Statistical plan: The Effect of Blood Pressure on Cerebral Blood Flow During Propofol Anesthesia

Brief Title: The Effect of Blood Pressure on Cerebral Blood Flow During Propofol Anesthesia

Official Title: The Effect of Blood Pressure on Cerebral Blood Flow During Propofol Anesthesia

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Statistical plan

Trial size: The minimal clinically important difference in internal carotid artery blood flow between evaluations at MAP 60-65 and 80-85 mmHg is considered to be 10% as evaluations using near-infrared spectroscopy indicate that intraoperative cerebral deoxygenation of > 10% associates to postoperative cognitive dysfunction. A power calculation indicated that at a 5% significance level and a power of 80% at least 18 patients are required to detect a difference in internal carotid artery blood flow of 10% corresponding to 19 ml/min assuming a standard deviation for the change of 27

ml/min (unpublished results from the study "Cerebral Blood Flow During Propofol Anaesthesia" NCT02951273). We plan to include 30 patients.

The primary outcome is change in internal carotid artery flow when MAP is set to 60-65 and 80-85 mmHg. Secondary outcomes are 1) change in internal carotid artery flow when MAP is set to 60-65 and 70-75 mmHg, 2) change in internal carotid artery flow when MAP is set to 70-75 and 80-85 mmHg, and 3) the slope of linear regression of MAP and internal carotid artery flow for the evaluations when MAP was 60-65 and 70-75 mmHg as compared to that of the evaluations when MAP was 70-75 and 80-85 mmHg.

Values are averaged over 2 min. The internal carotid artery flow and conductance are corrected for changes in $PaCO_2$ from the value at the evaluation at MAP 60-65 mmHg using a CO_2 reactivity of 18%/kPa and for the S_cO_2 a correction factor of 4.3%/kPa is used (unpublished results from the study "Cerebral Blood Flow During Propofol Anaesthesia" NCT02951273). Analysis of the time points when MAP was set to 60-65, 70-75, and 80-85 mmHg is by a repeated measure mixed model, fit by restricted maximum likelihood in a structured covariance model with time as a fixed effect (Proc mixed; SAS 9.4, SAS Institute, Cary, NC, USA). Analysis of variables not normally distributed is after logarithmic transformation or by a Friedman test and if the test is significant changes are evaluated using Wilcoxon signed rank sum test.

Difference in the slope of linear regression of changes in MAP and internal carotid artery flow for the evaluations at MAP 60-65 and 70-75 mmHg as compared to that for the evaluations when MAP was 70-75 and 80-85 mmHg is by a linear mixed model, fit by restricted maximum likelihood. The outcome parameter is relative change in internal carotid artery flow and the fixed effects are change in MAP, a condition factor for the two situations and an interaction factor to indicate a difference in slope. Values are presented as mean ± SD or median with interquartile range

for not normally distributed data and statistical significance is set at $P < 0.05$. Figures are drawn in R for Windows (version 3.4.1) using the package ggplot2.