Autoregulation-oriented therapy multicenter trial in severe TBI (COGiTATE)

V. Beqiri, 1 N.M. Wismans, 1 G. Meyfroidt, 1 B. Depreitere, 1 J. Donnelly, 1 J. Tas, 1 M. Cabreira, 2 A. Liberti, 1 R. Haeren, 1 C. Robba, 2 P. Hutchinson, 2 A. Kolias, 2 D. Menon, 3 A. Ercole, 3 P. Smielewski, 2 M. Czosnyka, 1 M. Aries 1

1. Maastricht University Medical Centre –, Department of Intensive Care and Neurosurgery, University of Maastricht; 2. Department of Clinical Neurosciences, Neurosurgery Department, University of Cambridge; 3. Academic Hospital Leuven, Department of Intensive Care and Neurosurgery, Leuven, Belgium; 4. Department of Technical Medicine, University of Twente, The Netherlands; 5. Division of Anaesthesiology, University of Cambridge, Addenbrooke’s Hospital, Cambridge, UK.

- Background
  - Individualising care is an important aspect of the intensive care management of traumatic brain injury (TBI).
  - Autoregulation assessment could provide a useful precision medicine cerebral perfusion pressure (CPP) target.
  - Numerous observational studies have shown improved outcomes in patients managed at a CPP for which autoregulation is best preserved (CPPopt), but this has never been prospectively evaluated.
  - Feasibility and safety need to be determined before a prospective outcome trial can be designed and conducted.

- Objectives
  - Primary objective: feasibility of targeting CPPopt in severe TBI.
  - Secondary objectives: safety and physiological effects of targeting CPPopt in severe TBI.

- Design
  - COGiTATE (CPPopt Guided Therapy Assessment Of Target Effectiveness) is a multicentre, phase II non-blinded, randomised controlled trial. Patients’ inclusion criteria, randomization and study procedure are described in figure 1. Participating centres are the Intensive Care Units (ICU) of Cambridge, Maastricht and Leuven.
  - Endpoints: Primary (feasibility): percentage of monitoring time for which CPP is within 5mmHg of CPPopt (calculated using an algorithm previously described). [1,2] Slightly modified. Secondary (safety): evaluation of changes in ICP, changes in autoregulation indexes and organ function parameters (tropin, ECG, serum creatinine, PaO2/FIO2 ratio).
  - Data collection is conducted using ICM+ software (http://icmplus.neurosurg.cam.ac.uk), supplemented by a dedicated plugin module designed specially for the COGiTATE trial, which includes an automated system of alert and review forms (figure 2).
  - The first patient was enrolled in February 2018. The recruitment will continue until 60 patients are studied.

- First patients
  - First patient enrolled in the control (CPP) arm.
  - The whole monitoring session of the first patient enrolled in the study is shown. The review time points are highlighted. Compliance with the study was 100% . ABP, mean arterial blood pressure; CPP, cerebral perfusion pressure; BTE, Brain Trauma Foundation; ICP, intracranial pressure.

- Discussion
  - This study will give evidence about feasibility of autoregulation oriented therapy concept in severe TBI patients.
  - This study is a prerequisite for a larger phase III outcome study.

- References: