Chapter 35
TBI in Pediatric Patients

Giselle Coelho and Eduardo Varjão Vieira

35.1 Historic/Epidemiology

Traumatic brain injury (TBI) is the leading cause of pediatric morbidity and mortality in the United States (US) and worldwide. In the United States, there are over 2 million cases of TBI per year, resulting in approximately 50,000 deaths [14, 19] and representing an important public health problem [13]. About 75% of all children hospitalized with trauma have a head injury [17].

The annual worldwide frequency of pediatric TBI is evaluated at 691 per 100,000 cases, with a noteworthy increment (60%) of emergency department (ED) visits from 1374.0 to 2193.8 per 100,000 from 2008 to 2010, respectively, in the United States [19, 38].

Severe TBI is a driving cause of mortality and disability in children. In the United States, it accounts for more than 2.8 million crisis office visits, more than 35,000 hospitalizations, and 2200 deaths per year [18, 39]. The estimated costs are colossal. Recently, the National Emergency Department Sample published an estimate of the initial hospital cost associated with TBI in the United States to be nearly $30 billion [34, 37].

It is important to emphasize that disability post-pediatric TBI is approximately 20%. Furthermore, different types of TBI are reported among different pediatric age groups. For example, in young infants, up to 30 per 100,000 babies under 1 year of age (average age 2–4 months) endure non-accidental injury (NAI) per year [29]. Considering patients 1–4 years of age, traumas result from falls, accounting for

G. Coelho (✉)
Department of Neurosurgery, Santa Marcelina Hospital, São Paulo, SP, Brazil

EDUCSIM Institute, São Paulo, SP, Brazil

E. V. Vieira
Department of Neurosurgery, Santa Marcelina Hospital, São Paulo, SP, Brazil

E. G. Figueiredo et al. (eds.), *Neurocritical Care for Neurosurgeons*,
https://doi.org/10.1007/978-3-030-66572-2_35

94–132 hospitalized children per 100,000. School-age children are more inclined to being hit by a car and to bicycle-related wounds. The secondary TBI in children reaches the highest peak during adolescence referring to motor vehicle accidents. Mortality rates for pediatric TBI range between 3.1 and 5.7 per 100,000 among different age groups between 0 and 14 years and dramatically increase to 24.3 per 100,000 in the 15–19 age group, according to the Centers for Disease Control and Prevention (CDC) [38, 41].

The pediatric traumatic brain injury (TBI) is remarkable, because the sequelae may extend beyond the evident physical impairment in the affected children to disrupt their psychosocial functioning. Damage may or may not resolve on the short term, often leaving them with long-term, deleterious deficits.

However, children may have very different outcomes when compared to adults, and the mechanism of injury may lead to completely different short-term and long-term results. In this context, it could be related to the concept of neuroplasticity, which is most prominent and active during time-sensitive periods of pre-natal and post-natal development [27, 38].

Aiming to standardize the medical care and therapeutic strategies, in 2003, the first *Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents* were published. Since then, the recommendations have been reexamined, and numerous studies have shown that guideline adherence is associated with reduced mortality and improved neurological outcome [22, 28, 34].

In general, the evidence resource used to write the guidelines consists of observational cohort studies and not randomized controlled trials. Therefore, there are some controversial questions in the management of TBI (especially in severe presentations), for example, the usefulness of the placement of an intracranial pressure (ICP) monitoring device and how to manage it and what are the most appropriate ICP therapies [34].

In this chapter, we discuss the main aspects of the TBI and its peculiar management in pediatric population.

35.2 Mechanisms of Injury

Interesting biomechanical and anatomical highlights of the growing cranium and brain lead to recognizing types of TBI in children compared to adults. Considering the proportion of head measure and weight to body between adults and children, it is possible to notice that the pediatric population is bigger than adults, which puts children's heads at higher risk of damage in any sort of trauma. Smaller cranium thickness and open sutures in newborn children allow more versatility and deformation, and then better absorption of the impact effects [11, 23].

Nevertheless, this could be considered unfavorable when combined with the fact that pediatric brains are less myelinated and contain a much bigger water content

compared to adults (89% versus 77%), which makes the pediatric brain more vulnerable to diffuse and shear damages [36, 38].

There are two principal phases of TBI. The first is the *primary injury* which involves the initial mechanical impact, resulting in loss of tissue and neuronal death. This primary injury cannot be repaired, and the damage is permanent.

The second phase is related to a *hyperexcitatory and inflammatory-mediated secondary injury* that occurs during the period of hours to days after the initial injury [43]. Consequently, there is a high blood-brain barrier (BBB) permeability and cerebral edema, resulting in rising intracranial pressure, potentially exacerbating cerebral ischemia [47].

The area of the brain surrounding the primary injury (penumbra) is susceptible to hypoxic events, and preservation of this region is one of the primary objectives in the management of TBI. For decades, secondary brain injury prevention has been the subject of significant research. Despite promising data from numerous preclinical researches, no therapy has improved outcomes in patients thus far.[31] Furthermore, we still have little corroboration about the effectiveness of every perspective of TBI management [13, 35].

The impact-loading mechanism occurs when the head is hit by a moving object or smashes into a stopped object, though impulsive-loading, moreover alluded to as "whiplash," happens when the head moves in reaction to fast movement of another body portion that is affected by an external action. After an impact-loading trauma, contusions, lacerations, and cranial fractures and coup-contrecoup brain damage (central and/or diffuse, parenchymal wounds, subarachnoid hemorrhage, etc.) are frequently observed [24].

The probabilities of injury types differ according to acceleration during an impulsive-loading trauma. Diffuse axonal injury (DAI) is related to coronal plane accelerations, while bridging veins damage and resultant subdural hematomas are more likely to occur in sagittal plane accelerations. The so-called shaken baby syndrome and DAI are representative sequelae of impulsive-loading trauma forced upon a weakly myelinated brain with less density [21, 38]. Once again, the differences between the pathophysiological responses to TBI in pediatrics compared to adults should be highlighted. Children tend to more frequently develop diffuse brain swelling [3] and early post-traumatic seizures after a moderate-to-severe TBI [5]. In addition, there is vulnerability to suffer consequences from low cerebral perfusion pressures, when compared to adults [15, 38].

35.3 Physical Examination/Image

Trauma victim care begins at accident stages. There is a consensus that the outcome for trauma patients is improved with a systematic initial evaluation from prehospital and hospital care teams. The primary assessment and the beginning of therapeutic approach to life-threatening injuries are described as ABCDE (Airway, Breathing,

Circulation, Disability, and Exposure). It is a mistake to initiate the approach of a patient with altered consciousness through neurological assessment. There are causes of coma that can be reversed following the steps of initial care, and it is not always associated with neurological problems. Secondary assessment begins after stabilization of the initial condition to search for other lesions that may endanger life or functionally affect the patient [6].

Children admitted to the emergency department and diagnosed with moderate and severe TBI should receive neurosurgical care. Neurosurgeons must obtain a complete history, sought characteristics of trauma mechanism, prior diseases, medications, and risk factors (i.e., seizures, otorrhagia, rhinorrhagia, unconsciousness, penetrating injury, nausea, vomiting, and headache). After obtaining history, it is important to detail neurological examination.

Neurological examination should begin by inspecting the child. Reactions or spontaneous interaction with the environment, general mobility, and posture will be evaluated. It is not possible to apply the techniques and maneuvers of adult neurological examination in children, particularly in neonates and infants. It is necessary to gain the child's confidence and through play and different maneuvers evaluate the different items of the neurological examination, which were not possible on simple inspection [42]. Pediatric facies, cranial bone, and scalp should be evaluated, searching for open or closed fractures, including signs of basilar skull fracture, and especially hematomas, and lacerations, because these can be cause of blood loss.

Despite some criticism, the Glasgow Coma Scale is still being used to report impairment of the level of consciousness and coma in traumatic injuries even in pediatric population, since some modifiers can be used to patients aged $\leq$2 years [12]. Neurological examination is a challenge in the unconscious child and should be direct to identify differences between focal and diffuse injuries. One of the important findings in infants is the presence of tense fontanelle that leads to intracranial hypertension suspicion. Other important findings are the clinical signs related to acute herniation of brain tissue. As transtentorial herniation progresses, the changes signs include pupillary changes and bradycardia. Foramen magnum herniation causes downbeat nystagmus, bradycardia, bradypnea, and hypertension. Clinical features of subfalcine herniation may be unilateral or bilateral weakness. Inappropriate motor responses such as decorticate or decerebrate rigidity reflect significant brainstem injury [33].

Head computed tomography enables quick detection of intracranial injury, signs of mass effect, and/or cerebral edema for pediatric patients with brain trauma [32]. This kind of image can affect therapeutic strategies, monitor effects of treatment, and evaluate progression or regression of some intracranial infections, although serial CT scans are controversial. Repeating CT scan can be useful when there is no evidence of neurological improvement despite medical and surgical treatment, neurologic deterioration, persistent or increasing intracranial pressure, or a condition that impedes neurologic status assessment, because of sedation or neuromuscular blockade. The adoption of scoring systems is useful to predict outcomes in patients

with severe trauma brain injury, including children. Higher Rotterdam head CT score rates are associated with greater mortality [16, 25, 32, 40], and the Marshall CT score has shown that scores 3 and 6 predict the most unfavorable outcomes [40].

35.4 Differential Diagnosis

Abusive head trauma is an important cause of severe brain injury. Although many of the clinical signs of accidental and abusive head injury are similar, the abusive mechanism should be investigated if suspected, because your diagnosis regards child protection [2].

35.5 Treatment Options

35.5.1 Severe Traumatic Brain Injury (sTBI)

Neurosurgeons have an important role in the TBI care process. The main goal is to recognize when acute herniation of brain tissue is imminent or ongoing to act as soon as possible. The latest released guideline for acute medical management of sTBI in children was published in 2019 [32]. In the following topics, monitoring, thresholds, and interventions are discussed.

35.6 General Recommendations

35.6.1 Ventilation

The cerebral circulation is controlled by homeostatic mechanisms, including partial pressure of carbon dioxide ($PaCO_2$), partial pressure of oxygen (PaO_2), cerebral autoregulation, metabolism, and blood viscosity. The sensitivity to changes in $PaCO_2$ makes it the most potent physiologic cerebral vasodilator [46]. Ventilation should be established in children who present deteriorating consciousness, respiratory failure, or decerebrate or decorticate posturing to decrease the incidence of brain impairment [45]. The settings for ventilation should be PaO_2 between 90 and 100 mmHg and $PaCO_2$ between 35 and 40 mmHg [33]. Prophylactic severe hyperventilation with $PaCO_2$ less than 30 mmHg in the initial 48 hours after injury is not suggested [32].

There is little data on the relationship between reversal of transtentorial herniation in children after TBI and the use of hyperventilation, although it is recommended as a component of the approach to the emergency treatment supported by

studies in adults. If hyperventilation is used in the management of refractory intracranial hypertension, advanced neuromonitoring for evaluation of cerebral ischemia may be necessary [32].

35.6.2 Blood Transfusion Therapy

Data suggests that children have higher oxygen consumption and a higher cardiac output to blood volume ratio than adults [9]. Cerebral blood flow rises as a result of improved rheology of the blood flow in cerebral vessel and as a compensatory reaction to decreased oxygen dispensation during anemia [46]. Although only a few studies of hemoglobin target have been published, evidence suggests a minimum hemoglobin target of 7.0 g/dl [33].

35.6.3 ICP Monitoring

Present data confirms that achieving adequately controlled ICP reduces mortality and is associated with better functional outcomes among children between 2 and 12 years with ICH [8]. However, there is not a specific recommendation for infants and children regarding CT and ICP monitoring after sTBI [32]. The presence of an open fontanel in infants does not preclude the development of intracranial hypertension and cerebral herniation [44], although the use of monitoring in children less than 2 years old has been less expected [32]. Importantly, in children younger than 5 years old with TBI, cerebral perfusion pressure (CPP) should be maintained greater than 40 mmHg, whereas in children between 6 and 17 years of age, a target greater than 50 mmHg is suitable [44].

35.6.4 Advanced Monitoring

As discussed earlier, the key issue of neurocritical care management of TBI patients is to optimize cerebral perfusion [33, 44]. Advanced neuromonitoring can improve overall outcomes [31]. Transcranial Doppler (TCD) may be performed within 72 hours of admission, and its frequency and duration will be guided by children clinical presentation and eventualities. It is useful for evaluation of cerebrovascular hemodynamics using measurements of intracranial cerebral arteries. Although there are no criteria for vasospasm for children, TCD appears to be a feasible method for CPP to predict response to medical treatment of intracranial hypertension [1, 32]. Sustaining a level of brain tissue oxygenation ($PbrO_2$) greater than 10 mmHg is

suggested when it is monitored. At this time, there is no strong evidence to support $PbrO_2$ monitoring, although its addition to other advanced neuromonitoring tools (i.e., microdialysis, examination of cerebral autoregulation, and electrophysiology assessments) is helpful to optimal critical care [32].

35.6.5 Hyperosmolar Therapy

Both mannitol and hypertonic saline (HTS) have been commonly used to manage raised intracranial hypertension. However, there is an absence of supportive mannitol clinical trials versus placebo, or other therapies in children. Bolus of 3% HTS has been recommended as hyperosmolar therapy in patients with intracranial hypertension. The dosing for acute use varies between 2 and 5 mL/kg over 10 and 20 minutes, and a continuous infusion of 0.1 and 1.0 mL/kg of body weight per hour can be used varying in accordance to minimum dose needed to maintain ICP less than 20 mmHg. Another option for hypertonic saline is bolus of 23.4% HTS for patients with existing hypervolemia. This has been shown to be effective for refractory ICP, and it can be delivered in a dosage of 0.5 mLkg with a maximum of 30 mL. The physiologic effect of higher serum sodium and serum osmolarity is to pull water from the intracellular and interstitial compartments of the brain, reducing cerebral edema [30]. However, the observation of a sustained high serum sodium greater than 160–170 mEq/L (>72 hour) may lead to complications like deep vein thrombosis, thrombocytopenia, and anemia, and it must be avoided [32].

35.6.6 Analgesics, Sedatives, and Neuromuscular Blocking

With the use of other interventions, the combination of benzodiazepine and opioid for sedative/analgesic therapy allows manipulation of ventilation, optimization of cerebral metabolic rate, cerebral blood flow, and intracranial pressure [20, 33]. Nevertheless, studies documented that bolus administration of midazolam and/or fentanyl during ICP rises has risks of cerebral hypoperfusion. Drugs and dosing should be chosen according to pediatrician experience and knowledge as there is absence of outcome data [32]. Nevertheless, long-term propofol use is not appropriate based on guidance from US Food and Drug Administration, because it may cause propofol infusion syndrome, presenting with lactic acidosis, cardiac dysfunction, and renal failure [20, 32]. Neuromuscular blockage has been demonstrated to achieve and maintain paralysis, and it can optimize patient-ventilator interactions and prevention of shivering, although at the expense of significant increased rates of respiratory tract infection, cardiovascular collapse, and myopathy [26].

35.6.7 CSF Drainage

Often, when ICP is increased, CSF drainage through an external ventricular drain can be used as a therapy. There are concerns regarding the potential for EVD to raise complications such as hemorrhage and infection [32].

35.6.8 Seizures Prophylaxis

A potential advantage of prophylactic treatment may be in decreasing early (within 7 days) post-traumatic seizure (PTS). Many risk factors have been shown to increase occurrence of PTS, including location of the lesion, cerebral contusions, retained bone and metal fragments, depressed skull fracture, focal neurologic deficits, loss of consciousness, GCS greater than 10, severity of injury, length of post-traumatic amnesia, subdural or epidural hematoma, penetrating injury, and age. There is a reduced seizure threshold in children, and it is especially challenging to recognize subtle clinical seizures. Thus, continuous electroencephalogram recording should be used, recognizing seizures occurrence in up to 70% of cases. There is no evidence that levetiracetam may be safe as an antiepileptic drug to use in TBI over phenytoin; therefore either is acceptable [32, 33].

35.6.9 Temperature Control/Hypothermia

Maintaining an adequate temperature between 35 °C and 38 °C after a traumatic brain injury is one of the goals to avoid secondary damage to the injured brain [32, 33]. Guidelines have used hypothermia as a treatment for ICP control, but its use in a prophylactic moderate way (32–33 °C) did not improve overall outcomes over normothermia. Moderate hypothermia therapy has been considered safe in children. It should be implemented at a rate of 0.5–1.0 °C every 12–24 hours or slower to avoid complications, and, if phenytoin is administered, monitoring and dosing have to be adjusted to minimize toxicity, particularly during the rewarming period [32].

35.6.10 Barbiturates

The suppression effects at cerebral circulation caused by high-dose barbiturates can be used if intracranial pressure is suboptimal after 4 hours dosing of osmotherapy and hyperventilation. Nevertheless, high-dose barbiturate therapy can cause hemodynamic instability, including decreased cardiac output, hypotension, and increased intrapulmonary shunt. Thus, barbiturates, particularly pentobarbital and thiopentone, are suggested in hemodynamically stable children, and consequently

vasopressors are commonly needed to maintain adequate CPP [32, 33]. The suggested dose for pentobarbital is a loading dosage of 10 mg/kg and a maintenance dose of 1 mg/kg/hr., aiming a burst suppression on electroencephalography. After 24 hours of reduced ICP, its infusion can be titrated and then withdrawn over 24–96 hours [33].

35.6.11 Decompressive Craniectomy

Decompressive craniectomy is used as a stand-alone procedure or associated with other surgical interventions such as hemorrhage evacuation to treat neurologic deterioration, strong suspicion of herniation, or intracranial hypertension (> 25 mmHg) refractory to optimal medical management [4, 32]. The surgical goal should be an anterior-to-posterior craniectomy diameter of at least 12 cm in children in a similar pattern to adults. There have been series showing that it is reasonable to adapt craniectomy size to age during infancy. However, a gain in a horizontal brain diameter of more than 1 cm might indicate serious brain herniation through the bone gap when an optimal hemicraniectomy is accomplished, associating with unfavorable outcome and long-term neuropsychological disturbances, similar to a post-traumatic pupillary dysfunction at admission [7, 10]. Autologous cranioplasty, even if complicated by bone flap resorption, is the chosen modality of cranial reconstruction, due to osteointegration, growing skull, and cost-effectiveness [10]. Although this can successfully decrease ICP, decompressive craniectomy is also associated with hygroma, hydrocephalus, and multiple types of infection (i.e., ventilator-associated pneumonia, bone flap sepsis).

35.6.12 Nutrition

Physiologically, in children, BTI increases metabolism, which requires caloric support during critical ill phase. Moreover, growing children have more nutritional needs for development. Because of this, early enteral nutritional support (within 72 hours from injury) is beneficial to reduce mortality and improve outcomes [32].

Pearls/Tips

- Considering the proportion of head measure and weight to body between adults and children, there are important population differences regarding cranioencephalic trauma and mechanisms of injury.
- Abusive head trauma should be recognized as a differential diagnosis in pediatric population.
- Autologous cranioplasty secondary to decompressive craniectomy should be chosen as the best option in children due to cranial growth pattern.

References

1. Abecasis F, Cardim D, Czosnyka M, Robba C, Agrawal S. Transcranial Doppler as a non-invasive method to estimate cerebral perfusion pressure in children with severe traumatic brain injury. Childs Nerv Syst. 2019; https://doi.org/10.1007/s00381-019-04273-2.
2. Adamsbaum C, Grabar S, Mejean N, Rey-Salmon C. Abusive head trauma: judicial admissions highlight violent and repetitive shaking. Pediatrics. 2010;126(3):546–55. https://doi.org/10.1542/peds.2009-3647. Epub 2010 Aug 9
3. Aldrich EF, Eisenberg HM, Saydjari C, Luerssen TG, Foulkes MA, Jane JA, et al. Diffuse brain swelling in severely head-injured children: a report from the NIH Traumatic Coma Data Bank. J Neurosurg. 1992;76:450–4.
4. Ardissino M, Tang A, Muttoni E, Tsang K. Decompressive craniectomy in paediatric traumatic brain injury: a systematic review of current evidence. Childs Nerv Syst. 2019;35(2):209–16. https://doi.org/10.1007/s00381-018-3977-5. Epub 2018 Sep 13
5. Arndt DH, Lerner JT, Matsumoto JH, Madikians A, Yudovin S, Valino H, et al. Subclinical early posttraumatic seizures detected by continuous EEG monitoring in a consecutive pediatric cohort. Epilepsia. 2013;54:1780–8.
6. ATLS Subcommittee; American College of Surgeons' Committee on Trauma; International ATLS working group. Advanced trauma life support (ATLS®): the ninth edition. J Trauma Acute Care Surg. 2013;74(5):1363–6. https://doi.org/10.1097/TA.0b013e31828b82f5.
7. Ballestero MFM, Furlanetti LL, Augusto LP, Chaves PHC, Santos MV, de Oliveira RS. Decompressive craniectomy for severe traumatic brain injury in children: analysis of long-term neuropsychological impairment and review of the literature. Childs Nerv Syst. 2019;35(9):1507–15. https://doi.org/10.1007/s00381-019-04274-1. Epub 2019 Jul 1
8. Banik S, Rath GP, Lamsal R, Sinha S, Bithal PK. Intracranial pressure monitoring in children with severe traumatic brain injury: a retrospective study. J Pediatr Neurosci. 2019;14(1):7–15. https://doi.org/10.4103/jpn.JPN_18_19.
9. Barcelona SL, Thompson AA, Coté CJ. Intraoperative pediatric blood transfusion therapy: a review of common issues. Part I: hematologic and physiologic differences from adults; metabolic and infectious risks. Paediatr Anaesth. 2005;15(9):716–26.
10. Beez T, Munoz-Bendix C, Ahmadi SA, Steiger HJ, Beseoglu K. From decompressive craniectomy to cranioplasty and beyond-a pediatric neurosurgery perspective. Childs Nerv Syst. 2019;35(9):1517–24. https://doi.org/10.1007/s00381-019-04303-z. Epub 2019 Jul 20
11. Bernardi B, Zimmerman RA, Bilaniuk LT. Neuroradiologic evaluation of pediatric craniocerebral trauma. Topics Magnetic Res Imag TMRI. 1993;5:161–73.
12. Borgialli DA, Mahajan P, Hoyle JD Jr, Powell EC, Nadel FM, Tunik MG, Foerster A, Dong L, Miskin M, Dayan PS, Holmes JF, Kuppermann N, Pediatric Emergency Care Applied Research Network (PECARN). Performance of the pediatric Glasgow coma scale score in the evaluation of children with blunt head trauma. Acad Emerg Med. 2016;23(8):878–84. https://doi.org/10.1111/acem.13014. Epub 2016 Aug 1.
13. Caplan HW, Cox CS. Resuscitation strategies for traumatic brain injury. Curr Surg Rep. 2019 Jul; 7(7): 14. Published online 2019 May 15. doi: https://doi.org/10.1007/s40137-019-0237-x.
14. Centers for Disease Control and Prevention. Report to congress on traumatic brain injury in the United States: epidemiology and rehabilitation. Atlanta: National Center for Injury Prevention and Control; Division of Unintentional Injury Prevention; 2015.
15. Chambers I, Stobbart L, Jones P, Kirkham F, Marsh M, Mendelow A, et al. Age-related differences in intracranial pressure and cerebral perfusion pressure in the first 6 hours of monitoring after children's head injury: association with outcome. Childs Nerv Syst. 2005;21:195–9.
16. Charry JD, Navarro-Parra S, Solano J, Moscote-Salazar L. Outcomes of traumatic brain injury: the prognostic accuracy of various scores and models. Neurol Neurochir Pol. 2019;53(1):55–60. https://doi.org/10.5603/PJNNS.a2018.0003. Epub 2019 Feb 11
17. Coulter IC, Forsyth RJ. Paediatric traumatic brain injury. Curr Opin Pediatr. 2019;31(6):769–74. https://doi.org/10.1097/MOP.0000000000000820.

18. DelSignore LA, Tasker RC. Treatment options for severe traumatic brain injuries in children: current therapies, challenges, and future prospects. Expert Rev Neurother. 2017;17:1145e1155.
19. Faul M, Xu L, Wald MM, Coronado V. Traumatic brain injury in the United States. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control: Atlanta; 2010.
20. Flower O, Hellings S. Sedation in traumatic brain injury. Emerg Med Int. 2012;2012:637171. https://doi.org/10.1155/2012/637171.
21. Gennarelli TA, Thibault LE, Adams JH, Graham DI, Thompson CJ, Marcincin RP. Diffuse axonal injury and traumatic coma in the primate. Ann Neurol. 1982;12:564–74.
22. Gerber LM, Chiu YL, Carney N, Hartl R, Ghajar J. Marked reduction in mortality in patients with severe traumatic brain injury. J Neurosurg. 2013;119:1583e1590.
23. Ghajar J, Hariri RJ. Management of pediatric head injury. Pediatr Clin N Am. 1992;39:1093–125.
24. Goldsmith W, Plunkett J. A biomechanical analysis of the causes of traumatic brain injury in infants and children. Am J Forensic Med Pathol. 2004;25:89–100.
25. Hale AT, Stonko DP, Brown A, Lim J, Voce DJ, Gannon SR, Le TM, Shannon CN. Machine-learning analysis outperforms conventional statistical models and CT classification systems in predicting 6-month outcomes in pediatric patients sustaining traumatic brain injury. Neurosurg Focus. 2018;45(5):E2. https://doi.org/10.3171/2018.8.FOCUS17773.
26. Hsiang JK, Chesnut RM, Crisp CB, Klauber MR, Blunt BA, Marshall LF. Early, routine paralysis for intracranial pressure control in severe head injury: is it necessary? Crit Care Med. 1994;22(9):1471–6.
27. Ismail FY, Fatemi A, Johnston MV. Cerebral plasticity: windows of opportunity in the developing brain. Eur J Paedatric Neurol. 2017;21:23–48.
28. Kannan N, Wang J, Mink RB, et al. Timely hemodynamic resuscitation and outcomes in severe pediatric traumatic brain injury: preliminary findings. Pediatr Emerg Care. 2018;34:325e329.
29. Keenan HT, Runyan DK, Marshall SW, Nocera MA, Merten DF, Sinal SH. A population-based study of inflicted traumatic brain injury in young children. JAMA. 2003;290:621–6.
30. Khanna S, Davis D, Peterson B, Fisher B, Tung H, O'Quigley J, Deutsch R. Use of hypertonic saline in the treatment of severe refractory posttraumatic intracranial hypertension in pediatric traumatic brain injury. Crit Care Med. 2000;28(4):1144–51.
31. Kochanek PM, Dixon CE, Mondello S, Wang KKK, Lafrenaye A, Bramlett HM, et al. Multicenter pre-clinical consortia to enhance translation of therapies and biomarkers for traumatic brain injury: operation brain trauma therapy and beyond. Front Neurol. 2018;9:640. https://doi.org/10.3389/fneur.2018.00640.
32. Kochanek PM, Tasker RC, Carney N, Totten AM, Adelson PD, Selden NR, Davis-O'Reilly C, Hart EL, Bell MJ, Bratton SL, Grant GA, Kissoon N, Reuter-Rice KE, Vavilala MS, Wainwright MS. Guidelines for the management of pediatric severe traumatic brain injury, third edition: update of the brain trauma foundation guidelines. Neurosurgery. 2019;84(6):1169–78. https://doi.org/10.1093/neuros/nyz051.
33. Kochanek PM, Tasker RC, Bell MJ, Adelson PD, Carney N, Vavilala MS, Selden NR, Bratton SL, Grant GA, Kissoon N, Reuter-Rice KE, Wainwright MS. Management of pediatric severe traumatic brain injury: 2019 consensus and guidelines-based algorithm for first and second tier therapies. Pediatr Crit Care Med. 2019;20(3):269–79. https://doi.org/10.1097/PCC.0000000000001737.
34. Lovett ME, O'Brien NF, Leonard JR. Children with severe traumatic brain injury, intracranial pressure, cerebral perfusion pressure, what does it mean? A review of the literature. Pediatr Neurol. 2019;94:3–20. https://doi.org/10.1016/j.pediatrneurol.2018.12.003. Epub 2019 Jan 11
35. Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol. 2017;16(12):987–1048. https://doi.org/10.1016/s1474-4422(17)30371-x.
36. Margulies SS, Thibault KL. Infant skull and suture properties: measurements and implications for mechanisms of pediatric brain injury. J Biomech Eng. 2000;122:364–71.

37. Marin JR, Weaver MD, Mannix RC. Burden of USA hospital charges for traumatic brain injury. Brain Inj. 2017;31:24e31.
38. Noureldine HA, Shimony N, Gassie K, Jallo GI. Chapter 6. Paediatric brain: injury susceptibility and plasticity. In: Narenthiran G, editor. Neurosurgery, vol. 1. London: Neurosurgery Listserv Press; 2019.
39. O'Brien NF, Maa T, Reuter-Rice K. Noninvasive screening for intracranial hypertension in children with acute, severe traumatic brain injury. J Neurosurg Pediatr. 2015;16:420e425.
40. Pargaonkar R, Kumar V, Menon G, Hegde A. Comparative study of computed tomographic scoring systems and predictors of early mortality in severe traumatic brain injury. J Clin Neurosci. 2019;66:100–6. https://doi.org/10.1016/j.jocn.2019.05.011. Epub 2019 May 15
41. Pinto PS, Poretti A, Meoded A, Tekes A, Huisman TA. The unique features of traumatic brain injury in children. Review of the characteristics of the pediatric skull and brain, mechanisms of trauma, patterns of injury, complications and their imaging findings— part 1. J Neuroimaging. 2012;22:e1–e17.
42. Rosemberg, Sergio. Neuropediatria Sergio Rosemberg. — 2. ed. — Sao Paulo: SARVIER, 2010.
43. Simon DW, McGeachy MJ, Bayir H, Clark RS, Loane DJ, Kochanek PM. The far-reaching scope of neuroinflammation after traumatic brain injury. Nat Rev Neurol. 2017;13(3):171–91. https://doi.org/10.1038/nrneurol.2017.13.
44. Stevens RD, Shoykhet M, Cadena R. Emergency neurological life support: intracranial hypertension and herniation. Neurocrit Care. 2015;23(Suppl 2):S76–82. https://doi.org/10.1007/s12028-015-0168-z.
45. Taylor A, Butt W, Rosenfeld J, Shann F, Ditchfield M, Lewis E, Klug G, Wallace D, Henning R, Tibballs J. A randomized trial of very early decompressive craniectomy in children with traumatic brain injury and sustained intracranial hypertension. Childs Nerv Syst. 2001;17(3):154–62.
46. Udomphorn Y, Armstead WM, Vavilala MS. Cerebral blood flow and autoregulation after pediatric traumatic brain injury. Pediatr Neurol. 2008;38(4):225–34. https://doi.org/10.1016/j.pediatrneurol.2007.09.012.
47. Unterberg AW, Stover J, Kress B, Kiening KL. Edema and brain trauma. Neuroscience. 2004;129(4):1021–9. https://doi.org/10.1016/j.neuroscience.2004.06.046.