Summary of results
NL65095.041.18 Optimization of cerebral perfusion after an ECIC bypass

Protocol ID **Netherlands Trial Register ID** **EudraCT number**	NL65095.041.18 NL7077 2018-002008-15
Name of Sponsor/Company	University Medical Center Utrecht, department of Anesthesiology Heidelberglaan 100, Local mail: Q04.2.313 P.O. Box 85500, 3508 GA Utrecht, The Netherlands Tel:+31 88 755 5555 Fax: +31 30 254 1828
Title of study	Optimal cerebral perfusion after an extracranial-intracranial bypass: should we increase blood pressure or cardiac output?
Investigators	Annemarie Akkermans, MD[1] (coordinating investigator) Judith van Waes, MD, PhD[1] Tristan van Doormaal, MD, PhD[2,3] Eric de Waal, MD, PhD[1] Gabriël Rinkel, MD, FRCP (E)[2] Albert van der Zwan, MD, PhD[2] Cor Kalkman[1] Wilton van Klei, MD, PhD[1] (principal investigator) *Affiliations* [1] Department of Anesthesiology, University Medical Center Utrecht, Utrecht University, The Netherlands [2] Department of Neurology and Neurosurgery, University Medical Center Utrecht, Brain Center, Utrecht University, The Netherlands [3] Department of Neurosurgery, University Hospital Zürich, Switzerland
Study centers	University Medical Center Utrecht, Utrecht, The Netherlands
Publication	Accepted for publication in the *British Journal of Anaesthesia* with title: "The effect of dobutamine and phenylephrine on cerebral perfusion in patients undergoing cerebral bypass surgery: a randomized crossover trial" – expected publication date July 2020
Study period	September 2018 – July 2019
Objectives	We hypothesized that inotropes – to increase cardiac output - rather than vasopressors – to increase blood pressure – are a key element for adequate graft flow and cerebral perfusion. Thus, we aimed to study the effect dobutamine administration versus the effect of phenylephrine administration on graft perfusion in patients undergoing cerebral bypass surgery.
Methodology	Randomized crossover study. Intraoperatively, patients randomly and sequentially received dobutamine to increase cardiac index and phenylephrine to increase mean arterial pressure (MAP). An increase of >10% in cardiac index and >10% in MAP was targeted, respectively. Before both interventions, a reference phase was implemented.
Number of patients (planned and analysed)	15 patients (17 procedures, two patients presented twice) assessed for eligibility. 6 declined to participate and 1 patient no longer met the inclusion criteria since the procedure changed. Total of included patients: 8 for 10 procedures.

Diagnosis and main criteria for inclusion	Adult patients (≥18 years) presenting for an extracranial-intracranial or intracranial-intracranial cerebral bypass were eligible for inclusion. Indication for their procedures was either moyamoya disease or atherosclerotid carotid artery occlussion.
Test product, dose and mode of administration	Dobutamine (2-15 µg kg-1 min-1); over central venous catheter
Duration of treatment	During hemostatis stage of procedure (+- 60 minutes)
Reference therapy, dose and mode of administration	Phenylephrine (0.15-1 µg kg-1 min-1); over central venous catheter.
Criteria for evaluation: efficacy	Graft flow increased with a median of 4.1 [IQR 1.7 – 12.0] ml min-1 after administration of dobutamine and with 3.6 [IQR 1.3 – 7.8] ml min-1 after administration of phenylephrine. The pseudomedian difference in increase in graft flow of dobutamine versus phenylephrine was -0.6 ml min-1, (95% CI -14.5 to 5.3).
Criteria for evaluation: safety	One patient developed a short episode of atrial arrhythmia when dobutamine was administered, which converted to sinus rhythm after discontinuation of dobutamine. There were no hemodynamic consequences. We did not see any other adverse effects of either dobutamine of phenylephrine administration.
Statistical methods	We compared the absolute flow difference between both interventions (Wilcoxon signed rank test) and constructed a random-effect linear regression model to explore treatment and carry-over effect
Summary – conclusions	Both dobutamine and phenylephrine increase graft flow during cerebral bypass surgery, without a preference for one method over the other.
Date of report	July 1st, 2020

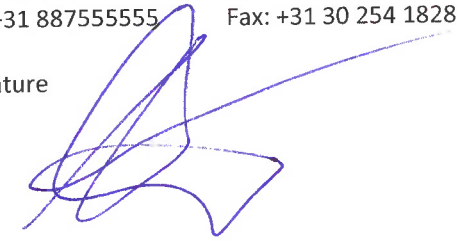
Signed for approval

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study

Principal Investigator

Prof. W. A. van Klei
University Medical Center Utrecht, Department of Anesthesiology Heidelberglaan 100, Local mail: Q04.2.313 P.O. Box 85500, 3508 GA Utrecht, The Netherlands Email: w.a.vanklei@umcutrecht.nl
Tel: +31 887555555 Fax: +31 30 254 1828

Signature

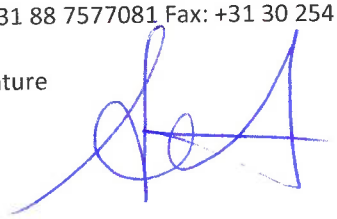


Date 6-7-2020

Coordinating investigator/project leader

Drs. A. Akkermans
University Medical Center Utrecht, Department of Anesthesiology Heidelberglaan 100, Local mail: Q04.2.313 P.O. Box 85500, 3508 GA Utrecht, The Netherlands Email: a.akkermans@umcutrecht.nl
Tel:+31 88 7577081 Fax: +31 30 254 1828

Signature



Date 13-7-2020