

On a Not-Dead Horse: CPP Deserves More Respect

Jennifer A Kosty, BA

Perelman School of Medicine

University of Pennsylvania

W Andrew Kofke, MD MBA

Departments of Anesthesiology and Critical Care and Neurosurgery

University of Pennsylvania

Twenty-two years ago, Michenfelder¹ in his Rovenstine Lecture on professional respect and then Crosby and Todd² in a follow-up editorial in this journal bemoaned the excessive preoccupation of that era with modest clinically insignificant rises in intracranial pressure secondary to the use of anesthetic agents. Two articles^{3,4} in this month's issue describe the clinical measurement of a related value, the cerebral perfusion pressure (CPP), and underscore the opposite concern: we are not preoccupied enough with CPP. Moreover, the seemingly small variations noted in these articles may be clinically significant. Moore et al.³ report an institutional failure to maintain the minimal suggested CPP during neurosurgical and trauma procedures, whereas Rasulo et al.⁴ call into question the acceptance of this threshold, providing evidence supporting a higher CPP threshold in patients with aneurysmal subarachnoid hemorrhage.

The study by Moore et al.³ examines the frequency of decreases in CPP to below 60 mmHg during both neurosurgical and trauma procedures. Using consecutive 5-minute epochs to examine the frequency of this occurrence, they report that 74% of neurosurgery cases and 82% of trauma cases had at least one epoch during which the median CPP was lower than 60 mmHg with a suggestion that CPP was lower than this threshold for some 15-20% of the time during these procedures. For reasons we will review, these observations should not be taken lightly.

Rasulo et al.⁴ investigate the use of the recently described autoregulation parameter, the pressure reactivity index, or PRx, in patients with subarachnoid hemorrhage (SAH). Although patients with a good outcome were younger with lower WFNS and GCS scores, in this group, significantly more time was spent with CPPs in the PRx-determined optimum CPP range. Interestingly, 19% of the patients had optimal CPPs greater than 91mmHg, and 45% had optimal CPPs greater than 81 mmHg. These findings support previous observations in patients with TBI that CPP management in a range near the PRx-defined optimum is associated with improved outcomes, and that some patients have PRx-defined optimal CPPs greater than 80 mmHg.⁵⁻⁷ Moreover, Rasulo et al.'s⁴ observations and those of others suggest that the goal CPP sought in Moore et al's³ study may be too low. Nonetheless, the notion that CPPopt is the new

standard for CPP must be considered an hypothesis at this point, albeit an attractive hypothesis.

These two articles raise several important points related to CPP that merit a brief examination. The first is the most basic: the actual method by which CPP is calculated. Lassen defined CPP in 1958 as “the pressure difference between cerebral arteries and veins... measured *at the level of the head.*”⁸ The importance of measuring MAP at the level of the tragus was reported by Rosner et al.⁹ who observed a 19 mmHg higher CPP when MAP was measured at heart instead of tragus with a 50 degree head of bed elevation. This gradient can be even higher in a tall patient, underscoring the importance of calculating CPP based on a tragus-level MAP. However, a recent survey¹⁰ reports that most neuroICUs in the United States calculate CPP using MAP measured at the level of the heart. This worrisome practice adds variability and likely widespread erroneously high estimates to the actual cerebral perfusion pressure thought to be experienced by the brain, further varying with the angle of the head of the bed, and the patient’s height. Underappreciation of this concept has led to devastating intraoperative strokes during shoulder surgeries that utilize the beach chair position when otherwise acceptable low normotension is induced and MAP is monitored at the level of the arm, or, worse, the leg.¹¹ In the reports in this issue, Moore et al.³ made MAP measurements in the supine position and Rasulo et al⁴ measured

CPP based on MAP measured at the level of the tragus (personal communication....notably this detail is missing in the article).

The next point that bears mention is the accepted CPP threshold for the lower limit of autoregulation (LLA). Moore et al³ reasonably assume this to be 60mmHg but this may be too low. Several authors have attempted to define LLA in normal humans. Lassen initially suggested the LLA was a MAP of 50 mmHg in normal humans.⁸ However, in a very interesting letter to the editor published almost 40 years later, Drummond¹² pointed out that the data points defining the LLA were defined by a study that involved inducing hypotension in normal pregnant women with hydralazine, a known cerebral vasodilator, and veratrum veride, which has unknown effects on cerebral circulation. With data from later original studies, he suggested that the LLA in normotensive individuals is likely a MAP of at least 70 mmHg and is probably even higher in hypertensive patients.

So what CPP threshold should be used to avoid breaching the LLA in TBI or SAH patients? Rosner et al¹³. suggested 70 mmHg and frequently higher as dictated by individualized observations, a recommendation based on the retrospective observation that his patients were managed at or above this level (83 ± 14 mmHg) and had better outcomes than historical controls. The Brain Trauma Foundation recommends a threshold of 60 mmHg based on several lines

of evidence including reports of worsened outcome with CPP less than 60mmHg^{14,15}. Other groups have suggested a higher threshold of 70 mmHg.^{16 17} Steiner et al.⁵, who determined the optimal CPP ranges for a large group of TBI patients, suggest that unlike healthy individuals, patients with severe neurological injury demonstrate intact or improved autoregulation within only a narrow range of CPP that is unique to each patient. Of the five studies cited by the Brain Trauma Foundation that suggest a cutoff of 60 mmHg, two measured MAP for calculated CPP relative to the right atrium,^{14,15} and one relative to the foramen of Monro.¹⁸ The methodologies for the other two studies^{19,20} could not be determined by the published methods or author contact. This methodological heterogeneity in the foundational research certainly further adds to the confusion on the appropriate LLA in TBI patients.

To conclude, the reports in this issue by Moore et al³ and Rasulo et al⁴ combined with work of others suggests: (1) commonly accepted CPP goals, which are possibly themselves too low, may not be regularly achieved during surgery, (2) autoregulation is not uniformly intact above a specific limit in patients with severe neurological injury but rather varies with CPP, (3) the LLA may be higher in some brain injured patients than in normal patients, and (4) an individualized approach to monitoring CPP with individualized goals ultimately may be the most appropriate approach as will need to be determined

in prospective studies. Finally, combining these observations with reports of morbidity and worse outcomes with low or not optimal CPP and concerns regarding systematic erroneous CPP assessment, it seems that CPP is a horse far from beaten; indeed, this living horse appears to merit a good deal more study and respect.

References

1. MICHENFELDER J. The 27th Rovenstine Lecture: Neuroanesthesia and the achievement of professional respect. *Anesthesiology* 1989;70 (4):695.
2. CROSBY G, TODD MM. On neuroanesthesia, intracranial pressure, and a dead horse. *J Neurosurg Anesthesiol* 1990;2:143-4.
3. MOORE LE, SHARIFPOUR M, SHANKS A, et al. Cerebral Perfusion Pressure Below 60 mmHg is Common in the Intraoperative Setting. *Journal of Neurosurgical Anesthesiology* 2011 in press.
4. RASULO FA, GIRARDINI A, LAVINIO A, et al. Are optimal cerebral perfusion pressure and cerebrovascular autoregulation related to longterm outcome in patients with aneurysmal subarachnoid hemorrhage? *journal of Neurosurgical Anesthesiology* 2011 in press.
5. STEINER LA, CZOSNYKA M, PIECHNIK SK, et al. Continuous monitoring of cerebrovascular pressure reactivity allows determination of optimal cerebral perfusion pressure in patients with traumatic brain injury. *Crit Care Med* 2002;30:733-738.
6. CZOSNYKA M, BRADY K, REINHARD M, et al. Monitoring of cerebrovascular autoregulation: facts, myths, and missing links. *Neurocrit Care* 2009;10:373-386.
7. ZWEIFEL C, LAVINIO A, STEINER LA, et al. Continuous monitoring of cerebrovascular pressure reactivity in patients with head injury. *Neurosurg Focus* 2008;25.
8. LASSEN NA. Cerebral blood flow and oxygen consumption in man. *Physiological reviews* 1959;39:183-238.
9. ROSNER MJ, COLEY IB. Cerebral perfusion pressure, intracranial pressure, and head elevation. *Journal of neurosurgery* 1986;65:636-41.
10. KOFKE WA, KOSTY J, KUMAR M, et al. Comparison of Clinician Practices for Measuring Cerebral Perfusion Pressure: A Review of the Literature and Survey of Members of the Neurocritical Care Society (abstract). *Journal of Neurosurgical Anesthesiology* 2011 in press
11. POHL A, CULLEN DJ. Cerebral ischemia during shoulder surgery in the upright position: a case series. *Journal of clinical anesthesia* 2005;17:463-9.

12. DRUMMOND JC. The lower limit of autoregulation: time to revise our thinking? *Anesthesiology* 1997;86:1431-3.
13. ROSNER MJ, ROSNER SD, JOHNSON AH. Cerebral perfusion pressure: management protocol and clinical results. *Journal of neurosurgery* 1995;83:949-62.
14. CHANGARIS DG, MCGRAW CP, RICHARDSON JD, et al. Correlation of cerebral perfusion pressure and Glasgow Coma Scale to outcome. *The Journal of trauma* 1987;27:1007-13.
15. CLIFTON GL, MILLER ER, CHOI SC, et al. Fluid thresholds and outcome from severe brain injury. *Critical care medicine* 2002;30:739-45.
16. MENZEL M, SOUKUP J, HENZE D, et al. Brain tissue oxygen monitoring for assessment of autoregulation: preliminary results suggest a new hypothesis. *Journal of neurosurgical anesthesiology* 2003;15:33-41.
17. VESPA P, PRINS M, RONNE-ENGSTROM E, et al. Increase in extracellular glutamate caused by reduced cerebral perfusion pressure and seizures after human traumatic brain injury: a microdialysis study. *Journal of neurosurgery* 1998;89:971-82.
18. KIENING KL, HARTL R, UNTERBERG AW, et al. Brain tissue pO₂-monitoring in comatose patients: implications for therapy. *Neurological research* 1997;19:233-40.
19. CHAN KH, DEARDEN NM, MILLER JD, et al. Multimodality monitoring as a guide to treatment of intracranial hypertension after severe brain injury. *Neurosurgery* 1993;32:547-52; discussion 552-3.
20. CHAN KH, MILLER JD, DEARDEN NM, et al. The effect of changes in cerebral perfusion pressure upon middle cerebral artery blood flow velocity and jugular bulb venous oxygen saturation after severe brain injury. *Journal of neurosurgery* 1992;77:55-61.