

Cerebral Perfusion Pressure Below 60 mm Hg is Common in the Intraoperative Setting

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Background: Maintaining adequate cerebral perfusion pressure (CPP) is of clinical concern in patients with neurological injury. Although there are extensive data on CPP in the ICU setting, there has been little quantitative study of CPP in the intraoperative setting.

Methods: We retrospectively analyzed the electronic intraoperative records of neurosurgical and trauma patients with concurrent intracranial and arterial pressure monitoring devices in continuous use for ≥ 45 minutes to calculate CPP (= mean arterial pressure – intracranial pressure). We assessed the total minutes and frequency of 5-minute epochs, during which the median CPP was < 60 mm Hg, and the associated risk factors.

Results: A total of 155 trauma and neurosurgical patients were studied. In the neurosurgery cohort ($n = 88$), 74% had at least one 5-minute epoch during which the median CPP was < 60 mm Hg and the median total minutes of CPP < 60 mm Hg was 39 [interquartile range (67), length of surgery 274 (300) min]. In the trauma cohort ($n = 67$), 82% had at least one 5-minute epoch of < 60 mm Hg, and the median total minutes CPP of < 60 mm Hg was 35 [(59), length of surgery 159 (160) min]. For the entire cohort ($n = 155$), patients with CPP < 60 mm Hg were found to have higher intracranial pressure compared with patients with CPP ≥ 60 mm Hg ($P < 0.001$). Unlike the neurosurgical cohort, trauma patients with CPP < 60 mm Hg had a greater frequency of episodes of mean arterial pressure < 70 mm Hg ($P = 0.001$).

Conclusions: CPP < 60 mm Hg is common in the intraoperative setting of a tertiary medical center in 2 different surgical populations with intracranial pathology. Prospective studies of intraoperative CPP and neurological outcomes are warranted.

Key Words: cerebral perfusion pressure, intracranial pressure, mean arterial pressure, neurosurgery, trauma surgery

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Low cerebral perfusion pressure [CPP = mean arterial pressure (MAP) – intracranial pressure (ICP)] is thought to influence the outcome of patients with neurological insult.^{1,2} In support of this, recent data suggest that CPP may play a role in determining brain tissue oxygenation in patients with subarachnoid hemorrhage, such that higher CPP values are associated with improved cerebral oxygenation and better outcomes.¹ There is also a general consensus that cerebral oxygenation is adversely affected below the lower autoregulatory limit of CPP.³ Most studies evaluating CPP in patients with intracranial pathology have been conducted in the intensive care unit setting and suggest that low CPP is a frequent event.⁴ However, quantitative studies directly assessing the frequency of low CPP and the factors associated with low CPP in the operating room are limited. Therefore, the objectives of this study were to (1) determine the frequency and duration in minutes during which the median CPP is < 60 mm Hg in patients with intracranial pathology and (2) assess the associated risk factors.

METHODS

With Institutional Review Board approval (University of Michigan, Ann Arbor), the electronic anesthesia records of adult patients undergoing emergent and elective surgery at the University of Michigan between July 2003 and March 2009 were screened for 3 qualifying criteria: (1) the presence of an ICP monitoring device; (2) the concurrent presence of an arterial catheter; and (3) the continuous use of both for at least 45 minutes. A threshold of 45 minutes was chosen to maximize data reliability by eliminating short, minor cases such as tracheostomy or brief periods of monitoring such as placement of the ventriculostomy at the conclusion of a surgical procedure. All procedures were performed with patients in the supine position. Perioperative patient information and intraoperative data were captured using Centricity (General Electric Healthcare, Waukesha, WI), an anesthesia information management system. ICP-monitoring devices consisted of intraventricular catheters (Codman Bactiseal or Integra) and Codman Microsensor ICP transducer systems. All intraventricular catheters and arterial lines were calibrated according to protocol at the initiation of anesthesia. CPP was defined as MAP – ICP; these data are presented in mm Hg. We were specifically interested in

patients with evidence of intracranial pathology requiring ICP monitoring; thus, patients with pressure recordings from lumbar drains were excluded from analysis. Patients were subdivided into 2 groups according to the procedure and surgical service, defined as neurosurgical or trauma (including orthopedic and general surgical procedures for patients with traumatic brain injury).

Intraoperative hemodynamic monitoring data were acquired by means of an automated, validated electronic interface from the physiological monitors (Solar 9500; General Electric Healthcare). The interface records 1 invasive arterial blood pressure and ICP measurement each minute. Each intraoperative anesthetic record was divided into consecutive 5-minute epochs. The median MAP, ICP, and CPP values for each 5-minute epoch were calculated. The use of a median value over 5 minutes filters out monitoring artifacts and transient changes with limited clinical significance.^{5,6} We assessed the frequency of 5-minute epochs with a median CPP < 60 mm Hg for patients who met the inclusion criteria. In addition, the median total time in minutes during which CPP was < 60 mm Hg and the median total case duration were calculated for patients meeting the inclusion criteria. Finally, the median CPP value for each case was determined by averaging the median CPP values of each 5-minute epoch of continuous monitoring. A CPP of 60 mm Hg was chosen as a threshold based on recommendations for the management of traumatic brain injury.⁷

Because both ICP and MAP determine CPP, we assessed the contributions of each of these variables in the neurosurgical and trauma cohorts. As with CPP, median ICP data were calculated for each case by averaging the median ICP value for each 5-minute epoch of continuous monitoring. The frequency of 5-minute epochs during which MAP was reduced was assessed by an absolute MAP value (MAP < 70, < 60, < 50, and < 40 mm Hg). By averaging the median data, our goal was to minimize artifacts.

Using preoperative assessments, the following preoperative risk factors were analyzed for an association with CPP < 60 mm Hg: sex, American Society of Anesthesiologists (ASA) physical status, premorbid history of hypertension or cardiac disease, antihypertensive therapy (specifically the preoperative use of β -blockers, Ca⁺⁺ channel blockers, and/or angiotensin-converting enzyme inhibitors), neurological examination, and body mass index. Intraoperative factors analyzed include the duration of the procedure, estimated blood loss and fluid administration, urine output, and administered anesthetic and nonanesthetic medications. For anesthetic agents, we assessed the intraoperative dosing of propofol, thiopental, and etomidate, and the expired concentrations of isoflurane, sevoflurane, and desflurane. Because this was a retrospective study, the anesthetic technique was not controlled.

Statistical analysis was performed using PASW version 18 (SPSS Inc., Chicago, IL). Patients meeting the inclusion criteria were analyzed both as a cohort and as neurosurgical and trauma subgroups. All patient data

were categorized as dichotomous variables: at least one 5-minute epoch with CPP < 60 mm Hg versus CPP \geq 60 mm Hg for the entire sampling period. Categorical data were analyzed using either the Pearson Chi-Square or the Fisher Exact Test. All continuous data elements were nonparametric and were analyzed using the Mann-Whitney *U* test. Statistical significance was considered as *P* value < 0.05.

RESULTS

A total of 524 cases with the concurrent use of an ICP monitor and an arterial catheter were identified. Patients without evidence of intracranial pathology (eg, aortic procedures with lumbar cerebrospinal fluid pressure monitoring) were excluded (*n* = 224, classified as "Others," Fig. 1). Of otherwise qualified patients with intracranial pathology, 104 patients who had undergone neurosurgical procedures and 41 patients who had undergone trauma procedures were excluded from analysis because continuous CPP measurement was < 45 minutes, the patient had a lumbar rather than an intracranial catheter, or because the patient was under 18 years of age (Fig. 1). A total of 155 cases met the inclusion criteria and were considered valid for analysis (88 neurosurgical and 67 trauma patients). The basic demographics for both patient groups are presented in Table 1. Notably, a greater proportion of trauma patients were ASA 4 and above compared with the neurosurgical cohort (*P* = 0.015). The diagnoses of neurosurgical patients were diverse and are summarized in Table 2.

Intraoperative 5-minute epochs during which the CPP was < 60 mm Hg were frequent in both surgical populations (Table 3). An overall 74% of neurosurgical patients had at least one 5-minute epoch with CPP < 60 mm Hg, with a range of 1 to 53 events per patient. The median CPP in neurosurgical patients with CPP < 60 mm Hg (*n* = 65) was 69 (interquartile range 14) mm Hg versus 84 (10) mm Hg in those with CPP \geq 60 mm Hg (*n* = 23, *P* < 0.001). In the trauma group, 82% of patients had at least 1 episode of CPP < 60 mm Hg, with a range of 1 to 90 events per patient. The median CPP in trauma patients with CPP < 60 mm Hg (*n* = 55) was 63 (16) mm Hg versus 78 (15) mm Hg in those with CPP \geq 60 mm Hg (*n* = 12, *P* < 0.001). The total duration during which CPP was < 60 mm Hg was also assessed in both surgical cohorts. For all neurosurgical patients (*n* = 88) the median total duration with CPP < 60 mm Hg was 39 (67) minutes, with a median length of surgery of 274 (300) minutes. For all trauma patients (*n* = 67), the median duration with CPP < 60 mm Hg was 35 (59) minutes, with a median length of surgery 159 (160) minutes.

For the entire cohort (*n* = 155) the overall median ICP was higher in patients with CPP < 60 mm Hg than in patients with CPP \geq 60 mm Hg [14 (9) mm Hg vs. 6 (7) mm Hg, *P* < 0.001]. The median ICP for neurosurgical patients was 9 (8) mm Hg in the CPP < 60 mm Hg group versus 5 (9) mm Hg in the CPP \geq 60 mm Hg group (*P* = 0.001). For trauma patients the median ICP was

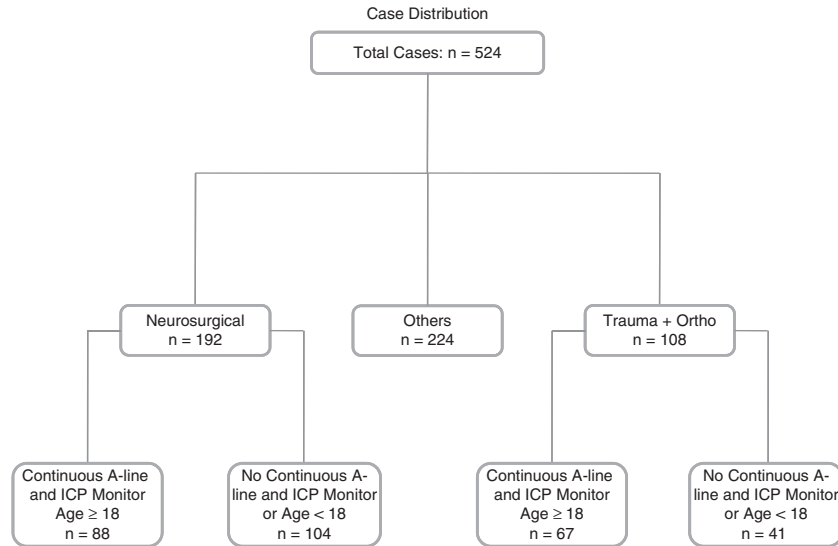


FIGURE 1. Case distribution from 524 cases identified as having both arterial line (A-line) and intracranial pressure (ICP) monitors. “Others” were vascular patients with no intracranial pathology. No continuous A-line and ICP monitor implies either lumbar drain or <45 continuous minutes during which cerebral perfusion pressure could be calculated. Patients under the age of 18 were excluded from analysis.

17 (9) mm Hg in the CPP < 60 mm Hg group versus 9 (13) mm Hg in the CPP ≥ 60 mm Hg group ($P = 0.009$). With regard to MAP, in the trauma cohort, patients with CPP < 60 mm Hg had a higher frequency of epochs with MAP < 70 mm Hg ($n = 55$, $P = 0.001$). There were no differences in the frequency of reduced MAP between the CPP < 60 mm Hg and the CPP ≥ 60 mm Hg subgroups in the neurosurgical cohort.

There were no associations between sex or ASA class and frequency of CPP < 60 mm Hg. Similarly, preoperative administration of vasopressors did not correlate with intraoperative CPP < 60 mm Hg. In terms of intraoperative clinical associations, neurosurgical patients with CPP < 60 mm Hg received both a greater number of boluses ($P = 0.04$) and a greater total dose (mcg) of phenylephrine hydrochloride ($P = 0.03$) compared with patients with CPP ≥ 60 mm Hg. There were no differences in vasopressor use between subsets in the trauma cohort. Finally, there were no significant differences in the

anesthetic technique between the two CPP subgroups in either surgical cohort.

DISCUSSION

The main finding of this study is that 5-minute epochs during which median CPP is below 60 mm Hg are common during the intraoperative care of adult neurosurgical and trauma patients with intracranial pathology at a tertiary medical center. Not only was there a high percentage of patients with at least one 5-minute epoch of CPP < 60 mm Hg (74% of neurosurgical patients and 82% of trauma patients), but both groups had multiple epochs and subsequently prolonged total minutes with CPP < 60 mm Hg despite the acceptable overall median CPP. Avoidance of low CPP is associated with improved outcome in patients with traumatic brain injury^{2,4} and subarachnoid hemorrhage,¹ but defining “adequate CPP” can be problematic. The most recent Brain Trauma Foundation recommendations for cerebral perfusion

TABLE 1. Demographic Summary

	Neurosurgery (N = 88)	Trauma (N = 67)
Age (y)	50 ± 16	45 ± 17
Sex (%)		
Male	43 (49%)	43 (64%)
ASA classification (%)		
1	1	1
2	13	3
3	44	23
4	24	38
5	3	2
BMI (kg/m ²)	28 ± 7	27 ± 6

Mean age (y), sex distribution (% male), American Society of Anesthesiologists (ASA) Classification (% of total), and body mass index (BMI, kg/m²).

TABLE 2. Summary of Diagnoses in Neurosurgical Cohort

Diagnosis	Count
Subarachnoid hemorrhage	45
Brain tumor	17
Subdural hematoma	13
Intraparenchymal hemorrhage	6
Unruptured aneurysm	2
Miscellaneous	5
Total	88

Neurosurgical diagnoses were diverse, unlike the trauma group, in which traumatic brain injury was the consistent mechanism of injury. Miscellaneous diagnoses include hydrocephalus (1), resection of ischemic brain tissue (3), and gun shot wound to head (1).

TABLE 3. Frequency of CPP <60 mm Hg

	CPP < 60 mm Hg	CPP ≥ 60 mm Hg	P
Neurosurgery (N = 88)			
Frequency	65 (74%)	23 (26%)	
Median ICP (mm Hg)	9 (8)	5 (9)	0.001
Median CPP (mm Hg)	69 (14)	84 (10)	<0.001
Trauma (N = 67)			
Frequency	55 (82%)	12 (18%)	
Median ICP (mm Hg)	17 (9)	9 (13)	0.009
Median CPP (mm Hg)	63 (16)	78 (15)	<0.001

Number (%) or median (interquartile range) is shown.

Median cerebral perfusion pressure (CPP) and intracranial pressure (ICP) data for patients having at least one 5-minute epoch with CPP < 60 mm Hg versus patients with continuous median CPP ≥ 60 mm Hg. The median ICP and CPP were calculated for each 5-minute epoch over the monitoring period to determine the value reported. Note that the overall median CPP in each group was ≥ 60 mm Hg, despite the frequency of 5-minute epochs in which the CPP was < 60 mm Hg.

thresholds conclude that the CPP target for traumatic brain injury patients ranges from 50 to 70 mm Hg.⁷ As the “critical threshold” for ischemia ranges between 50 and 60 mm Hg, the Foundation recommends a CPP threshold of approximately 60 mm Hg to provide a buffer against decreased CPP below the threshold for ischemia. This was the basis of our choice of 60 mm Hg as the lower limit of normal CPP.

Kuo et al⁸ studied CPP in 30 patients undergoing emergent craniotomy for hematoma evacuation; an ICP microsensor was placed in all patients after induction of anesthesia. Patients' CPP values were monitored intermittently and reported at predetermined procedural points including skull removal, dural opening, and hematoma evacuation. Patients were subdivided into groups with favorable outcomes (n = 19; those having a Glasgow Outcome Score of 4 to 5) and unfavorable (n = 11; having a Glasgow Outcome Score of 1 to 3). The mean intraoperative CPP in the favorable group was generally ≥ 60 mm Hg at dural opening, whereas the CPP in the unfavorable group was significantly below this. The range of CPP values reported in this article is similar to our own; our study has the advantage of a larger patient sample, 2 distinct patient populations, and continuous monitoring.

Although the overall median CPP was > 60 mm Hg in all subgroups of patients, there were differences in management that may indicate potential areas for clinical improvement. For example, both higher ICP and a greater frequency of MAP < 70 mm Hg were associated with CPP < 60 mm Hg in the trauma subgroup. By contrast, there was no difference in the frequency of decreased MAP between the neurosurgical CPP < 60 mm Hg and CPP ≥ 60 mm Hg subgroups. Thus, although ICP was the primary determinant of low CPP in the neurosurgical cohort, both reduced MAP and high ICP were contributory in the trauma low CPP subgroup. It is possible that the increased phenylephrine dosing in the neurosurgical CPP < 60 mm Hg subgroup resulted in less hypotension. Making recommendations regarding the management of MAP in traumatic brain injury patients is complicated because the use of vasopressors and fluids to elevate CPP, although effective at reducing the incidence of secondary ischemic events, has also been

associated with an increased risk of adult respiratory distress syndrome,⁹ and is specifically discouraged by the Brain Trauma Foundation Guidelines⁷ (Level II recommendation). We currently cannot make any recommendations regarding vasopressor use and CPP. Our data do, however, generate hypotheses that are testable in future prospective randomized studies.

The limitations of this study include a retrospective methodology, which precludes us from establishing the precise incidence of CPP < 60 mm Hg in the intraoperative setting. Furthermore, given the retrospective nature of our study and the diverse preoperative intracranial pathologies of our patients, we are unable to meaningfully assess correlations between CPP < 60 mm Hg and patient outcomes. Similarly, we are unable to comment on whether our study population of anesthetized patients was any more tolerant of low CPP (through reduction of cerebral oxygen requirements) than were ICU patients who are likely to receive sedation rather than general anesthesia. It could also be argued that a CPP < 60 mm Hg was targeted as the desired goal in some neurosurgical patients (eg, those with subarachnoid hemorrhage and unsecured aneurysms). However, the data in our study do not support this interpretation. First, the overall median CPP for the neurosurgical < 60 mm Hg cohort was 69 (14) mm Hg, suggesting that CPP ≥ 60 mm Hg was the goal and increased vasopressor dosing was used to achieve this. Second, the trauma population also had a high frequency of CPP < 60 mm Hg (82% of cases, with a range of 1 to 90 episodes in a given case). There would be no obvious reason to systematically target a lower CPP in the trauma patient. Thus, our interpretation is that, despite overall CPP means of > 60 mm Hg, discrete episodes of CPP < 60 mm Hg occur frequently across surgical populations, are unplanned, and may represent an opportunity for improved alerting and intervention. Finally, it is possible that the exclusion of CPP data from patients monitored for < 45 minutes could have altered our results. However, the majority of these cases related to brief procedures or intraventricular catheters that were placed at the end of surgery. Limited data points in these instances would render analysis less reliable, which is why these cases were excluded from the study.

In conclusion, our data demonstrate that intraoperative CPP <60 mm Hg is frequent in two different surgical patient populations with intracranial pathology, despite average CPP values >60 mm Hg. Further prospectively designed studies of intraoperative CPP monitoring, management, and outcomes are warranted.

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