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EDITORIAL

Are we ready for automated optimal cerebral perfusion pressure?

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Severe traumatic brain injury (TBI) may determine cerebral autoregulation derangements and cerebral blood flow (CBF) might become dependent on cerebral perfusion pressure (CPP).[1] Indeed, in healthy individuals CBF is adjusted by means of cerebral vessel vasodilatation and vasoconstriction, the so-called cerebral pressure autoregulation:[2] the uninjured brain physiologically responds to variations in cerebral perfusion pressure (CPP) through constant modifications of CBF and vascular resistances.

In order to counteract CPP dependency, and being CPP related to mean arterial pressure (MAP) and intracranial pressure (ICP), after severe TBI CPP is generally recommended to be kept between 60 and 70 mmHg during the whole intensive care unit (ICU) stay.[3] However, should CPP management in TBI patients be carefully tailored and individualized to each single patient? An "optimal and individual targeted therapy" is considered of importance in a wide variety of field in medicine, indeed.[4] The 2014 Neuromonitoring Guidelines already promoted the concept of patient autoregulation based monitoring and treatment;[4] nevertheless, the optimal cerebral perfusion pressure (CPPopt) targeting in patients with TBI represents an actual and vivid matter of debate and research,[5] mostly because, facing TBI pattern heterogeneity, CPP target management may be of efficacy only where autoregulation is best preserved.[6]

In patients with closed head injury, averaged cerebral autoregulation may be assessed by cerebrovascular pressure reactivity, using the Pressure Reactivity Index (PRx).[7] PRx does not need external stimuli, depending from the periodic variations in ICP and MAP, and it is routinely used as a marker for cerebral autoregulatory status.[4] Negative and positive PRx values indicates intact (that is a reduction in ICP in response to an increase in MAP) and impaired vascular pressure reactivity, respectively.

Indeed, PRx-CPP plotting generates a U-shaped curve which reveals the optimal CPP (CPPopt), corresponding to the smallest value of PRx where the cerebral autoregulation response is most active, while all other CPP values are associated with impaired cerebrovascular reactivity and thus with worse patient outcome.[6, 8]

As no golden standard is available for cerebral autoregulation or CPPopt management, in the past decades great research has been de-

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voted to the development of various software to automatically calculate CPPopt from the bedside.[9] Nevertheless, CPPopt curves may be difficult or awkward to handle, sometimes only partially present or definitively absent, determining the necessity of constant physician assessment and interpretation. It comes that the appraisal of the reliability and validity of an automated CPPopt calculation and display at the bedside is warranted as the basis of a CPPopt interventional study. On one hand, a possible CPPopt feasibility study would adapt the current ICP/CPP oriented treatment algorithm to individual CPPopt targets replacing the current 60-70 mmHg CPP guideline range; on the other, various brain pathologies (post-anoxic insult, acute stroke, neonatal encephalopathies, etc.) might benefit of a "tailored" cerebral perfusion target during intensive care management.[10-12]

In this issue of *Minerva Anestesiologica*, Steijn *et al*. presented the results of a survey on the validity of automated CCPopt.[13] The authors' primary objective was to test the agreement between the automatically-generated CPPopt values (automated CPPopt) and the values deduced from inspecting the CPPopt curve by selected clinicians with expertise interpreting CPPopt and PRx (clinicians' visual CPPopt), and to identify factors that might be associated with eventual disagreement. Their secondary objective was to explore how clinicians would adapt therapy when facing CPP deviation from CPPopt.

The validity of the presented survey was assured by Authors' consensus. They found a high level of agreement between the choices of clinicians and the automated CPPopt values: 46% of clinicians' visual CPPopt values completely agreed with the automated CPPopt value, and 48% of them agreed within a range of ±5 mmHg. Precisely, the agreement between automated CPPopt and visual judgement was excellent when the PRx-CPP relationship followed a well-defined U-shaped curve. Furthermore, when considering clinical choices, sub-optimal CPP values reached very high consensus for therapy change: most responders decided to change CPP in the direction of their selected CPPopt when the absolute difference between the patients' current CPP and clinicians' visual CPPopt was >5 mmHg; nevertheless, CPP above optimal led to more variable decisions. Thus, being the CPPopt concept a promising "biologically plausible" target that uses cerebrovascular pressure reactivity to guide individual CPP therapy in severe TBI patients, this survey adequately explored a CPPopt based treatment algorithm in patients with traumatic brain injury.

However, some important issues need to be discussed to better understand the impact of such findings in the clinical management of CPP in TBI patients.

First of all, it is difficult to merely conclude that these data support a routine use of automated CPPopt from the results of an unvalidated and relatively small-scale questionnaire, with only screenshots and limited physiological information provided, without clinical results. The selected 22 clinicians were all both "expert" in cerebral autoregulation and familiar with the CPPopt method. Thus, beside selection biased, the small judging cohort may not be representative of "non-expert" clinicians.

Second, three out of ten screenshots were deemed by more than 45% of clinicians not to be reliable enough to yield a trustworthy CPPopt. This limits the current CPPopt based treatment algorithm because as high as 30% of screenshots was not trustful. Different responses might have been produced with provided clinical scenarios and with more specific and longer screenshots. Possible solutions like automated weighting and (multiple) averaging are currently under investigation. Therefore, continuing research is required to find more sophisticated CPP-based treatment strategy.

Third, when CPPopt deviated more than 5 mmHg from the current patients' CPP, the majority of clinicians opted to change therapy. In daily clinical intensive care practice there would be no possibility to rely continuously on 'experts', so the CPPopt methodology should be much more robust than it is now.

Thus, with their survey, Steijn RK *et al.* made an essential step towards further designs of the first CPPopt feasibility study, so as to

properly prepare a randomized evaluation of "CPPopt-targeted" *versus* "current standard treatment" in TBI patients. Indeed, CPPopt should be first clearly defined as a physiologic target or a prognostic tool: it needs to be evaluated before recommendations can be made so as to know if and how CPPopt could be integrated into clinical decision making.[14-16] Meanwhile, both the CPP automated value and the PRx-CPP plot should be available for testing CPPopt guided management at the bedside to yield a trustworthy CPPopt.

Future prospective research should aim to better understand the potential mechanisms and effects of automated CPPopt and to clearly identify which patients would more benefit the most from such monitoring and therapeutic intervention.

References

1. Bouma GJ, Muizelaar JP. Cerebral blood flow, cerebral blood volume, and cerebrovascular reactivity after severe head injury. J Neurotrauma 1992;9(Suppl 1):S333-48.
2. Aaslid R, Lindegaard KF, Sorteberg W, Nornes H. Cerebral autoregulation dynamics in humans. Stroke 1989;20:45-52.
3. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, *et al*. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. Neurosurgery 2017;80:6-15.
4. Le Roux P, Menon DK, Citerio G, Vespa P, Bader MK, Brophy GM, *et al*. Consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care: A statement for healthcare professionals from the Neurocritical Care Society and the European Society of Intensive Care Medicine. Intensive Care Med 2014;40:1189-209.
5. Prabhakar H, Sandhu K, Bhagat H, Durga P, Chawla R. Current concepts of optimal cerebral perfusion pressure in traumatic brain injury. J Anaesthesiol Clin Pharmacol 2014;30:318-27.
6. Aries MJ, Czosnyka M, Budohoski KP, Steiner LA, Lavinio A, Kolias AG, *et al*. Continuous determination of optimal cerebral perfusion pressure in traumatic brain injury. Crit Care Med 2012;40:2456-63.
7. Czosnyka M, Smielewski P, Kirkpatrick P, Laing RJ, Menon D, Pickard JD. Continuous assessment of the cerebral vasomotor reactivity in head injury. Neurosurgery 1997;41:11-7.
8. Steiner LA, Czosnyka M, Piechnik SK, Smielewski P, Chatfield D, Menon DK, *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;30:733-8.
9. Schmidt JM, Kummer BR. Clinical Decision Support for Cerebral Perfusion Optimization After Traumatic Brain Injury. Crit Care Med 2016;44:1958-60.
10. Diedler J, Santos E, Poli S, Sykora M. Optimal cerebral perfusion pressure in patients with intracerebral hemorrhage: an observational case series. Crit Care 2014;18:R51.
11. da Costa CS, Czosnyka M, Smielewski P, Mitra S, Stevenson GN, Austin T. Monitoring of Cerebrovascular Reactivity for Determination of Optimal Blood Pressure in Preterm Infants. J Pediatr 2015;167:86-91.
12. Sekhon MS, Smielewski P, Bhate TD, Brasher PM, Foster D, Menon DK, *et al*. Using the relationship between brain tissue regional saturation of oxygen and mean arterial pressure to determine the optimal mean arterial pressure in patients following cardiac arrest: A pilot proof-of-concept study. Resuscitation 2016;106:120-5.
13. Steijn R, Stewart R, Czosnyka M, Donnelly J, Ercole A, Absalom A, *et al*. Survey in expert clinicians on validity of automated calculation of optimal cerebral perfusion pressure. Minerva Anestesiol 2018;84:40-8.
14. Lazaridis C, Smielewski P, Steiner LA, Brady KM, Hutchinson P, Pickard JD, *et al*. Optimal cerebral perfusion pressure: are we ready for it? Neurol Res 2013;35:138-48.
15. Depreitere B, Guiza F, Van den Berghe G, Schuhmann MU, Maier G, Piper I, *et al*. Pressure autoregulation monitoring and cerebral perfusion pressure target recommendation in patients with severe traumatic brain injury based on minute-by minute monitoring data. J Neurosurg 2014;120:1451-7.
16. Weersink CS, Aries MJ, Dias C, Liu MX, Kolias AG, Donnelly J, *et al*. Clinical and Physiological Events That Contribute to the Success Rate of Finding "Optimal" Cerebral Perfusion Pressure in Severe Brain Trauma Patients. Crit Care Med 2015;43:1952-63.

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