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

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■ 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 inpatients 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 increases of the Treatment Intensity Level, changes in autoregulation indexes and organ function parameters (troponin, 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.

Figure 1. Flow chart of the patients' inclusion, randomization and study procedures in the COGiTATE study

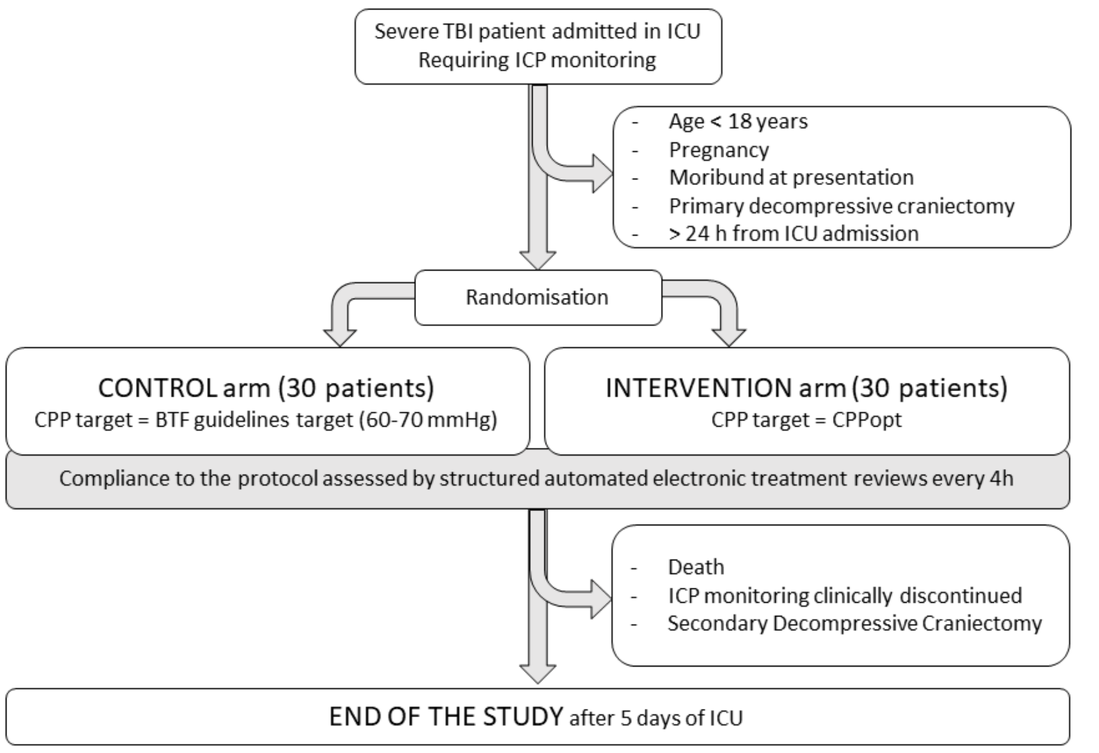
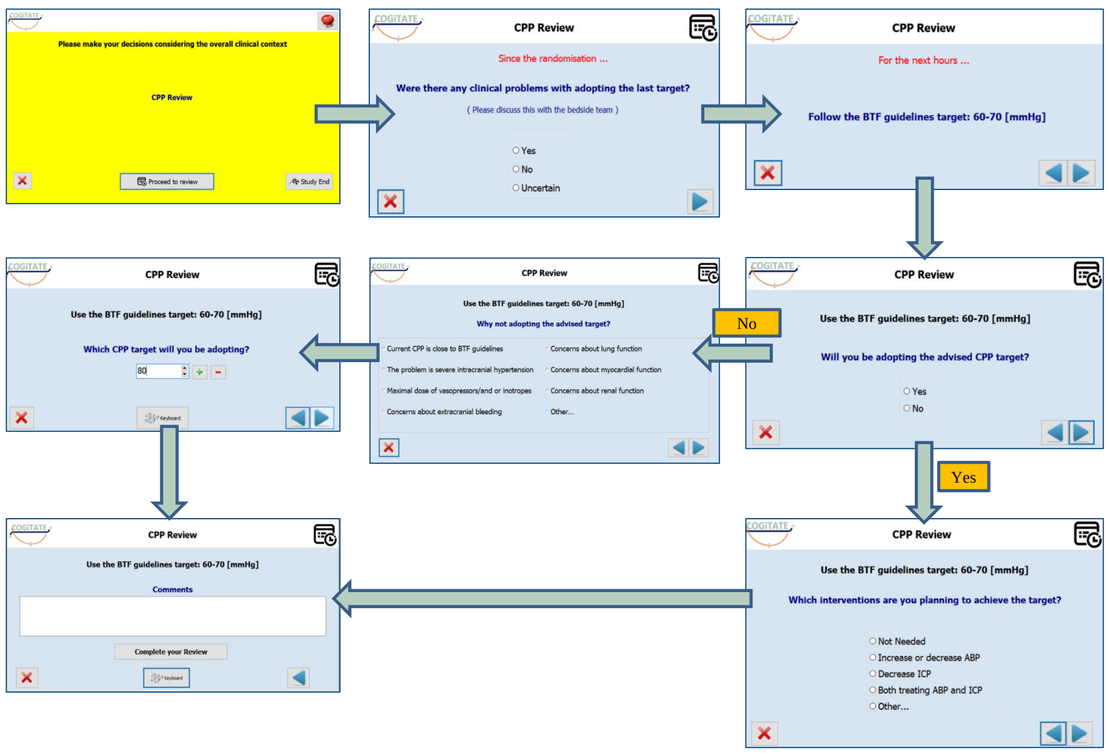


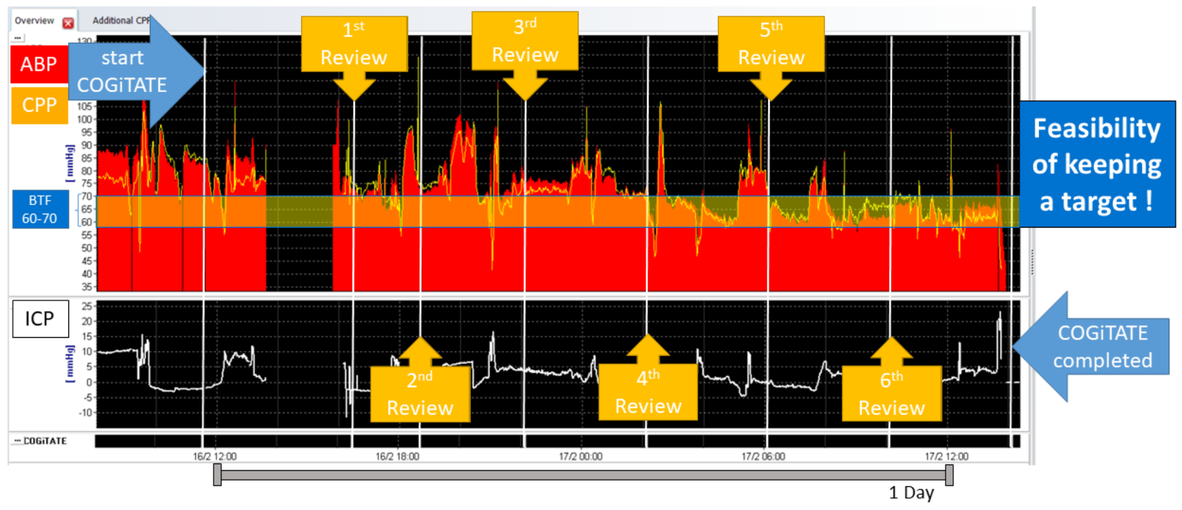
Figure 2. The automated system of alert and review forms, an example from the control group (CPP).



Every 4 h, at fixed time points, the COGiTATE module within ICM+ will pop up a review screen on the data collection computer at the bedside. The review screen will flash yellow, prompting an attending fellow to proceed to the review of the next recommended CPP target. The clinician's decision on the course of action and reasoning behind it will be documented using a set of forms, each comprising one question, with a simple decision tree logic guiding the answers. This will be discussed with the bedside staff and the new CPP target (for the next 4 hours) documented in the patient medical record.

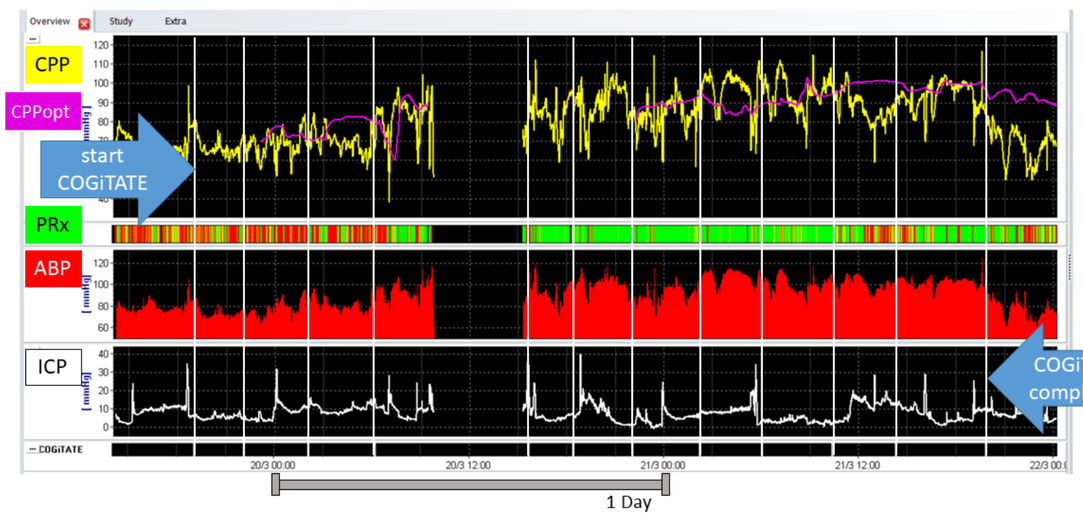
■ First patients

- 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; BTF, Brain Trauma Foundation; ICP, intracranial pressure*.

- First patient enrolled in the intervention (CPPopt) arm.



The whole monitoring session of the first patient enrolled in the intervention arm is shown. Compliance with the study was 100%. The target advised by the automated calculation of CPPopt, when available, was followed by the clinician. *CPP, cerebral perfusion pressure; CPPopt, optimal cerebral perfusion pressure; PRx, pressure reactivity index; ABP, mean arterial blood pressure; 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:

[1] Aries MJ et al. Continuous determination of optimal cerebral perfusion pressure in traumatic brain injury. Crit Care Med. 2012;40(8):2456-63.

[2] Liu X et al. Monitoring of Optimal Cerebral Perfusion Pressure in Traumatic Brain Injured Patients Using a Multi-Window Weighting Algorithm. *J Neurotrauma* 2017;15;34(22):3081–8.

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