

DISCLAIMER: These guidelines were prepared by the Department of Surgical Education, Orlando Regional Medical Center. They are intended to serve as a general statement regarding appropriate patient care practices based upon the available medical literature and clinical expertise at the time of development. They should not be considered to be accepted protocol or policy, nor are intended to replace clinical judgment or dictate care of individual patients.

SEVERE TRAUMATIC BRAIN INJURY MANAGEMENT

SUMMARY

Traumatic brain injury (TBI) is the leading cause of death for all age groups in the United States, contributing to over 50% of trauma deaths. Protocolized management of severe TBI [defined as a post-resuscitation Glasgow Coma Score (GCS) < 8] has been demonstrated to improve patient outcome. Primary endpoints in the management of severe TBI include minimizing cerebral edema and intracranial pressure (ICP) while simultaneously optimizing cerebral perfusion pressure (CPP) and tissue oxygenation to reduce secondary ischemic injury.

RECOMMENDATIONS

- **Level 1**
 - Maintain mean arterial pressure (MAP) > 80 mmHg or CPP > 60 mmHg if Glasgow Coma Score (GCS) < 8
 - Maintain ICP < 20 mmHg
 - Maintain patient temperature 36-37° Celsius; consider early antipyretics and cooling blankets
 - Do not administer high-dose steroids in TBI
- **Level 2**
 - Protect the patient's airway and intubate if GCS < 8
 - Maintain oxygenation (PaO₂ 80-120 mmHg) and normocarbica (PaCO₂ 35-40 mmHg)
 - Elevate head of bed 30 degrees at all times
 - Consider ICP monitor if GCS < 8 (after resuscitation) AND:
 - Abnormal head CT scan (hemorrhage, contusions, swelling, herniation, compressed basal cisterns)
 - Normal head CT scan AND two or more of the following: age > 40 years, unilateral or bilateral motor posturing, or systemic hypotension
 - Patient will not be examinable for a prolonged period of time
 - Provide judicious sedation and analgesia to control pain and agitation
 - Initiate norepinephrine if CPP < 60 mmHg despite appropriate volume resuscitation
 - If ICP is persistently greater than 20 mmHg, begin osmolar therapy
 - First line: 3% normal saline 100 mL IV q 2 hrs prn
 - Alternate: Mannitol 0.25-1.0 gm/kg IV q 6 hrs prn
 - Consider neuromuscular blockade for refractory ICP
 - Initiate seizure prophylaxis for the first 7 days post-injury
 - Consider continuous EEG to rule out non-convulsive status epilepticus
 - Ensure appropriate nutrition, stress ulcer, and deep venous thrombosis prophylaxis
- **Level 3**
 - Maintain hemoglobin > 9 gm during the patient's critical illness
 - Consider decompressive craniectomy for refractory ICP in consultation with Neurosurgery
 - If the patient is not a surgical candidate, consider pentobarbital coma for refractory ICP
 - Consider therapeutic hypothermia (temperature 33-34° Celsius) for refractory ICP

EVIDENCE DEFINITIONS

- **Class I:** Prospective randomized controlled trial.
- **Class II:** Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III:** Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment:** A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

TRAUMATIC BRAIN INJURY – TIERS OF THERAPY

TIER ZERO

The following interventions should be implemented in all patients with TBI:

- Maintain mean arterial pressure (MAP) > 80 mmHg if GCS < 8; otherwise target MAP > 70 mmHg
- Administer supplemental oxygen to maintain SpO₂ > 92%
- Elevate head of bed to 30 degrees
- Maintain head in neutral position to avoid jugular vein constriction
- Correct hyponatremia (serum Na⁺ < 140 mEq/L) with isotonic intravenous fluids (no dextrose)
- Correct coagulopathy with Prothrombin Complex Concentrate (PCC) in life-threatening bleeds
 - FEIBA NF 1000 units IV push over 5 minutes
- Transfuse platelets in patients with known history of antiplatelet agent use
- Avoid hyperthermia (temperature > 37°Celsius)
 - Acetaminophen 650 mg PO/PT q 4 hrs
- Avoid hyperglycemia (serum glucose > 180 mg/dL)
- Ensure early appropriate nutritional support
- Prevent deep venous thrombosis (DVT)
- Prevent gastrointestinal stress ulceration
- Prevent skin breakdown / decubitus ulcer formation through appropriate bed surface

TIER ONE

The following interventions should be added in all patients with Glasgow Coma Score (GCS) < 8:

- Ensure all physiologic goals from **Tier Zero** are met
- Airway / Breathing**
 - Intubate patient if GCS < 8 and as needed to protect the airway
 - Maintain PaCO₂ 35-40 mmHg
 - Maintain PaO₂ 80-120 mmHg
- Systemic and Cerebral Perfusion**
 - Insert an arterial line (leveled at the phlebostatic axis)
 - Insert a central venous catheter for central venous pressure (CVP) monitoring
 - Maintain euvolemia (fluid balance positive by 500-1000 mL in first 24 hrs, CVP > 8 mmHg)
 - Maintain MAP > 80 mmHg if ICP is unavailable
 - Maintain cerebral perfusion pressure (CPP=MAP-ICP) > 60 mmHg if ICP is available
 - If CPP < 60 mmHg, notify intensivist and:
 - If CVP < 8 mmHg, give normal saline 500-1000 mL bolus
 - If CVP > 8 mmHg, start norepinephrine 0-0.5 mcg/kg/min IV infusion to maintain CPP
 - Consider ICP monitoring
 - Indications
 - Salvageable patients with severe TBI (GCS 3-8 after resuscitation) and an abnormal CT scan (hemorrhage, contusions, swelling, herniation or compressed basal cisterns)
 - Patients with severe TBI and normal CT scan if two of the following are noted at admission: age > 40 yrs, unilateral or bilateral posturing, systolic BP < 90 mmHg
 - Patients with TBI who will not be examinable for a prolonged period of time
 - Management
 - Maintain ICP < 20 mmHg
 - Consider Osmolar Therapy (see below)
 - Consider short-term hyperventilation (PaCO₂ 30-34 mmHg) to acutely reduce ICP
 - Verify correct ICP waveform on extraventricular drain (EVD); notify neurosurgery if ICP waveform is incorrect or there is no CSF drainage
 - Level EVD at the external auditory meatus
 - Close EVD and level at 0 mmHg upon insertion to monitor ICP
 - If ICP > 20 mmHg for 10 minutes, open EVD at 0 mmHg for 15 minutes
 - If EVD is opened more than 3 times within 90 minutes, leave EVD open at 0 mmHg continuously and notify neurosurgery

- ❑ **Osmolar Therapy**
 - First line therapy
 - 3% normal saline IV bolus 100-250 mL q 2 hrs prn ICP > 20 mmHg for > 10 minutes
 - Alternate therapy
 - Mannitol 0.25-1.0 gm/kg IV q 6 hrs prn ICP > 20 mmHg
 - Measure serum osmolality and electrolytes q 6 hrs
 - Notify intensivist if serum Na changes by > 3 mEq/L from previous measurement
 - Hold hypertonic saline therapy for serum Na > 160 mEq/L
 - Hold mannitol therapy for serum osmolality > 320 mOsm
- ❑ **Protect the Brain**
 - Initiate continuous EEG monitoring to rule non-convulsive status epilepticus
 - Provide judicious analgesia and sedation to control pain and agitation
 - Fentanyl 25-150 mcg/hr IV infusion
 - Propofol 10-50 mcg/kg/hr IV infusion for Richmond Agitation Sedation Score (RASS) > -2
 - Exclude seizure activity
 - Keppra 500 mg IV BID for first 7 days (discontinue after 7 days if no seizure activity)
 - Avoid:
 - Hypotension (MAP < 70 mmHg)
 - Hypoxemia (SpO₂ < 92%)
 - Hypercarbia (PaCO₂ > 45 mmHg)
 - Hyponatremia (serum Na⁺ < 140 mEq/L)
 - Hyperglycemia (glucose > 180 mg/dL)
 - Hypovolemia
 - Fever (maintain temperature at 36-37° Celsius)
 - Anemia (maintain hemoglobin > 9 gm during the patient's critical illness)

TIER TWO

The following interventions should be considered if ICP is persistently > 20 mmHg for more than 60 minutes after discussion with neurosurgery and intensivist attendings:

- ❑ Ensure all physiologic goals from **Tier One** are met
- ❑ Consider head CT scan to rule out space-occupying lesion
- ❑ Consider continuous EEG monitoring to rule non-convulsive status epilepticus
- ❑ **Paralysis**
 - Start rocuronium (50 mg/kg loading dose, then 8 mcg/kg/hr); adjust dose according to Train of Four
- ❑ **Mild Hypothermia**
 - Induce hypothermia to 35° Celsius using the Arctic Sun™ cooling pads
- ❑ **Mild Hyperventilation**
 - Begin mild hyperventilation with goal PaCO₂ 30-34 mmHg

TIER THREE

The following interventions should be considered if ICP remains > 20 mmHg despite all Tier Two goals being met:

- ❑ Ensure that medical therapy with hypertonic saline is maximized
- ❑ Consider revised ICP threshold of 25 mmHg with strict adherence to CPP goals
- ❑ Initiate continuous EEG (if not already present)
- ❑ Consider 23.4% hypertonic saline 30 mL IVP for refractory ICP
- ❑ **Surgical Decompression**
 - Consider decompressive craniectomy in consultation with neurosurgery team
- ❑ **Hypothermia**
 - Consider hypothermia to 34° Celsius using the Arctic Sun cooling blanket
 - Once ICP < 20 mmHg for 48 hrs, rewarm at rate no greater than 0.1° Celsius/hr
- ❑ **Barbiturate Coma**
 - If not a surgical candidate, and refractory to all above interventions, consider pentobarbital coma
 - Pentobarbital 10 mg/kg IV over 10 minutes, then 5 mg/kg IV q 1 hr x 3, then 1 mg/kg/hr IV infusion
 - Titrate pentobarbital to the minimal dose required to achieve EEG burst suppression
 - Discontinue all other sedative agents and paralytics
 - Strongly consider invasive hemodynamic monitoring (such as pulmonary artery catheter) due to the negative inotropic effects of pentobarbital
 - Once ICP < 20 mmHg for 48 hrs, taper pentobarbital dose over the next 48-72 hrs

INTRODUCTION

TBI is a potentially lethal injury with mortality rates as high as 50%. Approximately 1.5 million people sustain TBI annually in the United States resulting in over 50,000 deaths and 500,000 individuals with permanent neurologic sequelae (1). Nearly 85% of TBI-related mortalities occur within the first two weeks of injury, reflecting the early impact of systemic hypotension and intracranial hypertension.

Patient outcome following severe TBI (defined by a post-resuscitation GCS < 8) is significantly improved when such patients are managed according to a comprehensive neuro-resuscitation protocol such as those recommended by the Brain Trauma Foundation (BTF) (www.braintrauma.org) or Neurocritical Care Society (www.neurocriticalcare.org) (1-3). A recent database analysis of TBI resuscitation and patient outcome in New York state demonstrated a decrease in mortality from 22% in 2001 to 13% in 2009 ($p < 0.0001$) when such guidelines were followed (1). Between these two time periods, guideline adherence increased from 56% to 75% ($p < 0.0001$), adherence to the cerebral perfusion pressure (CPP) recommendations increased from 15% to 48% ($p < 0.0001$), and the proportion of patients with ICP > 25 mmHg decreased from 42% to 29% ($p < 0.0001$).

The following guidelines outline an evidence-based medicine approach to the management of patients with severe TBI based upon the current medical literature and published consensus statements. The guidelines consist of three tiers of progressively escalating therapies targeted at controlling ICP. The importance of frequent and open communication between intensive care providers and the neurosurgery team cannot be overemphasized. Please note that patients with stroke, ruptured intracranial aneurysms, and those undergoing ICP monitoring for other neurological conditions should not be managed according to these TBI guidelines unless otherwise determined by the consulting neurosurgeon.

PATHOPHYSIOLOGY

Based on the Monroe-Kellie Doctrine, the intracranial volume [brain 80%, cerebral spinal fluid (CSF) 10%, and cerebral blood volume 10%] is fixed within the confines of the cranial vault and cannot expand. Since brain tissue has minimal compensatory capacity, in the presence of cerebral edema or space-occupying lesion, CSF and blood volume must decrease in order to regulate ICP. CSF may drain through the lumbar plexus and blood volume is tightly autoregulated by both the PaCO₂ and PaO₂. This allows cerebral blood volume to decrease, reducing ICP, while at the same time maintaining adequate CPP.

The goal of ICP monitoring and control in the TBI patient is to maintain an appropriate CPP [defined as mean arterial pressure (MAP) minus ICP] through either increasing MAP or decreasing ICP. A variety of therapies may be applied to lower ICP and reduce cerebral edema in an attempt to maintain sufficient CPP to provide adequate oxygen delivery to avoid secondary cerebral injury due to ischemia. There is a delicate balance between increasing cerebral perfusion and keeping ICP and cerebral edema minimized.

LITERATURE REVIEW

Initial Evaluation

All patients who present with suspected TBI should undergo a rapid primary and secondary survey with thorough evaluation of their airway, breathing, and circulation. Airway patency and adequate oxygenation and ventilation are paramount to avoiding secondary brain injury (4). The patient's cervical spine should be immobilized until cervical spine injury is ruled out. Urgent intubation to secure the patient's airway should be considered in any patient who presents with a GCS < 8 or in those who are unable to protect their airway. Intravenous access should be rapidly established. Bedside glucose testing should be performed in all unconscious patients and hypoglycemia rapidly treated if present. Thiamine (100 mg) should be administered in patients at risk for nutritional deficiency. If opioid toxicity is suspected (e.g., history of illicit drug use, apnea, bradypnea, small pupils), naloxone 0.4 mg IV should be administered and repeated as necessary, up to 4 mg. Appropriate laboratory tests [serum electrolytes, CBC with platelets, coagulation studies, arterial blood gas, urinalysis, and urine toxicology / alcohol level (as appropriate)] should be performed. If definitive neurosurgical care cannot be provided at the initial presenting institution, transfer to a higher level of care should be facilitated in a rapid fashion to preserve the "Gold Hour" and optimize the patient's outcome. Certain key resuscitative interventions should be initiated at the referring facility however to minimize secondary cerebral injury (Appendix 1).

Hypotension

Prehospital and in-hospital systemic hypotension independently increases morbidity and mortality following TBI (2). Systolic hypotension leads to cerebral ischemia and secondary brain injury. In the patient with GCS < 8, MAP should be maintained above 80 mmHg through the use of judicious isotonic intravenous fluids (without dextrose) until an ICP monitor is available. The goal should be to ensure an adequate CPP > 60 mmHg at all times (2,5). As the brain is very sensitive to anoxia, this will serve to improve oxygen delivery and further avoid secondary brain injury. If the patient's MAP cannot be maintained above 80 mmHg with intravenous fluid alone (or CPP > 60 mmHg if ICP monitoring is available), low-dose norepinephrine should be initiated (2,5).

Cerebral Perfusion Pressure (CPP)

CPP, defined as MAP minus ICP, is an important resuscitative parameter in the treatment of patients with TBI. The BTF recommends a CPP range of 50-70 mmHg with an optimal target of 60 mmHg (2). Measurements of cerebral blood flow, cerebral oxygenation [either jugular venous saturation (SjvO₂) > 50% or brain tissue oxygen tension (PbO₂) > 15 mmHg] and metabolism are considered complimentary tools in the management of TBI when available (2). Maintenance of CPP > 70 mmHg should be avoided due to an increased risk of over-resuscitation and acute respiratory distress syndrome (ARDS). CPP < 50 mmHg should be avoided due to the risk of low cerebral blood flow, cerebral hypoxia, and secondary brain injury.

Head of Bed Elevation

All patients with TBI should have their head of bed elevated 30 degrees to reduce cerebral edema and augment venous drainage from the cranial vault. Elevation of the head may also lower ICP without adverse impact upon either cerebral blood flow or CPP (6). In patients with suspected or documented spine injury, this is best achieved by placing the patient's bed in the reverse Trendelenburg position. Elevation of the head of bed greater than 30 degrees has not been demonstrated to be beneficial.

Normothermia

Elevated body temperature / fever has a significant deleterious impact upon the brain. While fever is typically defined as a core body temperature greater than 38.3° Celsius, temperatures in excess of 37° Celsius can significantly impact the already impaired brain parenchyma. Elevated body temperature increases the patient's inflammatory response by elevating levels of pro-inflammatory cytokines and neutrophils. This can increase sympathetic tone, resting energy expenditure, oxygen consumption, heart rate, and minute ventilation. While fever occurs in 30-45% of the non-neurologically injured, it may be seen in up to 70% of those with TBI. In these patients, an infectious etiology is present less than 50% of the time, with the remainder being classified as "central fever." Central fever is believed to be due to direct damage to the thermoregulatory centers of the brain, which are found in the preoptic nucleus of the hypothalamus and focal centers of the pons. Severe damage to these centers can also result in profound hypothermia, which can result in coagulopathy, cardiac arrhythmias, or depressed immune function.

Significantly worse outcomes occur in patients with intracerebral hemorrhage who develop a body temperature greater than 37.5° Celsius within the first 72 hours (7). Early fever following TBI has been associated with lower GCS, presence of diffuse axonal injury, cerebral edema, hypotension, hypoglycemia, and leukocytosis (8). Fever within the first week is associated with increased intracranial pressure, neurologic impairment, and prolonged ICU stay (9). Among 846 patients with TBI, fever at any time in the first week was associated with intermediate decline and poor overall long-term outcome (10).

Hypothermia is also associated with worse outcomes in TBI. Among 1,403 ICU patients with TBI, a core temperature less than 35° Celsius was observed in 10.9% of patients (11). Patients in the hypothermia group were less likely to survive (p<0.013) and were more likely to have penetrating injury, Injury Severity Score>25, and need for exploratory laparotomy. In a multivariable logistic regression model adjusted for demographics and injury characteristics, the odd's ratio for death among hypothermic patients was 1.7 times that of normothermic patients (12).

Aggressive efforts to control temperature in the TBI patient should be implemented including early intravenous and enteral antipyretic medications, control of room temperature, and cooling blankets or

pads. Due to the deleterious effect of temperature on brain parenchyma, therapy should be initiated when patient temperature exceeds 37° Celsius rather than waiting until the traditional definition of fever has been reached.

Therapeutic Hypothermia

Therapeutic hypothermia has been demonstrated to improve neurologic outcome following witnessed arrest from ventricular fibrillation or pulseless ventricular tachycardia (13). Data supporting its use following TBI has been less convincing. In 2001, 392 TBI patients were randomly assigned to hypothermia (core body temperature of 33° Celsius using ice, cold gastric lavage, and surface cooling for 48 hours) or normothermia. Poor outcomes, defined as severe disability, persistent vegetative state, or death, occurred in 57% of patients in both groups. Mortality was essentially the same (28% vs. 27%) in both groups (p=0.79). The authors concluded that therapeutic hypothermia was not effective in improving outcomes in TBI (14). Two additional randomized trials comparing therapeutic hypothermia with normothermia similarly found no benefit in TBI patients (15,16). The routine use of therapeutic hypothermia following TBI cannot be recommended at this time.

While normothermia has few potential side effects, the potential complications of therapeutic hypothermia include hypotension, arrhythmia, electrolyte disorders, impaired coagulation, shivering, hyperglycemia, and increased risk of infection.

Therapeutic hypothermia may have a role in the treatment of patients with severe TBI and refractory ICP, but should only be used after consultation between the attending intensivist and neurosurgeon. When therapeutic hypothermia has been initiated, therapy should be continued until ICP < 20 mmHg for 48 hrs at which time patients may be rewarmed at a rate not to exceed 0.1° Celsius per hour with close monitoring for the development of rebound intracranial hypertension.

Shivering management (Appendix 2)

When body temperature is lowered, the physiologic response is to prevent further heat loss through vasoconstriction. When vasoconstriction is no longer effective, shivering occurs to counterbalance heat loss. In the context of induced hypothermia, shivering is undesirable because it causes patient discomfort, increases body temperature, increases metabolic / oxygen demand, and increases intraocular and intracranial pressures (17,18). A step-wise approach to the prevention of shivering appears appropriate. Pharmacologic options for the control of shivering include: meperidine, morphine, fentanyl, propofol, magnesium, benzodiazepines, and neuromuscular blockers (19). It is important to consider that data on pharmacologic interventions for shivering control are based upon experience with either health volunteers or in the postoperative setting (20-23). Therefore, the effect of repetitive dosing and prolonged use of these agents in therapeutic hypothermia is lacking (i.e. CNS toxicity associated with meperidine).

Targeted Temperature Management (Appendix 3)

With the deleterious effects of fever and hypothermia established for TBI patients, many modalities of achieving either normothermia or therapeutic hypothermia have been described (19). Conventional cooling methods include skin exposure, ice, cold packs, infused cold fluid, peritoneal lavage, and antipyretics. There are also many commercially available cooling devices available. The Blanketrol™ (Cincinnati Subzero, Cincinnati, OH) is a water-circulating blanket system that utilizes two large cooling blankets, one beneath and one on top of the patient, to maintain the desired patient temperature. The Arctic Sun™ (Medivance, Jugenheim, Germany) circulates water through gel pads that are applied to the patient's back, abdomen, and thighs, automatically controlled by a rectal thermometer. Several intravascular cooling systems are also commercially available. These systems infuse cold fluids via a closed-loop central venous catheter to maintain the desired body temperature. In a prospective study of ICU patients, Hoedemakers et al found superior temperature control using water-circulating blankets, gel-pads, and intravascular cooling as compared to conventional cooling techniques and air-circulating blankets (24).

Seizure Prophylaxis

Post-traumatic seizures may be classified as early (\leq 7 days post-injury) or late ($>$ 7 days post-injury) (2). Both early and late seizures should be avoided. Anticonvulsant therapy, using either levetiracetam or

phenytoin, is indicated to decrease the incidence of early post-traumatic seizures in severe TBI, but not mild or moderate TBI. Levetiracetam does not require blood level monitoring as does phenytoin and recent studies suggest decreased long-term functional outcome among patients who receive phenytoin prophylaxis. Routine prophylaxis of late post-traumatic seizures is not recommended (see “Seizure Prophylaxis in Patients with Traumatic Brain Injury” guideline). Seizure prophylaxis can generally be discontinued after 7 days of therapy in the absence of seizure activity.

Corticosteroids

Multiple prospective, randomized studies have demonstrated no benefit in lowering ICP or improvement in patient outcome through the use of high-dose corticosteroids in acute TBI (2). The use of methylprednisolone in patients with moderate to severe TBI has been demonstrated to increase mortality and is contraindicated.

Hyperventilation

Hypercapnea is a potent cerebral vasodilator and should be avoided in patients with cerebral edema and elevated ICP. Hyperventilation reduces ICP by causing cerebral vasoconstriction and reducing cerebral blood flow. Aggressive hyperventilation has been used for years in the treatment of elevated ICP, but has been demonstrated to have a deleterious outcome (10). Prophylactic hyperventilation ($\text{PaCO}_2 < 25$ mmHg) is no longer recommended (2). A PaCO_2 target of 35-40 mmHg is appropriate in the initial resuscitation of the patient with severe TBI. In patients with refractory elevations in ICP, a revised target of 30-34 mmHg may be appropriate. Hyperventilation should be avoided in the first 24 hours post-injury when cerebral blood flow is often critically reduced. Hyperventilation may have a role as a temporizing measure in the acute reduction of elevated ICP. When hyperventilation is used for more than a brief period of time, monitoring of cerebral oxygenation using either jugular venous bulb oximetry (SjvO_2) or brain tissue oxygen tension (PbrO_2) should be considered.

Hyperosmolar Therapy

Hyperosmolar therapy, using either mannitol or hypertonic saline, has been demonstrated to be beneficial in reducing both cerebral edema and elevated ICP (2). Mannitol has the additional desirable properties of decreasing blood viscosity, increasing free radical scavenging, and inhibiting cellular apoptosis. These agents serve to establish an osmotic gradient across the blood brain barrier. They must be used with caution, however, as excessive use can lead to hypovolemia, hypernatremia, and worse patient outcome. Arterial pressure monitoring and serial sodium and osmolality measurements are essential to appropriate titration of these therapies.

Mannitol should be administered in doses of 0.25-1 gm/kg every 6 hours as needed to reduce ICP (25,26). Mendelow et al. have shown that mannitol improves MAP, CPP, cerebral blood flow, and ICP (27). Mannitol should not be administered in the absence of ICP monitoring unless the patient is showing signs of transtentorial herniation (2).

Hypertonic saline reduces cerebral edema while simultaneously lowering ICP and augmenting CPP by increasing MAP. 3%, 7.5%, and 23.4% hypertonic saline have all been studied in severe TBI. 3% normal saline may be administered in boluses of 100 mL every 2 hours as needed to reduce ICP. Hypotensive patients with severe TBI may benefit from either 250 mL of 7.5% or 30 mL of 23.4% saline as an acute resuscitative intervention to raise MAP, reduce ICP, and avoid crystalloid over-resuscitation. Wade et al. demonstrated that hypotensive TBI patients resuscitated with hypertonic saline were twice as likely to survive compared to those that received normal saline resuscitation ($p < 0.05$) (28). Vasser et al. showed that trauma patients with a GCS ≤ 8 receiving hypertonic saline had a significant improvement in survival to discharge compared to either normal saline or Lactated Ringer’s solution (29).

Intracranial Pressure (ICP) (Appendix 4)

ICP ≥ 15 mmHg has been independently associated with increased mortality following TBI (30). ICP < 20 mmHg has been demonstrated to predict improved outcome (31). The goal of ICP treatment should be reduce ICP below 20 mmHg wherever possible, balancing the risks of continued intracranial hypertension against the potential iatrogenic risks of overtreatment.

ICP cannot be reliably predicted by CT scan alone. As a result, ICP monitors should be placed and utilized to guide resuscitative therapy in the following three patient populations (2):

1. Salvageable patients with severe TBI (GCS 3-8 after resuscitation) and an abnormal CT scan (hemorrhage, contusions, swelling, herniation or compressed basal cisterns)
2. Patients with severe TBI and a normal CT scan if two of the following are noted at admission: age > 40 years, unilateral or bilateral posturing, systolic BP < 90 mmHg
3. Patients with TBI who will not be examinable for a prolonged period of time

ICP monitors should not be placed in patients that are deemed to have a non-survivable injury or who will undergo neurosurgical intervention within four hours of the initial injury.

Hemoglobin Resuscitation

A restrictive red blood cell transfusion threshold of 7 gm/dL is commonly utilized in the critically ill based upon the results of the TRICC trial (32). It is important to recognize that this study evaluated patients who had already been resuscitated and excluded patients who were traumatically injured with ongoing blood loss. A subsequent subgroup analysis of patients with cardiac disease found that red blood cell transfusion was actually protective and improved survival (33). There is a theoretical benefit to maintaining elevated hemoglobin concentrations in the TBI patient who is at risk for cerebral ischemia. Retrospective clinical trials and meta-analyses to assess the potential benefit of a liberal red blood cell threshold in severe TBI have failed to identify a beneficial transfusion threshold, but may well have been underpowered. Sekhon et al. have recently conducted a retrospective cohort study of 273 TBI patients (34). They identified that a mean hemoglobin concentration < 9 gm/dL during the first seven days post-injury is associated with an increased risk of mortality (relative risk 3.1; 95% confidence interval 1.5-6.3; p=0.03).

Analgesia and Sedation

Analgesia and sedation in the TBI patient have the advantages of reducing elevated ICP, controlling blood pressure, preventing temperature elevation, and facilitating mechanical ventilation (2). These goals must be balanced against the potential loss of a reliable neurologic examination and iatrogenic reduction in systemic blood pressure and cerebral perfusion.

Analgesia is best obtained using continuous narcotic infusions. Fentanyl has minimal hemodynamic effects and a short half-life (10-20 minutes) allowing rapid titration on and off for neurologic examination. Propofol is a sedative hypnotic agent that has a favorable pharmacokinetic profile and beneficial effects on both cerebral metabolic rate and ICP following TBI. It has a short half-life (9 minutes) making it easy to titrate on and off for neurologic examination. Propofol does depress respiratory drive and must be used in conjunction with mechanical ventilation. It is also a cardiac depressant and directly reduces preload, contractility, and systemic vascular resistance, potentially leading to systemic hypotension if used inappropriately. High dose propofol infusions (>83 mcg/kg/min for greater than 24 hours) have been associated with fatal acidosis, rhabdomyolysis, and refractory arrhythmias (known as "Propofol Infusion Syndrome") (35). In general, doses of less than 50 mcg/kg/min are both effective and safe. Short-term infusions of high dose propofol (> 50 mcg/kg/min) may be deemed necessary to control ICP after discussion with both the patient's neurosurgeon and intensivist.

Neuromuscular paralysis

Pharmacologic neuromuscular paralysis can be beneficial in the control of refractory intracranial hypertension by reducing cerebral metabolic rate. Few studies exist to support this as a routine practice. Prophylactic paralysis is associated with increased pneumonia and ICU stay and should be instituted only after failure to respond to less invasive therapies (36).

Barbiturate Coma

The beneficial effects of high-dose barbiturates in reducing ICP have been known since the 1930s (2). These agents are powerful myocardial depressants, however, and have deleterious effects on other organ systems as well. The prophylactic administration of barbiturates to reduce ICP and induce burst suppression on EEG is not recommended. High dose barbiturates are recommended to control elevated

ICP that is refractory to maximal medical and surgical management. When implemented, invasive hemodynamic monitoring, such as with a pulmonary artery catheter, is essential.

Infection Prevention

Nosocomial infection is a significant concern in the critically ill. Central line-associated bloodstream infection (CLABSI) and catheter-associated urinary tract infection (CAUTI) should be prevented. Ventilator-associated pneumonia (VAP) should be reduced through the use of early extubation and tracheostomy where appropriate. Routine ventricular catheter exchange and prophylactic antibiotic administration has not been demonstrated to reduce the risk of infection (2).

Routine Critical Care Management

Appropriate critical care management should be initiated in any patient with TBI. Gastrointestinal stress ulcer prophylaxis should be administered in patients using either an H₂-blocker or proton pump inhibitor (see "Stress Ulcer Prophylaxis" guideline). Deep venous thrombosis prophylaxis should be initiated once active cerebral hemorrhage has ceased using subcutaneous heparin 5000 IU q 8 hrs (see "Deep Venous Thrombosis Prophylaxis in the Critically Ill" guideline). Early enteral nutritional support should be initiated in all TBI patients to avoid the development of protein-calorie malnutrition (see "ICU Enteral Feeding Guidelines"). Patients should receive full-caloric replacement by day 7 post-injury. Skin breakdown and decubitus ulcer formation should be prevented through the use of appropriate pressure-reduction bed surfaces.

REFERENCES

The evidence based medicine guidelines referenced in the text above may be accessed at: www.surgicalcriticalcare.net/guidelines.

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Surgical Critical Care Evidence-Based Medicine Guidelines Committee

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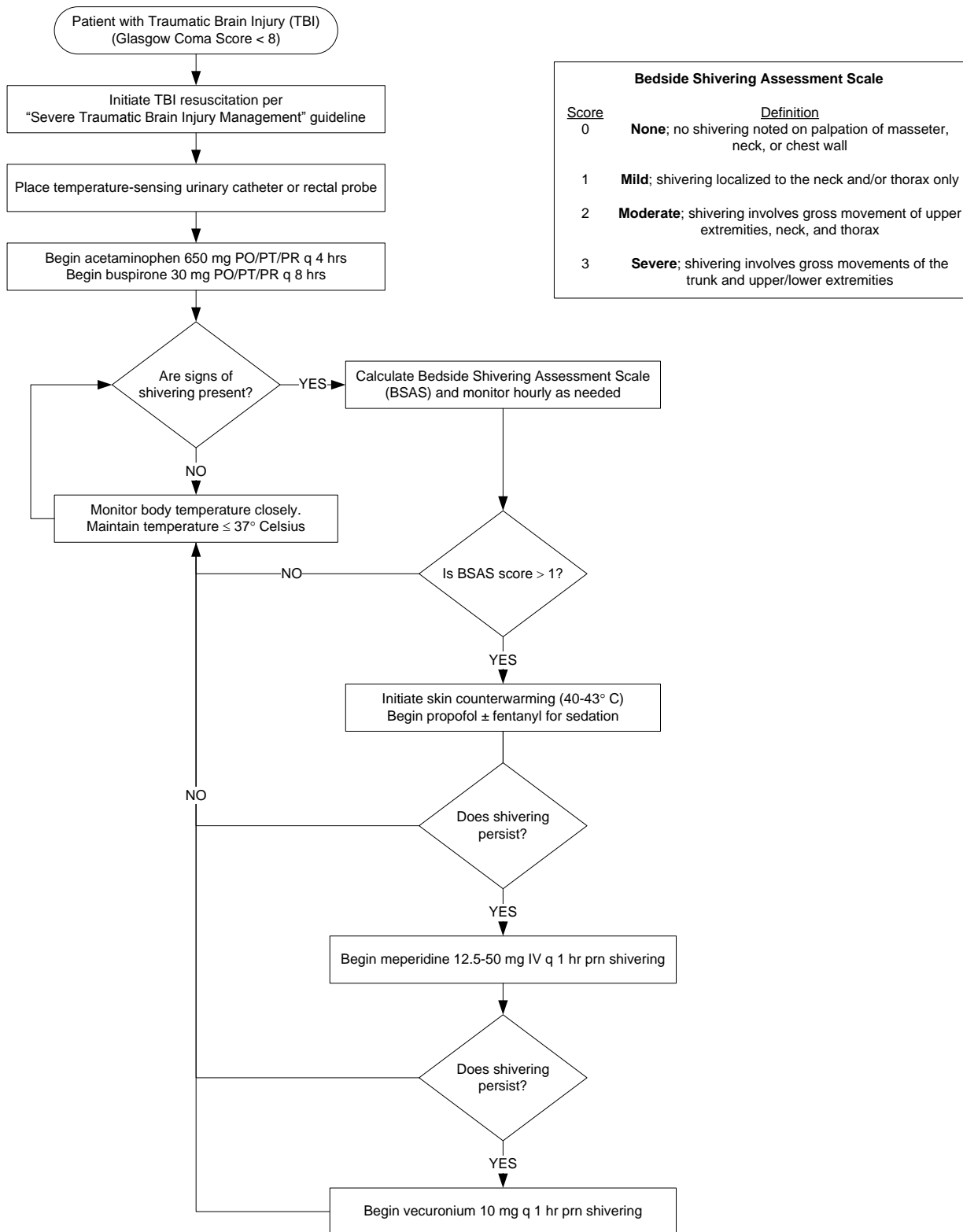
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APPENDIX 1: TRAUMATIC BRAIN INJURY – EMERGENCY DEPARTMENT CHECKLIST

The following interventions should be implemented in all patients with TBI who are awaiting transfer to definitive neurosurgical care:

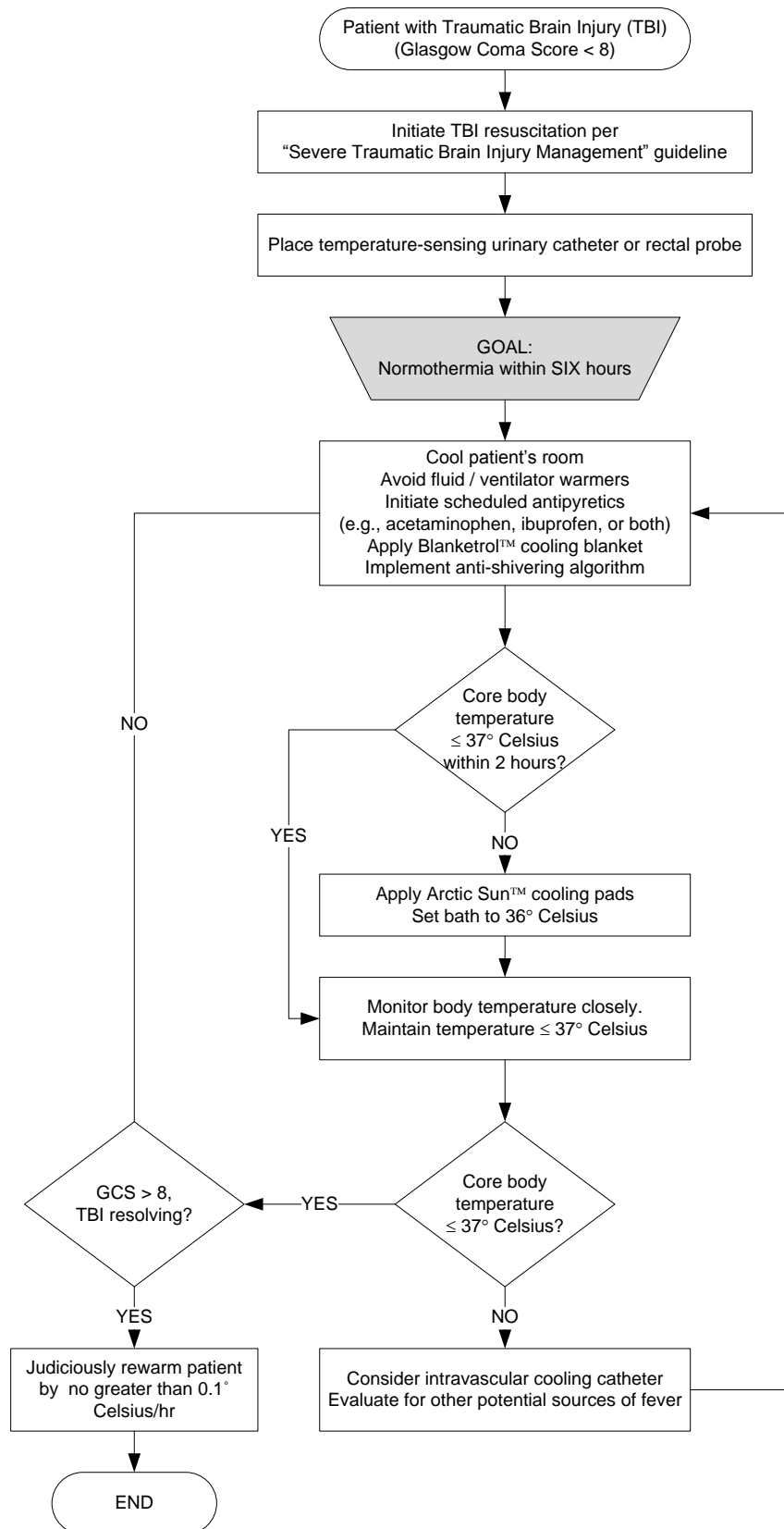
- ❑ Perform head CT scan to define extent of TBI
 - Do not delay transfer to obtain other radiographic studies
- ❑ Maintain mean arterial pressure (MAP) > 80 mmHg if GCS < 8; otherwise target MAP > 70 mmHg
- ❑ Administer supplemental oxygen to maintain SpO₂ > 92%
- ❑ Intubate patient if GCS < 8 and as needed to protect the airway
 - Maintain PaCO₂ 35-40 mmHg, PaO₂ 80-120 mmHg
- ❑ Elevate head of bed to 30 degrees (use Reverse Trendelenburg position if spine precautions)
- ❑ Maintain head in neutral position to avoid jugular vein constriction
- ❑ Administer isotonic intravenous fluids (no dextrose)
- ❑ Correct coagulopathy with Prothrombin Complex Concentrate (PCC) in life-threatening bleeds
 - FEIBA NF 1000 units IV push over 5 minutes
- ❑ Transfuse platelets in patients with known history of antiplatelet agent use
- ❑ Consider mannitol or hypertonic saline bolus if patient demonstrates blown pupil and imminent cerebral herniation
- ❑ Avoid:
 - Hypotension (MAP < 70 mmHg)
 - Hypoxemia (SpO₂ < 92%)
 - Hypercarbia (PaCO₂ > 45 mmHg)
 - Hyperglycemia (glucose > 180 mg/dL)
 - Hypovolemia
 - Fever (temperature > 37°Celsius)

APPENDIX 2: SHIVERING MANAGEMENT IN TBI PATIENTS (37)



Bedside Shivering Assessment Scale	
Score	Definition
0	None ; no shivering noted on palpation of masseter, neck, or chest wall
1	Mild ; shivering localized to the neck and/or thorax only
2	Moderate ; shivering involves gross movement of upper extremities, neck, and thorax
3	Severe ; shivering involves gross movements of the trunk and upper/lower extremities

APPENDIX 3: TARGETED TEMPERATURE MANAGEMENT IN TBI PATIENTS



APPENDIX 4: TROUBLESHOOTING EXTERNAL VENTRICULAR DRAINS

