

Chapter 8. Cerebral perfusion pressure

I. RECOMMENDATIONS

A. Standards. There are insufficient data to support treatment standards for this topic.

B. Guidelines. A cerebral perfusion pressure (CPP) >40 mm Hg in children with traumatic brain injury (TBI) should be maintained.

C. Options. A CPP between 40 and 65 mm Hg probably represents an age-related continuum for the optimal treatment threshold. There may be exceptions to this range in some infants and neonates.

Advanced cerebral physiologic monitoring may be useful to define the optimal CPP in individual instances.

Hypotension should be avoided.

D. Indications from the Adult Guidelines. The adult guidelines (1) stated there were insufficient data to support either a treatment standard or guideline. Under *Options*, it stated, "Cerebral perfusion pressure (CPP) should be maintained at a minimum of 70 mm Hg." (1)

II. OVERVIEW

Global or regional cerebral ischemia is an important secondary insult to the acutely injured brain. Grossly, the CPP—defined as the mean arterial pressure minus the intracranial pressure (ICP)—defines the pressure gradient driving cerebral blood flow (CBF), which, in turn, is related to metabolic delivery of essential substrates. The posttraumatic brain has a significant incidence of vasospasm that may increase the cerebral vascular resistance and decrease the CPP, producing ischemia. With the use of continuous monitoring capabilities including invasive blood pressure and ICP equipment, the CPP could be manipulated in an attempt to avoid both regional and global ischemia.

III. PROCESS

We searched Medline and Healthstar from 1966 to 2001 by using the search

strategy for this question (see Appendix A) and supplemented the results with literature recommended by peers or identified from reference lists. Of 53 potentially relevant studies, five were used as evidence for this question (Table 1).

IV. SCIENTIFIC FOUNDATION

There is abundant evidence that CBF declines following TBI and may frequently reach the ischemic threshold for brain tissue (2–6). Regional CBF may be even more reduced in the vicinity of intracranial hematomas and contusions (7, 8). There is much debate on how best to measure CBF and at what threshold there is actual tissue ischemia. Cerebral perfusion pressure is relatively easy to measure and appears to correlate well with CBF when measured. A low CPP is highly correlated with poor outcome, but there is less evidence that manipulating the CPP can change eventual neurologic outcome in both adults and children.

There is little quality evidence for the role of CPP in pediatric patients. The comprehensive literature search for this guideline only found one class II study and no class I studies.

A retrospective cohort, class II study collected data on all pediatric TBI patients presenting to both level I pediatric trauma centers in Oregon who received an ICP monitor (118 patients, Glasgow Coma Scale [GCS] 6 ± 3 , age 7.4 ± 4.6 yrs). By logistic regression methods, the authors found mortality rate significantly associated with a mean CPP <40 mm Hg ($p < .01$) and mean ICP >20 mm Hg ($p < .001$). Mean arterial pressure <70 mm Hg (their definition of "hypotension") was not statistically independently associated with death. They also found no incremental reduction of mortality rate or improved 3-month Glasgow Outcome Scale score associated with mean increases of CPP >40 mm Hg. However, only 60% of patients had documented follow-up at 3 months (9).

Barzilay et al. (10) studied 56 consecutive admissions to their pediatric inten-

sive care unit (PICU) with coma from TBI, central nervous system infections (five cases), and miscellaneous etiologies (ten cases) for at least 6 hrs before admission. Mean arterial pressure and CPP were treated in an uncontrolled fashion, and patients were followed until hospital discharge only. Comparison of survivors and nonsurvivors showed results in Table 2. The difference in minimum CPP is significant at $p < .001$.

Elias-Jones et al. (11) studied 39 consecutive PICU admissions for TBI with an initial GCS ranging from 3 to 11 and an age range of 2 months to 13 yrs (average age 7.8 yrs) who had multiple interventions for ICP >20 mm Hg or CPP <50 mm Hg. They showed that all but one survivor (of total 30) had CPP >40 mm Hg, and CPP was <40 mm Hg in seven of nine fatalities ($p < .00002$, Fisher's exact test). The interventions included hypothermia to 32°C and hyperventilation to a $Paco_2$ of 3.0–3.5 kPa for all patients. Severe hypocapnia was associated with a worse outcome.

Another retrospective case series of 24 consecutive admissions to a PICU of patients with a GCS <8, average age 6.3 yrs, with ten patients between 1 and 5 yrs of age, showed that all survivors had CPP >50 mm Hg ($p < .005$, Fisher's exact test) (12).

Sharples et al. (13, 14) studied a convenience sample of 17 pediatric patients (2–16 yrs old, average age 7 yrs) with TBI and GCS 3–8 by measuring continuous mean arterial pressures and ICPs and calculating CBF and cerebral vascular resistance by using the nitrous oxide method. The authors found cerebral vascular resistance was proportional to CPP (Pearson $r = .32$, $p = .0003$) and the relationship was even closer in those patients deemed to have a "good" outcome (i.e., near-normal neurologic function).

Key Elements from the Adult Guidelines Relevant to Pediatric TBI

A large randomized controlled trial of 189 patients with severe TBI (15% with a

Table 1. Evidence table

Reference	Description of Study	Data Class	Conclusion
Barzilay et al. (10), 1988	Retrospective analysis of survival at hospital discharge with minimum CPP in 56 patients (41 with severe TBI, five with CNS infections, and ten miscellaneous).	III	CPP 65.5 ± 8.5 mm Hg for survivors vs. 6.0 ± 3.9 mm Hg for nonsurvivors ($p < .001$).
Elias-Jones et al. (11), 1992	Retrospective analysis of neurologic outcome at 2.5 yrs (0.5–5 yrs) post-TBI (GCS 5.5, 3–11) associated with extremes of CPP in 39 patients (average age 7.8 yrs, 2 mos–13 yrs).	III	CPP >40 mm Hg in all but one survivor, <40 mm Hg in seven of nine fatalities ($p < .00002$).
Kaiser and Pfenninger (12), 1984	Retrospective analysis of 24 patients (average age 6.3 yrs) with severe TBI (all GCS <8), 21.5% with ICH, GOS follow-up 2.5 yrs (1.5–4.4 yrs).	III	All survivors with minimum CPP >50 mm Hg ($p < .005$).
Sharples et al. (13), 1995	Retrospective analysis of 17 patients (convenience sample), aged 2–16 yrs (average 7 yrs), neurologic outcome (“good and moderate” vs. “severe and died”). CPP, CBF, and CMRO ₂ calculated.	III	CVR proportional to CPP ($r = .32, p = .0003$). CVR not related to age, GCS, or time from injury.
Downard et al. (9), 2000	Retrospective cohort study of 118 patients (age 7.4 ± 4.6 yrs) with ICP monitors established within 24 hrs of admission, GCS 6 ± 3, 50% with space occupying lesions, hourly CPP calculations. GOS last recorded in chart.	II	No survivors with mean CPP <40 mm Hg ($p < .01$); no relationship for increments of CPP >40 mm Hg.

CPP, cerebral perfusion pressure; TBI, traumatic brain injury; CNS, central nervous system; ICH, intracranial hemorrhage; GOS, Glasgow Outcome Scale; CBF, cerebral blood flow; CMRO₂, cerebral metabolic rate of oxygen; CVR, cerebral vascular resistance; GCS, Glasgow Coma Scale.

Table 2. Comparison of cerebral perfusion pressure (CPP) and intracranial pressure (ICP) in survivors vs. nonsurvivors (10)

	Minimum CPP, mm Hg	Maximum ICP, mm Hg
Survivors	65.5 ± 8.5	16.9 ± 3.1
Nonsurvivors	6.0 ± 3.9	53.7 ± 10.8

gunshot wound) compared ICP-targeted therapy with CBF-targeted therapy that resulted in a CPP >50 mm Hg in the first group and a CPP >70 mm Hg in the second. It showed no difference in 3- or 6-month Glasgow Outcome Scale score, but there was an increased risk of adult respiratory distress syndrome in the second group (15). Another large prospective study of 353 severe TBI patients, with 178 receiving continuous monitoring and management of cerebral oxygen extraction in addition to management of CPP, showed that the additional intervention was associated with better neurologic outcome at 6 months (16). A retrospective study by Changaris et al. (17) in 136 adult patients showed that all patients with a CPP <60 mm Hg on the second day of injury died and more patients with a CPP >80 mm Hg had a better outcome. Another retrospective study of 221 patients followed for a year after TBI also showed better outcomes including mortality rate ($p < .001$) if CPP >80 mm Hg (18). Multiple prospective studies evaluating interventions such as hypothermia, barbiturate coma, and controlling jugu-

lar venous oxygen content used CPP >70 mm Hg as a target without directly evaluating this variable alone (19–23). Two studies looked at the relationship of artificially raising the mean arterial pressure in TBI patients with inotropes, and these studies found that this intervention had little effect on the ICP, thereby raising CPP and CBF. The studies were too small to find an effect on ultimate outcome (24, 25). Another small study ($n = 21$) showed that an increase of CPP from an average of 32 to 67 mm Hg significantly improved brain tissue Po₂ but that further increases did not improve this variable (26).

V. SUMMARY

A CPP <40 mm Hg is consistently associated with increased mortality, independent of age. It is unclear whether this value represents a minimal threshold or whether the optimal CPP may be above this in children (e.g., 50–65 mm Hg), based on available data. There are likely to be age-related differences in optimal CPP goals that are indiscernible due to small numbers in these pediatric studies. No study demonstrates that active maintenance of CPP above any target threshold in pediatric TBI is responsible for improved mortality or morbidity.

VI. KEY ISSUES FOR FUTURE INVESTIGATION

Controlled, prospective, randomized studies in children are needed to deter-

mine optimal CPP levels in various pediatric age groups and mechanisms of injury. The relative importance of ICP and CPP-targeted therapies needs to be assessed by using age-appropriate long-term (>1 yr) functional outcomes.

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Controlled, prospective, randomized studies in children are needed to determine optimal cerebral perfusion pressure levels in various pediatric age groups and mechanisms of injury.

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APPENDIX: LITERATURE SEARCH STRATEGIES

SEARCHED MEDLINE AND HEALTHSTAR FROM 1966 TO 2001

Chapter 8. Cerebral Perfusion Pressure

1. exp craniocerebral trauma/
2. head injur\$.tw.
3. brain injur\$.tw.
4. 1 or 2 or 3
5. cerebral perfusion pressure.tw.
6. cerebrovascular circulation/ and blood pressure/
7. 5 or 6
8. 4 and 7
9. limit 8 to (newborn infant <birth to 1 month> or infant <1 to 23 months> or preschool child <2 to 5 years> or child <6 to 12 years> or adolescence <13 to 18 years>)
10. limit 9 to english language