An estimated 1 in 10 (5.3 million) of the 54 million Americans living with disabilities have a disability caused by TBI (www.hhs.gov). Approximately 475,000 TBIs occur among children ages 0–14 years old every year in the US (www.cdc.gov), and the current leading cause of death in children more than 1 year old is TBI. Different pediatric age groups experience different causes for their injury. In infants, the most common causes are falls and physical assaults. In toddlers and young children, car accidents and falls are most common. In children and teenagers, car accidents and sports are the most common causes.50

Proper management and care of pediatric patients is therefore crucial to improve functional outcome in this population. Adequate management and care of pediatric patients is critical to ensure the best functional outcome in this population. In their controversial trial, Cooper et al. concluded that decompressive craniectomy following TBI did not improve clinical outcome of the analyzed adult population. While the study did not target pediatric populations, the results do raise important and timely clinical questions regarding the effectiveness of decompressive surgery in pediatric patients. There is still a paucity of evidence regarding the effectiveness of this therapy in a pediatric population, and there is an especially noticeable knowledge gap surrounding age-stratified interventions in pediatric trauma. The purposes of this review are to first explore the anatomical variations between pediatric and adult populations in the setting of TBI. Second, the authors assess how these differences between adult and pediatric populations could translate into differences in the impact of decompressive surgery following TBI. (DOI: 10.3171/2011.8.FOCUS11177)

**Key Words**  • clinical trial  • pediatric  • traumatic brain injury  • decompressive surgery

Traumatic brain injury (TBI) is the current leading cause of death in children over 1 year of age. The study did not explicitly target pediatric populations; however, the results of the study do raise important and timely clinical questions regarding the effectiveness of decompressive surgery in pediatric patients. There is still a paucity of evidence regarding the effectiveness of this therapy in this population, and there is an especially noticeable knowledge gap surrounding age-stratified interventions in pediatric trauma.

We have several goals in this review. First, we explore the anatomical variations between pediatric and adult populations in the setting of TBI. Second, the authors assess how these differences between adult and pediatric populations could translate into differences in the impact of decompressive surgery following TBI by analyzing current knowledge on the utilization of craniectomy as a treatment in these different populations.

**Physiology**

Pediatric populations represent an important but often under-defined population in the literature investigating TBI. Many adult trials of decompressive craniectomy following TBI include patients as young as 10 or 15 years old in their protocols,16,26 demonstrating a failure to dis-
tistinguishing between adult and pediatric populations. However, significant physiological, anatomical, and pathological differences exist between the ages of birth and adulthood, resulting in the need for clear definitions in patient populations. For the purposes of this review, the pediatric population includes children from the moment of birth until 18 years of age.

Damage following TBI is the result of primary and secondary injuries on the brain. Primary injury is largely due to shearing forces between brain tissue of different densities, specifically between skull and dura mater, dura mater and gray matter, and white matter and gray matter.12 Secondary physiological injury, however, is also responsible for a large amount of morbidity and death. Secondary injury can result from impaired cerebral blood flow, regional edema, hemorrhage, elevated ICP and therefore reduced CPP, dysfunction of ion pumps, excessive release of neurotransmitters, cascade of cellular destruction via reactive oxygen species, proteolysis, and inflammation.38 These processes can often lead to ischemia, infarct, and necrosis.

Intracranial pressure is one of the most important brain physiological variables, especially following TBI.21,25,30,42 Control of ICP is therefore crucial in preventing secondary injury. Healthy adults normally maintain ICP values below 20–25 mm Hg, although this exact threshold is not clear in any age group.10

Anatomy

There are multiple anatomical mechanisms for injury to the brain. In both pediatric and adult populations, the brain is cushioned by a surrounding layer of CSF and infused by layers of vessels that provide structural and nutritional support. The brain is protected further by layers of pia, arachnoid, and dura mater, surrounded by a bony skull. In young children, the skull has not yet calcified completely and is less capable of distributing pressure. By adulthood, the skull has hardened into a sandwich of cortical bone around a spongy diploë and can resist impact fracture at 11 times the force strength of neonates.36 Anatomical and mechanical variations between adults and children explain some of the differences between the 2 age groups for severity of and response to TBI. Children have smaller brains than adults, and researchers have demonstrated in chimpanzee models that upon subjection to whiplash, smaller brains are less vulnerable than larger brains to the same amount of angular acceleration inducing injury.39 Relative to their body and compared with adults, however, children have large and heavy heads with weaker cervical neck muscles, which allows for a more forceful impact and a more severe injury. In young children, the skull is more pliable and incapable of withstanding bending loads. Cranial sutures are not yet fused, and upon impact, the soft skull deforms into the brain. More severe trauma is associated with plastic deformation and cracking of the skull.38

Differences in TBI Within the Pediatric Population

Many elements influence outcome following TBI, including patient age, impact severity, physiological variables, anatomical variations, and especially control of ICP. Although not definitively proven, children are believed to have stratified values of normal ICP based on their age. Infants maintain ICP of 2–4 mm Hg, while older children typically maintain their normal ICP range between 5 and 15 mm Hg. These values of ICP correlate with CPP guidelines implemented in 1997, whereby adequate CPP per age group is defined as ≥ 30 (neonate), ≥ 40 (1 month to 1 year), ≥ 50 (1–4 years), ≥ 60 (5–8 years), and ≥ 70 mm Hg (> 8 years).11,48 (Table 1). However, a more recent clinical trial has noted lower values for critical minimum CPP, with values of 48, 54, and 64 mm Hg for children ages 2–6, 7–10, and 11–15, respectively (Table 1).13 The thresholds for ICP hypertension in children requiring treatment are generally considered to be lower than in adults, with the threshold in infants approximately 15 mm Hg and in young children between 15 and 20 mm Hg.7 Several clinical studies support these age-stratified values in pediatrics, noting that neurological outcome is improved when medical treatments targeted at maintaining ICP below 20 mm Hg are used.20,46

Recent studies, both clinical and basic science, show variation in clinical outcome following TBI between children and adults (Table 2). Worse outcomes might be predicted in pediatrics because children have a higher incidence of edema following TBI and a reduced antioxidative capacity compared with adults.6,38 Also, children experience a higher incidence of hypotensive episodes following TBI, which decreases CPP.8 Finally, the young brain normally receives a higher percentage of cardiac output compared with the adult brain, and children are therefore at higher risk for ischemia following TBI due to their dependence on a higher perfusion rate.45,55 Recent evidence has shown that older teens generally demonstrate better outcomes than younger children, perhaps due to greater vulnerability among younger children to more severe physical injury.3,4,28,32 Despite these factors, however, children overall tend to have better clinical outcomes following TBI than adults.3,4,28

To investigate the reasons for such differences in outcomes, many animal models have been used to compare young versus old age and TBI. Studies have examined the role of biomechanics,35 metabolism,49 cell death,4,25 electrophysiology,7,44 and glutamatergic neurotransmission23,24 as possible mechanisms to explain the improved clinical outcome in pediatric compared with adult patients. An additional mechanism by which immature brain tissue may recover better following TBI is due to the presence of low levels of chondroitin sulfite proteoglycan glycoproteins compared with adult tissue. This important matrix component provides rigidity and support to the brain parenchyma, and lower levels of the glycoprotein are associated with increased plasticity. This lower level may be 1 mechanism by which the developing brain can maintain plasticity and rapidly remodel following injury.5,41,51

Surgical Interventions for TBI in the Pediatric Population

Because ICP following TBI is widely regarded as an
Traumatic brain injury and decompressive surgery in pediatrics

TABLE 1: Comparison of 2 different clinical measures of minimum adequate CPP

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Age</th>
<th>Adequate CPP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bullock et al., 1996</td>
<td>neonate</td>
<td>≥ 30</td>
</tr>
<tr>
<td></td>
<td>1 month–1 yr</td>
<td>≥ 40</td>
</tr>
<tr>
<td></td>
<td>1–4 yrs</td>
<td>≥ 50</td>
</tr>
<tr>
<td></td>
<td>5–8 yrs</td>
<td>≥ 60</td>
</tr>
<tr>
<td></td>
<td>&gt;8 yrs</td>
<td>≥ 70</td>
</tr>
<tr>
<td>Chambers et al., 2006</td>
<td>2–6 yrs</td>
<td>&gt; 48</td>
</tr>
<tr>
<td></td>
<td>7–10 yrs</td>
<td>&gt; 54</td>
</tr>
<tr>
<td></td>
<td>11–15 yrs</td>
<td>&gt; 60</td>
</tr>
</tbody>
</table>

TABLE 2: Comparison of prognostic factors following TBI between children and adults

<table>
<thead>
<tr>
<th>Prognosticator</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>edema</td>
<td>higher incidence</td>
<td>lower incidence</td>
</tr>
<tr>
<td>antioxidative capacity</td>
<td>lesser</td>
<td>greater</td>
</tr>
<tr>
<td>hypotensive episodes</td>
<td>higher incidence</td>
<td>lesser incidence</td>
</tr>
<tr>
<td>% of cardiac output</td>
<td>higher</td>
<td>lesser</td>
</tr>
<tr>
<td>age stratification</td>
<td>younger children</td>
<td>more vulnerable to severe injury</td>
</tr>
<tr>
<td>age stratification</td>
<td>younger adults</td>
<td>more favorable outcome</td>
</tr>
<tr>
<td>basement membrane glycoproteins</td>
<td>lower levels of chondroitin sulfate</td>
<td>higher levels of chondroitin sulfate</td>
</tr>
<tr>
<td>physiological variables examined in animals</td>
<td>death, metabolism, electrophysiology, glutamatergic neurotransmission</td>
<td>death, metabolism, electrophysiology, glutamatergic neurotransmission</td>
</tr>
</tbody>
</table>

important physiological determinant of brain function and clinical outcome.\textsuperscript{21,25,30,42} many approaches have been developed to control ICP. However, despite the existence of guidelines for management following TBI, there is a lack of data surrounding specific interventions, especially in pediatric populations. Most guidelines focus on ICP control as a means to maintain adequate CPP.\textsuperscript{34} Current medical treatments to reduce ICP include hyperosmolar therapy (such as mannitol or hypertonic saline),\textsuperscript{53} hyper-ventilation\textsuperscript{15,47} sedation and paralytics, and head of bed elevation. In addition, barbiturate-induced coma\textsuperscript{2} and hypothermia\textsuperscript{19} have been shown to reduce cerebral metabolic rate and oxygen demands, offering a protective role.\textsuperscript{2} If medical treatment is ineffective in normalizing ICP, several types of surgical intervention are possible. Surgical methods used include hematoma evacuation, ventricular drains, and craniectomy. Hematoma evacuation is indicated in the setting of a hemorrhagic mass lesion, while a ventricular drain is used in the setting of hydrocephalus or when CSF drainage is desired. The third method, craniectomy, is the subject of many current clinical trials. The overall goal is to increase the total volume of the cranial cavity by removing a large portion of the skull, thereby lowering ICP and reducing the incidence of secondary injury to the brain.

Several approaches to decompressive craniectomy exist. In both children and adults, a bilateral frontotemporoparietal craniectomy is often used for diffuse bilateral swelling, while a unilateral frontotemporoparietal craniectomy is chosen for unilateral brain swelling.\textsuperscript{21,25,30} A variety of specialized techniques have also been reported in children, including smaller, 4-cm bitemporal craniectomies,\textsuperscript{49} larger craniectomies,\textsuperscript{25,28} and craniectomy combined with expansion duraplasty.\textsuperscript{14,18,42} To date no study has compared the efficacy of the various techniques in improving outcome. Furthermore, the timing of decompressive craniectomy and its effect on clinical outcome have not been clearly established in pediatric patients.

Current opinion on the effectiveness of craniectomy in improving clinical outcome in pediatric patients following TBI is divided. Reduction of refractory ICP has been shown to be a major predictor of mortality following TBI.\textsuperscript{21,25,30,42} and many studies have confirmed the positive effects of craniectomy on reducing ICP following TBI.\textsuperscript{14,18,42,50} However, few randomized controlled studies exist that specifically address the effectiveness of craniectomy in pediatric populations to improve clinical outcome. In most current adult and pediatric studies, refractory ICP hypertension is often defined as ICP > 20 mm Hg for some defined time period.\textsuperscript{14,20,40} However, no standard definition of ICP hypertension exists in pediatric patients, which poses difficult challenges for designing and comparing clinical trials and results.

Clinical Trials of TBI

Traumatic brain injury trials are inherently challenging. Guidelines recommend prespecified baseline prognostic criteria, broad inclusion criteria, and ordinal statistical analysis to maximize efficiency and generalizability of the results.\textsuperscript{33} Additionally, because functional outcome following TBI can change greatly from 1 to 5 years postincident, long follow-up periods greater than 1 year are needed.\textsuperscript{15} The 5 trials summarized in Table 3 are the most significant and recent in the field of craniectomy following pediatric and adult TBI. Of these studies, only the Taylor et al.\textsuperscript{48} and Kan et al.\textsuperscript{27} trials are dedicated pediatric studies. The remaining 3 studies analyze primarily adult populations with overlap into the pediatric age range. All 5 studies were of small sample size, with numbers of patients ranging from 27 to 309. Additionally, 2 of the 5 studies, conducted by Polin et al.\textsuperscript{42} and Kan et al.,\textsuperscript{27} were retrospective studies.

Taylor et al., 2001

Completed in 2001, the Taylor et al.\textsuperscript{48} RCT investigated the clinical effectiveness of very early application of craniectomy in children with TBI. Using functional outcome at 6 months after intervention as the primary outcome and the control of ICP as a secondary outcome, the authors demonstrated positive outcomes in craniectomy patients compared with noncraniectomy patients, as well as a large decrease in ICP.

The inclusion criteria for study participants were refractory intracranial hypertension, defined as sustained ICP during the 1st day after admission (> 20 mm Hg for
### TABLE 3: Comparison of 5 clinical studies of decompressive surgery following pediatric mild TBI*

<table>
<thead>
<tr>
<th>Study Characteristics</th>
<th>Taylor et al., 2001</th>
<th>Polin et al., 1997</th>
<th>Kan et al., 2006</th>
<th>Cooper et al., 2011</th>
<th>Hutchinson et al., TBD</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>27</td>
<td>70</td>
<td>51</td>
<td>155</td>
<td>309 (to date)</td>
</tr>
<tr>
<td>age range or median</td>
<td>10.7 yrs</td>
<td>18.7 yrs</td>
<td>6.6 yrs</td>
<td>23.7 yrs (surgery)/24.6 yrs (SOC)</td>
<td>15–59 yrs</td>
</tr>
<tr>
<td>methods</td>
<td>RCT; ICP ≤20 mm Hg; surgery &lt;6 hrs postrandomization; 4-cm bitemporal craniotomy via bilateral vertical incision in midtemporal region</td>
<td>retrospective study; bifrontal craniectomy to relieve refractory ICP; surgical patients matched w/ SOC control</td>
<td>retrospective study; decompressive craniectomy performed in children between 1996 and 2005</td>
<td>RCT; ICP maintained ≤20 mm Hg; Marshall criteria; injury severity score; trauma score; treatment &lt;72 hrs postictus</td>
<td>RCT; ICP ≤25 mm Hg</td>
</tr>
<tr>
<td>description</td>
<td>clinical effectiveness of very early craniectomy in children w/ TBI</td>
<td>retrospectively compared craniectomy following TBI to appropriately matched controls</td>
<td>analyzed postop mortality and morbidity following TBI in children</td>
<td>clinical effectiveness of craniectomy following brief refractory ICP HTN after TBI</td>
<td>clinical effectiveness of craniectomy following brief refractory ICP HTN after TBI</td>
</tr>
<tr>
<td>inclusion criteria</td>
<td>&gt;12 mos old w/ head injury; refractory ICP HTN (&gt;20 mm Hg/30 min, &gt;25 mm Hg/10 min, &gt;30 mm Hg/1 min); evidence of herniation</td>
<td>head injury; refractory ICP HTN (despite mild hyperventilation, elevation of bed, mannitol, or barbiturate); max ICP &gt;20 mm Hg</td>
<td>severe head trauma; elevated ICP</td>
<td>head injury; abnormal CT scan requiring ICP monitoring; ICP &gt;20 mm Hg &gt;15 min despite first-line treatments</td>
<td>head injury; abnormal CT scan requiring ICP monitoring; refractory ICP (&gt;25 mm Hg for 1–12 hrs)</td>
</tr>
<tr>
<td>exclusion criteria</td>
<td>none</td>
<td>GCS score &gt;7</td>
<td>none</td>
<td>cerebral mass lesion; successful control of ICP w/ first therapies</td>
<td>bilat fixed and dilated pupils; bleeding diathesis; devastating injury not expected to survive &gt;24 hrs</td>
</tr>
<tr>
<td>major findings</td>
<td>positive outcomes in craniectomy group; decreased ICP in surgical group vs SOC</td>
<td>surgery group had better functional outcome vs SOC; decreased ICP in surgical vs SOC; in most favorable pediatric population, large advantage of craniectomy</td>
<td>high rate of mortality in children undergoing decompressive surgery for raised ICP; hydrocephalus and epilepsy common complications of surgery following TBI</td>
<td>better outcome following second-line medical therapy after brief, modest elevation in ICP unresponsive to first-line medical therapy</td>
<td>TBD</td>
</tr>
<tr>
<td>limitations</td>
<td>small trial size; no age stratification; long study over 7 yrs; functional outcome only studied at 6 mos</td>
<td>narrow inclusion criteria; low population sample; retrospective protocol; &quot;favorable population&quot; defined narrowly: surgery within 48 hrs, no ICP &gt;40 mm Hg; age of the population</td>
<td>small study population; retrospective protocol; only 6 patients underwent craniectomy for raised ICP only</td>
<td>large screened population w/ narrow inclusion population; baseline patient differences (pupil dilation); inappropriate low threshold for ICP; large crossover rate (23%); interquartile ICP 18–22 mm Hg, questionable if meaningful HTN</td>
<td>TBD</td>
</tr>
</tbody>
</table>

* HTN = hypertension; SOC = standard of care; TBD = to be determined.
Traumatic brain injury and decompressive surgery in pediatrics

30 minutes, > 25 mm Hg for 10 minutes, or > 30 mm Hg for 1 minute), or clinical evidence of herniation, represented by pupil dilation. Of the control group patients, 1 patient had fixed pupils preoperatively, and in the surgery group, 3 patients had fixed pupils preoperatively. Surgery was performed within 6 hours of randomization, with each patient in the surgery group receiving a 4-cm bitemporal craniotomy via a bilateral vertical incision in the midtemporal region. As noted in the Adelson guidelines, this surgical operation is smaller than historical craniectomies for relief of ICP.25,29 Cranioplasty was performed several months later if indicated.

The study demonstrated positive results for the implementation of early craniectomy in children with TBI. Seven of 13 surgery patients obtained a favorable outcome at 6 months, while only 2 of 14 medical patients obtained a favorable outcome (p = 0.046). However, due to the nature of the repeated significance testing performed during the test, a p value < 0.021 was required for statistical significance for this test, per the explanation of the authors. Additionally, surgery patients demonstrated an ICP decrease of 8.98 mm Hg during the 48-hour period following intervention (95% CI 4.987–12.968), while medical patients demonstrated a decrease of 3.39 mm Hg over the same 48-hour period (95% CI –0.435 to 7.807). Finally, surgery patients demonstrated fewer ICP spikes (> 20 mm Hg) than medical patients (107 vs 223, respectively).

In comparison with the recent adult craniectomy trials described below, the Taylor et al. 2001 pediatric trial has important findings and implications. The authors hypothesized that the implementation of an early craniectomy in refractory ICP hypertensive patients would result in better patient outcomes than the historical standard of care, which reserved surgery as a final intervention in refractory ICP hypertension following TBI.21,42 Based on their preliminary findings, the use of early craniectomy may result in better functional outcomes at 6 months in pediatric patients. However, this trial is limited by several factors. First, there was a small trial size of only 27 patients, and future studies would need to greatly expand the patient number. Second, there are numerous anatomical, mechanical, and physiological differences between the infant brain and the adolescent brain, as explained earlier, and future trials will need to address these issues through age stratification. Third, the study was long, lasting over 7 years, and functional outcome evaluation was only performed early in the recovery period, at 6 months. Another study has noted that long-term recovery following TBI can change greatly from 1 to 5 years postincident.12

Kan et al., 2006

A small patient study, the Kan et al.27 analysis of clinical effectiveness of craniectomy following severe TBI in children was completed in 2006. The study was a retrospective analysis of 51 children’s records following craniectomy to either relieve ICP (6 children) or to relieve ICP and evacuate a hematoma (45 children). The authors found that craniectomy for the purpose of relieving ICP alone was associated with high levels of morbidity and mortality; however, strong conclusions cannot be drawn as only 6 patients were included in this specific cohort.

Few additional studies exist that specifically investigate the role of craniectomy in pediatric populations following TBI. The Taylor et al. study is the largest study to date, but has a small sample size of 27 patients. In a smaller study, Cho and colleagues41 reported significant decreases in ICP in 10 children < 2 years old (from a mean of 59 mm Hg preoperatively to a mean of 12 mm Hg postoperatively).

Polin et al., 1997

Rather than performing a prospective RCT, Polin et al.42 selected 35 patients who had undergone a bifrontal craniectomy for the purpose of relieving refractory ICP following TBI. Refractory ICP was defined in this study as patients who possessed elevated ICP despite hyperventilation, elevation of the head of the bed, mannitol administration, or barbiturate administration. The average patient age was 18.7 years old, all but 2 patients had a maximum ICP > 20 mm Hg, and no patient had a GCS score > 7 at the time of surgery. All surgical patients were matched with appropriately selected controls who had similar characteristics but did not undergo craniectomy. The average reduction in ICP in the surgery group was from 34.9 to 21.6 mm Hg and the average reduction in ICP in the control group was from 33.2 to 29.4 mm Hg (p = 0.026), indicating an advantage in the surgical group.

Most importantly, patients undergoing craniectomies demonstrated greater functional outcomes than control patients: 37% of craniectomy patients had a favorable outcome, compared with 16% of control patients (p = 0.014). When restricted to pediatric populations (< 18 years old), the difference was 44% versus 22%, respectively, although not statistically significant (p = 0.079). Finally, when the patient population was restricted to the most favorable target for craniectomy, defined as surgery performed within 48 hours of injury and no sustained ICP > 40 mm Hg, pediatric populations receiving craniectomies had an 80% favorable outcome but the control group demonstrated a 24% favorable outcome (p = 0.002).

Due to the trial’s narrow inclusion criteria, low population sample, and retrospective analysis protocol, conclusions are limited. A significant implication, however, is that when the pediatric patient population is appropriately screened for therapeutic benefit as per the definitions of Polin et al., the use of craniectomy appears to improve functional outcome over the standard practice of medical care.

Cooper et al., 2011

The authors of the DECRA trial recently published controversial trial results implicating worse outcome following craniectomy in patients with a brief, modest elevation in ICP following TBI (Table 3).

While it does not target pediatric craniectomy patients, and no pediatric data were reported, this study does raise important, controversial questions for the field. Additionally, the age range of participants in the study overlaps with pediatrics, including people from 15 to 59 years.
old. The randomized, nonblinded study suggests that patients with brief, modest elevations in ICP unresponsive to first-line medical therapy who subsequently received second-line medical therapy (and life-saving surgery at the discretion of the surgeon) have better outcomes than those patients who undergo immediate decompression. Completed between December 2002 and April 2010, the trial enrolled 155 participants. The principal comparison was between the effectiveness of decompressive craniectomy and medical standard of care following TBI; endpoints examined were functional outcome at 6 months (primary outcome) and the ICP hypertension index (secondary outcome). The only surgical option considered was a bifrontal temporoparietal craniectomy with bilateral dural opening and without falx cerebri division. Based on the study’s definition of inclusion criteria, ICP threshold, patient population characteristics, and intent to treat analysis, a larger unfavorable outcome was associated with surgery over medical therapy in their cohort, which included mostly adult patients. However, the trial did demonstrate reduced hourly ICP and reduced the ICP hypertension index among the surgery patients.

The trial suffers from several limitations, both specific and for the purposes of this review. The study included confounding variables including baseline patient differences, unquestionably low threshold for ICP hypertension, and a large crossover rate. The majority of patient characteristics were similar at baseline, with the large exception that the craniectomy group included a higher percentage of participants with nonresponsive pupils than the standard of care group (27% vs 12%, respectively), which is an indicator of more severe prognosis. The authors designated 20 mm Hg as their threshold for intracranial hypertension. While this value is generally accepted in pediatric studies, it has not received a Level I

The trial suffers from several limitations, both specific and for the purposes of this review. The study included confounding variables including baseline patient differences, unquestionably low threshold for ICP hypertension, and a large crossover rate. The majority of patient characteristics were similar at baseline, with the large exception that the craniectomy group included a higher percentage of participants with nonresponsive pupils than the standard of care group (27% vs 12%, respectively), which is an indicator of more severe prognosis. The authors designated 20 mm Hg as their threshold for intracranial hypertension. While this value is generally accepted in pediatric studies, it has not received a Level I recommendation for the threshold for instituting therapy in adult populations.

For the purpose of this review, the trial is timely and controversial; however, the results must be cautiously interpreted within the pediatric field as no specific conclusions were implemented regarding children. It is difficult to apply the results of the DECRA study to pediatric or any group of patients, due to the variety of confounding variables present in the study.

Hutchinson et al.

A trial in the United Kingdom (RESCUEicp) is currently underway with similar study aims as the DECRA trial but with important differences, such as including participants as young as 10 years old (Table 3). Comparable to the DECRA protocol, the RESCEUicp trial makes provisions for physicians to deliver care in the best interest of the patient, including craniectomy for the medicine group or barbiturates for the surgery group if the situation becomes an emergency (for example, prolonged ICP > 40 mm Hg with compromised CPP). Both studies use multiple-observer readings of CT scans following injury to stage the severity of the injury at baseline, a key component for an efficient trial. The RESCEUicp study has the potential to generate a more powerful analysis of the outcome from craniectomy in both pediatric and adult patients and may be instrumental in directing future standard of care guidelines.

Discussion

Clinical outcomes following craniectomy after TBI in children are controversial. Taylor et al.48 reported clear favorable outcomes in 7 of 13 patients receiving craniectomy and in only 2 of 14 patients receiving full medical management. Polin et al.49 compared the rate of favorable outcomes in their pediatric and adult populations and report 44% and 29% favorable, respectively. However, this study had no control group. In a mixed-age prospective study, Guerra et al.25 used highly restrictive patient selection criteria to analyze the effects of craniectomy on clinical outcome, and the results failed to support young age as a predictor of improved outcome.

Current guidelines are sparse and based on little clinical evidence. Adelson et al.2 recommend the following criteria for selecting favorable patients for craniectomy in children: 1) diffuse cerebral swelling on cranial CT imaging; 2) within 48 hours of injury; 3) no episodes of sustained ICP > 40 mm Hg before surgery; 4) GCS score > 3 at some point subsequent to injury; 5) secondary clinical deterioration; and 6) evolving cerebral herniation syndrome.

At the moment, thorough investigations examining the clinical effectiveness of craniectomy in pediatric patients suffering from TBI are lacking. An important consideration, which arises from these discussions, is the appropriate selection of patients for craniectomy. The 2003 guidelines for surgical treatment of pediatric intracranial hypertension state “patients who experience a secondary deterioration on the Glasgow Coma Scale (GCS) and/or evolving cerebral herniation syndrome within the first 48 hours after injury may represent a favorable group. Patients with an unimproved GCS of 3 may represent an unfavorable group.”

Previous findings22,49 support a functionally higher outcome in pediatric patients compared with adult patients, especially when recipient patients are appropriately screened for maximum ICP < 40 mm Hg and surgery is implemented within 48 hours. Additionally, the ongoing RESCEUicp study is very similar to the DECRA study but includes patients as young as 10 years old, which may illuminate the effectiveness of the procedure in pediatric populations in the near future. Based on the current paucity of data within the pediatric field, it would be beneficial for the authors to perform subgroup analysis within their pediatric cohort. Additionally, specific goals for future trials might include the following: large pediatric patient database, stratified by age; similar baseline characteristics; minimization of crossover; accordance with guidelines in selecting threshold for refractory ICP hypertension; appropriate selection of long-term (> 5 years) measures of clinical outcome; and specific, nonexcepted exclusion criteria including established characteristics for worse outcome.

Conclusions

To date, decompressive surgery following TBI re-
mains controversial. Current questions that remain include the following. Which patients are appropriate for selection for craniectomy following TBI? Is young age a predictor of improved outcome? How can we optimize the surgical approach to refractory ICP hypertension in pediatric patients? How can we better understand the various physiological measurements (ICP, CPP, cerebral blood flow, and others) to tailor the surgical therapy to the patient? What role, if any, does the age of the patient play in targeting their therapeutic ICP level? Future RCTs are needed to address these and other questions, with special importance being placed on age stratification in pediatric patient populations.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Appelboom, Zoller, Szpalski, Anderson. Acquisition of data: McDowell. Drafting the article: Appelboom, Zoller, Feldstein. Critically revising the article: Zoller, Piazza, Szpalski, Zacharia, Hickman. Reviewed submitted version of manuscript: Zoller. Administrative/technical/material support: Bruce, D’Ambrosio. Study supervision: Appelboom, Vaughan, D’Ambrosio, Feldstein, Anderson.

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