Critical Care Management of Traumatic Brain Injury

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Abstract

Traumatic brain injury (TBI) is a significant public health problem. It is the leading cause of death and disability despite advancements in its prevention and treatment. Treatment of a patient with head injury begins on the site of trauma and continues even during her/his transportation to the trauma care center. Knowledge of secondary brain injuries and timely management of those in the prehospital period can significantly improve the outcome and decrease mortality after TBI. Intensive care management of TBI is guided by Brain Trauma Foundation guidelines (4th edition). Seventy percent of blunt trauma patients will also suffer from some degree of head injury. The management of these extracranial injuries may influence the neurological outcomes. Damage control tactics may improve early mortality (control hemorrhage) and delayed mortality (minimize systemic inflammation and organ failure). Neuromonitoring plays an important role in the management of TBI because it is able to assess multiple aspects of cerebral physiology and guide therapeutic interventions intended to prevent or minimize secondary injury. Bedsides, multimodality monitoring predominantly comprises monitoring modalities for cerebral blood flow, cerebral oxygenation, and cerebral electrical activity. Establishing a reliable prognosis early after injury is notoriously difficult. However, TBI is a much more manageable injury today than it has been in the past, but it remains a major health problem.

Keywords
- traumatic brain injury
- critical care
- polytrauma
- multimodality monitoring
- prognostication

Introduction

Centers for Disease Control and Prevention defines a traumatic brain injury (TBI) as a disruption in the normal function of the brain that can be caused by a bump, blow, or jolt to the head, or by a penetrating head injury.[1] Everyone is at the risk of a TBI, especially children and older adults. Common types of TBIs are coup–contrecoup injury, concussion, brain contusion, diffuse axonal injury, penetrating injury, and shaken baby syndrome.[2] TBI, a significant public health problem, is a leading cause of disability and mortality in all regions of the globe despite advancements in its prevention and treatment. Its global incidence is rising, and it is predicted to surpass many diseases as a major cause of death and disability by the year 2020.[3] TBI is the main cause of one-third to one-half of all trauma deaths and the leading cause of disability in people under 40 years of age.[1] The World Health Organization estimates that almost 90% of deaths due to injuries occur in low- and middle-income countries and 85% of people survive with significant morbidity, contributing to global health burden.[1] TBI is a leading cause of mortality, morbidity, disability, and socioeconomic losses in India as well. It is estimated that nearly 1.5 to 2 million persons are injured, and 1 million die every year in India.[1] India and other developing countries are facing the major challenges of prevention, prehospital care, and rehabilitation of patients with TBI.[4] Currently, the severity of TBI is categorized based on the Glasgow Coma Scale (GCS) as mild (score: 13–15), moderate (score: 9–12), or severe (score: <9).[5] Primary injury refers to the initial impact that causes the brain to be displaced within the skull resulting in either (1) focal brain damage causing intracerebral hemorrhage, contusion, or laceration or (2) diffuse brain damage due to acceleration/deceleration forces. Secondary injuries gradually occur as a consequence of ongoing cellular events that cause subsequent damage. Ninety-five

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percent of mortality after TBI in India is attributed to lack of optimal management instituted early within the "golden hour" period. This review article attempts to elaborate the management strategies involved for patients with TBI. Comprehensive care of a patient with TBI begins in the field (prehospital) where brain trauma is sustained and continues up until the hospital management, prognostication, outcome assessment, and rehabilitation.

1. **Prehospital care of head injury:** Secondary brain injury, the sequel of trauma to the brain tissue, is potentially treatable and most of the therapies are targeted to prevent it.[6] Secondary injury is amplified by various cofactors such as hypoxemia, hypotension, hypercarbia, hypoglycemia, hyperglycemia, hypothermia, hyperthermia, and seizures. "Time is brain." Time is a crucial factor for the occurrence as well as the prevention of secondary brain injury. Assessment of the level of consciousness, inspection of pupillary size, reactivity to light and symmetry, and recording blood pressure, oxygenation, and respiratory rate should be routinely used in the prehospital triage of patients with TBI.[6–8] Initial management in the prehospital setting should aim toward correction of hypoxemia, hypocarbia/hypercarbia, and hypotension.
2. **Critical care management of patients with TBI:** Prehospital resuscitation is continued in the emergency department of the trauma center. A noncontrast head computed tomography (CT) is recommended at the earliest to rule out skull fractures, intracranial hematomas, and cerebral edema. Extradural hematoma larger than 30 cm^3 or an acute subdural hematoma >10 mm in thickness along with a midline shift > 5 mm on CT should be surgically evacuated, regardless of the patient's GCS score. For traumatic intracerebral hemorrhage (ICH) involving the cerebral hemisphere, surgical indications are not clearly described. Evacuation is recommended if the ICH exceeds 50 cm^3 in volume, or if the GCS score is 6 to 8 in a patient with a frontal or temporal hemorrhage greater than 20 cm^3 with a midline shift of at least 5 mm and/or cisternal compression on CT scan. Elevation and debridement are suggested for open skull fractures that are depressed greater than the thickness of the cranium or if there is dural perforation, significant intracranial hematoma, frontal sinus involvement, cosmetic deformity, wound infection or contamination, or pneumocephalus.

Management as per Brain Trauma Foundation guidelines: Fourth edition of brain trauma foundation (BTF) guidelines addresses evidence-based treatment interventions, monitoring, and treatment thresholds that are concerning TBI (►**Table 1**).[9]

a. **Head injury and sedation:** General indications of sedation in patients with TBI are control of anxiety, pain, discomfort, agitation, and facilitation of mechanical ventilation.[10] Neuro-specific indications of sedation in neuro-intensive care unit (ICU) are to decrease the cerebral metabolic rate for oxygen and restrict the cerebral blood flow–metabolism mismatch, control of intracranial pressure (ICP), seizure suppression, and control of cortical spreading depolarization.[11] Clinical conditions in neuro-ICU that mandate sedation and/or analgesia are targeted temperature management, suppression of paroxysmal sympathetic activity, and control of ICP and status epilepticus. Commonly used sedatives, their indications, advantages, and disadvantages are listed in ►**Table 2**.

Fentanyl, remifentanil, and morphine are commonly used analgesics in neuro-ICU. Bolus doses of opioids may decrease the mean arterial pressure (MAP) and thereby decrease the cerebral perfusion pressure (CPP). However, careful titration of the drug dose and use of infusion will maintain the desired CPP. Use of midazolam infusion at a dose of 0.01 to 0.06 mg/kg/hour as a sedative along with an infusion of an analgesic agent such as remifentanil (0.05 μg/kg/min) or fentanyl (2.0 μg/kg/hour) will facilitate to achieve optimal CPP/ICP targets without compromising MAP.[10] Periodic sedation holiday is given for neurological monitoring. Propofol sedation may be preferred in the setting of ICP elevation, which is refractory to light sedation. Propofol decreases the cerebral metabolic demand and has a short duration of action, allowing periodic clinical neurological assessment.[11] Neuromuscular blockers may prevent ICP elevations secondary to patient–ventilator dys-synchrony. However, routine use of neuromuscular agents should be avoided since use of these agents may result in prolonged neuromuscular weakness and increase in the duration of mechanical ventilation.[11]

b. **Use of antibiotics in patients with TBI:** Incidence of CSF leak is 1 to 3% of all TBIs, 9 to 11% with penetrating head injuries, 10 to 30% with skull base fractures, and 36% with Le Forte fractures.[12] Treatment involves reduction and fixation of fractures as appropriate. Spontaneous resolution of CSF rhinorrhea occurs in 98% of the patients over 10 days and otorrhea stops completely in nearly all cases.[12] Rhinorrhea increases the risk of meningitis by 23-fold and otorrhea increases the risk by 9-fold. Incidence of meningitis is 10% in patients with penetrating fractures, 0.8 to 1.5% after craniotomy, and 4 to 17% after external ventricular drains.[13] Antibiotic prophylaxis covering most common pathogens of meningitis such as *Streptococcus pneumoniae* and *Haemophilus influenzae* should be started in high-risk patients.[14] Duration of antibiotics should be 1 week after CSF leak resolution. If suspected for meningitis, CSF cultures should be obtained and empiric treatment with vancomycin and second-generation cephalosporins should be initiated till culture reports are obtained. Broad-spectrum antibiotics are indicated in patients with penetrating head injury or body injury. In patients with TBI, it is important to prevent antibiotic resistance with appropriate choice of antibiotics after evaluating culture and sensitivity reports.[15]
c. **Use of antiseizure drugs in patients with traumatic brain injury:** Incidence of early post-traumatic seizures in patients with TBI is 30%.[16] Incidence of nonconvulsive seizures as diagnosed by electroencephalogram monitoring is 15 to 20%.[17] Antiseizure medications are used to decrease the incidence of early seizures in patients with TBI. However, prophylactic antiseizure medication

Table 1 Fourth edition of Brain Trauma Foundation guidelines[9]

Parameter	Level of recommendation	Recommendations
Decompressive craniectomy	IIA	A large frontotemporoparietal DC not < 12 x 15 cm or 15 cm in diameter is recommended to reduce mortality and improve outcomes in patients with severe TBI In patients with sustained increase in ICP > 20 mm Hg despite first-tier therapy and those with diffuse brain injury, bifrontal DC is not recommended as it is not associated with better outcome
Prophylactic hypothermia	IIB	Early (2.5 h) and short duration (48 h) prophylactic hypothermia is not recommended to improve outcomes in patients with diffuse injury
Hyperosmolar therapy	IIB	It is recommended to use hyperosmolar therapy to reduce intracranial pressure in patients with severe traumatic brain injury. However, there are no recommendations on the use of any specific hyperosmolar agent
Cerebrospinal fluid drainage	III	Use of CSF drainage to lower ICP in patients with an initial GCS < 6 during the first 12 h after injury may be considered. The EVD system to be zeroed at the level of midbrain with continuous drainage of CSF for effective management of ICP
Ventilation therapies	IIB	Avoid prolonged prophylactic hyperventilation with $PaCO_2$ of 25 mm Hg or less. Avoid hyperventilation during the first 24 h when cerebral blood flow is alarmingly reduced
Anesthetics, analgesics, and sedatives	IIB	EEG burst suppression using barbiturates as prophylaxis against development of raised ICP is not recommended High-dose barbiturates are recommended in a setting of sustained intracranial hypertension refractory to standard medical and surgical therapy in the background of stable hemodynamics during and before therapy No recommendations on the use of propofol have been made and should be used with caution
Steroids	I	Steroids are associated with increased mortality and thus their use for the management of ICP is not recommended
Nutrition	IIA	Initiation of enteral feeding by 5th day and at the most by 7th day post injury is recommended
	IIB	Transgastric jejunal feeding is recommended to reduce the incidence of ventilator-associated pneumonia
Infection prophylaxis	IIA	Use of early tracheostomy is found to be associated with reduced mechanical ventilation days. However, there is no evidence regarding reduction in mortality or the incidence of nosocomial pneumonia The use of PI oral care is not recommended to reduce ventilator-associated pneumonia
	III	Antimicrobial-impregnated EVD catheters may be considered to prevent catheter-related infections
DVT prophylaxis	III	Use of pharmacological prophylaxis with LMWH or low-dose unfractioned heparin in combination with mechanical prophylaxis is to be considered when the benefit is found to outweigh risk of cerebral bleeding No evidence regarding the preferred agent, dose, or timing of pharmacological prophylaxis for deep vein thrombosis
Seizure prophylaxis	IIA	Phenytoin is recommended to decrease the incidence of early PTS (within 7 days of injury) Use of phenytoin or valproate for prophylaxis against late PTS is not recommended
Intracranial pressure monitoring	IIB	Management of intracranial hypertension using information from an ICP monitor is recommended to reduce in-hospital and 2-week post-injury mortality in patients with severe TBI
Cerebral perfusion pressure monitoring	IIB	Management of severe TBI patients using guidelines-based recommendations for CPP monitoring is recommended to decrease 2-week mortality
Advanced cerebral monitoring	III	Jugular bulb monitoring of arteriovenous oxygen content difference ($AVDO_2$) may be considered to reduce mortality and improve outcomes at 3 and 6 months of post-injury

(continued)

Table 1 *(continued)*

Parameter	Level of recommendation	Recommendations
Blood pressure thresholds	III	Maintaining SBP at ≥100 mm Hg for patients 50 to 69 years old or at ≥110 mm Hg or above for patients 15 to 49 or over 70 years may be considered to decrease mortality and improve outcomes
Intracranial pressure thresholds	IIB	Treating ICP above 22 mm Hg is recommended as it is associated with increased mortality
	III	Treatment to be guided by ICP values, clinical condition, and brain CT findings
Cerebral perfusion pressure thresholds	IIB	Treatment directed at achieving a target CPP between 60 and 70 mm Hg as it is associated with favorable outcome
	III	Avoiding aggressive attempts to maintain CPP above 70 mm Hg with fluids and pressors may be considered because of the risk of adult respiratory failure
Advanced cerebral monitoring thresholds	III	Prevention and treatment of jugular venous saturation < 50% to reduce mortality and improve outcomes

Abbreviations: CSF, cerebrospinal fluid; CPP, cerebral perfusion pressure; DC, decompressive craniectomy; DVT, deep vein thrombosis; EEG, electroencephalogram; EVD, external ventricular drain; GCS, Glasgow Coma Scale; ICP, intracranial pressure; ICU, intensive care unit; LMWH, low molecular weight heparin; PI, povidone-iodine; PTS, post traumatic seizures; SBP, systolic blood pressure; TBI, traumatic brain injury.

Table 2 Commonly used sedatives and analgesics in neurointensive care unit for patients with TBI[10]

Sedatives	Indications	Physiological effects			Advantages	Disadvantages
		CBF	$CMRO_2$	ICP		
Propofol	Standard sedation Raised ICP Status epilepticus	⇓	⇓	⇓	Rapid onset and short duration of action	No analgesic effect Propofol infusion syndrome Hemodynamic instability
Midazolam	Standard sedation Status epilepticus	⇓	⇓	⇓	Amnesia Hemodynamic stability	Tolerance and tachyphylaxis Prolonged duration of mechanical ventilation ICU delirium
Dexmedetomidine	Agitation delirium	⇔	⇔	⇓	Sedative, anxiolytic and analgesic with minimal respiratory depression	Limited clinical experience in patients with TBI
Barbiturates	Refractory increase in ICP Status epilepticus	⇓⇓	⇓⇓	⇓⇓	Drug of choice when other drugs fail	Hypothermia/ immune-suppression/infections

Abbreviations: $CMRO_2$, cerebral metabolic rate of oxygen; ICP, intracranial pressure; ICU, intensive care unit; TBI, traumatic brain injury.

does not prevent later development of epilepsy.[18] While guidelines recommend phenytoin to prevent early post-traumatic seizures, phenytoin use in other neurological conditions such as subarachnoid hemorrhage is associated with long-term cognitive dysfunction.[9,19] A randomized clinical trial (RCT) comparing levetiracetam with phenytoin for seizure prophylaxis in patients with TBI revealed similar efficacy for seizure prevention but improved functional outcome with levetiracetam.[20]

d. **Deep vein thrombosis prophylaxis:** Risk of thromboembolism in patients with isolated TBI is 11 to 25%. However, the risk increases when TBI is associated with polytrauma.[21] Venous thromboembolism can be prevented with antithrombotic therapy but risks of intracranial hemorrhage expansion are greatest in the first 24 to 48 hours in patients with TBI.[22,23] A pilot study randomized 62 patients to either enoxaparin or placebo group. Radiological and subclinical progression of intracranial hemorrhage was common in the enoxaparin group; however, none of the patients developed clinically significant hemorrhage. And one patient in the placebo group developed deep vein thrombosis (DVT).[24] A recent meta-analysis of clinical trials and observational trials recommended that use of pharmacological prophylaxis was safe when initiated within 24 to 48 hours of TBI with periodic intracranial imaging to rule out hemorrhage.[25] As per BTF guidelines, use of pharmacological prophylaxis with low molecular weight heparin or low-dose unfractionated heparin in combination with mechanical prophylaxis is to be considered when the benefit is found to outweigh the risk of cerebral bleed.[9] Periodic ultrasonographic examination to rule out DVT is recommended in high-risk patients.

e. **Management of coagulopathy:** Approximately one-third of the patients with severe TBI manifest coagulopathy.[26] Coagulopathy is associated with intracranial hematoma expansion, poor neurological outcome, and death. There is lack of recommendations on coagulation reversal in patients with TBI.[27] Patients taking warfarin may be infused fresh frozen plasma, prothrombin complex concentrate, and vitamin K.[27] A target of international normalized ratio (INR) < 1.4 may be achieved. In patients with thrombocytopenia, platelet transfusion is recommended to maintain a platelet concentration of >75,000/mm^3. In a cohort study, a platelet count of < 13,5000/mm^3 was associated with a 12.4 times higher risk of hemorrhage expansion, and a platelet count of < 95,000/ mm^3 was associated with 31.5 times higher risk of neurosurgical intervention.[28] In patients with TBI, recombinant factor VIIa did not show any mortality benefit.[29]

f. **Ventilation:** Hyperventilation should be avoided in patients with TBI at least in the first 24 hours.[9] Decreases in the partial pressure of carbon dioxide ($PaCO_2$) cause vasoconstriction, thus reducing CBF to an injured brain. Thus, hyperventilation can trigger secondary ischemia. Mild-to-moderate hyperventilation may be instituted after 48 hours as a temporary measure. However, $PaCO_2$ < 30 mm Hg should be avoided.[30,31] In one randomized study, patients with TBI who were hyperventilated for 5 days had a worse outcome as compared to non-hyperventilated patients. Application of positive end expiratory pressure (PEEP) to patients with TBI has raised theoretic concerns of increases in ICP. But studies have showed no effects of PEEP up to 15 to 20 cm H_2O on ICP.[32,33] However, in one retrospective study, patients of TBI having severe lung injury showed a statistically significant effect on ICP (0.31 mm Hg rise in ICP for every 1 cm H_2O rise in PEEP).[34] Use of PEEP in TBI patients with acute respiratory distress syndrome has been shown to improve cerebral oxygenation.[35] Hypoxia should be avoided and PaO_2 of > 60 mm Hg should be maintained.[30]

g. **Temperature management:** Well-designed RCTs (BHYPO and EuroTherm 3235)[36] with therapeutic hypothermia below 35C for severe TBI have mostly failed to show a significant improvement in mortality rates. However, there are no RCTs till date evaluating the effects of modest cooling in patients with TBI. Fever worsens the outcome after TBI by precipitating secondary brain injury.[37] Induced normothermia using endovascular cooling and a continuous feedback loop system has been shown to lower fever burden and improve ICP control.[38] Studies have not shown convincing improvements with long-term clinical outcome. Noninduced hypothermia has been associated with an increase in mortality after TBI.[39] A systematic Cochrane review including 3,110 TBI patients subjected to mild-to-moderate cooling (32–35C) demonstrated that there was no meaningful long-term outcome after hypothermia.[40] Other systematic reviews and meta-analyses showed borderline benefits for death and neurological outcome but with increased risks of pneumonia.[41,42] Considerable disparity among studies in the degree and duration of hypothermia, as well as the rate of rewarming, limits the aptness of these studies in clinical practice. Majority of literature disfavors therapeutic hypothermia for severe TBI. However, based on the results of recent trials hypothermia may be beneficial in patients with focal neurological deficits.

h. **Osmotic therapy:** Many observational studies, RCTs, meta-analysis, and systematic reviews have found that either agents—mannitol or 3% NaCl—decrease the ICP.[43–46] Hypertonic saline (HS) appears to lead to fewer ICP treatment failures. However, there is no evidence to suggest superiority of either agent to improve outcomes such as mortality or functional recovery.[9] HS has many theoretical advantages over mannitol. HS is a suitable osmotic agent in TBI patients with ongoing blood loss. It does not produce hypovolemia and volume depletion. HS has a reflection coefficient of 1 as against 0.9 for mannitol.[47] HS does not leak into the brain tissues and cause cerebral edema. Potential adverse effects are circulatory overload, pulmonary edema, and hyperchloremic acidosis. Hyperosmolar agents should be tapered slowly after initiation to prevent rebound cerebral edema as a consequence of reversal of osmotic gradient. Majority of studies do suggest improved control of ICP and improvements with cerebral perfusion and oxygenation with HS.

i. **Intravenous fluids:** Isotonic fluids such as normal saline should be used in TBI. In post hoc analysis of SAFE trial of TBI patients, resuscitation with albumin in ICU was associated with increased mortality as compared to normal saline.[48] Balanced crystalloid solutions decrease the risk of acute kidney injury as compared to normal saline in general ICU patients. Balanced solutions are not routinely used in TBI patients as they are relatively hypotonic and may worsen cerebral edema. The SMART ICU trial compared saline with balanced solutions in critically ill patients. Among the TBI patients enrolled in the trial, no benefit was seen with the use of balanced fluids.[49]

j. **Glucose management:** Both hypo- and hyperglycemia are associated with poor outcome in severe TBI.[9] This is presumed to be due to precipitation of secondary brain injury. A target range of 140 to 180 mg/dL is recommended. In one case series, tight glucose control in the range of 80 to 110 mg/dL was found to be associated with reduced cerebral glucose availability and increased mortality.[50]

k. **Management of refractory intracranial pressure:** Patients with refractory ICP elevations generally have poor outcome. Further interventions should be made after risk–benefit discussions with family. All patients should be assessed for impending cerebral herniation. Clinical signs include pupillary asymmetry, decorticate or decerebrate posturing, respiratory depression, and Cushing's triad of hypertension, bradycardia, and irregular respiration. Endotracheal intubation and brief hyperventilation to a $PaCO_2$ of 25 to 30 mm Hg should be instituted. Presence of a cerebral oxygenation monitor such as near infrared spectroscopy or jugular oximetry would indicate impending cerebral ischemia during hyperventilation.[9] Head end elevation to 30 to 45,

intravascular osmotic agents, and sedation and analgesia with anesthetic agents are the management strategies in the event of impending cerebral herniation. Decompressive craniectomy is a life-saving procedure in patients with refractory elevations in ICP.[9] Decompressive craniectomy is considered in patients with raised ICP refractory to CSF drainage, sedation and analgesia, osmotic therapy, and pharmacotherapy to maintain optimal CPP. A craniectomy defect of at least 11 to 12 cm in diameter is recommended when performing hemicraniectomy for unilateral injury. A large bifrontal craniectomy is recommended for a diffuse injury. Middle cranial fossa should be adequately decompressed to prevent uncal herniation and generous durotomy, and lax duraplasty should be considered to decrease ICP. Decompressive craniectomy in diffuse traumatic brain injury (DECRA)[51] is a randomized trial of 155 adults with diffuse TBI and ICP > 20 mm Hg for 15 minutes within 1-hour period despite first-tier medical therapies. In such patients, bifrontal craniectomy was compared with continued medical care. Surgery was associated with greater reductions in ICP with shorter length of stay in the ICU but was associated with worse outcome on extended Glasgow Outcome Scale (GOS) at 6 months. RESCUEicp[52] is another randomized trial of 408 patients aged 10 to 65 years with refractory ICP > 25 mm Hg for 1 to 2 hours despite medical therapy. In these patients, craniectomy was compared with medical therapy. ICP was better controlled in the surgical group. But similar to DECRA, patients in the craniectomy group had lower mortality (27 vs. 49%) but higher rates of vegetative state (8.5 vs. 2.1%). Also, the surgical group had higher disability reflecting those of patients in the surgical group who would not have otherwise survived. However, a prespecified analysis of outcomes at 1 year showed that the craniectomy group had a higher rate of favorable outcome in terms of disability (45 vs. 32%).

l. **Paroxysmal sympathetic overactivity:** Paroxysmal sympathetic overactivity (PSH) occurs in 10% of the patients with TBI. PSH consists of episodes of hypertension, tachycardia, tachypnea, hyperthermia, diaphoresis, increased tone, and posturing, of varying severity.[53] Management includes intermittent doses of midazolam or fentanyl for short episodes of PSH. Persistent PSH is tackled with propranolol 10 mg thrice daily or clonidine 0.1 mg thrice daily or gabapentin 100 to 300 mg thrice daily or bromocriptine 1.25 to 2.5 mg thrice daily.[54]

3. **TBI and systemic effects:** The incidence of systemic organ dysfunction and failure in patients with acute severe TBI is as follows: cardiovascular, 52% and 18%; respiratory, 81% and 23%; coagulation, 17% and & 4%; renal, 8% and 0.5%; and hepatic, 7% and 0%.[55] Failure of optimal management of organ dysfunction may have deleterious adverse effects on the injured brain.

Cardiovascular system Hemodynamic instability is the most common cardiovascular abnormality. Initial hyperdynamic response is followed by hypotension. Sympatholytic drugs mitigate catecholamine surge and hypertensive response. However, sympatholytic drugs need to be used cautiously due to their adverse effects on blood pressure. TBI-induced hypotension is normally fluid responsive. Noradrenaline infusion may be used in patients who are adequately hydrated but still low on blood pressure and CPP. Vasopressin infusion is to be considered in cases of refractory hypotension. Cardiac dysfunction and electrocardiographic changes (prolongation of the QT interval, ST segment abnormalities, flat or inverted T waves, U waves, peaked T waves, Q waves, and widened QRS complexes) that occur in association with acute TBI secondary to catecholamine surge revert to normal spontaneously after a variable period.

Respiratory system In the event of neurogenic pulmonary edema secondary to catecholamine surge, PEEP may be used to optimize oxygenation and to reduce extravascular lung water. Diuretics are used to maintain optimal CPP.

Renal system Systemic inflammatory response triggered by cytokines in patients with TBI plays a key role in the pathogenesis of renal dysfunction. Sympathetic surge may lead to severe hypertension causing red cell fragmentation, hemolysis, and acute kidney injury. Hypothalamic–pituitary–adrenal axis dysregulation causes acute changes in renal sodium handling and also causes cerebral salt wasting. Renal replacement therapy should be considered in patients with progressive kidney disease.

4. **Neuro-FAST:** Neuro focused assessment with sonography for trauma is essential in neuro-ICU. On admission and periodically, patients undergo transcranial Doppler assessment of cerebral blood flow velocities and optic nerve sheath diameter. Neuro-FAST guides neuro-intensivists in the assessment of cerebral compliance and ICP noninvasively. Hemodynamics need to be targeted to optimize cerebral blood flow and reduction in ICP. Echocardiography and lung ultrasound are routinely used in ICU to diagnose and manage cardiac and respiratory dysfunctions.

5. **Management of head injury in association with polytrauma:** Seventy percent of blunt trauma patients will suffer from some degree of head injury.[56] There is also often an under appreciation of some of these extracranial injuries in TBI patients. The management of these extracranial injuries can influence the neurological outcomes. Judicious application of current concepts and management protocols may ensure the best outcomes in these patients. In India, > 100,000 lives are lost every year with polytrauma.[1] This is likely because 95% of trauma victims in India do not receive optimal care during the "golden hour" period after an injury is sustained.

a. **Definition of polytrauma:** As per the New Berlin Definition,[57,58] polytrauma is described as a case with Abbreviated Injury Score (AIS) > 3 in two or more AIS regions and one or more additional variable from physiological parameters, that is, systolic blood pressure < 90, GCS <8, acidosis with base excess <–6, coagulopathy with partial thromboplastin time > 40 sec, INR >1.4, and age > 70 years. The AIS is an anatomically based, consensus-derived, global

severity scoring system that classifies each injury by body region according to its relative importance on a 6-point ordinal scale (AIS1, minor; AIS2, moderate; AIS3, serious; AIS4, severe; AIS5, critical; AIS6, maximal: currently untreatable).[59] Once the diagnosis of polytrauma is established, concept of golden hour and platinum 10 minutes is vital.[60] This theory states that the best chance of survival in trauma patients occurs when they receive emergency management within 1 hour of injury. Of this only 10 minutes (platinum 10 minutes) of the golden hour should be used for on-scene activities. Mortality after polytrauma has a trimodal distribution: (a) immediate—severe brain injury, transection of great vessels, or other major hemorrhage; (b) early (minutes to hours)—brain injury (epidural/subdural bleed), hemo/pneumothorax, diaphragm rupture, pelvis/long bone fractures; and (c) delayed (days)—sepsis, multiple organ failure. Thus, the first peak is immediately after traumatic injury, and the second one is during the first hour of the post-traumatic period. This generated the concept of "golden hour." In the modern and very efficient trauma systems, evidence indicates decreased mortality with bimodal and unimodal distribution of mortality.[61]

b. **Damage control strategy:** Damage control tactics may improve early mortality (control hemorrhage) and delayed mortality (minimize systemic inflammation and organ failure).[25] Damage control refers to an operative strategy predicated on immediately treating only life-threatening injuries and purposefully delaying definitive operative repair of injuries until the patient's physiology has returned to normal. The timing of definitive repair of injuries temporized during damage control surgery is determined by the patient's physiologic status but typically starts 24 to 48 hours after the initial injury. Surgical management of a patient with polytrauma involves stepwise prioritization of the procedure as per the severity and extent of life-threatening injury[62] (►**Fig. 1**).

c. **Algorithm for fracture care in TBI:**

- In an unstable patient with severe head injury (GCS < 9), consider only damage control surgery.
- In a stable patient with mild head injury (GCS 13–15), consider definitive surgery 5 days after primary insult.
- Consider early total care (within 36 hours) in optimally resuscitated, stable patients.

Concurrent management of head injury as per BTF should continue in the perioperative period as well as in the ICU. Ideal blood pressure target in a patient with polytrauma and head injury is still not defined. CPP of 60 to 70 mm Hg may be required in TBI. However, there exists an increased risk of bleeding in a patient with injuries to liver or spleen when MAP is > 60 mm Hg. A hybrid protocol of a lower MAP till the abdominal bleeding is controlled may be considered. At the time of hybrid protocol, consider monitoring vitals of brain using multimodality monitoring. Continuous perioperative and intensive care resuscitation should be continued to achieve euvolemia and normal tissue oxygenation. Damage control resuscitation principles should be applied throughout all phases of damage control.[62] Any further testing or imaging that is needed to better define the full extent of injuries is also obtained.

6. **Multimodal monitoring in ICU:** Neuromonitoring plays an important role in the management of TBI because it is able to assess multiple aspects of cerebral physiology and guide therapeutic interventions intended to prevent or minimize secondary injury. No single neuromonitor is able to identify comprehensively the spectrum of pathophysiologic changes after TBI, and multimodality monitoring—the measurement of several variables simultaneously—provides a more comprehensive picture of the (patho)physiology of the injured brain and its response to treatment.[63] Clinical assessment using objective scales to assess consciousness and motor power is a key component of neuromonitoring. The GCS[5] was the first attempt to standardize assessment of neurologic state after TBI by recording best eye opening and verbal and motor responses to standardized verbal and physical stimuli. Multimodality monitoring along with clinical monitoring and radiological imaging shall facilitate critical care management of patients with TBI. Several monitoring techniques are available for clinical use (►**Table 3**). Expert consensus guidelines on multimodality neuromonitoring have been published by the Neurocritical Care Society and the European Society of Intensive Care Medicine after comprehensive review of the literature.[64] Bedside multimodality monitoring comprises monitoring modalities for cerebral blood flow, cerebral oxygenation, and cerebral electrical activity. Supplementary to the above, ICP monitoring and bedside neuroimaging such as CT of the brain will provide additional information of the intracranial condition.
7. **Prognostication of TBI in ICU:** TBI is a leading cause of death and disability. No head injury is too severe to despair of, nor too trivial to ignore. Establishing a reliable prognosis early after injury is notoriously difficult. Prognostication after head injury is essential to guide and counsel the relatives of a patient regarding the probable outcomes. It helps in decision making regarding the present condition and allocating the resources accordingly. ►**Table 4** lists parameters that significantly affect the prognosis of a patient with TBI.

Most common prognostic models used in TBI are composed of parameters listed in ►**Table 2**. They are mortality, GOS (extended), International Mission for Prognosis and Analysis of Clinical Trials in TBI (IMPACT) (online calculator available at http://www.tbi-impact.org/?p=impact/calc), and CRASH score (online calculator available at http://www.crash.lshtm.ac.uk/Risk%20calculator/index.html)

8. **Quality-of-life indicators for TBI patients after discharge from ICU:** Survivors of TBI often have variety of physical and psychological deficits affecting their day-to-day life. Current management of TBI relies mainly on the traditional outcome measures that focus mainly on the survival and physical disability but not on the functional disability and cognitive impairment. In contrast, many of the

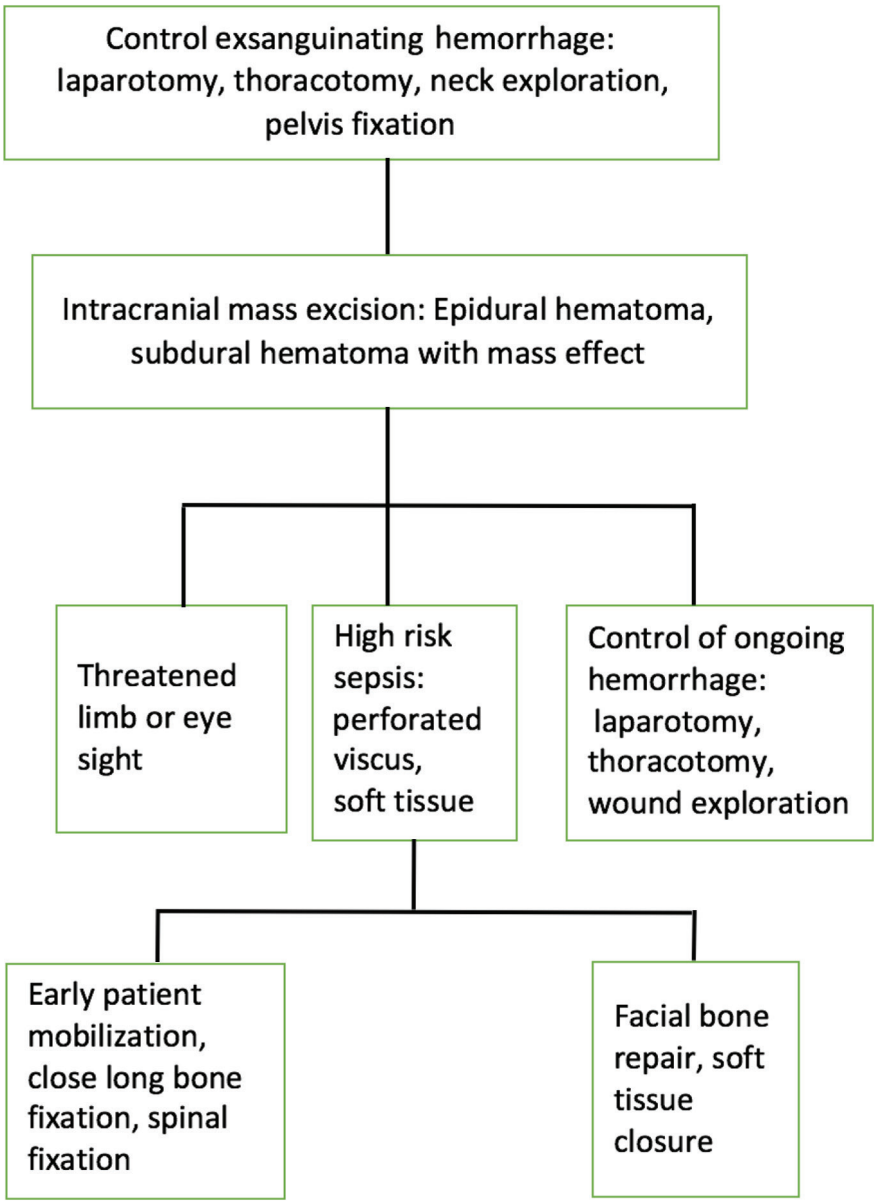

Fig. 1 Surgical algorithm in a patient with polytrauma.

Table 3 Multimodal neuromonitoring in traumatic brain injury[63,64]

Technique	Advantages	Disadvantages	Thresholds for intervention
Cerebral blood flow and metabolism monitors			
TCD	Noninvasive Real-time, continuous monitoring	Relative rather than absolute cerebral blood flow Operator dependent Failure rate in up to 10% of patients; absent acoustic window	Increased blood flow velocity and pulsatility index
Thermal diffusion flowmetry	Continuous measurement of absolute regional cerebral blood flow	Concerns over reliability Limited clinical data	Not determined
Cerebral microdialysis	Measurement of brain tissue biochemistry Early detection of hypoxia/ischemia Monitoring ischemic and nonischemic causes of cellular bioenergetic distress	Focal measure Thresholds for intervention uncertain	Glucose < 0.7 mM Lactate:pyruvate ratio > 25–40 Lactate > 4.0 mM

(continued)

Table 3 *(continued)*

Technique	Advantages	Disadvantages	Thresholds for intervention
Cerebral oxygenation monitors			
Jugular venous oximetry	Straightforward to perform Easy to interpret Real-time and continuous Global trend monitor	Insensitive to regional ischemia Requires correct catheter placement to avoid contamination from extracranial circulation Invasive procedure; risk of hematoma, carotid puncture, and vein thrombosis	Jugular venous oxygen saturation ≤ 50–55%
Brain tissue PO_2	Global trend monitor Gold standard for bedside cerebral oxygenation monitoring Real-time and continuous focal monitoring of critically perfused tissue Low complication rate–hematoma risk < 2%, no reported infections	Invasive Utility dependent on probe location; at-risk but viable tissue; regional monitor; normal-appearing frontal lobe; global measure 1h run-in period required	Brain tissue PO_2 ≤ 15–20 mm Hg
Near-infrared spectroscopy	Noninvasive assessment of regional cerebral tissue oxygenation High spatial and temporal resolution Assessment over multiple regions of interest simultaneously	Lack of standardization between commercial devices Ischemic thresholds not defined Signals affected by extracerebral tissue Not recommended for routine clinical use	Not determined
Cerebral autoregulation	Identification of optimal CPP range Interpretation of relationships between cerebral blood flow, oxygen delivery/demand, and cellular metabolism	Requires high-frequency signal processing Insufficient data to support recommendation for routine clinical use	Not available
Monitors for cerebral electrical activity: EEG			
Scalp EEG	Noninvasive Correlates with ischemic and metabolic changes Assessment of nonconvulsive seizures/status epilepticus	Skilled interpretation required Affected by anesthetic/sedative agents Misses some seizure activity Cannot identify cortical spreading depolarizations	Not available
Invasive EEG (subdural strip/depth electrodes)	Identifies abnormalities missed by scalp EEG monitoring Only method to monitor cortical spreading depolarizations	Invasive Labor intensive	Not available
ICP monitors			
Ventricular catheter	Measures global pressure Therapeutic drainage of cerebrospinal fluid to manage ICP In vivo calibration	Placement technically difficult Risk of hemorrhage Risk of infection	ICP > 22 mm Hg
Microsensor	Intraparenchymal/subdural placement Low procedural complication rate Low infection risk	Risk of infection In vivo calibration not possible Measures localized pressure	ICP > 22 mm Hg
Noninvasive methods Optic nerve sheath diameter, calculated ICP value from TCD parameters	Low risk Use in coagulopathic patients	Insufficiently accurate for routine clinical use Many unable to offer continuous monitoring	
Bedside brain Imaging			
CT	Noninvasive Easy to read and interpret	Not real-time No information on cerebral physiology	CT findings to be correlated clinically

Abbreviations: CPP, cerebral perfusion pressure; CT, computed tomography; EEG, electroencephalogram; ICP, intracranial pressure; TCD, transcranial Doppler.

Table 4 Prognostication of brain trauma

Parameter	Prognosis
Clinical parameters	
Age > 40 y[65,66]	Worse with increasing age
Motor component of initial GCS post-resuscitation[67]	Increasing incidence of death with GCS <6 (12.5% to 88.9%)
Pupillary reaction[30]	Bilaterally absent pupillary reflex has >70% PPV of poor prognosis
Secondary insults	
Hypotension[68]	Systolic blood pressure < 90 mm Hg has a 67% PPV for-poor outcome
Hypoxia[68]	Hypotension with hypoxia has a 79% PPV of poor outcome
Anemia[69]	Hematocrit < 30 increases mortality
Glucose[70]	Glucose levels > 150 mg/dL is associated with poor outcome
Radiological parameters[71–73]	
Midline shift >1.5 cm on CT brain	70% PPV of mortality
SAH in basal cisterns on CT brain	70% PPV of mortality
Gray–white matter ratio < 1.16 on MRI of brain	100% specific and 38% sensitive in predicting poor outcome
Injuries to corpus callosum, corona radiata, and dorsolateral Brain stem on MRI brain	Poor outcome
Decreased *N*-acetylcholine/creatinine ratio and increased choline levels in the injured region on brain MRI	Poor outcome
Electrophysiological parameters[74,75]	
Bilateral absence of N20 response after 48 to 72 h after resuscitation	Predicts poor outcome in patients who have not under-gone therapeutic hypothermia
Burst suppression on EEG > 50%	Predicts poor outcome
Genetic parameters[76]	
Presence of apo E ε4 allele	Predicts poor prognosis as apo E ε4 allele is associated with significant levels of biomarkers S-100B and NSE
Microsomal RNA 9	Decreased expression increases cell survival and increased expression promotes cell death
Biomarkers[77,78]	
Blood S100B within 6 hours of TBI	< 0.1 μg/L is a marker of discharging patients
Serum glial fibrillary acid protein levels > 1.5 ng/mL at admission and up to 14 days after TBI	Unfavorable outcome at 6 months
Increased cerebrospinal fluid Tau level 6 hours after TBI and up to 6 days	Poor outcome
Initial fall in serum cortisol levels immediately after TBI	Associated with increased mortality and morbidity

Abbreviations: CT, computed tomography; EEG, electroencephalogram; GCS, Glasgow Coma Scale; MRI, magnetic resonance imaging; PPV, positive predictive value; TBI, traumatic brain injury.

health-related quality of life (HRQOL) indices focus on the outcomes from the patient's perspective of functional independence, mental health, and community life after TBI.[79,80] QOL in brain injury overall scale[43,45] is a HRQOL index developed for TBI patients. This is a six-item scale addressing physical condition, cognition, emotions, functions in daily life, personal and social life, and current situations and future prospects. Satisfaction in these areas is rated on a five-point scale. The resulting score gives a measure of QOL out of a total possible score of 100. Other popular HRQOL indices used for TBI patients are Short Form 36 (SF-36),[81] Glasgow Outcome Scale - Extended (GOS-E),[82] quality of life after Brain Injury (QOLIBRI)[83] and Telephone Interview for Cognitive Status and Brain Injury Grief Inventory (BIGI).[84]

9. Interventions with uncertain or no benefit

Hemostatic treatments: There is no evidence that hemostatic therapy[27] benefits non-coagulopathic patients with severe TBI. Two trials found a statistically significant decrease in hemorrhage expansion following TBI with the use of tranexamic acid, along with a trend toward improved outcomes.[85]

Neuroprotective treatment: A wide range of agents[86] (intravenous progesterone, magnesium, hyperbaric oxygen, cyclosporine, etc.) targeting various aspects of the brain injury cascade have been tested in clinical trials. Women have been shown to have decreased morbidity and mortality after TBI as compared to age-matched men. Administration of progesterone is associated with reduced mortality, improved neurological outcome, and a reduction in neuronal apoptosis. Progesterone-mediated neuroprotection is through its direct antioxidant effects, modulation on inflammatory response, effects on astrocytes and microglia, cerebral perfusion, and metabolism. To date, no neuroprotective agents or strategies (including induced hypothermia) have been shown to produce an improved outcome.

Glucocorticoids: The use of glucocorticoid therapy following head trauma was found to be harmful rather than beneficial in a large trial of patients with moderate-to-severe TBI.[87]

Conclusion

TBI is a much more manageable injury today than it has been in the past, but it remains a major health problem. Our understanding of TBI is improving constantly. BTF continues to define the best practices in treating brain injury. Although there is lack of effective treatment for TBI recovery today, the efforts for developing therapeutic strategies on TBI recovery have been continuously made over the past several decades. Standard medical and surgical interventions always play a significant role in the acute management for TBI patients. With existing better acute management guidelines in the acute phase of TBI, the number of TBI survivors with various disabilities has risen. This calls for major research of TBI to be shifted into the area of neurorestoration and neurorehabilitation.

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Conflict of Interest
None declared.

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