Chapter 4. Threshold for treatment of intracranial hypertension

I. RECOMMENDATIONS

Strength of Recommendation: Weak. Quality of Evidence: Low, from poor-quality class III studies.

A. Level I

There are insufficient data to support a level I recommendation for this topic.

B. Level II

There are insufficient data to support a level II recommendation for this topic.

C. Level III

Treatment of intracranial pressure (ICP) may be considered at a threshold of 20 mm Hg.

II. EVIDENCE TABLE (see Table 1)

III. OVERVIEW

In children with severe traumatic brain injury (TBI), mortality is often the result of a refractory increase in ICP. Furthermore, the need to prevent raised ICP is recognized as central to current neurocritical care of children after severe TBI. Management of severe TBI in the pediatric intensive care unit is largely focused on the management of raised ICP and preservation of cerebral perfusion pressure (CPP). Brief increases in ICP that return to normal in <5 mins may be insignificant; however, sustained increases of ≥20 mm Hg for ≥5 mins likely warrant treatment (1). Based in large part on studies in adults, an ICP treatment threshold of 20 mm Hg has been used in most centers for decades. However, the optimal ICP target or targets for pediatric TBI remain to be defined. Normal values for mean arterial blood pressure and hence CPP are lower in children, particularly in infants and young children. It has also been shown in anesthetized children without TBI that the lower CPP limit of autoregulation of cerebral blood flow is, surpris-

ingly, similar in young children vs. older children—and does not decrease below approximately 60 mm Hg (2). Thus, young children have less autoregulatory reserve than older children—i.e., the difference in CPP between normal and the lower limit of autoregulation is smaller in infants and young children than it is in older children. This suggests the possible need to set a lower ICP therapeutic target for infants and young children than older children or adults with TBI. As shown in the "Scientific Foundation" section, most of the evidence specific to pediatrics supports an ICP threshold of 20 mm Hg; however, individual reports do support lower ICP thresholds (as low as 15 mm Hg). However, some pediatric studies suggest higher thresholds (35 or even 40 mm Hg). Thus, although an ICP threshold of 20 mm Hg is generally used, and even lower threshold may physiologically make sense for infants and young children, the optimal threshold for ICP-directed therapy and whether or not it should be adjusted for children of different ages deserves additional investigation. It should also be recognized that some of the studies defining the ICP threshold used therapies that are not contemporary such as aggressive hyperventilation. Finally, in light of the heterogeneity of the pathology and pathophysiology in pediatric TBI, ICP management may need to be individualized in some cases.

IV. PROCESS

For this update, MEDLINE was searched from 1996 through 2010 (Appendix B for search strategy), and results were supplemented with literature recommended by peers or identified from reference lists. Of 60 potentially relevant studies, nine were added to the existing table and used as evidence for this topic.

V. SCIENTIFIC FOUNDATION

Eleven poor-quality class III studies met the inclusion criteria for this topic and provide evidence to support the recommendations (3–13).

No prospective or retrospective studies were identified that specifically compared the effect of ICP-directed therapy on outcome (either short or long-term) using two (or more) predefined thresholds in pediatric TBI. One study examined this issue within the context of a randomized controlled trial (9).

We are thus left with various studies, both prospective and retrospective, that examined the association between outcome and different ICP thresholds in patients who, for the most part (5 of 13) (3–5, 8, 11), were managed with a therapeutic goal of <20 mm Hg for ICP-directed therapy. Of the 11 studies in the evidence table, one study used an ICP treatment threshold of 15 mm Hg (10) and another specifically used CPP rather than ICP treatment thresholds to guide treatment (13). One study described target "ranges" for the ICP threshold including 15–25 mm Hg and 20–25 mm Hg (12), and one used an age-dependent ICP treatment threshold ranging from 15 mm Hg in infants to 20 mm Hg in older children (9). Thus, it must be recognized that most of the studies in this evidence table have an inherent bias—ICP <20 mm Hg was the *a priori* therapeutic target for some or all of the patients. In addition to this limitation, statistical approaches to adjust for confounding variables in examining the association between ICP and outcome were variably used. Another important limitation of these studies is that there was no consistent approach to assess the relationship with outcome between either the time of assessment of ICP after TBI or the duration of time ICP was above a given threshold value. Generally mean or peak values or ICP values within a given epoch were used.

Although defining a safe ICP threshold has proved elusive, all but one of the 11 studies report that sustained intracranial hypertension is associated with mortality or poor outcome in children after severe TBI.

A study by Pfenninger et al (4) retrospectively reviewed 24 patients with severe TBI. The stated goal of the treatment was "to maintain ICP <20 mm Hg and abolish ICP elevations that were >25–30 mm Hg that lasted for >3 min." The treatment regimen that was used included severe hyperventilation ($Paco_2$ 25–30 mm Hg), fluid restriction, mild hypothermia (rectal temperature 35.5–

Table 1. Evidence table

Reference	Study Description	Data Class, Quality, and Reasons[a]	Results and Conclusion
Studies from previous guidelines			
Esparza et al, 1985 (3)	Design: single-center retrospective review N = 56 Age: 3 months to 14 yrs Treatment threshold set at ICP >20 mm Hg Protocol: Treatment regimen not contemporary and included severe hyperventilation and dexamethasone	Class III Poor quality: no control for confounders; unclear if outcome assessment was unbiased No statistical comparison made between groups	13 of 13 (100%) patients with ICP >40 mm Hg had poor outcome (severe disability, vegetative, or dead) and all the patients with poor outcome died 4 of 14 (approximately 28%) patients with ICP 20–40 mm Hg had poor outcome 2 of 29 (approximately 7%) patients with ICP 0–20 mm Hg had poor outcome
Pfenninger et al, 1983 (4)	Design: single-center retrospective review N = 24 Age: 3 month to 14 yrs GCS: ≤7 Protocol: Treatment threshold was defined to maintain ICP ≤ 20 mm Hg, abolish ICP >25–30 mm Hg (sustained for >3 mins) and maintain CPP >50 mm Hg	Class III Poor quality: no control for confounders	ICP >40 mm Hg was associated with higher mortality ($p < .001$) 13 of 16 patients with ICP 20–40 mm Hg had good outcome or moderate disability; three of 3 patients with ICP <20 mm Hg had good outcome or moderate disability
Studies from other chapters of previous guidelines			
Alberico et al, 1987 (5)	Design: single-center, prospective, observational study N = 100 Age: 0–19 yrs GCS: ≤7 Protocol: treatment threshold set at 20 mm Hg Treatment regimen included severe hyperventilation Outcome: GOS	Class III Poor quality: no control for confounders	70% good outcome GOS in children with ICP <20 mm Hg with treatment vs. 8% good outcome in children with ICP refractory to treatment (>20 mm Hg), $p < .05$
Chambers et al, 2001 (6)	Design: single-center retrospective study N = 84 Age: 3 months to 16 yrs Protocol: the ICP threshold for treatment and the specific treatments used were not provided Data recordings were made for a median of 41 hrs; ROC curves calculated to determine threshold value for ICP and CPP; for ICP, the ROC curves were created over 1-mm Hg intervals over the range of 0–90 mm Hg Outcome: dichotomized 6-month GOS	Class III Poor quality: no control for confounders; unclear if patient selection was unbiased	Overall, thresholds of 35 mm Hg for ICP and 45 mm Hg for CPP were the best predictors of outcome The ROC-defined cutoffs varied depending on the Marshall computed tomography classification and ranged from 21 mm Hg to 59 mm Hg
Downard et al, 2000 (7)	Design: two-center retrospective study N = 118 Age: <15 yrs GCS: ≤8 in 99 patients (84%) Protocol: no standard treatment protocol; sedation, mannitol, hyperventilation, vasopressors, ventriculostomy, or decompressive craniectomy used at the discretion of the treating physician	Class III Poor quality as an intervention study Moderate quality as a prognosis study: logistic regression performed to determine factors associated with GOS; but no comparison of groups based on any intervention	In a stepwise logistic regression analysis, mean ICP >20 mm Hg in the initial 48 hrs was significantly associated with an increased risk of death It was not indicated whether or not other ICP thresholds were investigate
Kassof et al, 1988 (8)	Design: single-center, retrospective, observational study N = 25 Age: 3 months to 17 yrs Protocol: treatment threshold set at 20 mm Hg Treatment regimen not contemporary and included severe hyperventilation and dexamethasone	Class III Poor quality: no control for confounders; unclear if patients selection was unbiased	Mean of peak ICP in patients who died (N = 5) was 81 mm Hg (range, 55–120 mm Hg); in contrast, mean of peak ICP was 18.7 mm Hg (range, 10–30 mm Hg) in patients who did not require additional treatment for ICP and there were no deaths; no statistical analysis was presented

Table 1.—*Continued*

Reference	Study Description	Data Class, Quality, and Reasons[a]	Results and Conclusion
New studies			
Adelson et al, 2005 (9)	Design: prospective multicenter randomized controlled trial of moderate hypothermia vs. normothermia plus medical management N = 47 Age: <13 yrs Protocol: ICP treatment threshold varied with age and included 15 mm Hg, 18 mm Hg, or 20 mm Hg, for children 0–24 months, 25–96 months, and 97–156 months, respectively Contemporary guidelines-based treatment regimen including randomized use of moderate hypothermia Outcome: *post hoc* analysis of relationship between ICP and outcome (3- and 6-month GOS)	Class III Poor quality: no control for confounders in ICP analysis	Mean ICP was lower in children with good (11.9 ± 4.7 mm Hg) vs. poor (24.9 ± 26.3 mm Hg, $p < .05$) outcome; the percent time with ICP <20 mm Hg differed significantly in the good (90.8% ± 10.8%) vs. poor (68.6% ± 35.0%, $p < .05$) outcome groups ICP >20 mm Hg was the most sensitive and specific for poor outcome
Cruz et al, 2002 (10)	Design: single-center prospective study N = 45; children with ICP <15 mm Hg were excluded Age: 1–12 yrs Protocol: the ICP threshold for treatment was ≥ 15 mm Hg Treatment protocol to maintain normalized ICP, CPP, and cerebral oxygen extraction, included sedation, mannitol, severe hyperventilation (PaCO$_2$ <30 mm Hg), barbiturates, and decompression for ICP >25 mm Hg Outcome: 6-month GOS	Class III Poor quality: no control for confounders	ICP peaked on day 4 in both groups ICP was significantly higher ($p ± .02$) on days 2–5 in children with unfavorable vs. favorable outcomes Daily mean ICP values ranged between 15 and 21 mm Hg on days 2–5 in the favorable outcome group and between 19 and 26 mm Hg on days 2–5 in the unfavorable outcome group Uncontrolled ICP >40 mm Hg occurred in the two children who died 82% of the patients had a favorable outcome
Grinkeviciute et al, 2008 (11)	Design: single-center prospective study N = 48 Age: 2.4 months to 18 yrs Protocol: treatment threshold defined as ICP >20 mm Hg Patients were treated according to ICP-targeted protocol of the management of severe pediatric traumatic brain injury 27.1% of patients with decompressive craniectomy Outcome: 6-month dichotomized GOS	Class III Poor quality: no control for confounders. Insufficient power to detect outcome	The survival rate was remarkably high at 97.9% for children admitted to the pediatric intensive care unit Differences in peak ICP (22.2 mm Hg vs. 24.6 mm Hg, respectively) in groups with favorable vs. unfavorable outcomes were not statistically significant; also no difference was seen between groups in minimal CPP Only 5 patients were described as having poor outcome
Pfenninger and Santi, 2002 (12)	Design: single-center retrospective observational study N = 51 of whom 26 underwent ICP monitoring and critical care management Age: 1 month to 16 yrs Protocol: an ICP target of 20–25 mm Hg was used ICP-directed therapy included diuretics, hypertonic saline, hyperventilation, pressors, and barbiturate coma Outcome: dichotomized 6- to 12-month GOS	Class III Poor quality: no control for confounders, potential selection bias in children who received ICP monitoring	Mean sustained ICP ≥ 20 mm Hg was associated with poor outcome ($p < .05$)
White et al, 2001 (13)	Design: single-center retrospective observational study N = 136; 37 of these patients underwent ICP monitoring Age: 0–17 yrs Protocol: an ICP target was not identified, but a CPP target of ≥ 50 mm Hg in infants and ≥ 70 mm Hg for children was used A contemporary treatment regimen was used	Class III Poor quality: no control for confounders for ICP analysis, potential selection bias in patients who received ICP monitoring	14% of survivors and 41% of nonsurvivors had ICP >20 mm Hg in the first 72 hrs; no other threshold was specifically examined. ICP maximum and ICP measured 6, 12, and 24 hrs after admission were all significantly lower in survivors

ICP, intracranial pressure; GCS, Glasgow Coma Scale; CPP, cerebral perfusion pressure; GOS, Glasgow Outcome Scale; ROC, receiver operating characteristic.

[a]No study provided data for a comparison between specific ICP thresholds for initiation of therapy on outcome.

36.5°C), dexamethasone, and barbiturate infusion for refractory ICP >20 mm Hg. Sustained ICP >40 mm Hg was associated with death (p < .001). Thirteen of 16 patients with sustained ICP 20–40 mm Hg had a good outcome or moderate disability. The three patients with ICP <20 mm Hg had a good outcome or moderate disability.

A study by Esparza et al (3) was a retrospective review of 56 pediatric children with severe TBI. The study included two victims of abusive head trauma. Treatment threshold was also ICP >20 mm Hg. The treatment regimen used again was not contemporary in that it included severe hyperventilation and dexamethasone. The group of patients with an ICP >40 mm Hg had a mortality rate of 100%, those with ICP >20–40 mm Hg had a mortality rate of 28%, whereas those with ICP 0–20 mm Hg had an incidence of poor outcome (severe disability, vegetative, or dead) of only approximately 7%, supporting use of an ICP treatment threshold ≤20 mm Hg.

A study by Alberico et al (5) was carried out as a prospective, observational study of 100 children (age range, 0–19 yrs) with severe TBI using an ICP treatment threshold again of 20 mm Hg. The treatment regimen once again included severe hyperventilation, limiting somewhat the ability to generalize the findings to current treatment. Patients with ICP maintained <20 mm Hg had a 70% good outcome (Glasgow Outcome Scale) in contrast to those with refractory intracranial hypertension who had only an approximately 8% good outcome. This study also supports an ICP treatment threshold of 20 mm Hg.

A retrospective, observational study by Kasoff et al (8) reported on data from 25 children (ages 3 months to 17 yrs). The patients included one victim of abusive head trauma. An ICP treatment threshold was again set at 20 mm Hg along with a CPP threshold of 40 mm Hg. The treatment regimen again was not contemporary and included both severe hyperventilation and dexamethasone. Only a limited amount of data on the relationship between ICP and outcome was presented, although it was clear from the study that severe refractory ICP was associated with poor outcome. The mean of peak ICP in patients who died (n = 5) was 81 mm Hg (range, 55–120 mm Hg), whereas the mean of peak ICP was 18.7 mm Hg (range, 10–30 mm Hg) and there were no deaths in patients who did not require ICP-directed therapies. However,

no statistical analysis was performed. Given the practicalities associated with clinical use of a threshold, for the purpose of making guideline recommendations, we have categorized this study as supporting a threshold of 20 mm Hg.

A study by Downard et al (7) was a retrospective observational study that included two level I trauma centers in the state of Oregon, the Oregon Health Sciences University trauma registry and the Legacy Emanuel Hospital and Health Center. A total of 118 children <15 yrs of age were included. Glasgow Coma Scale score was ≤8 in 99 patients (84%). No standard treatment protocol was described; therapies including sedation, mannitol, hyperventilation, vasopressors, ventriculostomy, or decompressive craniectomy were used at the discretion of the treating physician. It was not indicated that an ICP of 20 mm Hg was the treatment threshold; however, it was the only ICP threshold that was included in the logistic regression. A stepwise logistic regression analysis showed that a mean ICP >20 mm Hg in the initial 48 hrs was significantly associated with an increased risk of death with an odds ratio of 2.39. It was not indicated whether or not other ICP thresholds were investigated. A CPP <40 mm Hg was also associated with poor outcome.

A study by Chambers et al (6) retrospectively reviewed data on 84 children with severe TBI and receiver operating characteristic curves were calculated to determine threshold values for CPP and ICP. ICP treatment thresholds and specific therapies used were not specified. Data recordings were made for a median of 41.2 hrs. Using receiver operating characteristic curves, an ICP threshold of 35 mm Hg was determined to correlate best with Glasgow Outcome Scale at 6 months. The receiver operating characteristic-defined cutoffs varied greatly depending on the Marshall computed tomography classification. Specifically, for types I, II, and III diffuse injury, the ICP cutoffs were 21 mm Hg, 24 mm Hg, and 33 mm Hg, respectively. For evacuated and unevacuated mass lesion categories, the cutoffs were 40 mm Hg and 59 mm Hg, respectively. Thus, this report supports an ICP treatment threshold of 35 mm Hg and also suggests that optimal ICP thresholds may differ for different computed tomography classifications. However, caution is advised given that the sample size in the various subgroups is limited, the study was retrospective,

and biological plausibility for some of the thresholds is questionable. Nevertheless, this study raises the question as to whether or not ICP thresholds should be different in children with diffuse injury vs. focal contusion.

A retrospecitve study by White et al (13) reported on 136 children with severe TBI (Glasgow Coma Scale score ≤8) of whom 37 were managed with ICP monitoring. A CPP-directed protocol with targets of >50 mm Hg in infants and >70 mm Hg in children, rather than a specific ICP target, was used to direct therapy. A contemporary approach to treatment was used with only mild or no hyperventilation along with sedation, osmolar therapy, barbiturates, and vasopressors. Hypothermia was not used. They reported that 41% of nonsurvivors vs. 14% of the survivors had ICP >20 mm Hg in the first 72 hrs. No other ICP threshold was specifically examined. The highest recorded ICP value was 26 ± 18 mm Hg vs. 59 ± 33 mm Hg in survivors vs. nonsurvivors (p = .03). ICP values measured 6, 12, and 24 hrs after admission were all significantly lower in survivors (19 ± 29, 18 ± 18, 16 ± 24 mm Hg) vs. nonsurvivors (43 ± 27, 45 ± 27, 43 ± 34 mm Hg), respectively. It is not clear why only 27% of children with severe TBI received ICP monitoring in this study. Nevertheless, they revealed an association between ICP >20 mm Hg and mortality in a cohort of patients that were not specifically treated using an ICP target of 20 mm Hg.

A study by Cruz et al (10) reported data from 45 children with severe TBI prospectively studied using a unique protocol that targeted an ICP threshold of ≥15 mm Hg along with prevention of increased cerebral oxygen extraction as a surrogate marker of cerebral ischemia assessed with a jugular venous bulb catheter. The treatment protocol included sedation, fast high-dose mannitol (0.7–1.2 g/kg), barbiturates, and surgical decompression for refractory ICP >25 mm Hg. Outcome was defined using dichotomized 6-month Glasgow Outcome Scale score. ICP peaked on day 4 in both groups and was significantly (p < .05) higher on days 2–5 in children with unfavorable vs. favorable outcomes (6-month Glasgow Outcome Scale). Daily mean ICP values ranged between 15 and 21 mm Hg on days 2–5 in the favorable outcome group and between 19 and 26 on days 2–5 in the unfavorable outcome group. Uncontrolled ICP >40 mm Hg occurred in the two children who died. This article is

unique in using an ICP treatment threshold of 15 mm Hg across the age spectrum in pediatric TBI, although they did not necessarily achieve that target. Nevertheless, using that threshold for treatment, favorable outcome was seen in tier analysis at a value of <19 mm Hg. Given the practicalities associated with clinical use of a numerical threshold, for the purpose of making guideline recommendations, we have categorized this study as supporting a threshold of 20 mm Hg rather 19 mm Hg.

A study by Pfenninger and Santi (12) retrospectively reviewed data from 51 children with severe TBI and compared it with data from two historical cohorts (1994–1998 vs. 1978–83 and 1988–92). Within the more contemporary cohort, 51% of the children underwent ICP monitoring. Nonmonitored patients were not salvageable (n = 5), underwent immediate decompressive craniectomy for early deterioration (n = 2), or underwent jugular bulb venous saturation monitoring instead (n = 17). ICP-directed therapy included diuretics, hypertonic saline, hyperventilation, and barbiturate coma targeting an ICP of 20–25 mm Hg. Neither decompressive craniectomy nor hypothermia was used to control ICP. Mean sustained ICP ≥20 mm Hg was associated with poor outcome ($p < .05$) defined as a dichotomized 6- to 12-month Glasgow Outcome Scale score. Favorable outcome was observed in all eight children with maximum mean sustained ICP <20 mm Hg, eight of 15 with ICP 20–40 mm Hg, and one of three children with ICP >40 mm Hg. This study is complex in that the treatment threshold appeared to be a range of 20–25 mm Hg and suggests and ICP threshold of <20 mm Hg associated with a favorable outcome.

A study by Adelson et al (9) was a prospective multicentered randomized controlled trial of moderate hypothermia vs. normothermia plus medical management in 47 children <13 yrs of age with severe TBI. The study was unique in that the ICP treatment threshold varied with age using 15 mm Hg, 18 mm Hg, or 20 mm Hg for children 0–24 months, 25–96 months, and 97–156 months, respectively. Although this study was rated level II for assessment of effect of hypothermia, it was rated level III as evidence pertaining to ICP threshold. A contemporary guidelines-based treatment regimen was used that also included randomized treatment with or without moderate hypothermia. *Post hoc* analysis of the relationship between ICP and outcome (3- and 6-month Glasgow Outcome Scale) was carried out with the expressed purpose (stated in the text) of addressing a gap in the pediatric TBI guidelines. That analysis examined the association between outcome and ICP from 0 to 90 mm Hg in children treated with this specific regimen. Mean ICP was lower in children with good (11.9 ± 4.7 mm Hg) vs. poor (24.9 ± 26.3 mm Hg, $p < .05$) outcome. The percent time with ICP <20 mm Hg differed significantly in the good (90.8% ± 10.8%) vs. poor (68.6% ± 35.0%, $p < .05$) outcome groups. ICP >20 mm Hg was the most sensitive and specific for poor outcome. Based on these findings, this study supports an ICP treatment threshold of 20 mm Hg. However, it should be recognized that hypothermia could represent an important confounder in the report. This study also represents the only study in the evidence table to guide ICP-directed treatment with age, although the impact of these age-dependent thresholds on outcome within the three age categories was not assessed.

A prospective study by Grinkeviciute et al (11) of 48 children with severe TBI who underwent ICP monitoring and ICP-directed therapy at a target of 20 mm Hg using a contemporary therapeutic regimen included decompressive craniectomy in >27% of cases. The survival rate was remarkably high at 97.9% for children admitted to the pediatric intensive care unit, although the total denominator for all severe TBI victims presenting to the emergency department was not provided. Surprisingly, differences in peak ICP (22.2 mm Hg vs. 24.6 mm Hg, respectively) in groups with favorable and unfavorable outcomes (6-month dichotomized Glasgow Outcome Scale score) were not statistically significant. Similarly, no difference between outcome groups was seen for minimal CPP. However, despite the fact that many patients had ICP >25 mm Hg, >90% of the patients had a favorable outcome and this study included only five patients with a poor outcome; thus, the statistical power to examine the relationship of raised ICP across outcomes was limited. In addition, the use of peak ICP could also limit data interpretation.

Only class III studies are available and although the studies support several different thresholds for ICP treatment, given that eight of the 11 class III studies supported a threshold of approximately 20 mm Hg, that level represents the most strongly supported value for ICP and thus is the threshold supported as a level III recommendation. We recognize that additional studies in pediatric patients with TBI are needed to determine the optimal ICP threshold or thresholds for infants and children and also define whether or not the threshold is dependent on age, injury mechanism, computed tomography injury pattern, location of the monitor, and/or other factors.

VI. INFORMATION FROM OTHER SOURCES

A. Indications From the Adult Guidelines

There is level II evidence that treatment should be initiated at an ICP threshold of 20 mm Hg as stated in the recommendations section of the adult guidelines document (14). In addition, in the summary section of the adult guidelines, it is stated that current data support 20–25 mm Hg as an upper threshold to initiate treatment. There are no large randomized trials in adults that directly compare different ICP treatment thresholds.

In a study by Marmarou et al (15), 428 patients with severe TBI were prospectively analyzed for monitoring parameters that determined outcome and their ICP threshold values. Using logistic regression, the threshold value of 20 mm Hg best correlated with 6-month Glasgow Outcome Scale score. The proportion of hourly ICP reading >20 mm Hg was a significant independent determinant of outcome. There are small, noncontrolled studies that suggest a range of 15–25 mm Hg. In one of these studies, Saul and Ducker (16) changed the ICP threshold from 25 to 15 mm Hg in two sequentially treated groups of patients and found a decrease in mortality from 46% to 28%. In the same study by Chambers et al (4) (see evidence table; Table 1) for which we used data from pediatric patients as evidence for this document, 207 adult patients were also assessed. They had ICP and CPP monitoring, and receiver operating characteristic curves were used to determine whether there were significant thresholds for the determination of outcome. The sensitivity for ICP rose for values >10 mm Hg, but it was only 61% at 30 mm Hg. In a smaller prospective study by Ratanalert et al (17) of 27 patients grouped into ICP treatment thresholds of 20 or 25 mm Hg, there was no difference in outcome between this

narrow range of treatment threshold. Finally, in a report by Schreiber et al (18) of 233 patients with ICP monitoring analyzed prospectively, an opening ICP >15 mm Hg was identified as one of five risk factors associated with a higher mortality rate.

Any chosen ICP threshold must be closely and repeatedly corroborated with the clinical examination and computed tomography imaging in an individual patient because pupillary abnormalities occurred in patients with ICP values as low as 18 mm Hg (19).

In addition, the critical value of ICP and its interaction with CPP and with other measures (jugular venous oxygen saturation, partial pressure of brain tissue oxygen, cerebral blood flow) remains unknown. The adult guidelines conclude that because the importance of these other parameters is recognized, the absolute value of ICP may be less important (14). The relationship between partial pressure of brain tissue oxygen and ICP in children has only recently begun to be explored (20).

VII. SUMMARY

There is evidence (eight of 11 class III studies) that sustained elevations in ICP (>20 mm Hg) are associated with poor outcome in children after severe TBI, and thus the level III recommendation. What is not well established is the absolute target for ICP-directed therapy that is needed to maximize outcome since this was not specifically addressed prospectively in any of the studies reviewed. Although one of these studies was carried out in the setting of a randomized controlled trial, no randomized controlled trial has directly compared the effect of two or more thresholds for ICP-directed therapy on outcome in pediatric TBI. There are also individual poor-quality level III studies that support either lower (a range of 15–25 mm Hg) or higher (35 or 40 mm Hg) threshold values than 20 mm Hg, although thresholds <20 mm Hg do, as discussed previously, have theoretical support for infants and young children. Finally, based on the fact that normal values of blood pressure and ICP are age-dependent, it is anticipated that the optimal ICP treatment threshold may be age-dependent. However, data on this point are extremely limited; only a single study on this topic in children that met the inclusion criteria varied the ICP treatment threshold with age using 15 mm Hg, 18 mm Hg, or 20 mm Hg for children 0–24 months, 25–96 months, and 97–156 months, respectively (9).

VIII. KEY ISSUES FOR FUTURE INVESTIGATION

- A direct comparison of two specific ICP treatment thresholds on outcome in children, particularly values <20 mm Hg.
- Investigation to determine whether threshold values for ICP-directed therapy are age-dependent.
- Determination whether or not injury mechanism (e.g., abusive head trauma) or computed tomography pattern changes the optimal ICP treatment threshold.
- Examination of physiological and biochemical surrogates (e.g., microdialysis, partial pressure of brain tissue oxygen, pressure volume index) of outcome are needed either to complement or supplant ICP-directed therapy in children.
- Assessment as to whether the treatment threshold for ICP-directed therapy changes with either time after injury or duration of intracranial hypertension.
- Investigations that better define the relative value of ICP- vs. CPP-directed therapy in pediatric TBI.

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