TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Severe Traumatic Brain Injuries
Evidence-Based Guideline

Definition: A traumatic brain injury (TBI) is any injury to the head that leads to a disruption in the normal function of the brain. TBIs fall in a range of severity and are typically assessed through the use of the Glasgow Coma Scale (GCS). Mild TBI is defined by a GCS score of 13-15, moderate TBI by a GCS score of 8-12 and severe TBI by a GCS score of <8.[13]

Epidemiology: TBI is a leading cause of morbidity and mortality in children in the United States (CDC, 2018). In 2013 alone, there were approximately 640,000 emergency department visits, 18,000 hospitalizations, and 1,500 deaths related to TBI in children aged 14 years and younger.[53]

Etiology: TBI can be caused by any force or impact to a child's skull. Falls, being struck by or against an object, and motor vehicle accidents are the leading causes of TBI in children less than 14 years of age.[53] Due to the lack of currently available treatments specific to primary brain trauma, the main goal for TBI care is prevention of secondary injuries such as cerebral ischemia, cerebral hypoxia, and increased cerebral oxygen demand.[42] Achievement of this goal requires time-sensitive, coordinated, and goal-directed decision making between services in order to address rapidly changing organ systems.[42]

Inclusion Criteria
- Children with suspected severe TBI
- Glasgow Coma Scale (GCS) score ≤8 (post-resuscitation)
- Children 2 years-18 years of age

Exclusion Criteria
- Children <2 years of age
- Patients >18 years of age

Diagnostic Evaluation
History: Assess for
- Non-accidental trauma

Physical Examination:
- Thorough clinical assessment
- Fontanelles (if applicable)
- Pupil size and reactivity
- GCS score
- Neurological assessment
- Other areas of trauma (if applicable)

Laboratory Tests:
- Chemistry 10 Panel
- CBC with Platelets and Diff
- Type and Screen
- Electrolytes
- Nursing Glucose Point of Care (POC)
- Blood Osmolality
- Nursing Blood Gas POC
- Non Accidental Trauma Panel (if suspected)

Critical Points of Evidence*

TCH Evidence-Based Recommendations

Evidence Supports

- Place an intracranial pressure (ICP) monitor in children with severe traumatic brain injuries (TBI) and a post-resuscitation Glasgow Coma Scale (GCS) score of ≤8, as determined by a Neurosurgeon. [2,3,7,8,20,37,57] – Strong recommendation, very low quality evidence

  Remarks: Despite the lack of controlled evidence to support the use of ICP monitors in children with severe TBI, this recommendation places high value on maintaining ICP within the targeted threshold. Without the placement of ICP monitors the effectiveness of interventions aimed at lowering ICP are unknown, especially in children that are sedated and intubated. The team recognizes that the initial post-resuscitation GCS score can be affected by other variables (i.e. medications), therefore placement of an ICP monitor should be based on the Neurosurgeon's assessment and evaluation.
- Administer IV 3% hypertonic saline for the treatment of intracranial hypertension (ICH) in children with severe TBI and a post-resuscitation GCS score ≤8. [28,43,45,46,48,52] – Strong recommendation, very low quality evidence

  Administration: Begin first with an IV bolus dose of 3% hypertonic saline 2 mL/kg-5 mL/kg administered over 10-20 minutes. Subsequent doses may be administered PRN. [28]

  If IV bolus doses of 3% hypertonic saline are not effective in reducing intracranial hypertension, consider initiating a continuous IV infusion of 3% hypertonic saline 0.1-1.0 mL/kg/hour, administered on a sliding scale.

  The team recommends that the patient's serum sodium level be closely monitored while receiving 3% hypertonic saline.

  Remarks: For severe TBI patients in the Emergency Center (EC) with a strong clinical suspicion of ICH, the team recommends beginning 3% hypertonic saline IV administration (as outlined above) in the EC in order to reduce treatment delay.

  If 3% hypertonic saline is not available, the team recommends considering the use of IV mannitol for treatment of ICH.
- Avoid early, prophylactic moderate hypothermia (32°-33°C) with a goal of maintaining normothermia (36°-37°C) in children with severe TBI and a post-resuscitation GCS score of ≤8. [1,16,33,51,60] – Strong recommendation, moderate quality evidence

Remarks: If a patient is hypothermic (<36°C) when assessed by the Kangaroo Crew, upon Emergency Center (EC) arrival, or in the Pediatric Intensive Care Unit (ICU), initiate rewarming as soon as possible as outlined in the EC Resuscitation and Trauma Room Normothermia Guideline or PICU Targeted Temperature Management Protocol, depending on patient location.

- Place an external ventricular drain (EVD) in children with severe TBI and a post-resuscitation GCS score of ≤8, based on a Neurosurgeon's assessment of ventricle size and confidence in successfully placing an EVD. [9,19,25,29,32] – Strong recommendation, very low quality evidence
  Remarks: Decision to place an EVD should be made in conjunction with review of admission head CT (Nav/Stealth) of ventricle size.
  If unable to place an EVD, consider placement of an intraparenchymal ICP and brain oxygenation monitor to monitor ICP.
  Placement of dual, simultaneous EVD and intraparenchymal ICP monitors may be considered after discussion of the patient's status and anticipated needs with the Neurosurgery Attending.
  No more than 3 attempts to place an EVD per patient should be made.
- Consider the use of high dose barbiturate therapy in hemodynamically stable children with severe TBI (post-resuscitation GCS score ≤8) and refractory ICH despite maximal medical and/or surgical management (decompressive craniectomy). [21,34,35,48] – Weak recommendation, very low quality evidence
  Administration: PENTobarbital 5-10 mg/kg IV bolus dose (rate <50 mg/min) followed by 0.5-5 mg/kg/hr continuous IV infusion to achieve continuous electroencephalography (cEEG) burst suppression.
  Remarks: PENTobarbital is associated with respiratory depression, myocardial depression, hypotension, and low cardiac output and practitioners should be prepared to treat these complications.
  Patients who receive PENTobarbital administration should have cEEG and continuous hemodynamic monitoring initiated immediately, if not already in place.
  If cEEG monitoring is not possible, Train-of-Four monitoring should be used to monitor burst suppression.
  While receiving PENTobarbital, consider the use of vasoactive agents in order to maintain mean arterial pressure (MAP) and cerebral perfusion pressure (CPP) within therapeutic goal range.
- Consider decompressive craniectomy in children with severe TBI and a post-resuscitation GCS score of ≤8, who are showing early signs of neurologic deterioration or herniation or are developing ICH that is refractory to medical management. [15,21,23,27,41,44,54] – Weak recommendation, very low quality evidence
- Administer IV levETIRAcetam for antiseizure prophylaxis for children with severe TBI and a post-resuscitation GCS score of ≤8. If the patient is in status epilepticus, follow the Status Epilepticus Guideline.[12,14,24,26,28,31,40,50,58,59] – Strong recommendation, low quality evidence
  Administration: Administer an IV loading dose of levETIRAcetam 60 mg/kg in the EC (obtain a levETIRAcetam level two hours after administration of loading dose).
  Begin IV levETIRAcetam maintenance therapy within 12 hours of the initial loading dose at 15 mg/kg/DOSE every 12 hours.
  Remarks: If no evidence of electrographic/subclinical or clinical seizures is observed within 7 days of admission, discontinue antiseizure prophylaxis therapy.
  Currently, there is insufficient evidence to recommend levETIRAcetam over phenytoin based on either efficacy in preventing early post-traumatic seizures (PTS) or toxicity. [28]
- Utilize continuous electroencephalography (cEEG), upon admission to a PICU, for children with severe TBI and a post-resuscitation GCS score ≤8.). [4,39,55] – Strong recommendation, very low quality evidence
  Remarks: If a seizure lasting ≥5 minutes is observed (electrographic/subclinical or clinical), administer IV LORazepam 0.1 mg/kg (max dose: 4 mg), and notify Neurology and Neurosurgery immediately.
  If a seizure lasting <5 minutes is observed (electrographic/subclinical or clinical), consult Neurology and Neurosurgery immediately.
- Maintain a targeted core temperature of 36°C-37°C in children with severe TBI and a post-resuscitation GCS score of ≤8. [10,30] – Strong recommendation, very low quality evidence

Evidence Against

- Do not obtain a routine repeat computed tomography (RHCT) scan greater than 24 hours after the admission and initial follow-up study in the absence of neurologic deterioration or increasing ICP, in children with severe TBI and a post-resuscitation GCS score of ≤8. [5,6,22] – Strong recommendation, very low quality evidence

Evidence Lacking/Inconclusive

- In the context of multiple ICP-related therapies as well as the appropriate use of analgesia and sedation, avoid additional bolus administration of midazolam and/or fentanyl for ICP control due to the risks of cerebral hypoperfusion. Focus the use of analgesics and sedatives on adequate pain control and/or sedation for children with severe TBI and a post-resuscitation GCS score of ≤8. [28, 47,55] – Consensus recommendation
- Avoid prophylactic severe hyperventilation (to a $PaCO_2$ <30 mmHg) in children with severe TBI and a post-resuscitation GCS score of ≤8. – Consensus recommendation
- Do NOT administer corticosteroids in attempts to reduce ICP in children with severe TBI and a post-resuscitation GCS score of ≤8.– Consensus recommendation
- Do NOT consider the use of an immune-modulating diet as a treatment to improve outcomes in children with severe TBI and a post-resuscitation GCS score of ≤8. – Consensus recommendation
- Consider routine use of acetaminophen as adjunct therapy for targeted temperature management.-Consensus recommendation
  Remarks: PICU Targeted Temperature Management Protocol

Recommendations Adopted/Adapted from National Guidelines

- Treatment to maintain a cerebral perfusion pressure (CPP) at minimum of 40 mmHg is suggested. A CPP target between 40 and 50 mmHg is suggested to ensure that the minimum value of 40 mmHg is not breached. There may be age-specific thresholds with infants at the lower end and adolescents at or above the upper end of this range. (28)
  Remarks: This recommendation was adopted from the Brain Trauma Foundation: Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition.
- *Safety recommendation:* In the context of multiple ICP-related therapies, avoiding sustained (>72 hours) serum sodium >170 mEq/L is suggested to avoid complications of thrombocytopenia and anemia, whereas avoiding a sustained serum sodium >160 mEq/L is suggested to avoid the complication of deep vein thrombosis. (28)
  Remarks: This Safety recommendation was adopted from the Brain Trauma Foundation: Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition.
- Initiation of early enteral nutritional support (within 72 hours from injury) is suggested to decrease mortality and improve outcomes. (28)
  Remarks: This recommendation was adopted from the Brain Trauma Foundation: Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition
- If $PbrO_2$ monitoring is used, maintaining a level >10 mmHg is suggested. (28)
  Remarks: This recommendation was adopted from the Brain Trauma Foundation: Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition.

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

General:

Acute Emergency Center (EC) Management and Stabilization

- Complete Primary Survey per Advanced Trauma Life Support Guidelines.
- Assess initial GCS and pupil size and reactivity.
- Consider 3% hypertonic saline IV boluses/infusion for suspected intracranial hypertension 2.0 mL/kg-5.0 mL/kg administered over 10-20 minutes. Subsequent doses may be administered PRN.
  If IV bolus doses of 3% hypertonic saline are not effective in reducing intracranial hypertension, consider initiating a continuous IV infusion of 3% hypertonic saline 0.1-1.0 mL/kg/hour, administered on a sliding scale.
- Monitor the patient's serum sodium level closely while receiving 3% hypertonic saline.
- Begin antiseizure prophylaxis: Administer an IV loading dose of levETIRAcetam 60 mg/kg in the EC.

Acute Radiology Management

- STAT Head CT with Nav/Stealth feature

Neurointensive Care Unit Management

- Insert EVD or ICP and $PbtO_2$ monitor (can also occur in the EC or Operating Room).
- Ensure adequate vascular access, if not already present.
- Avoid hypotonic IV fluid.
- Ensure and maintain adequate sedation and analgesia for pain control.
- Initiate PICU Targeted Temperature Management Protocol.
- Initiate cEEG.
- Obtain a levETIRAcetam level two hours after administration of loading dose.
- Begin IV levETIRAcetam maintenance therapy within 12 hours of the initial loading dose at 15 mg/kg/DOSE every 12 hours.
- If a seizure lasting ≥5 minutes is observed (electrographic/subclinical or clinical), administer IV LORazepam 0.1 mg/kg (max dose: 4mg), and notify Neurology and Neurosurgery immediately.
- Maintain ICP <20 mmHg, CPP 40-50 mmHg (there may be age-specific thresholds with infants at the lower end and adolescents at or above the upper end of this range), Temperature: 36°-37°C, $PaCO_2$ 35-42 mmHg, Serum Glucose: 80-180 mg/dL, and Serum Na: 140-150 mEq/dL.

Consults/Referrals:

- Neurology
- Neuropsychology
- Physical Therapy/Occupational Therapy
- Physical Medicine and Rehabilitation
- Speech-Language Pathology
- Social Work
- Child Life

Follow-Up Care

- Traumatic Brain Injury Clinic within one month after discharge

Measures

Process

- Number of ICP monitors placed
- Number of specialty consults placed during the acute phase of care

Outcome

- Mortality
- Morbidity
- Glasgow Outcome Scale
- Number of early posttraumatic seizures

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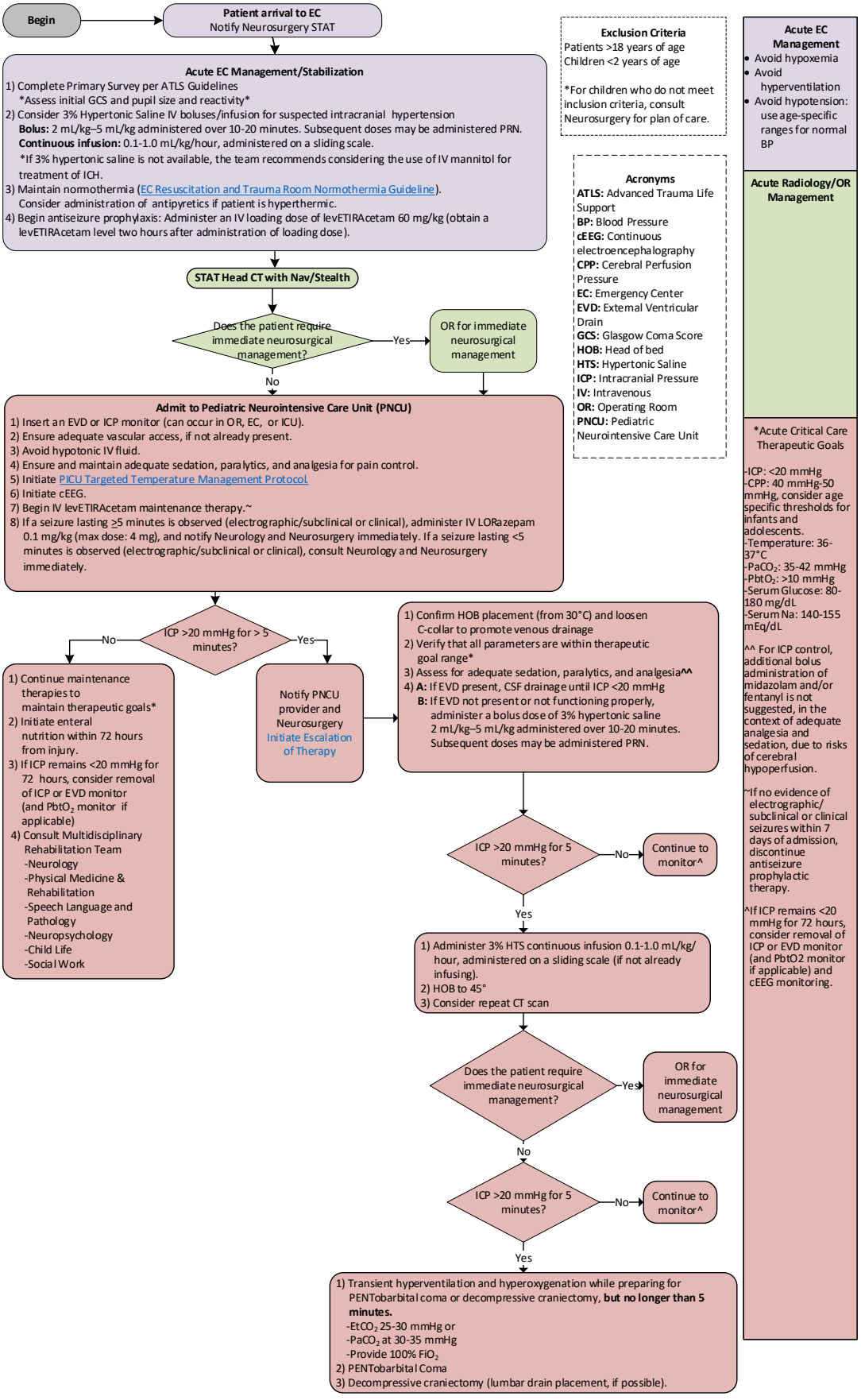
TCH Evidence-Based Outcomes Center
Clinical Algorithm for Severe Traumatic Brain Injuries-Initial Management



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Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts

2. Review of Existing External Guidelines
   - "ACR Appropriateness Criteria® head trauma-child"
   - Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents-third edition"
   -"Head injury: assessment and early management"
   -"Head injury. Triage, assessment, investigation and early management of head injury in children, young people and adults"
   -"Severe Traumatic Brain Injury (TBI) Clinical Pathway-Emergency, ICU, and Inpatient"
3. Literature Review of Relevant Evidence
   - Searched: PubMed, Cochrane, CINAHL
     *Re-affirmed May 2023 with no new literature search.

4. Critically Analyze the Evidence
   - 5 meta-analyses, 5 randomized controlled trials, and 45 nonrandomized studies

5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Severe Traumatic Brain Injuries evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.
"Evidence Supports" provides evidence to support an intervention
"Evidence Against" provides evidence against an intervention.
"Evidence Lacking/Inconclusive" indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence.*

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the management of Severe Traumatic Brain Injuries in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

Version History

Date	Comments
August 2018	Originally Completed
September 2019	The third edition of the Brain Trauma Foundation's Guidelines for the Management of Pediatric Severe Traumatic Brain Injury was reviewed. Recommendations were adopted and updated for the following areas: • Brain oxygenation monitoring • CPP thresholds • Hypertonic saline bolus dose range and safety recommendations • Avoidance of additional midazolam and/or fentanyl administration for ICP control in the context of appropriate analgesia and sedation • Initiation of enteral nutrition within 72 hours of injury
November 2020	Updated LevETIRAcetam dosing for maintenance therapy.
May 2023	Reaffirmed