Chapter 5. Cerebral perfusion pressure thresholds

I. RECOMMENDATIONS

Strength of Recommendations: Weak.

Quality of Evidence: Low, from poor- and moderate-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

A minimum cerebral perfusion pressure (CPP) of 40 mm Hg may be considered in children with traumatic brain injury (TBI).

A CPP threshold 40–50 mm Hg may be considered. There may be age-specific thresholds with infants at the lower end and adolescents at the upper end of this range.

II. EVIDENCE TABLE (see Table 1)

III. OVERVIEW

Global or regional cerebral ischemia is an important secondary insult to the acutely injured brain. CPP, as defined by mean arterial pressure (MAP) minus the mean intracranial pressure (ICP), is the pressure gradient driving cerebral blood flow, which, in turn, in the normal state is autoregulated and coupled with cerebral metabolic rate for oxygen. Autoregulation and coupling between cerebral blood flow and cerebral metabolic rate for oxygen may be disrupted in the brain after TBI, and a decrease in CPP may therefore induce cerebral ischemia. With the use of continuous monitoring capabilities including invasive blood pressure and ICP equipment, the CPP could be manipulated by treatment in an attempt to avoid both regional and global ischemia. The optimal CPP threshold and therapeutic approach to achieve it both remain to be defined.

There are age-related differences in MAP, cerebral blood flow, and cerebral metabolic rate for oxygen from infancy through to adulthood. Because pediatric values are, in the main, lower than adult values, we need to know whether there are age-specific thresholds or targets for CPP that should be used during the critical care management of pediatric severe TBI.

Cerebral perfusion pressure is relatively easy to measure. The main reason for undertaking the invasive monitoring required for calculating this number is to titrate treatment using the level of each of the constituent parameters as a guide (i.e., CPP, ICP, and MAP) (1, 2). There are three main limitations in comparing CPP data from various studies for the purpose of identifying whether low CPP is harmful or whether there is an age-related "critical threshold" that should be targeted in treatment.

First, there may be a problem with the measurement of CPP, particularly when it is not standardized. Theoretically, to calculate actual CPP both MAP and ICP need to be zero-calibrated to the same level. Intraparenchymal fiber-tip sensors measure ICP at the tip of the device in relation to atmospheric pressure and no adjustment is possible. When using other types of devices, it is common practice to calibrate blood pressure to the right atrium and ICP to the level of the foramen of Monro. The calculation of CPP will underestimate actual CPP by an error proportional to the distance between the two zeroing points multiplied by the sine of the angle of bed elevation. For a given bed elevation, this error increases with increasing size of the patient, and for a given size of child, this error increases with increasing bed elevation. From first principles, across the pediatric age range, at bed elevation of 30°, adolescents will have almost double the error of infants (11 vs. 6 mm Hg). At a given size, increasing the bed elevation by 30° will double the error when adolescents are compared with infants (10 vs. 5 mm Hg). The studies included as evidence for this chapter describe practice in children covering the full pediatric age range. Bed elevation is only described in two studies: at 0–30° elevation (3) and 15–30° elevation (4). The ICP monitoring devices that were used are not described in two studies (5, 6) and three studies used cerebral intraparenchymal monitoring (4, 7, 8). The reference levels for zero calibration of ICP or blood pressure are not described in any of the reports.

Second, the real-time numerical value of CPP not only reflects intracranial tissue and fluid dynamics, but also the CPP level that is being targeted by those at the bedside. Four studies do not describe any ICP- or CPP-directed strategy in their management (5, 9–11). One study used an ICP threshold of 20 mm Hg to direct therapy (7). The other four studies used an age-related scale in threshold for CPP-directed intervention. In two studies, the lower limit of the scale that was used was 40 mm Hg (6, 8), and in the other two studies, it was 45 mm Hg (3, 4). The upper threshold in the scale was 50–70 mm Hg. It is evident from these data that low level of CPP will, therefore, also indicate failure to achieve the CPP target as well as a failure to respond to treatment. Table 2 provides a summary of the targets and treatments used in each of the studies included in the evidence table.

Third, the CPP summary statistic that is used in the analysis is different in many of the studies (Table 2). Minimum or lowest CPP during monitoring is used in four studies (5, 6, 9, 11). The other five studies report mean CPP: as an initial value (4), average in the first 24 hrs and daily for 5 days (3), or as an average for the whole period of monitoring (7, 8, 10). Another important consideration in regard to the summary statistic is whether or not preterminal data in nonsurvivors were included. Only one report describes excluding preterminal data (10); the rest of the reports do not discuss whether these data are included or excluded.

Taken together, caution should be applied when interpreting the results from

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Table 1. Evidence table

Reference	Study Description	Data Class, Quality, and Reasons	Results and Conclusion
Studies from previous guidelines			
Barzilay et al, 1988 (9)	Design: retrospective case series with analysis of minimum CPP N = 56 Age: mean age 6.2 yrs; 41 with severe TBI, 5 with central nervous system infection, and 10 miscellaneous conditions GCS: 54 cases with GCS ≤8 Purpose: patients were treated for increased or decreased CPP Protocol: CPP management protocol was not specified Outcome: survival at hospital discharge	Class III Poor quality: no control for confounders	Among 41 patients with severe TBI: CPP was 65.5 ± 8.5 mm Hg for survivors vs. 6.0 ± 3.9 mm Hg for nonsurvivors ($p < .01$)
Downard et al, 2000 (12)	Design: retrospective case series with analysis of mean hourly CPP calculation in the first 48 hrs of care N = 118 Age: mean 7.4 ± 4.6 yrs GCS: mean GCS 6 ± 3 (99 severe cases), 50% with space-occupying lesions Protocol: intracranial pressure monitors established within 24 hrs of admission Outcome: last recorded GOS in records at ≥ 3 months, and dichotomized to "good" and "poor" outcomes	Class III Moderate quality: outcome assessment methods not clearly described, otherwise met all criteria	All children with mean CPP <40 mm Hg died No significant difference in GOS when mean CPP was divided into deciles from 40 to >70 mm Hg More patients had a good outcome than poor outcome when mean CPP was >50 mm Hg, but there was no analysis of this in the publication
Kaiser and Pfenninger, 1984 (10)	Design: retrospective case series with analysis of minimum CPP N = 24 Age: mean 6.3 yrs GCS: all with GCS <8, 21.5% with intracranial hemorrhage Protocol: CPP management included intubation, hyperventilation, control of body temperature, dexamethasone, barbiturates, and osmotic agents Outcome: GOS follow-up at mean 2.5 yrs (range, 1.5–4.4 yrs) after injury	Class III Poor quality: unclear if selection methods unbiased; no control for confounders	All survivors (N = 19) had minimum CPP >50 mm Hg; 3 of the 5 children who died also had CPP >50 mg Hg
New studies			
Adelson et al, 2005 (3)	Design: randomized controlled trial of hypothermia therapy with analysis of average CPP over the first 5 days of care N = 102 Age: <17 yrs (mean age in two-part study 6.89 and 6.95 yrs) CPP management goal was targeted by age using 45–50 mm Hg, 50–55 mm Hg, and 55–60 mm Hg for children aged 0–24 months, 25–96 months, and 97–156 months (first cohort) or 97–214 (second cohort), respectively Protocol: not specified Outcome: GOS was dichotomized at 6 months after injury	Class III Poor quality: no control for confounders in CPP analysis (for hypothermia, this is a class II study)	Mean CPP on day 1 was higher in the hypothermia group (70.75 mm Hg) than the normothermia group (64.84 mm Hg), $p = .037$ There were no statistically significant differences between groups on days 2 to 5, and GOS was not assessed in relation to differences in CPP on day 1 Average CPP was 69.19 ± 11.96 mm Hg for favorable vs. 56.37 ± 20.82 mm Hg for unfavorable ($p = .0004$) outcome groups; the percent time with CPP >50 mm Hg was 94.2% ± 16.9% for favorable vs. 87.3% ± 29.5% for unfavorable ($p = .0001$)
Barlow et al, 1999 (11)	Design: retrospective case series with analysis of lowest CPP N = 17 Age: 1–20 months (mean, 5.1 months) with inflicted TBI Protocol: not specified; increased intracranial pressure and decreased CPP were treated in all cases Outcome: a 6-point outcome scale assessed 3–122 months (mean, 33 months) postinjury	Class III Poor quality: no control for confounders; unclear if selection and outcome assessment measures were unbiased	Lowest CPP correlated with poor outcome ($p < .005$)

Table 1. —*Continued*

Reference	Study Description	Data Class, Quality, and Reasons	Results and Conclusion
Chaiwat et al, 2009 (5)	Design: retrospective case series analysis of lowest CPP in the first 72 hrs after severe TBI; a Doppler-derived cerebral blood flow autoregulatory index was also studied and calculated as percent change in estimated cerebrovascular resistance per percent change in CPP N = 36 patients (2 inflicted TBI) Age: 9.1 ± 5.3 yrs (range, 0.8–16 yrs) Protocol: when ICP was not monitored, CPP or mean arterial blood pressure was increased according to whichever following variable was greater: 1) 20% above baseline; or 2) a set value of 80 mm Hg for the group <9 yrs and 90 mm Hg for the group aged 9–16 yrs, respectively Outcome: GOS dichotomized at 6 months after discharge	Class III Moderate quality: the methods for outcome were adequate and nonbiased but the adequacy of the sample size is unclear	On univariate analysis CPP <40 mm Hg during the first 72 hrs had no association with poor outcome When logistic regression was performed, using a number of factors, only impaired autoregulatory index remained an independent predictor of poor outcome
Chambers et al, 2001 (13)	Design: retrospective case series with analysis of CPP N = 84 Age: 3 months to 16 yrs (median, 10 yrs) Outcome: GOS dichotomized at 6 months	Class III Poor quality: no control for confounders; unclear if patient selection was unbiased	Poor outcome in all 8 cases with CPP <40 mm Hg; more patients had good outcome than poor outcome when mean CPP was >40 mm Hg
Figaji et al, 2009 (4)	Design: prospective case series with analysis of CPP data N = 52 Age: <15 yrs (median, <7 yrs) Protocol: patient management based on treatment recommendations in previous edition of the Pediatric Guidelines; target values for CPP were >50 mm Hg in children >2 yrs old and >45 mm Hg in children <2 yrs old Outcome: GOS was dichotomized into "favorable" and "unfavorable" outcome ≥ 6 months after injury	Class III Moderate quality: outcome assessment methods not clearly described, otherwise met all criteria	Median (interquartile range) for lowest CPP was significantly lower in unfavorable outcome patients: 29 (20–45) mm Hg vs. 44 (35–51) mm Hg, $p = .023$ Unfavorable outcome patients also had more episodes of CPP <40 mm Hg: 3 (0–10 vs. 0 0–1), $p = .03$ There was no difference in the number of episodes of CPP <50 mm Hg
Kapapa et al, 2010 (6)	Design: retrospective case series with analysis of CPP in relation to age-specific lower limit (up to 1 month, >40 mm Hg; 2 months up to 1 yr, >45 mm Hg; 1 yr up to 7 yrs, >50 mm Hg; >7 yrs, 55–60 mm Hg) N = 16 Age: 0–16 yrs GCS: <9 Protocol: treatment algorithm including CPP management was used Outcome: GOS was dichotomized at varied times after injury	Class III Poor quality: small sample size with inadequate case selection and outcome measures; unclear details of the regression analysis reporting the relationship between CPP and outcome	Patients with CPP value below the age-specific lower limit for just a single occurrence had a significantly worse outcome ($p = .013$)
Narotam et al, 2006 (7)	Design: prospective case series with analysis of mean CPP N = 16 Age: 1.5–18 yrs (mean, 14 yrs) GCS: 3–12 (mean, 5; 15 cases were severe) Protocol: patients were managed for prevention of cerebral ischemia with ventilation, vasopressors, respiratory treatments, etc. Outcome: GOS at 3 months after injury	Class III Poor quality: no control for confounders for GOS analysis; unclear if selection and outcome assessment methods unbiased	All survivors had good outcome; mean CPP was 81.52 ± 16.1 mm Hg for survivors vs. 50.33 ± 31.7 mm Hg for nonsurvivors ($p < .033$)

Table 1. —*Continued*

Reference	Study Description	Data Class, Quality, and Reasons	Results and Conclusion
Stiefel et al, 2006 (8)	Design: retrospective case series with analysis of mean daily CPP N = 6 Age: 6–16 yrs Protocol: treatment targeted age-appropriate CPP (≤40 mm Hg) Outcome: GOS was dichotomized at discharge	Class III Poor quality: no control for confounders, very small sample, unclear if selection methods unbiased	Mean daily CPP in survivors was 75.63 ± 11.73 mm Hg

CPP, cerebral perfusion pressure; TBI, traumatic brain injury; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale.

Table 2. Summary of treatments, cerebral perfusion pressure target, and cerebral perfusion pressure statistics used in studies

	Treatments Used					
Reference	Hyperventilation	Induced Hypothermia	Barbs	Decompressive Craniectomy	CPP Target Strategy	CPP Statistic
Adelson et al, 2005 (3)	No	Yes	Yes	Yes	Age-related 45 mm Hg	Mean CPP
Barlow et al, 1999 (11)	TH	TH	TH	TH	TH	Lowest CPP
Barzilay et al, 1988 (9)	Yes	Yes	Yes	No	—	Lowest CPP
Chaiwat et al, 2009 (5)	—	—	—	—	—	Lowest CPP
Chambers et al, 2001 (13)	TH	TH	TH	TH	TH	Minimum CPP
Downard et al, 2000 (12)	Yes	No	No	Yes	—	Mean CPP 48 hrs
Figaji et al, 2009 (4)	Yes	Yes	Yes	Yes	Age-related 45 mm Hg	Initial and lowest CPP
Kaiser and Pfenninger, 1984 (10)	Yes	Yes	Yes	No	—	Mean CPP
Kapapa et al, 2010 (6)	Yes	Yes	Yes	Yes	Age-related 40 mm Hg	Lowest CPP
Narotam et al, 2006 (7)	Yes	No	No	No	Intracranial pressure-related	Mean CPP
Stiefel et al, 2006 (8)	—	—	—	—	Age-related 40 mm Hg	Mean CPP

CPP, cerebral perfusion pressure.

In the studies that describe therapy: "Yes" denotes use of therapy and "No" denotes where treatment is not used. "TH" denotes where the study is aimed at defining a threshold about burden from CPP insult and outcome rather than it being an intervention study. Dashes (—) indicate where no information is given in the report.

the pediatric TBI CPP studies and applying the information to treatment strategies for TBI.

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 77 potentially relevant studies, eight were added to the existing table and used as evidence for this topic.

V. SCIENTIFIC FOUNDATION

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

A randomized controlled trial of hypothermia (32–33°C) therapy, a class II study for the evidence about hypothermia, but class III for the evidence about CPP, reported average CPP over the first 5 days of care as well as for the total 5 days of care (3). The study was performed in two parts: part 1, 48 cases of pediatric TBI with Glasgow Coma Scale score ≤8, aged 6.89 ± 3.46 yrs; and part 2, 27 cases of pediatric TBI with Glasgow Coma Scale score ≤8, aged 6.95 ± 5.68 yrs. The authors used dichotomized Glasgow Outcome Scale outcome (good in 28 cases, 14 hypothermia patients and 14 normothermia patients; poor in 40 cases, 18 hypothermia patients and 22 normothermia patients) assessed at 6 months after injury to examine differences in CPP. The average CPP for all 5 days was higher in the good outcome group: good outcome 69.19 ± 11.96 mm Hg vs. poor outcome 56.37 ± 20.82 mm Hg (p = .0004). In

addition, the percent time with CPP >50 mm Hg was higher in the good outcome group: good outcome 94.2% ± 16.9% vs. poor outcome 87.3% ± 29.5% (p = .0001).

Five studies found higher CPP associated with better outcomes and their findings were as follows. A study by Barzilay et al (9) studied 41 consecutive TBI admissions to their pediatric intensive care unit with coma for at least 6 hrs before admission. Survivors had higher minimum CPP than nonsurvivors: 65.5 ± 8.5 vs. 6.0 ± 3.9 mm Hg, respectively (p < .01). A study by Figaji et al (4) studied prospectively 52 children with TBI and found median lowest CPP experienced during the course of monitoring was higher in those with better outcome. By using dichotomized Glasgow Outcome Scale outcome assessed at least 6 months after injury, those with favorable outcome had lowest CPP median (interquartile range) of 44 (35–51) mm Hg vs. 29 (20–45) mm Hg in those with an unfavorable outcome (p = .023). A study by Narotam et al (7) analyzed data from 16 children aged 1.5–18 yrs (mean, 14 yrs), 15 of whom had Glasgow Coma Scale score ≤8. All ten survivors had an excellent recovery at 3 months (Glasgow Outcome Scale score 5). Mean CPP was higher in survivors (81.52 ± 16.1 mm Hg) than nonsurvivors (50.33 ± 31.7 mm Hg, p = .033). A study by Stiefel et al (8) studied brain tissue oxygen monitoring in six patients (aged, 6–14 yrs, Glasgow Coma Scale score 3–7) and found mean daily CPP in the five survivors was 75.63 ± 11.73 mm Hg. Last, in a sample of TBI cases restricted to 17 young children with inflicted injury (aged 1–20 months; mean, 5.1 months), Barlow et al (11) reported that higher lowest CPP during intensive care was associated with better outcomes in a 6-point scale 3–122 months (mean, 33 months) after injury (p = .0047).

Four studies reported findings in relation to a threshold in CPP of 40 mm Hg. In the study reported by Figaji et al (4) (see previously), the authors found that more episodes of CPP <40 mm Hg were observed in those with an unfavorable (3 [0–10]) vs. favorable (0 [0–1]) outcome (p = .03). In the other study, a more complex relationship between CPP and outcome involved data from autoregulation of cerebral blood flow. A study by Chambers et al (13) analyzed 84 children aged 3 months to 16 yrs (median, 10 yrs) and examined minimum CPP in relation to dichotomized Glasgow Outcome Scale at 6 months. Sixty-three of 76 cases with CPP >40 mm Hg had good outcome and all eight cases with CPP <40 mm Hg had a poor outcome (p < .0001, Fisher's exact test). A study by Downard et al (12) analyzed 118 pediatric TBI cases aged up to 15 yrs (mean age, 7.4 yrs; 99 cases with Glasgow Coma Scale score 3–8) and reported dichotomized Glasgow Outcome Scale score at 3 months or later in relation to CPP thresholds. Seventy-two of 96 patients with CPP >40 mm Hg had a good outcome, whereas all 22 cases with CPP <40 mm Hg died. The difference in mortality was statistically significant (p < .0001, Fisher's exact test). A study by Chaiwat et al (5) analyzed 36 cases of TBI for predictors of poor outcome. ICP of >20 mm Hg and CPP <40 mm Hg during the first 72 hrs were not associated with outcome. However, on logistic regression, an estimate of impaired cerebral blood flow autoregulation using Doppler ultrasonography—the autoregulatory index—was an independent predictor of poor outcome (adjusted odds ratio, 23.1; 95% confidence interval, 1.9–279.0). Impaired autoregulatory index was an independent risk factor when the authors entered CPP <40 mm Hg, systolic blood pressure lower than the fifth percentile for age and gender during the first 72 hrs after TBI, low middle cerebral artery velocity, and impaired autoregulatory index into the model (adjusted odds ratio, 29.8; 95% confidence interval, 1.7–521.4). Because autoregulatory index is calculated as the percent change in cerebrovascular resistance per percent change in CPP, and cerebrovascular resistance is defined as the ratio of CPP to middle cerebral artery velocity, it is impossible to disentangle the relationship between outcome and CPP. Autoregulatory index represents a research tool.

Five class III studies contain data concerning CPP threshold >40 mm Hg. Two retrospective case series support the idea that there may be an age-related CPP threshold >40 mm Hg. A study by Kapapa et al (6) analyzed 16 children aged <16 yrs and reported dichotomized Glasgow Outcome Scale in relation to age-specific lower limits in CPP (i.e., >40 mm Hg, infants up to 1 month; >45 mm Hg, infants aged 2 months to 1 yr; >50 mm Hg, children aged between 1 and 7 yrs; 55–60 mm Hg, children aged >7 yrs). The authors found that patients with CPP values below the age-specific lower limit for just a single occurrence had a significantly worse outcome (p = .013). A study by Kaiser and Pfenninger (10) reported findings in 24 consecutive admissions to their pediatric intensive care unit of patients with a Glasgow Coma Scale score <8, average age = 6.3 yrs (ten patients between 1 and 5 yrs) and showed that all survivors had CPP >50 mm Hg (p < .005, Fisher's exact test). The two remaining studies in this group of four did not observe a threshold >40 mm Hg. In the study reported by Figaji et al (4) (see previously), the authors also reported outcome in relation to the number of episodes during monitoring that CPP was <50 mm Hg; there was no difference in the number episodes in those with an unfavorable (8 [2–18.5]) vs. favorable (3 [0–8.8]) outcome (p = .137). Of note, two-thirds of the children in this series were <8 yrs. As discussed, in the study reported by Downard et al (12), 100% of children with mean CPP <40 mm Hg died as compared with only 25% of children who had a CPP >40 mm Hg. The difference in mortality was statistically significant (p < .0001, Fisher's exact test). Last, in the study of young children with inflicted TBI reported by Barlow et al (11) (see previously), only one infant in the series of 17 had the lowest CPP of >50 mm Hg.

These studies, in aggregate, suggest that in the pediatric age range, there may be an age-related threshold between 40 and 50 mm Hg with infants at the lower end and adolescents at the upper end of this range. Finally, studies specifically focused on assessment of the optimal upper limit for CPP management in pediatric TBI were lacking.

VI. INFORMATION FROM OTHER SOURCES

A. Indications From the Adult Guidelines

In adults, with respect to CPP, it appears that the critical threshold for cerebral ischemia generally lies in the region of 50–60 mm Hg and can be further delineated in individual patients by ancillary monitoring (14). It is becoming increasingly apparent that elevating the CPP through pressors and volume expansion is associated with serious systemic toxicity, may be incongruent with frequently encountered intracranial conditions, and is not clearly associated with any benefit in terms of general outcome.

A study by Clifton et al (15) was a *post hoc* analysis of the data on CPP within the data set from 392 patients in the randomized controlled trial of therapeutic hypothermia for severe TBI. When they analyzed individual predictive variables separately, they found CPP of <60 mm Hg to be associated with an increased proportion of patients with poor outcome. They found similar associations for ICP >25 mm Hg, MAP <70 mm Hg, and fluid balance <−594 mL. When these variables were combined into a stepwise logistic regression model, however, low CPP had no effect on outcome, although the other three variables remained within the group of most powerful variables in determining outcome. Based on a purely pragmatic assessment of these data, the authors noted that a CPP target threshold should be set approximately 10 mm Hg above what is determined to be a critical threshold to avoid dips below the critical level (15). The overall assessment of the adult CPP guidelines therefore suggests "a general threshold in the realm of 60 mm Hg, with further fine-tuning in individual patients based on monitoring of cerebral oxygenation and metabolism and assessment of the status of pressure autoregulation" (14).

The adult guidelines state that there are insufficient data to support a level I recommendation for this topic. Under "Options," it states the following: aggressive attempts to maintain CPP >70 mm Hg with fluids and pressors should be avoided because of the risk of adult respiratory distress syndrome; CPP of <50 mm Hg should be avoided; and CPP values to target lie within the range of 50–70 mm Hg. Patients with intact pressure autoregulation tolerate higher CPP values and ancillary monitoring of cerebral parameters including blood flow, oxygenation, or metabolism may facilitate CPP management.

VII. SUMMARY

Survivors of severe pediatric TBI undergoing ICP monitoring consistently have higher CPP values vs. nonsurvivors, but no study demonstrates that active maintenance of CPP above any target threshold in pediatric TBI reduces mortality or morbidity. In comparing the findings from pediatric and adult TBI studies, there does appear to be an age-related difference in CPP threshold. Whether these differences are the result of differences in measurements, goal in CPP management, or the makeup in age range of the small numbers in the pediatric studies remains unclear. CPP should be determined in a standard fashion with ICP zeroed to the tragus (as an indicator of the foramen of Monro and midventricular level) and MAP zeroed to the right atrium with the head of the bed elevated 30°.

VIII. KEY ISSUES FOR FUTURE INVESTIGATION

- A standard method for measuring CPP level and duration and reporting data would be useful across pediatric TBI studies that focus on targeting CPP.
- Multimodal neuromonitoring studies to help determine the relationships between CPP and autoregulation and between CPP and ischemia in individual patients.
- Controlled, prospective, randomized studies in children to determine optimal level of CPP based on ischemia monitoring in various pediatric age groups and mechanisms of injury.
- Long-term (>1 yr), age-appropriate functional outcome studies to assess the relative importance of ICP- and CPP-targeted therapies as well as analyses evaluating outcomes in relation to treatment responders and nonresponders.
- Studies to determine whether a CPP target threshold set above (e.g., 10 mm Hg) what is determined to be a critical threshold could avoid dips below the critical CPP level.

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