



CRITICAL UPDATE ON THE THIRD EDITION OF THE GUIDELINES FOR MANAGING SEVERE TRAUMATIC BRAIN INJURY IN CHILDREN

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Background Severe traumatic brain injury (TBI) is associated with high rates of death and disability. As a result, the revised guidelines for the management of pediatric severe TBI address some of the previous gaps in pediatric TBI evidence and management strategies targeted to promote overall health outcomes.

Objectives To provide highlights of the most important updates featured in the third edition of the guidelines for the management of pediatric severe TBI. These highlights can help critical care providers apply the most current and appropriate therapies for children with severe TBI.

Methods and Results After a brief overview of the process behind identifying the evidence to support the third edition guidelines, both relevant and new recommendations from the guidelines are outlined to provide critical care providers with the most current management approaches needed for children with severe TBI. Recommendations for neuroimaging, hyperosmolar therapy, analgesics and sedatives, seizure prophylaxis, ventilation therapies, temperature control/hypothermia, nutrition, and corticosteroids are provided. In addition, the complete guideline document and its accompanying algorithm for recommended therapies are available electronically and are referenced within this article.

Conclusions The evidence base for treating pediatric TBI is increasing and provides the basis for high-quality care. This article provides critical care providers with a quick reference to the current evidence when caring for a child with a severe TBI. In addition, it provides direct access links to the comprehensive guideline document and algorithms developed to support critical care providers. (*American Journal of Critical Care*. 2020;29:e13-e18)

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Traumatic brain injury (TBI) is a major cause of mortality in the United States, accounting for 30% of all injury-related deaths.¹ In addition, the health care burden of TBIs continues to increase; about 2.8 million TBI-related emergency department visits, hospitalizations, and deaths occurred in the United States in 2013.¹ More specifically, approximately 56 800 TBI-related deaths occurred in 2014, including 2529 deaths of children.² Of those children living with moderate to severe TBI, more than 61% experience a disability.³

The use of intensive care management protocols focused on intracranial pressure (ICP) measurement and medical/surgical treatment of intracranial hypertension are critical to prevent secondary injury.⁴ Secondary injury results from a pathophysiological cascade of events that reduces perfusion of surviving neural tissue, oxygen and metabolite delivery, and clearance of metabolic waste and toxins, ultimately leading to intracranial hypertension, further focal ischemic injury, brainstem compression, and, if untreated, death.⁵⁻⁷

“Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation Guidelines,”⁸ published in *Pediatric Critical Care Medicine* in 2018, provides updated evidence-based recommendations applicable to the management of children with severe TBI

in the intensive care unit (ICU) and directly addresses some of the previous gaps in the pediatric TBI literature. As the number of children who arrive in the ICU with severe TBI continues to increase and because neurocritical care is provided in ICUs, it is vital that critical care providers be aware of the most current practice recommendations. Therefore, in this article, we describe the process behind the development of the third edition guidelines and focus on the highlighted

These updated guidelines provide the most up-to-date evidence-based practice recommendations for children with severe traumatic brain injury.

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new evidence and recommended best practice approaches for a child with a severe TBI.

Methods

The revision of the third edition of the guidelines for the management of pediatric severe TBI was approached in 2 phases (Figures 1 and 2): (1) the systematic review, which included the identification, assessment, and synthesis of literature, and (2) the use of that foundation to develop evidence-based recommendations. The key criteria for inclusion in the guidelines were (1) the study population included pediatric patients (≤ 18 years) with severe TBI (score of 3-8 on the Glasgow Coma Scale [GCS]) and (2) the study assessed for and included outcome data such as neurologic function, mortality, or appropriate intermediate targeted topic outcomes. All included studies were then assessed for potential bias and internal validity. Key data elements were then selected and placed into tables summarized by topic, each assigned a class (1-3) depending on the quality of the evidence (see Figure 1 for a description of the classes). The final phase of the evidence review was the synthesis, which is described for each topic in the third edition of the guidelines in the section titled, “Evaluation of the Evidence.”

Next, the quality of the body of evidence was assessed using the 4 domains described in Figure 1. The number of studies and number of study participants included were also considered when assessing the quality of the body of evidence. An overall assessment was then made as to whether the quality of the body of evidence was high, moderate, low, or insufficient. Finally, the applicability of studies is discussed for each topic in the guidelines found in the “Quality of the Body of Evidence” and “Applicability” sections.

Decisions to use identified evidence when formulating recommendations were based on both the quality and the applicability of the body of evidence. If no evidence was identified, no recommendations were formulated. If the identified evidence was extremely limited, it could be considered insufficient to formulate a recommendation. Even if a recommendation was not made, the studies contributing

evidence remained in the full guidelines to acknowledge their place in the body of evidence and to make the evidence accessible for possible future consideration. Recommendations were then designated as level I, II, or III (defined further in Figure 2).

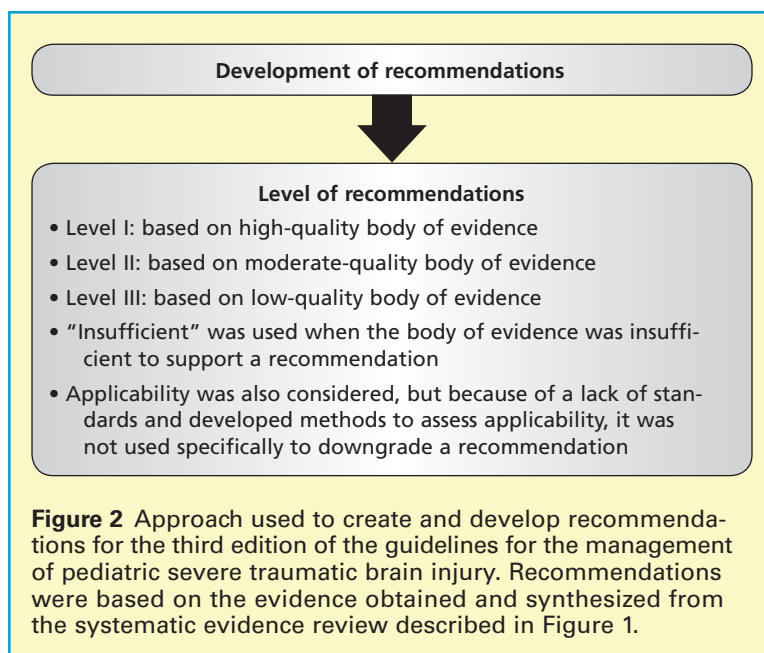
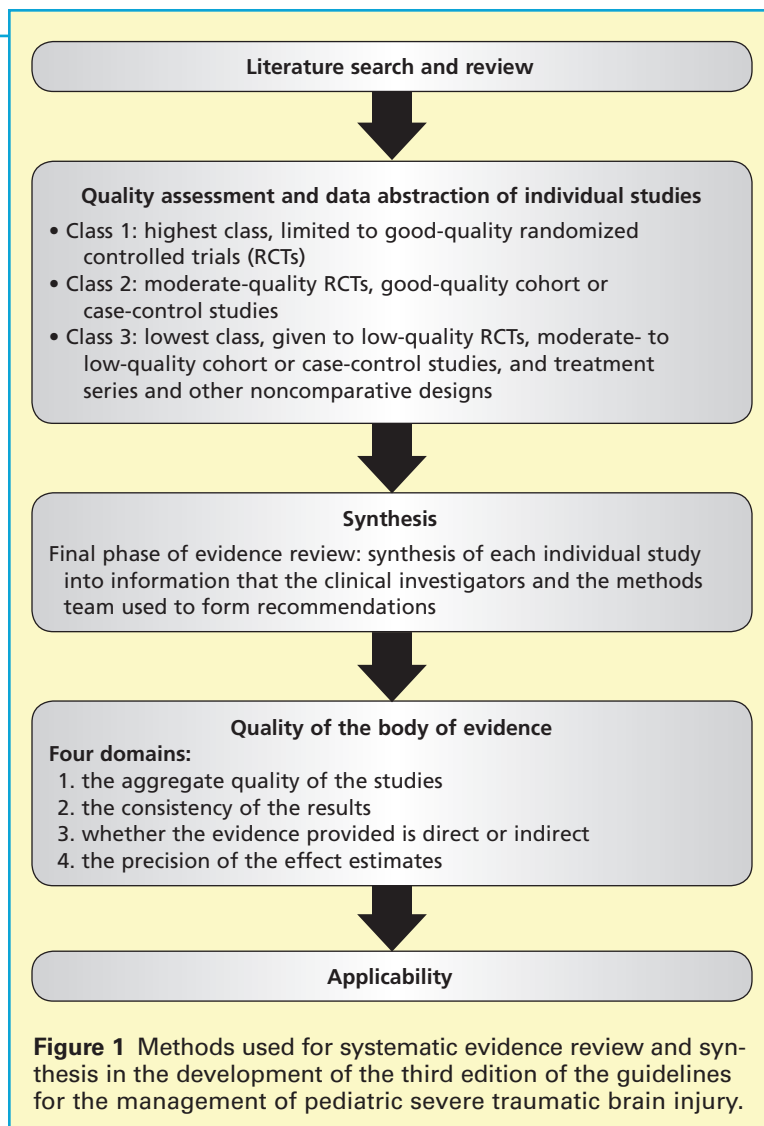
The guideline authors chose to include all topics found in the second edition of the guidelines and did not add any new topics. Major changes for the third edition are described within the guidelines' Appendix C. Supportive data that were included in the third edition are representative of the most current literature at the time of the guidelines' revision, and the rationale for replacing old data is explained within the guidelines' Appendix E. Likewise, recommendations were changed or removed from the second edition in instances where the current literature provided more accurate or newer information for the third edition.

Critical Update of an Evidence-Based Guideline on Pediatric Severe TBI

The third edition of the guidelines for the management of pediatric severe TBI aims to optimize and standardize evidence-based care of children with severe TBI with a methodologically, rigorously updated (2010-2017) systematic review that incorporated 48 new studies. The new and existing evidence resulted in 22 level II or III evidence-based recommendations. Eight new recommendations now support interventions for neuroimaging, hyperosmolar therapy, analgesics and sedatives, seizure prophylaxis, temperature control, and nutrition. The third edition of the guidelines provides recommendations on monitoring, thresholds, and treatments in children ages 0 to 18 years with TBI and GCS scores less than 9. Three primary end points are addressed: (1) outcomes including mortality, morbidity, and function; (2) control of ICP; and (3) prevention of posttraumatic seizures. The third edition of the guidelines is available for free and can be accessed at [3rd Edition Guidelines for the Management of Pediatric Severe TBI](#). An [executive summary](#) is also available in the journals *Neurosurgery* and *Pediatric Critical Care Medicine*. A companion algorithm was also developed to supplement the recommendations with expert consensus and organization of interventions and can be found at [Management of Pediatric Severe TBI: Guidelines-Based Algorithm](#).⁹

Provider Approach to and Recommendations for a Child With Severe TBI

Several new and relevant findings in the recommendations provided in the guidelines address the monitoring and treatment of children with severe



Table

Key clinical recommendations for critical care providers: summary of findings from the third edition of the guidelines for the management of pediatric severe traumatic brain injury

Monitoring

- Critical care providers should *not* routinely obtain a repeat computed tomography scan more than 24 hours after admission and initial follow-up unless there is evidence of increasing ICP or neurologic deterioration.

Treatment

- Critical care providers should administer a bolus of 3% hypertonic saline in patients with intracranial hypertension at a dose of 2 to 5 mL/kg over 10 to 20 minutes; for persistent intracranial hypertension, administer a continuous infusion of hypertonic saline at a dose of 0.1 to 1.0 mL/kg body weight per hour on a sliding scale.
- Critical care providers should *avoid* bolus administration of midazolam and/or fentanyl during intracranial pressure crises; avoid continuous infusion of propofol in the management of refractory intracranial hypertension or sedation.
- Critical care providers should use antiseizure prophylaxis to reduce the occurrence of early posttraumatic seizures within 7 days of injury.
- Critical care providers should *avoid* prophylactic severe hypoventilation as measured by a $Paco_2 < 30$ mm Hg in the first 48 hours after injury.
- Critical care providers should *avoid* prophylactic moderate (32°C-33°C) hypothermia to improve overall outcomes of pediatric patients with a severe TBI; however, moderate (32°C-33°C) hypothermia is recommended for ICP control.
- Critical care providers should initiate enteral feedings within 72 hours of injury. An immune-modulating diet is *not* recommended for pediatric patients with a severe TBI.
- Critical care providers should *avoid* use of corticosteroids to improve the outcome or reduce ICP in pediatric patients with a severe TBI.

Abbreviations: ICP, intracranial pressure; TBI, traumatic brain injury.

TBIs (see Table). The threshold recommendations from the previous edition did not change.¹⁰ The following sections highlight the relevant changes.

Monitoring Recommendations

The new guidelines do not recommend routinely repeating computed tomography (CT) scans, unless signs of neurologic deterioration or increasing ICP

are apparent.¹¹ Therefore, routine repetitive CT scans are not recommended to guide decisions in neurosurgical intervention, especially after the initial CT scan or more than 24 hours after admission. The new guidelines also suggest that the decision to insert and use any monitoring device for a child with severe TBI depends on understanding the data, information derived from the monitor, and how such data and information may permit targeted evidence-based care. Because indications

The guidelines include 8 new recommendations.

for intracranial hypertension remain limited or nonexistent, the guidelines recommend ICP monitoring. Detection of elevated ICP with monitoring allows for more timely delivery and accurate titration of treatment.^{4,12}

Treatment Recommendations

Hyperosmolar Therapy. Use of hypertonic saline (HTS) in children with severe TBI has been associated with lower ICP and reduced need for other interventions.¹³ Hypertonic saline administration has also been associated with a 2-fold faster resolution of intracranial hypertension when compared with a bolus dose of fentanyl or pentobarbital.¹⁴ Bolus HTS 3% is recommended in patients with acute intracranial hypertension, with a dose range of 2 to 5 mL/kg administered in 10 to 20 minutes. Continuous infusion of HTS is recommended for further treatment in patients with intracranial hypertension, with a continuous infusion of 3% saline ranging between 0.1 and 1.0 mL/kg of body weight per hour administered on a sliding scale with a titration goal to maintain ICP at less than 20 mm Hg. A bolus of 23.4% HTS is recommended for refractory ICP, with a suggested dose of 0.5 mL/kg and a maximum dose volume not to exceed 30 mL. Finally, avoiding sustained (>72 hours) serum sodium levels greater than 170 mEq/L is recommended to reduce complications of thrombocytopenia and anemia in the context of multiple ICP-related therapies. Furthermore, avoiding a sustained serum sodium level greater than 160 mEq/L is recommended to avoid the complication of deep vein thrombosis. Although mannitol is commonly used in the management of increased ICP in pediatric TBI, no new studies were identified as evidence for its use within the guidelines.

Analgesics, Sedatives, and Neuromuscular Blocking Agents. Analgesics and sedatives are necessary for comfort, tolerance, and when severe TBI requires rapid-sequence intubation and mechanical ventilation.¹⁵ Alternatively, the use of neuromuscular blocking agents is not routinely necessary, unless preparing for rapid-sequence intubation or when an acute lung injury interferes with optimal ventilation. The guidelines recommend that bolus administration of midazolam and/or fentanyl during ICP crises be avoided because of the risks of cerebral hypoperfusion, specifically when multiple ICP-related therapies are actively being used. No new recommendations for the use of ketamine for ICP control were described because of the lack of confidence in the evidence. No new evidence was found to support the use of continuous infusion of propofol for either the

management of refractory intracranial hypertension or sedation; therefore, it is not recommended.

Seizure Prophylaxis. Posttraumatic seizures (PTSs) are described as occurring early, within 7 days of injury, or late, beyond 8 days of recovery.¹⁶ Several risk factors are associated with the occurrence of PTSs, such as retained bone and metal fragments, depressed skull fracture, location of the lesion, loss of consciousness, GCS score greater than 10, and age. Lower seizure thresholds in infants and children make subtle clinical seizures more challenging to recognize, and therefore the use of continuous electroencephalography and antiseizure prophylaxis is recommended. Antiseizure prophylaxis reduces the occurrence of early PTSs within 7 days of injury.^{17,18} However, no evidence based on either efficacy in preventing early PTS or toxicity supports the use of levetiracetam versus phenytoin for antiseizure prophylaxis.

Ventilation Therapies. Airway protection and controlled mechanical ventilation and oxygenation are essential in the management of pediatric severe TBI.¹⁹ Reduced Paco_2 as a result of hyperventilation can decrease cerebral blood flow despite decreased ICP and increased cerebral perfusion pressure.²⁰ Prophylactic severe hyperventilation to a Paco_2 less than 30 mm Hg in the first 48 hours after injury is therefore not recommended. Furthermore, if hyperventilation is used in the management of refractory intracranial hypertension, advanced neuromonitoring for evaluation of cerebral ischemia is recommended.

Temperature Control/Hypothermia. Hyperthermia is associated with poorer outcomes and should be prevented in children with severe TBI.^{21,22} Therapeutic hypothermia has been used to limit secondary brain injury because of its role in decreasing inflammation, lipid peroxidation, cerebral metabolic demands, excitotoxicity, cell death, and acute seizures.^{23,24} However, the third edition of the guidelines reports ample published evidence to discourage the use of prophylactic moderate (32°C-33°C) hypothermia over normothermia to improve overall outcomes in children with severe TBI. Moderate (32°C-33°C) hypothermia is, however, recommended for ICP control.²⁵⁻²⁷ If moderate hypothermia is used and rewarming is initiated, it should be carried out at a rate of 0.5°C to 1.0°C every 12 to 24 hours or slower to avoid rewarming complications. Furthermore, if phenytoin is used during hypothermia, monitoring and dosing should be adjusted to minimize toxic effects, specifically during the rewarming period.

Nutrition. Traumatic brain injury causes an increase in metabolism, and thus increased caloric support is necessary for patients with TBI during the critical phase of injury. Children have additional nutritional needs for growth and development, so children with TBI may require an even greater relative increase in caloric support compared with adults who have TBI. For children with severe TBI, use of an immunomodulating diet is not suggested.²⁸ However, initiation of early enteral support (within 72 hours from time of injury) is recommended to decrease mortality and improve patients' outcomes. Posttraumatic hyperglycemia is associated with poorer outcomes for patients with severe TBI; however, the data are insufficient to recommend or discourage tight glucose control for children with severe TBI and persistent hyperglycemia. Tight glycemic control should be used cautiously with vigilant monitoring to prevent hypoglycemia in children with severe TBI.

Corticosteroids. The use of corticosteroids is not recommended to improve the outcome or reduce ICP in children with severe TBI.^{29,30} Corticosteroids are appropriate in patients with severe TBI with recognized adrenal suppression, with injury to the hypothalamic-pituitary axis, or those who have a history of requiring chronic steroid replacement therapy.

Conclusion

Critical care providers play a vital role in the recognition, management, and treatment of pediatric severe TBI. Beginning and maintaining the appropriate course of care throughout a patient's hospitalization can directly influence a patient's risk of morbidity and mortality. "Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation Guidelines" provides evidence for best practice in the care of pediatric patients with severe TBI to promote improved patient outcomes. Such best-practice interventions include administration of 3% hypertonic saline in patients with acute intracranial hypertension, providing antiseizure prophylaxis to reduce the occurrence of early posttraumatic seizures, and initiating early enteral support within 72 hours from time of injury to reduce morbidity and mortality. As the number of children with severe TBI continues to grow, much work still must be done to continue to develop

The guidelines provide the most current scientific evidence to improve outcomes in pediatric severe traumatic brain injury.

and advance evidence-based treatment to improve outcomes for children who sustain severe TBI.

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