

# Determination of selective antegrade perfusion flow rate in aortic arch surgery to restore baseline cerebral near-infrared spectroscopy values: a single centre observational study

Jan-Oliver Friess MD<sup>1,2</sup>, Maurus Beeler MD<sup>1</sup>, Murat Yildiz MD<sup>3</sup>, Dominik Guensch MD<sup>1</sup>, Anja Levis MD<sup>1</sup>, Daniel Gerber MD<sup>1</sup>, Jakob Wollborn MD<sup>4</sup>, Hansjoerg Jenni<sup>3</sup>, Markus Huber<sup>1</sup>, Florian Schönhoff MD<sup>1</sup>, Gabor Erdoes MD<sup>1</sup>

- 1) Department of Anaesthesiology and Pain Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland.
- 2) Department of Anesthesiology, Critical Care and Pain Medicine, Boston Children's Hospital, Harvard Medical School, Boston, United States.
- 3) Department of Cardiac Surgery, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland.
- 4) Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, United States.

**Key Question:** What flow rate is necessary to maintain rSO<sub>2</sub> baseline during selective antegrade perfusion in aortic arch surgery?

**Key finding(s):** rSO<sub>2</sub> was lower than baseline at 6ml/kg/min. Flow rates of 8 and 10 ml/kg/min resulted in rSO<sub>2</sub> that did not differ from the baseline.

**Take-home message:** Baseline rSO<sub>2</sub> is more likely met at 8 than 6 ml/kg/min. A flow rate of 10 ml/kg/min does not further increase the rSO<sub>2</sub> significantly.

Word count: 4653

Meeting presentation:  
2019 EACTA Annual Congress. Ghent, Belgium. September 4-6, 2019

ClinicalTrials.gov Identifier: NCT03484104

Corresponding author:

Jan-Oliver Friess MD

[jan-oliver.friess@insel.ch](mailto:jan-oliver.friess@insel.ch)

[jan-oliver.friess@childrens.harvard.edu](mailto:jan-oliver.friess@childrens.harvard.edu)

Inselspital, Bern University Hospital, Freiburgstrasse 18, CH 3010 Bern, Switzerland and

Boston Children's Hospital, 300 Longwood Ave, Boston, MA 03115, USA, Phone: +1 857 204 0373

The Author(s) 2023. Published by Oxford University Press on behalf of the European Association for Cardio-Thoracic Surgery. All rights reserved.

1 **Abstract**

2  
3 **Objective**

4 Neuroprotection during aortic arch surgery involves selective antegrade cerebral perfusion. The parameters  
5 of cerebral perfusion, e.g. flow rate, are inconsistent across centers and are subject of debate. The aim of  
6 this study was to determine the cerebral perfusion flow rate during hypothermic circulatory arrest required  
7 to meet preoperative awake baseline regional cerebral oxygen saturation (rSO<sub>2</sub>).

8  
9 **Methods**

10 Patients scheduled for aortic arch surgery with hypothermic circulatory arrest were enrolled in this  
11 prospective observational study. After initiation of hypothermic circulatory arrest, bilateral selective  
12 antegrade cerebral perfusion was established and cerebral flow rate was continuously increased. The  
13 primary endpoint was the difference of cerebral saturation from baseline during cerebral perfusion flow  
14 rates of 6 ml/kg/min, 8 ml/kg/min, and 10 ml/kg/min.

15  
16 **Results**

17 A total of 40 patients were included. During antegrade cerebral perfusion rSO<sub>2</sub> was significantly lower than  
18 the baseline at 6ml/kg/min (-7.3, 95%-CI: -1.7,-12.9;  $p=0.0015$ ). In contrast flow rates of 8 and 10  
19 ml/kg/min resulted in rSO<sub>2</sub> that did not significantly differ from the baseline (-2; 95%-CI: -4.3,8.3;  $p>0.99$   
20 and 1.8; (95%-CI: -8.5%, 4.8%;  $p>0.99$ ). Cerebral saturation was significantly more likely to meet baseline  
21 values during selective antegrade cerebral perfusion with 8ml/kg/min than at 6ml/kg/min (44.1%; 95%-CI:  
22 27.4%,60.8% vs 11.8%; 95% CI: 0.9%,22.6%;  $p=0.0001$ ).

23  
24 **Conclusion**

25 At 8 ml/kg/min cerebral flow rate during selective antegrade cerebral perfusion regional cerebral oximetry  
26 baseline values are significantly more likely to be achieved than at 6 ml/kg/min. Further increasing the  
27 cerebral flow rate to 10 ml/kg/min does not significantly improve rSO<sub>2</sub>.

28

## 1 **Introduction:**

2  
3 Aortic arch surgery requires neuroprotective techniques to protect the brain from transient ischemia. The  
4 mainstay of neuroprotection includes systemic hypothermia and regional cerebral perfusion. Lowering the  
5 body temperature generally reduces the metabolic rate of a tissue. This is especially important for the brain  
6 tissue that only has a limited tolerance for malperfusion and hypoxemia. Cerebral metabolism decreases  
7 markedly with decreases in body temperature.[1, 2] A technique to reduce the metabolic demands of the  
8 brain by cooling the patient on cardiopulmonary bypass (CPB) and then arresting the circulation for the  
9 duration of aortic arch repair, the hypothermic circulatory arrest (HCA), applies this concept to aortic arch  
10 surgery.[3] Furthermore, HCA in combination with regional cerebral perfusion prolongs the window for  
11 cessation of aortic blood flow, as supply with cold oxygenated blood to the brain is maintained. This  
12 technique is proven to be feasible and save.[4-6] Whereas many techniques of delivering cerebral perfusion  
13 have been described, bilateral selective antegrade perfusion (sACP) of the right and left common carotid  
14 artery is the standard in many centers.[7] The detailed parameters applied for flow rate and perfusion  
15 pressure during sACP remain subject of debate. Animal studies showed that the lower threshold for  
16 selective antegrade flow rate is 6 ml/kg/min before cerebral tissue ischemia develops,[8] whereas high flow  
17 rates have the burden of luxury perfusion, an increase in intracranial pressure and risk of cerebral edema.[9]  
18 While the optimal flow rate for selective antegrade cerebral perfusion in humans remains yet unknown,  
19 maintaining regional cerebral oxygenation (rSO<sub>2</sub>) as measured by near infrared spectroscopy (NIRS) at  
20 awake baseline values is a commonly employed strategy. The objective of this study was to determine what  
21 flow rate is necessary to maintain awake baseline cerebral oxygenation during selective antegrade perfusion  
22 in aortic arch surgery. We hypothesized that a flow rate between 6 and 10 ml/kg/min will be necessary to  
23 achieve this endpoint.

## 24 **Methods**

25  
26  
27 With local ethics committee approval (Cantonal Ethics Committee Bern, Switzerland), patients scheduled  
28 for elective aortic arch repair with planned hypothermic circulatory arrest and bilateral sACP were included  
29 in this prospective observational single centre study. Patients were enrolled from June, 2018 until  
30 December, 2020. Informed consent was obtained before study inclusion. This study was registered on  
31 [clinicaltrials.gov](https://clinicaltrials.gov) (NCT03484104).

### 32 *Anesthesia technique*

33  
34 Patients were monitored with standard monitoring tools according to American Society of Anesthesiology,  
35 including bilateral frontal NIRS optodes. Anesthesia induction was conducted according to institutional

1 practice. After measurement of the rSO<sub>2</sub> baseline at room air intravenous access was obtained. A single dose  
2 of 1 mg midazolam was applied before placement of an arterial line. Prior to induction, patients were  
3 oxygenated with 100% oxygen until the expiratory oxygen fraction reached 80%. During preoxygenation  
4 a sufentanil bolus of 0.5 mcg/kg adjusted to total body weight (TBW) was administered. Induction was  
5 initiated with titration of propofol (1-2 mg/kg TBW) or etomidate (0.2-0.6 mg/kg TBW), followed by  
6 rocuronium (1 mg/kg adjusted to ideal body weight (IBW)) after loss of consciousness. Following  
7 endotracheal intubation every patient had a central venous line and a multi access catheter preferably placed  
8 in the right internal jugular vein. Temperatures were monitored at four sites: bladder (via Foley catheter,  
9 considered as reference for body core temperature), pharynx and tympanum bilaterally. Anesthesia  
10 maintenance was provided with isoflurane (via ventilator and during CPB via vapor in fresh gas flow to  
11 oxygenator).

### 13 *Neuromonitoring*

14 Bifrontal rSO<sub>2</sub> measurement by NIRS was started prior to anesthesia induction and continuously recorded  
15 throughout the case with a Masimo Root®, O3® (Irvine, CA, USA) regional oximetry device. This  
16 technique is recommended by international societies for aortic arch procedures and is widely accepted for  
17 monitoring sACP during HCA.[10] The initial measurement obtained in the awake patient breathing room  
18 air was defined as baseline. EEG monitoring was initiated with a Masimo Sedline® (Irvine, CA, USA)  
19 utilizing the same Masimo Root® device at the same time.

### 21 *Hypothermic circulatory arrest and selective antegrade cerebral perfusion*

22 HCA and sACP were performed according to institutional standards: After central aortic cannulation and  
23 initiation of CPB cooling was started and ice pads were placed on the forehead. When reaching a core  
24 temperature of 26-28°C on CPB, HCA was initiated. After opening the aortic arch and visualizing the  
25 orifices of the supra-aortic branches, balloon perfusion catheters were inserted into the left and right carotid  
26 arteries (via the innominate artery). Cerebral perfusion was performed using a separate roller pump and the  
27 two balloon-tipped perfusion catheters (distal perfusion catheter 12 F, LeMaitre Vascular Inc. Burlington,  
28 MA, USA). Cerebral perfusate was drawn from the CPB oxygenator, the temperature of the perfusate was  
29 20°C, and the pressure in the common ACP line was monitored close to the roller pump.

30 Flow through the perfusion catheters was consecutively slowly increased in every patient by the perfusionist  
31 according to institutional routine. The effect of sACP was monitored by bifrontal NIRS. The increase in  
32 perfusion flow was halted when the cerebral perfusion met rSO<sub>2</sub> values that were approximating those  
33 recorded on CPB before initiation of HCA. However, if the line pressure was meeting values of >300  
34 mmHg, the increase in flow was stopped and the flow decreased to maintain a pressure below 300mmHg.

### 1 *Study specific data collection*

2 rSO<sub>2</sub> values were continuously recorded in the anesthesia documentation system. For this study rSO<sub>2</sub> values  
3 were specifically noted by a study nurse at awake baseline, after preoxygenation, on CPB before HCA,  
4 after initiation of HCA at sACP flow of 6, 8 and 10 ml/kg ideal body weight per min, at the end of sACP,  
5 back on CPB and after administration of protamine after separation from CPB. For the objective of this  
6 study the observational data collection at the initiation of sACP was of utmost importance. During this  
7 phase of the procedure continuous increase of the sACP flow rate exposed the individual patient to sACP  
8 flow alterations and subsequent variations in rSO<sub>2</sub>.

### 9 10 *Clinical endpoints*

11 The primary outcome was the bifrontal rSO<sub>2</sub> value at 6 ml/kg/min, 8 ml/kg/min and 10 ml/kg/min sACP  
12 flow rates. We calculated the difference from those values to the awake baseline rSO<sub>2</sub> as primary endpoint.  
13 An important secondary clinical outcome was the occurrence of neurologic deficits. Those were defined as  
14 neurological deficits that were not present before the day of surgery and included ischemic stroke, transient  
15 ischemic attack (TIA), delirium and postoperative cognitive decline (POCD).

### 16 17 *Sample size*

18 Until now no data for sACP flow that is necessary to meet the awake rSO<sub>2</sub> baseline were reported. Based  
19 on a lack of evidence and derived from clinical observations (of a steep increase of rSO<sub>2</sub> during initiation  
20 of sACP) we assumed a medium standardized effect size and opted for a sampling with a sample size of 40  
21 patients.

### 22 23 *Statistical analysis*

24 Categorical variables are reported as frequency and percentages. Continuous variables are reported as mean  
25 and standard deviation in case of normally distributed values and as median and interquartile range  
26 otherwise.[11] The repeated measurements of rSO<sub>2</sub> values were statistically modelled using a Generalized  
27 Estimation Equation (GEE) model (R package *geepack*) with an exchangeable correlation structure.[12] A  
28 binomial outcome distribution of the GEE allowed the computation of the probability of reaching the  
29 baseline rSO<sub>2</sub> values as a function of the flow rate. Predicted probabilities are illustrated using estimated  
30 marginal means (R package *emmeans*).[13] A Gaussian outcome distribution in a separate GEE allowed  
31 the pairwise comparisons of rSO<sub>2</sub> values at different timepoints whose *p* values were adjusted using  
32 Tukey's method. Pairwise comparisons of rSO<sub>2</sub> were only possible for those patients arriving a 10  
33 kg/ml/min flow rate (N=13). A *p* value < 0.05 was considered significant and statistical analysis was  
34 performed with R version 4.0.2.[13, 14]

## 1 Results

### 3 *Population*

4 A total of 40 patients with HCA and sACP were enrolled in this study. Fifteen patients (38%) were female  
5 (Table 1). Mean body weight and BMI were  $83.3 \pm 15.7$  kg and  $27.8 \pm 5$  kg/m<sup>2</sup>, respectively. One case was  
6 a redo procedure. Thirty-two patients (80%) had arterial hypertension and 18 (45%) patients had  
7 concomitant coronary artery disease (CAD). One patient had a history of myocardial infarction. Renal  
8 insufficiency (>grade 1, KDIGO) was present in 13 (33%) patients. Two patients had a history of stroke.  
9 Atrial fibrillation was known in 6 (15%) patients. The median Euroscore II was 3.93 [IQR:2.26-6.46].

### 11 *Surgical procedures*

12 Overall surgical procedures were mostly combinations of procedures including replacement of the of the  
13 supracoronary aorta in 22 (55%) patients and a composite graft (Bentall procedure) in 18 patients (45%).  
14 Out of these two groups two patients had a replacement of the aortic arch, one with and one without a  
15 Bentall procedure (Table 2). Every patient had at least an open distal anastomosis for which bilateral sACP  
16 was needed. The median duration of surgery was 272 [IQR:236-331] min, whereas the duration of  
17 cardiopulmonary bypass run was 154 [IQR:133-178] min. The median HCA duration was 16 [IQR:13.0-  
18 19.2] min, including 11 [IQR:8.0-14.0] min for bilateral sACP.

### 20 *Cerebral oximetry*

21 Median awake cerebral oximetry was 63.0 [IQR:59.9-65.1] (Table 3). Preoxygenation resulted in an  
22 increase of rSO<sub>2</sub> to 67.5 [IQR:64.4-70.5]. During sACP the median NIRS values were 57.0 [IQR:53.0-  
23 61.9], 60.5 [IQR:56.5-65.4] and 61.5 [IQR:57.1-63.6] with the corresponding sACP flow rates of 6, 8 and  
24 10 ml/kg/min respectively.

25 The rSO<sub>2</sub> was significantly lower than the baseline at 6ml/kg/min for patients that reached all three levels  
26 of sACP flow rates (difference: -7.3; 95%-CI: -1.7, -12.9;  $p=0.0015$ , pairwise comparison Table A3). In  
27 contrast flow rates of 8 and 10 ml/kg/min resulted in rSO<sub>2</sub> that did not significantly differ from the baseline  
28 awake rSO<sub>2</sub> (difference: -2; 95%-CI: -4.3, 8.3;  $p>0.99$  and 1.8; 95%-CI: -8.5%, 4.8%);  $p>0.99$ ). Table 4  
29 shows the number of patients that reached each level of sACP flow rate.

30 The predicted probability to achieve the baseline rSO<sub>2</sub> during sACP with a flow of 6ml/kg/min was 11.8%  
31 (95%-CI: 0.9%, 22.6%) for the cohort of 34 patients that achieved perfusion steps 6 and 8 ml/kg/min. The  
32 probability was significantly higher at a flow of 8 ml/kg/min (44.1%; 95%-CI: 27.4%,60.8%;  $p=0.0001$ )  
33 (Fig.2 A).

34

1 For the cohort of patients that achieved three perfusion rate levels (6-8-10ml/kg/min) the probability was  
2 7.1% (95%-CI: -6.3%,20.6%), 42.9% (95%-CI: 16.9%,68%) and 57.1% (95%-CI: 32.2%,83.1%) (Fig 2 B)  
3 for 6, 8 and 10ml/kg/min flow rate, respectively. The difference in probabilities was significant between 6  
4 and 8ml/kg/min and 6 and 10 ml/kg/min flow. Although 10ml/kg/min flow achieved higher probabilities  
5 than 8ml/kg/min the difference was not significant ( $p=0.278$ ).

### 6 7 *Clinical outcomes*

8 Fourteen (35%) patients in our cohort had neurologic deficits. Nine (23%) patients had postoperative  
9 delirium, 4 (10%) motor deficits, and 2 (5%) patients had a reduction in visual acuity. All neurologic deficits  
10 were transient, and all patients were symptom-free at discharge. In 9 (23%) patients cerebral neuroimaging  
11 with either computed tomography or magnetic resonance imaging was performed and showed ischemic  
12 lesions in 4 (10%) patients. Three of these lesions were described embolic (Appendix Table A4). There  
13 were no statistically significant differences in patients with and without neurological deficits concerning  
14 the proportion of patients meeting the baseline  $rSO_2$  values and the flows that were achieved during sACP  
15 (Appendix Tables A1 and A2). No patient died during hospitalization.

### 16 17 **Discussion**

18  
19 In this study of 40 patients undergoing aortic arch surgery with HCA, we found that sACP flows of 8 and  
20 10ml/kg/min were able to approximate the baseline  $rSO_2$ , whereas a flow of 6ml/kg/min resulted in  
21 significantly lower  $rSO_2$  than baseline. The probability of achieving awake cerebral oximetry baseline  
22 values with an sACP flow of 6 ml/kg/min was significantly lower than with 8 ml/kg/h. Further increase of  
23 flow rate to 10ml/kg/min did not result in a significant increase in the probability to achieve the baseline  
24  $rSO_2$ .

25 This study is the first to report sACP flow rates, resulting  $rSO_2$  values with the flow rates and probabilities  
26 to achieve the baseline cerebral oximetry measurements in humans during HCA for surgical interventions  
27 of the thoracic aorta.

28 Evidence on how to perform sACP until now was derived from animal studies. Haldenwang et al. used  
29 similar flow rate of 8ml/kg/min in an animal model and compared it to 18ml/kg/min, with the latter leading  
30 to increased intracranial pressure and not providing any benefit.[9] In our study there was no significant  
31 increase in probability to meet the baseline when further increasing the flow to 10ml/kg/min when baseline  
32 value were not achieved with 8ml/kg/min. However, a recent survey revealed an average flow of 10-  
33 15ml/Kg/min used for sACP in many centers.[7] The majority of our patients did not meet these flow rates.  
34 Nevertheless, our measurements of cerebral oximetry as well as our clinical results are reassuring of our

1 strategy. Higher flow rates were hindered in our setting by in-line pressures that were approaching the  
2 hemolysis threshold. Due to that pressure build up in the 3/16" sACP perfusion line, the increase in sACP  
3 flow was halted routinely, when reaching 300mmHg and maintained at the achieved level. The line pressure  
4 was measured close to the roller pump of the sACP line. It is important to consider that most of the pressure  
5 build up is due to in-line resistance to flow of the 150 cm long line and does not equal the intra-vascular or  
6 cerebral perfusion pressures. That may indicate that generating high intra-line pressures may not be worth  
7 the risk of hemolysis because flow rates beyond 8ml/kg/min might have limited effects on additional tissue  
8 oxygenation. Higher flow may also increase cerebral perfusion pressure and animal data show that high-  
9 pressure perfusion did not result in better outcomes than a low-pressure approach.[15]  
10 The lower flow rate of 6ml/kg/min resulted in a low probability to achieve baseline rSO<sub>2</sub>. In addition a  
11 relative decrease of 20% in rSO<sub>2</sub> from baseline is acknowledged as the threshold to initiate treatment  
12 measures during adult cardiac surgery.[16] Thus, the lower flow rate of 6ml/kg/min in our study was not  
13 able to prevent a substantial decrease of rSO<sub>2</sub> of this magnitude in all patients. This observation is in line  
14 with an animal study that suggests an ischemic threshold with sACP at 20°C is close to the flow rate of  
15 6ml/Kg/min.[8] Furthermore a retrospective analysis in surgical patients showed that blood flow in the  
16 middle cerebral artery during sACP, measured by transcranial doppler, was not detectable below a flow of  
17 5ml/kg/min.[17]  
18 Although a flow of 8ml/Kg/min restored baseline values with a probability of 42.9% close observation of  
19 the individual response to initiation of sACP on cerebral oximetry is obligatory. Our records suggest that  
20 there is a wide interindividual variation for demands of flow rate during sACP (Figure 3). Real time  
21 monitoring with cerebral oximetry can augment the adjustment of the flow rate to each individual patient.  
22  
23 Due to the limited volume of brain tissue monitored by bifrontal NIRS multimodal neuromonitoring with  
24 EEG and transcranial doppler may be able to expand the amount of dependent brain tissue monitored and  
25 to survey the effective flow delivered. Further studies to evaluate the practice of sACP and impact of  
26 different flow rates on cerebral oximetry and clinical outcome are needed to confirm our findings and add  
27 to generalizability. These findings must be interpreted in the context of the study design as the nature of  
28 this study is observational the sACP was commenced according to institutional standards. The sACP flow  
29 was continuously increased to approximate the reference rSO<sub>2</sub> values on CPB before HCA in each patient.  
30 We utilized that initiation phase to observe the effect of different flow rates on rSO<sub>2</sub>. However, there was  
31 no study specific protocol for sACP commencement and flow rates. This allowed also for individual  
32 adaption of the flow rate and surgical demands. We did not monitor the intra-vascular cerebral perfusion  
33 pressure (or estimates thereof in the right radial-, carotid- or temporal artery). This is not a routine procedure  
34 in our institution. Thus, we cannot correlate flow rates and resulting cerebral oximetry values to achieved



1 intravascular cerebral perfusion pressures. Since the right-sided perfusion catheter was introduced through  
2 the innominate artery a potential run-off of perfusate into the right arm cannot be excluded. As described  
3 above the in-line pressure in the sACP perfusion line limited the increase beyond 8ml/kg/min in 27 patients,  
4 resulting in a limited number of patient going through all three levels of flow rates (6, 8 and 10ml/kg/min).  
5 In general HCA in our population were short in duration (Table 2). However, they were longer than safe  
6 HCA durations suggested earlier for the given core temperatures without sACP, thus justifying the sACP  
7 even for relatively short durations. Our results with our institutional approach may not ad hoc be  
8 generalizable to other institutions. Thus, our findings need to be confirmed in other settings. However, the  
9 results indicate that prior evidence from animal studies concerning the lower limit of sACP flow rates may  
10 be applicable to human patients.

### 11 *Conclusion*

12 At 8 ml/kg/min cerebral flow rate during selective antegrade cerebral perfusion, cerebral oximetry baseline  
13 values are significantly more likely to be achieved than at 6 ml/kg/min. Further increasing the cerebral flow  
14 rate to 10 ml/kg/min does not significantly increase the probability to achieve baseline rSO<sub>2</sub>.  
15

ACCEPTED MANUSCRIPT

1 **Data Availability Statement**

2 The data underlying this article will be shared on reasonable request to the corresponding author  
3 and after approval of the local ethics committee according to local regulations.

4

5 **Table 1:** Patient demographics and comorbidities

6

<b>Gender</b> (female)	15/40 (38%)
<b>Height</b> (cm)	173 (10.1)
<b>Weight</b> (kg)	83.3 (15.7)
<b>BMI</b> (kg/m <sup>2</sup> )	27.8 (5.00)
<b>Ideal body weight</b> (male; kg)	73.9 (6.65)
<b>Ideal body weight</b> (female; kg)	55.7 (5.37)
<b>Prior cardiac surgery</b>	1 (3%)
<b>Cerebrovascular disease</b>	0 (0%)
<b>Prior Stroke<sup>†</sup></b>	2 (5%)
<b>TIA</b>	3 (8%)
<b>Atrial Fibrillation:</b>	6 (15%)
<b>Coronary artery disease</b>	18 (45%)
<b>History of myocardial infarction</b>	1 (3%)
<b>COPD</b>	2 (5%)
<b>Arterial hypertension</b>	32 (80%)
<b>Diabetes</b>	1 (3%)
<b>Renal failure (&gt; grade I, KDIGO):</b>	13 (33%)
<b>Creatinine at 1<sup>st</sup> day of hospital stay [mmol/L]</b>	81.5 [IQR: 67.0-90.8]

7

8 **Table 1:** Summary of patient demographics and comorbidities. BMI: body mass index, TIA:  
9 transient ischemic attack, COPD: chronic obstructive pulmonary disease, KDIGO: Kidney  
10 Disease: Improving Global Outcomes (Scale for grading kidney disease).

11

1 **Table 2:** Procedural data

2

<b>Primary aortic procedures</b>	
<b>Supracoronary aortic replacement</b>	22 (55%)
<b>Composite Graft (Bentall procedure)</b>	18 (45%)
<b>Further cardiac or aortic procedures (combined procedures)</b>	
<b>Aortic arch replacement</b> (Frozen elephant trunk, FET)	2 (5%)
<b>Aortic valve procedure</b> (replacement/repair including Composite grafts/Bentall procedures)	29 (73%)
<b>Tricuspid valve procedure</b>	1 (3%)
<b>CABG</b>	14 (35%)
<b>PFO Closure</b>	9 (23%)
<b>ASD Closure</b>	1 (3%)
<b>Aortic segments included in procedure:</b>	
aortic root	18 (45%)
zone 0	40 (100%)
zone 1	3 (8%)
zone 2	2 (5%)
zone 3	2 (5%)
<b>Procedure duration</b> (min)	272 [236;331]
<b>CPB time</b> (min)	154 [133;178]
<b>Aortic cross-clamp time</b> (min)	106 (36.8)
<b>HCA time</b> (min)	16.0 [13.0;19.2]
<b>sACP time</b> (min)	11.0 [8.00;14.0]
<b>Length of hospital stay</b> (days)	9.00 [7.00;13.0]
<b>Euroscore 2</b>	3.93 [2.26;6.46]

3

4 Legend **Table 2:** Summary of procedural data. CABG: coronary artery bypass graft, PFO:  
5 persistent foramen ovale, ASD: atrial septal defect, CPB: Cardiopulmonary bypass, HCA:  
6 hypothermic circulatory arrest. sACP: selective antegrade cerebral perfusion.

**Table 3:** Intraoperative data

	Awake Baseline	Preoxygenated	After intubation	CPB before HCA	sACP 6ml/kg/min	sACP 8ml/kg/min	sACP 10ml/kg/min	At end of sACP	At end of CPB	After separation from CPB (after protamine)
<b>Flow of 6ml/kg/min achieved</b>	.	.	.	.	40 (100%, 95%-CI: 91.2% - 100%)	.	.	.	.	.
<b>Flow of 8ml/kg/min achieved</b>	.	.	.	.	.	34 (85.0%, 95%-CI: 70.2% - 94.3%)	.	.	.	.
<b>Flow of 10ml/kg/min achieved</b>	.	.	.	.	.	.	13 (32.5%, 95%-CI: 18.6% - 49.1%)	.	.	.
<b>Total flow (ml/min)</b>	.	.	.	.	402 (SD:64.7)	523 (SD:86.7)	585 (SD:107)	543 (SD:87.9)	.	.
<b>rSO<sub>2</sub> left</b>	62.5 [59.8;65.2]	68.5 [63.0;71.0]	65.5 [62.8;70.0]	65.0 [59.0;72.0]	58.0 [51.5;63.0]	60.0 [57.0;66.0]	62.5 [57.2;64.8]	63.0 [57.0;69.0]	63.0 [57.8;67.2]	63.0 [59.5;67.0]
<b>rSO<sub>2</sub> right</b>	64.0 [59.0;66.2]	68.0 [65.8;71.0]	67.0 [63.0;71.0]	66.0 [61.0;73.0]	57.0 [53.8;61.2]	59.5 [55.0;66.8]	61.0 [56.2;66.2]	62.5 [58.0;68.2]	64.0 [58.8;67.2]	64.0 [62.0;68.5]
<b>rSO<sub>2</sub> averaged</b>	63.0 [59.9;65.1]	67.5 [64.4;70.5]	66.0 [62.4;71.6]	65.0 [59.5;72.1]	57.0 [53.0;61.9]	60.5 [56.5;65.4]	61.5 [57.1;63.6]	62.5 [58.8;66.6]	62.8 [57.6;67.6]	64.0 [60.8;67.2]
<b>Hb (g/l)</b>	.	.	130 [122;140]	104 [92.5;115]	.	.	.	.	98.5 [88.5;105]	98.5 [89.0;104]
<b>Temperatures (°C)</b>										
<b>left tympanal</b>	.	.	.	24.6 [23.6;26.1]	24.9 [23.4;25.6]	24.9 [23.4;25.5]	25.1 [24.9;25.6]	23.6 [22.6;24.4]	.	.
<b>right tympanal</b>	.	.	.	24.2 [23.3;25.7]	24.3 [23.2;25.4]	24.4 [23.3;25.5]	25.2 [23.9;25.4]	23.6 [22.5;24.3]	.	.
<b>bladder (core)</b>	.	.	.	28.3 [27.1;29.4]	27.5 [26.6;28.8]	27.6 [26.7;28.6]	27.5 [26.8;28.0]	27.5 [26.6;28.5]	.	.
<b>Naso-pharyngeal</b>	.	.	36.2 [35.9;36.3]	24.8 [23.8;26.3]	24.8 [23.7;26.3]	25.1 [23.7;26.2]	25.3 [24.5;25.9]	23.4 [22.8;24.9]	.	.
<b>etCO<sub>2</sub> (mmHg)</b>	.	.	33.0 [31.8;35.0]	.	.	.	.	.	.	32.5 [29.0;34.8]
<b>pH</b>	.	.	7.35 [7.33;7.37]	7.31 [7.28;7.34]	.	.	.	.	.	7.33 [7.32;7.36]
<b>pCO<sub>2</sub> (mmHg)</b>	.	.	45.0 [42.2;48.3]	47.5 [44.0;51.2]	.	.	.	.	.	45.8 [42.0;48.0]
<b>pO<sub>2</sub> (mmHg)</b>	.	.	47.4 [42.4;50.7]	348 [304;397]	.	.	.	.	.	45.6 [41.8;50.0]

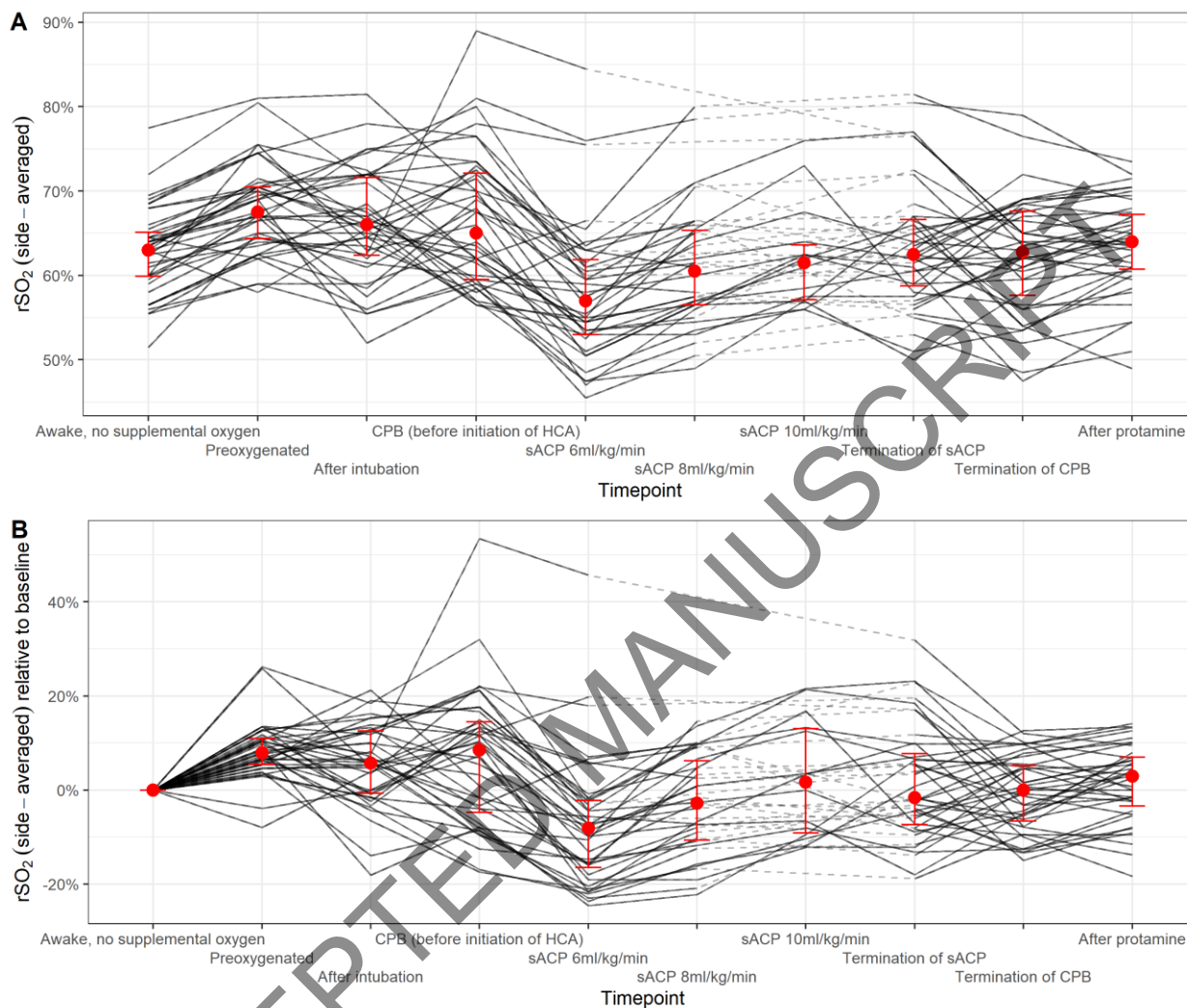
Legend **Table 3:** Summary of. sACP: selective antegrade cerebral perfusion. rSO<sub>2</sub>: regional cerebral oxygenation, Hb: hemoglobin,

**Table 4.** Number of patients at or above the baseline rSO<sub>2</sub> during sACP (side-averaged).

Time point	Patients at or above baseline rSO <sub>2</sub>
Preoxygenated	38/40 (95%)
After intubation	29/40 (73%)
sACP 6ml/kg/min	7/40 (18%)
sACP 8ml/kg/min	15/34 (44%)
sACP 10ml/kg/min	8/13 (62%)
Termination of sACP	19/40 (48%)
Termination of CPB	21/40 (53%)

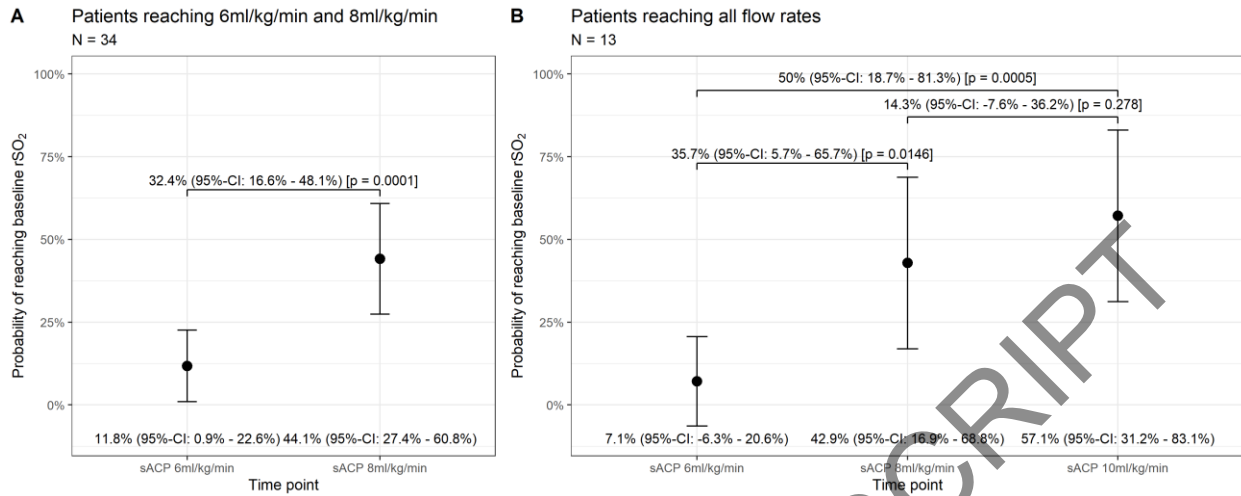
Legend **Table 4:** Summary of patients that achieved or exceeded their exact baseline rSO<sub>2</sub> at various time points during the procedure. rSO<sub>2</sub>: regional cerebral oxygenation, sACP: selective antegrade cerebral perfusion, CPB: Cardiopulmonary bypass.

ACCEPTED MANUSCRIPT

**Figure 1:** Time evolution of cerebral rSO<sub>2</sub> over the course of the procedure

Legend **Figure 1:** **A** rSO<sub>2</sub> plotted over time points of procedures. **B** relative rSO<sub>2</sub> changes from the awake rSO<sub>2</sub> baseline values (0%). Median and interquartile ranges are shown in red. Individual patients are shown in black lines. Dotted lines indicate that the sACP flow was not achieved. rSO<sub>2</sub>: regional cerebral oxygenation, sACP: selective antegrade cerebral perfusion

**Figure 2:** Predicted probabilities for rSO<sub>2</sub> values with specific SACP flow



Legend **Figure 2:** Predicted probabilities to achieve the baseline rSO<sub>2</sub> with each sACP flow rate. **A** patients that were perfused with sACP flow rates of 6ml/kg/min and increased to 8ml/kg/min. **B** patients that were perfused with increase from 6ml/kg/min through 8ml/kg/min and 10ml/kg/min. rSO<sub>2</sub>: regional cerebral oxygenation, sACP: selective antegrade cerebral perfusion.

ACCEPTED MANUSCRIPT

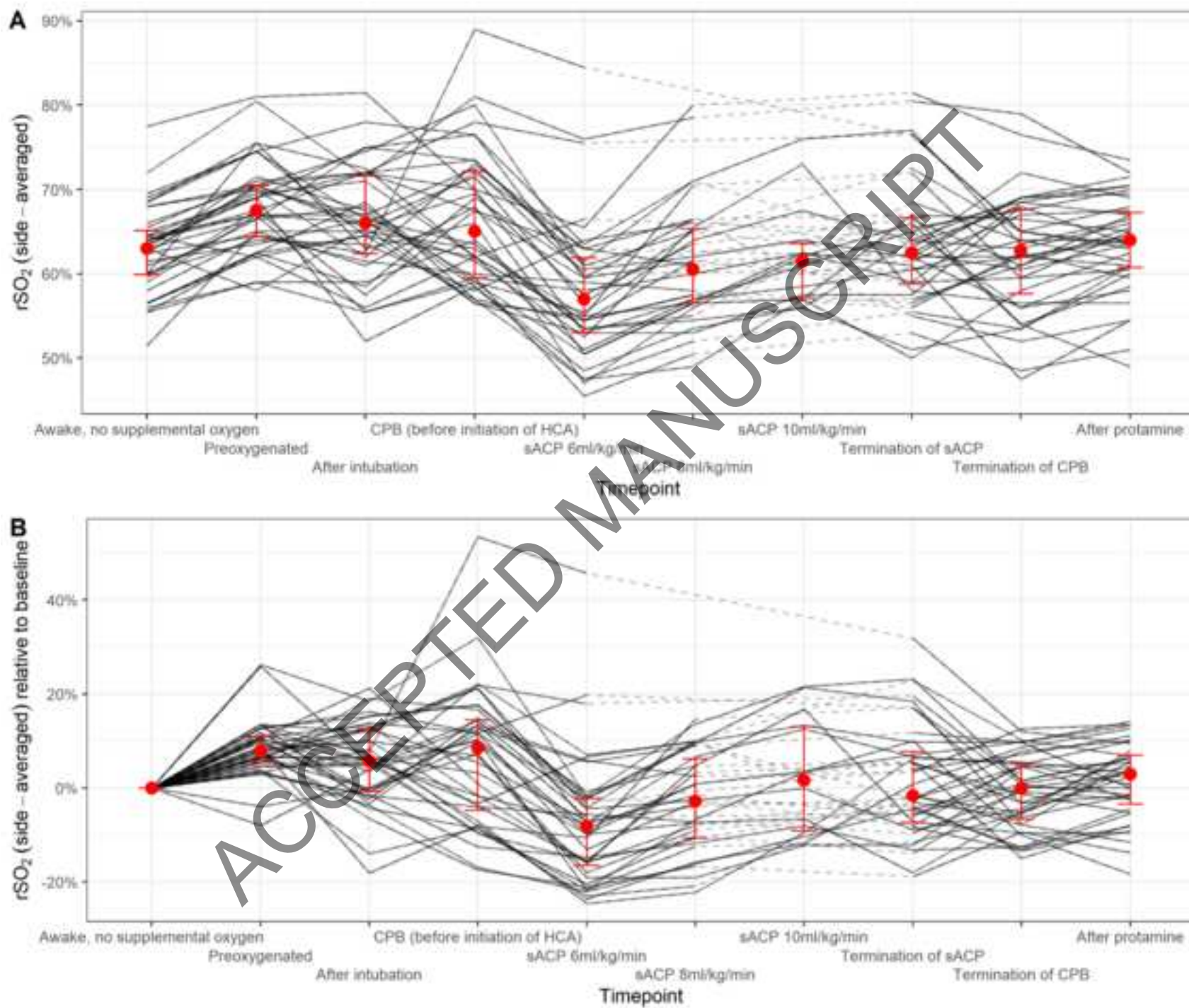
## References:

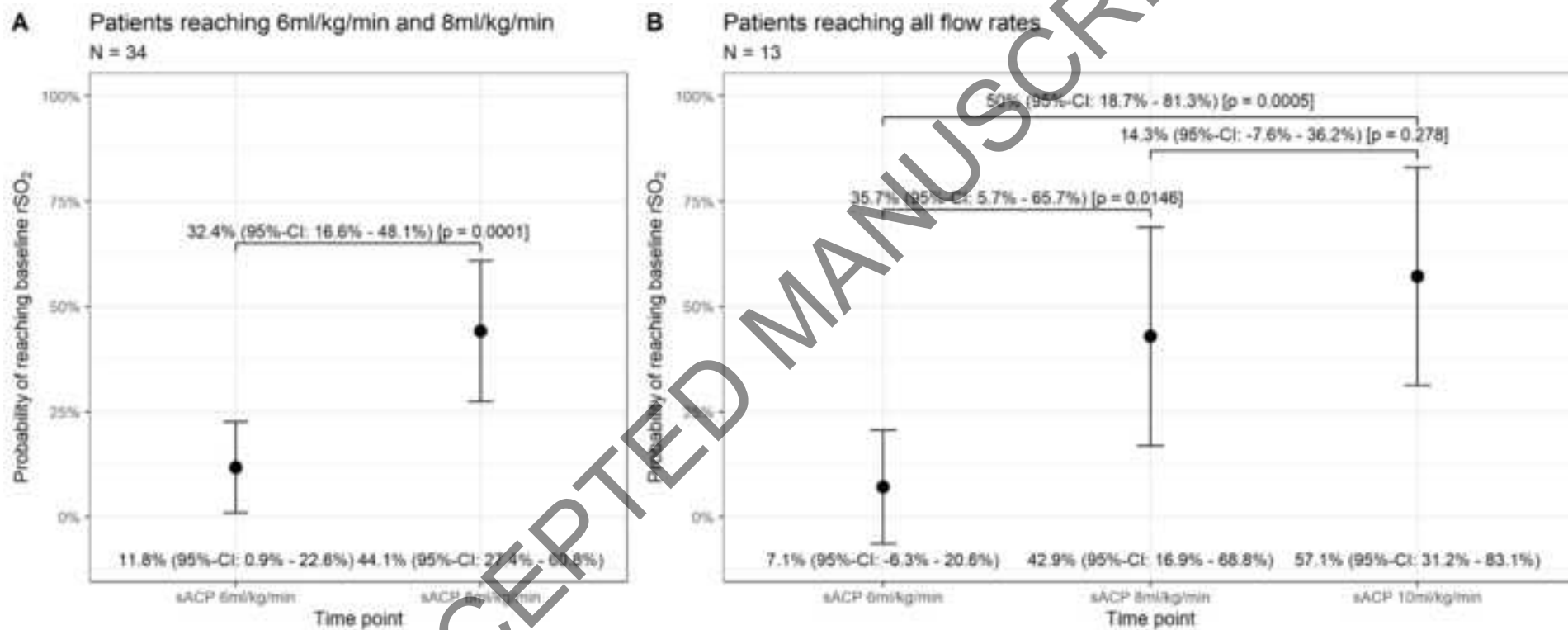
- [1] McCullough JN, Zhang N, Reich DL, Juvonen TS, Klein JJ, Spielvogel D *et al.* *Cerebral metabolic suppression during hypothermic circulatory arrest in humans.* *Ann Thorac Surg* 1999;**67**:1895-9; discussion 919-21.
- [2] Michenfelder JD, Milde JH. *The effect of profound levels of hypothermia (below 14 degrees C) on canine cerebral metabolism.* *J Cereb Blood Flow Metab* 1992;**12**:877-80.
- [3] Griep RB, Stinson EB, Hollingsworth JF, Buehler D. *Prosthetic replacement of the aortic arch.* *J Thorac Cardiovasc Surg* 1975;**70**:1051-63.
- [4] Kazui T, Kimura N, Yamada O, Komatsu S. *Surgical outcome of aortic arch aneurysms using selective cerebral perfusion.* *Ann Thorac Surg* 1994;**57**:904-11.
- [5] Bachet J, Guilmet D, Goudot B, Termignon JL, Teodori G, Dreyfus G *et al.* *Cold cerebroplegia. A new technique of cerebral protection during operations on the transverse aortic arch.* *J Thorac Cardiovasc Surg* 1991;**102**:85-93; discussion 93-4.
- [6] Harrer M, Waldenberger FR, Weiss G, Folkmann S, Gorlitzer M, Moidl R *et al.* *Aortic arch surgery using bilateral antegrade selective cerebral perfusion in combination with near-infrared spectroscopy.* *Eur J Cardiothorac Surg* 2010;**38**:561-7.
- [7] De Paulis R, Czerny M, Weltert L, Bavaria J, Borger MA, Carrel TP *et al.* *Current trends in cannulation and neuroprotection during surgery of the aortic arch in Europe.* *Eur J Cardiothorac Surg* 2015;**47**:917-23.
- [8] Jonsson O, Morell A, Zemgulis V, Lundström E, Tovedal T, Einarsson GM *et al.* *Minimal safe arterial blood flow during selective antegrade cerebral perfusion at 20° centigrade.* *Ann Thorac Surg* 2011;**91**:1198-205.
- [9] Haldenwang PL, Strauch JT, Amann I, Klein T, Sterner-Kock A, Christ H *et al.* *Impact of pump flow rate during selective cerebral perfusion on cerebral hemodynamics and metabolism.* *Ann Thorac Surg* 2010;**90**:1975-84.
- [10] Czerny M, Schmidli J, Adler S, van den Berg JC, Bertoglio L, Carrel T *et al.* *Current options and recommendations for the treatment of thoracic aortic pathologies involving the aortic arch: an expert consensus document of the European Association for Cardio-Thoracic surgery (EACTS) and the European Society for Vascular Surgery (ESVS).* *Eur J Cardiothorac Surg* 2019;**55**:133-62.
- [11] Hickey GL, Dunning J, Seifert B, Sodeck G, Carr MJ, Burger HU *et al.* *Statistical and data reporting guidelines for the European Journal of Cardio-Thoracic Surgery and the Interactive CardioVascular and Thoracic Surgery.* *Eur J Cardiothorac Surg* 2015;**48**:180-93.
- [12] Højsgaard S, Halekoh U, Yan J. *The R Package geepack for Generalized Estimating Equations.* *Journal of Statistical Software* 2005;**15**:1 - 11.
- [13] Lenth RV. emmeans: Estimated Marginal Means, aka Least-Squares Means. 2021.
- [14] R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, 2014.
- [15] Halstead JC, Meier M, Wurm M, Zhang N, Spielvogel D, Weisz D *et al.* *Optimizing selective cerebral perfusion: deleterious effects of high perfusion pressures.* *J Thorac Cardiovasc Surg* 2008;**135**:784-91.
- [16] Denault A, Deschamps A, Murkin JM. *A proposed algorithm for the intraoperative use of cerebral near-infrared spectroscopy.* *Semin Cardiothorac Vasc Anesth* 2007;**11**:274-81.

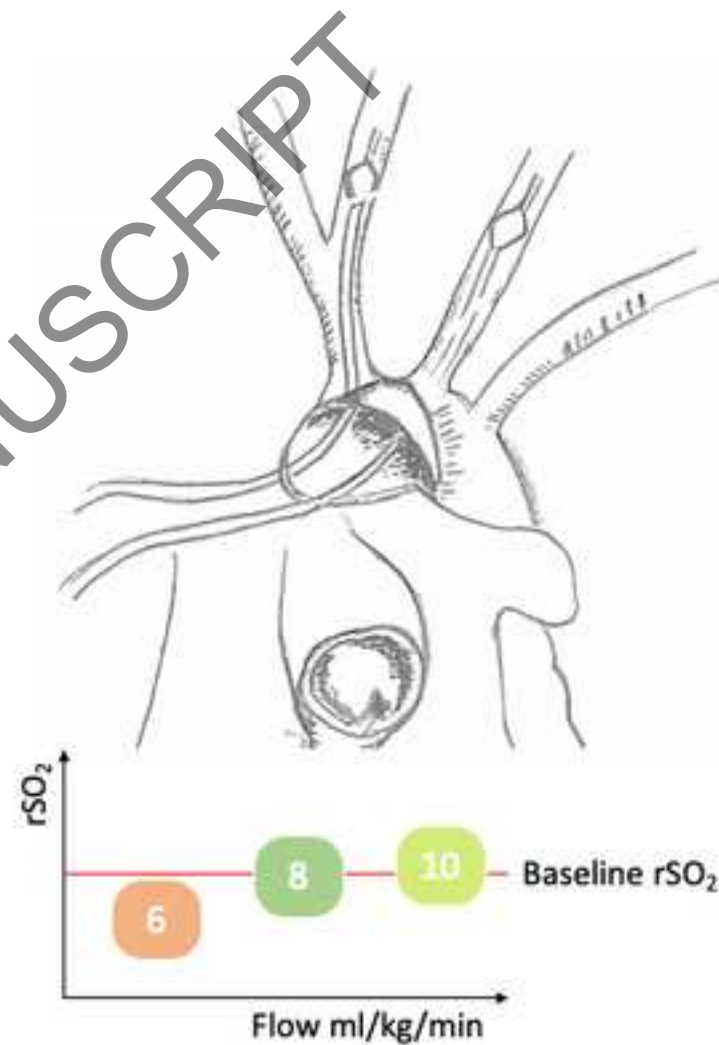
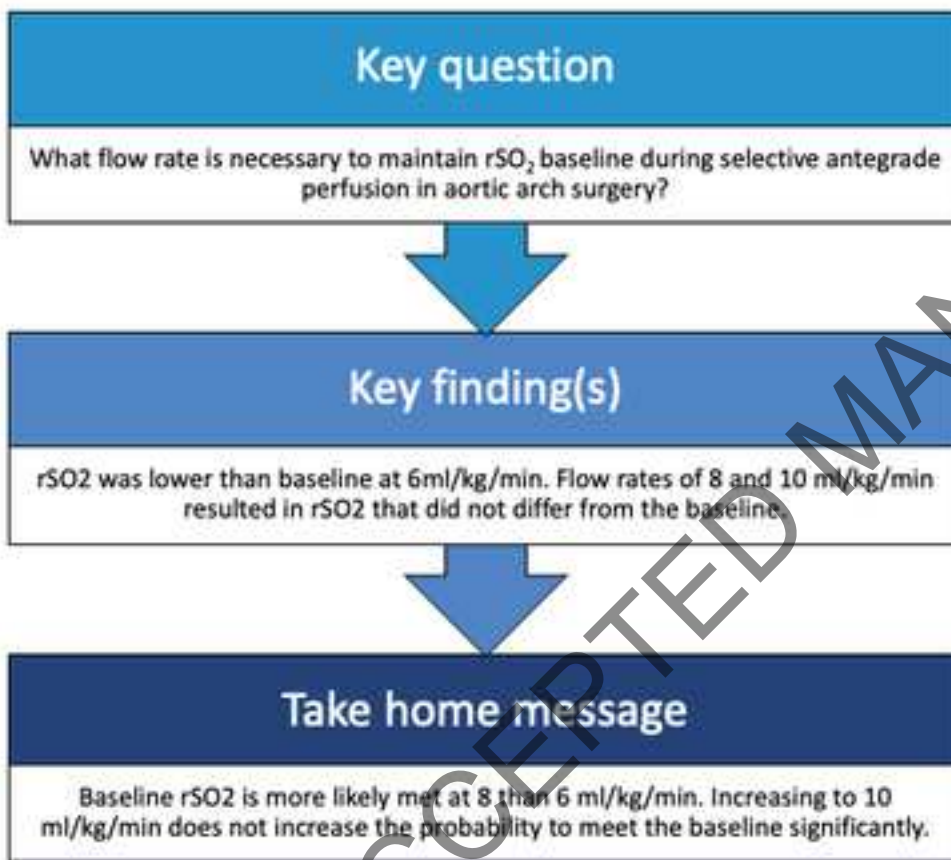


[17] Wang X, Ji B, Yang B, Liu G, Miao N, Yang J *et al.* *Real-time continuous neuromonitoring combines transcranial cerebral Doppler with near-infrared spectroscopy cerebral oxygen saturation during total aortic arch replacement procedure: a pilot study.* *Asaio j* 2012;**58**:122-6.

ACCEPTED MANUSCRIPT







ACCEPTED MANUSCRIPT