate pain control and sedation are very simple and effective methods to reduce intracranial pressure.

- The American Academy of Neurology's practice guideline suggests using phenytoin for seizure prevention only in the first 7 days after TBI. Newer anti-epileptic drugs with an improved safety profile may be a reasonable alternative. If prophylactic antiepileptics are used, they need to be discontinued after 7 days of use (if there has been no convulsive or nonconvulsive seizures).

- The significant head injury (CRASH) trial demonstrated no benefit and increased mortality rate in TBI patients randomized to 3 g of methylprednisolone in the first 72 hours after injury.

- The Brain Trauma Foundation guidelines state that intracranial pressure should be monitored in those with a postresuscitation GCS of 3 to 8 and an abnormal computed tomography scan, and further for those with a similar severity and a normal CT scan if two of the following are present: age older than 40 years, posturing, or hypotension. CPP thresholds should be maintained within a range of greater than 50 mm Hg and less than 70 mm Hg.

- CNS storming episodes are typically characterized as sudden onset of exaggerated sympathetic responses including hypertension, tachycardia, tachypnea, high fever, sweating, and papillary dilation, along with occasional dystonic posturing. Bromocriptine, β-blockers such as propranolol, morphine sulfate, dantrolene, and clonidine may be helpful.
## Key Physiological Parameters in TBI

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Management</th>
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<tbody>
<tr>
<td>Blood pressure</td>
<td>Avoid systolic blood pressure &lt;90 mmHg</td>
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<tr>
<td></td>
<td>Admission hypotension is associated with poor outcome</td>
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<tr>
<td>Oxygenation</td>
<td>Avoid PaO₂ &lt;60 mmHg and SaO₂ &lt;90 %</td>
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<tr>
<td></td>
<td>Hypoxia on admission is associated with poor outcome</td>
</tr>
<tr>
<td>Temperature</td>
<td>Avoid fever (temp &gt;38.3)</td>
</tr>
<tr>
<td>Intracranial pressure</td>
<td>Treatment of ICP above 20 mmHg is recommended</td>
</tr>
<tr>
<td>Cerebral perfusion pressure (CPP)</td>
<td>A CPP value of approximately 60 mmHg is recommended</td>
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<tr>
<td></td>
<td>Attempts to keep CPP above 70 mmHg with fluids and pressors are discouraged</td>
</tr>
<tr>
<td></td>
<td>due to the risk of ARDS</td>
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<tr>
<td></td>
<td>CPP &lt;50 mmHg should be avoided</td>
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<tr>
<td>Brain oxygen</td>
<td>PbtO₂ &lt;15 mmHg and SjO₂ &lt;50 % are recommended as treatment thresholds</td>
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</tbody>
</table>
• QUESTIONS?

• THANK YOU FOR ATTENDING!