

Title: Are we ready for Optimal CPP-oriented management of TBI patients?

Authors: V. Beqiri, M. Aries, A. Ercole, J. Donnelly, J. Tas, M. Czosnyka, D. Menon, P.J. Hutchinson, P. Smielewski

Objective: Monitoring cerebral autoregulation (CA) is important for TBI patients,¹ as impaired CA correlates with poor outcome.²⁻³ Today, automated algorithms allow to assess CPP for which autoregulation is best preserved (CPPopt) continuously and present it at the bedside⁵⁻⁶. Individualising CPP treatment using CPPopt is attractive and this has been recognised in published guidelines. However there are no specifications for its use clinically and it has therefore never been prospectively evaluated¹. Numerous logistic, technical, feasibility and safety questions remain before the idea of selecting individual CPP treatment targets based on the state of CA⁴ can be incorporated into clinical practice. How far are we from strict guidelines on the incorporation of this methodology into TBI protocols?

Design: Literature review

Subjects:

Methods: Systematic review

Results: The feasibility of CPPopt-guided therapy has only been evaluated retrospectively and in non-clinical ways, whereas no studies exist on its safety. A prospective investigation of CPPopt-guided therapy has been initiated with 'Cpopt Guided Therapy: Assessment of Target Effectiveness' (COGiTATE), a multicenter randomized trial assessing feasibility and safety of a continuous CA monitoring-based therapy in adult TBI patients.

Conclusions: COGiTATE seems to be the first step to define the physiological effect of targeting CPPopt and should pave the way toward establishing the exact protocol of CPPopt-oriented therapy and the phase III study.

References:

1. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. *Neurosurgery*. 2016;80(1):1. doi:10.1227/NEU.0000000000001432.
2. Hlatky R, Furuya Y, Valadka AB, et al. Dynamic autoregulatory response after severe head injury. *J Neurosurg*. 2002;97(5):1054-1061. doi:10.3171/jns.2002.97.5.1054.
3. Czosnyka M, Czosnyka Z, Smielewski P. Pressure reactivity index: journey through the past 20 years. doi:10.1007/s00701-017-3310-1.
4. 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(4):733-738. <http://www.ncbi.nlm.nih.gov/pubmed/11940737>. Accessed December 28, 2017.
5. Aries MJH, Czosnyka M, Budohoski KP, et al. Continuous determination of optimal cerebral perfusion pressure in traumatic brain injury*. *Crit Care Med*. 2012. doi:10.1097/CCM.0b013e3182514eb6.
6. Liu X, Maurits NM, Aries MJH, et al. Monitoring of Optimal Cerebral Perfusion Pressure in Traumatic Brain Injured Patients Using a Multi-Window Weighting Algorithm. *J Neurotrauma*. 2017;34(22):3081-3088. doi:10.1089/neu.2017.5003.
7. Depreitere B, Güiza F, Berghe G Van Den, 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(120):1451-1457. doi:10.3171/2014.3.JNS131500.

8. Güiza F, Meyfroidt G, Piper I, et al. Cerebral Perfusion Pressure Insights and Associations with Outcome in Adult Traumatic Brain Injury. doi:10.1089/neu.2016.4807.
9. Oshorov A V, Savin IA, Goriachev AS, Popugaev KA, Potapov AA, Gavrilov AG. [The first experience in monitoring the cerebral vascular autoregulation in the acute period of severe brain injury]. *Anesteziol Reanimatol.* (2):61-64. <http://www.ncbi.nlm.nih.gov/pubmed/18540464>. Accessed January 1, 2018.
10. Donnelly J, Czosnyka M, Adams H, et al. Individualizing Thresholds of Cerebral Perfusion Pressure Using Estimated Limits of Autoregulation. *Crit Care Med.* 2017;45(9):1464-1471. doi:10.1097/CCM.0000000000002575.
11. Dias C, Silva MJ, Pereira E, et al. Optimal Cerebral Perfusion Pressure Management at Bedside: A Single-Center Pilot Study. *Neurocrit Care.* 2015;23(1):92-102. doi:10.1007/s12028-014-0103-8.
12. Jaeger M, Dengl M, Jü, Schuhmann MU. Effects of cerebrovascular pressure reactivity-guided optimization of cerebral perfusion pressure on brain tissue oxygenation after traumatic brain injury*. *Crit Care Med.* 2010;38(5):1343-1347. doi:10.1097/ccm.0b013e3181d45530.