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Research Article

Cerebral Events are not Predicted by Near-Infrared Spectroscopy during Anesthesia for Aortic Arch Surgery with Bilateral Antegrade Selective Cerebral Perfusion and Hypothermic Circulatory Arrest

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Abstract

Background: Near-infrared spectroscopy (NIRS) for brain monitoring has an uncertain value. We prospectively assessed the association of decreased NIRS tissue oxygenation index (TOI) with cerebral events in adults undergoing aortic arch repair with hypothermic circulatory arrest and bilateral antegrade selective cerebral perfusion.

Methods: 76 consecutive patients (mostly aortic arch dissections/aneurysms) were studied. Desaturation was defined as unilateral or bilateral TOI decrease to <50% or to <80% of the individual patients' baseline. No intervention was based on TOI data and the end-point was postoperative cerebral events shown by imaging.

Results: Baseline TOI on left/right foreheads averaged 70.4% ± 10.8 (SD) and 67.9% ± 9.1, and did not change significantly thereafter. Twenty-six of 76 patients (34%) showed a TOI decrease to <50% and 55 (72%) a decrease to <80% from baseline. Cerebral complications occurred in 26/76 patients (34%), i.e., regional brain infarction (n=22) or edema (n=4). Twenty-six of 76 (34%) patients, 11 (42%) with and 15 (58%) without decreased TOI, had cerebral events but neither absolute TOI nor its decrease from baseline was predictive (p=0.206). Conversely, in patients with events, the incidence of decreased TOI was not different (11 vs. 15 of 26; 42% vs. 58%; p=0.206), whereas duration of hypothermic circulatory arrest (59min ± 34 vs. 43 ± 33, p=0.049) and bilateral antegrade selective cerebral perfusion (66min ± 27 vs. 50 ± 26, p=0.013), hospital-stay (p=0.001), and mortality (p=0.014) were different.

Conclusions: Thus, while duration of hypothermic circulatory arrest with bilateral antegrade selective cerebral perfusion was predictive of postoperative cerebral events, the absolute or relative decrease in NIRS TOI was not.

ABBREVIATIONS

NIRS: Near-Infrared Spectroscopy; TOI: Tissue Oxygenation Index (as measured by NIRS); HCA: Hypothermic Circulatory Arrest; BASCP: Bilateral Antegrade Selective Cerebral Perfusion; CPB: Cardiopulmonary Bypass; ICU: Intensive Care Unit

INTRODUCTION

Despite efforts for brain protection by bilateral antegrade selective cerebral perfusion (BASCP) and hypothermic circulatory arrest (HCA) cerebral complications after aortic arch surgery range from overt stroke [1] and bleeding to other deficits [2].

Near-infrared spectroscopy (NIRS) is proposed for monitoring brain oxygenation during aortic arch surgery [3-5] and studies have suggested an association between reductions in NIRS derived oxygenation and postoperative cognitive dysfunction, stroke, and delirium in patients undergoing coronary artery bypass graft surgery [6-9]. However, NIRS in adults may measure skin rather than brain oxygenation and a "brain tissue oxygenation" of 50% was even reported when sensors were attached to the foreheads of dead human corpses [10].

Thus, while NIRS in adults might help to predict critically decreased perfusion to the head and hence cerebral damage, its merits are controversial [11-13] and it is unclear, whether NIRS during aortic arch surgery with HCA and BASCP predicts cerebral complications [5,14,15].

Accordingly, we assessed in adults undergoing aortic arch surgery with BASCP and HCA, whether 1) predefined decrements in NIRS tissue oxygenation index (TOI) predict cerebral events and, conversely, 2) patients postoperatively revealing cerebral complications had shown unilateral or bilateral TOI desaturation intraoperatively.

MATERIALS AND METHODS

Patients

Following local ethics committee approval (13-5667-BO), we enrolled (study DRKS00006073) 78 consecutive patients undergoing aortic arch surgery using BASCP combined with moderate HCA with continuous bifrontal NIRS. Preoperative characteristics are shown in Table 1. Data from 2 other patients were excluded because these patients died during surgery and hence could not be evaluated postoperatively. Six patients with a history of out-of-hospital cardiopulmonary resuscitation were included since they had shown normal pupillary diameters and reactions to light before surgery. Of the latter 6 patients none had apparent neurological complications and while 3 of these patients died following prolonged intensive care unit (ICU) the other 3 patients were discharged without sequelae.

Diagnoses included aortic arch aneurysmal disease in 20 (26%) patients, acute aortic type I dissection in 39 (51%), chronic type I dissection in 7 (9%), retrograde type III aortic arch dissection in 6 (8%), and severe aortic valve stenosis with dissected porcelain aorta in 4 (5%). Surgery included total aortic arch replacements in 49 (64%) patients and hemi-arch replacements in 27 (36%). Forty-two patients (55%) had emergency surgery.

Anesthesia

Besides non-invasive monitoring, catheters were inserted into both radial arteries and a femoral artery and the internal jugular veins (7.5 F, 12 F) for measurements of arterial pressures, detection

Table 1: Cerebral events, demographic, and perioperative data from patients undergoing NIRS monitoring during aortic arch surgery with hypothermic circulatory arrest and bilateral antegrade selective cerebral perfusion, with or without a decrease of tissue oxygenation index (TOI) to less than 50%, and with and without a decrease of TOI to less than 80% of the individual patients` baseline.

	Tissue oxygenation index			Tissue oxygenation index		
Variable	**Desaturation to <50% (n=26)**	**No desaturation (n=50)**	**p value**	**Desaturation to <80% of individual baseline (n=55)**	**No desaturation (n=21)**	**p value**
Neurologic outcome						
Postoperative cerebral event	11 (42%)	15 (58%)	0.206	19 (73%)	7 (27%)	0.573
Cerebral regional ischemia	9 (41%)	13 (59%)	0.299	16 (73%)	6 (27%)	0.600
Frontal lobe	0 (0%)	2 (100%)	0.430	2 (100%)	0 (0%)	0.521
Lateral lobe	2 (40%)	3 (60%)	0.561	4 (80%)	1 (20%)	0.576
Posterior lobe	0 (0%)	3 (100%)	0.279	3 (100%)	0 (0%)	0.373
Global	7 (58%)	5 (42%)	0.059	7 (58%)	5 (42%)	0.199
Generalized brain edema	2 (50%)	2 (50%)	0.423	3 (75%)	1 (25%)	0.695
Patient characteristics						
Age, years	60 ± 13	62 ± 11	0.361	60 ± 12	65 ± 9	0.151
Male	18 (30%)	41 (70%)	0.164	42 (71%)	17 (29%)	0.462
Female	8 (47%)	9 (53%)	0.164	13 (76%)	4 (24%)	0.462
Weight, kg	79 ± 18	86 ± 15	0.299	82 ± 17	93 ± 18	0.276
Height, cm	172 ± 13	177 ± 10	0.288	175 ± 12	178 ± 7	0.598
Perfusion variables						
Duration of HCA, min	51 ± 37	47 ± 33	0.600	50 ± 34	43 ± 34	0.418
Duration of BASCP, min	52 ± 27	56 ± 28	0.522	56 ± 27	49 ± 28	0.270
Core temperature during HCA and BASCP, °C	26 ± 1	26 ± 0	0.980	25 ± 1	26 ± 1	0.790
Postoperative variables						
Length of ICU stay, days	23 ± 28	23 ± 31	0.994	21 ± 24	31 ± 41	0.191
Length of hospital stay, days	32 ± 30	30 ± 29	0.812	28 ± 24	36 ± 39	0.291
In-hospital mortality	5 (26%)	14 (74%)	0.292	12 (63%)	7 (37%)	0.227

Data are expressed as means ± SD, numbers, or proportion of values from 76 patients.
Abbreviations: BASCP: bilateral antegrade selective cerebral perfusion, HCA: hypothermic circulatory arrest, ICU: intensive care unit, NIRS: near-infrared spectroscopy, TOI: tissue oxygenation index

Table 2: Tissue oxygenation index, demographic, and perioperative data from patients experiencing or not cerebral events following aortic arch surgery with hypothermic circulatory arrest and bilateral antegrade selective cerebral perfusion.

Variable	Cerebral event (n=26)	No cerebral event (n=50)	Regional brain ischemia (n=22)	No regional brain ischemia (n=54)	All patients (n=76)
Desaturation in NIRS					
TOI decrease < 50%	11 (42%)	15 (58%)	9 (35%)	17 (65%)	26 (34%)
TOI decrease to < 80% of individual baseline	19 (35%)	36 (65%)	16 (29%)	39 (71%)	55 (72%)
Patient characteristics					
Age, years	61 ± 10	62 ± 12	61 ± 10	61 ± 12	61 ± 11
Male	20 (34%)	39 (66%)	16 (27%)	43 (73%)	59 (78%)
Female	6 (35%)	11 (65%)	6 (35%)	11 (65%)	17 (22%)
Weight, kg	84 ± 17	82 ± 17	84 ± 18	82 ± 17	83 ± 17
Height, cm	173 ± 10	176 ± 12	174 ± 11	176 ± 12	175 ± 11
Perfusion variables					
Duration of HCA, min	59 ± 34*	43 ± 33	61 ± 35#	43 ± 33	48 ± 34
Duration of BASCP, min	66 ± 27*	50 ± 26	65 ± 27#	51 ± 26	55 ± 27
Core temperature during HCA and BASCP, °C	25 ± 1	26 ± 1	25 ± 1	25 ± 1	26 ± 1
Postoperative variables					
Length of ICU stay, days	46 ± 39*	12 ± 13	48 ± 40#	14 ± 16	24 ± 30
Length of hospital stay, days	51 ± 37*	21 ± 17	53 ± 38#	22 ± 19	31 ± 29
In-hospital mortality	11 (58%)*	8 (42%)	9 (47%)#	10 (53%)	19 (25%)

Data from 76 patients expressed as means ± SD, numbers, or proportion of values. Tissue oxygenation index values are given as absolute low values <50% and as values relative to each individual patients baseline.
Abbreviations: BASCP: bilateral antegrade selective cerebral perfusion, HCA: hypothermic circulatory arrest, ICU: intensive care unit, NIRS: near-infrared spectroscopy, TOI: tissue oxygenation index
*p<0.05 vs. no cerebral event
#p<0.05 vs. no cerebral ischaemia

of potential malperfusion, blood sampling, and transfusion. To measure pulmonary artery pressure, thermodilution cardiac output, and blood temperature a pulmonary catheter was advanced. Anaesthesia was initiated by sufentanil (1µg.kg^{-1}, Sufenta®), etomidate (0.3mg.kg^{-1}, Hypnomidat®), and rocuronium (0.6mg.kg^{-1}, Esmeron®). Following intubation, patients were ventilated with oxygen in air so as to achieve normocarbia. A gastric tube, an esophageal temperature probe, and a Foley catheter with bladder temperature thermistor were also placed. Anesthesia was maintained by isoflurane (0.7-0.8% end-tidal), with additional sufentanil as required.

Before hypothermic cardiopulmonary bypass (CPB), patients received tranexamic acid (2g iv.) and heparin (400 units.kg body weight^{-1}) to achieve an activated clotting time >400s. During CPB, isoflurane was continued via a vaporizer incorporated into the extracorporeal gas supply. Before and after CPB (initial pump blood flow: 2.4 l.min^{-1}.m^{-2}) mean arterial pressure was targeted to exceed 60mmHg using neosynephrine or norepinephrine, if required. Lactated Ringer's solution was added to the CPB circuit to maintain reservoir volume and packed red blood cells were added when hemoglobin concentration decreased to <7g.dl^{-1}. The off-CPB trigger for red cell transfusion was 9g.dl^{-1}. After rewarming the patient to 37°C and separation from CPB, reversal of heparin by protamine, appropriate coagulation therapy guided by thrombelastography, and sternal closure, patients were transferred to the intensive care unit (ICU).

Surgical procedures

CPB was instituted via an aortic or right subclavian arterial cannula and a two stage right atrial cannula using a median sternotomy. Right subclavian or axillary artery cannulation was the cannulation site in 39 (51%) patients. In case of computed tomography (CT) scan-proven brachiocephalic trunk dissection or in very unstable patients due to cardiac tamponade, aortic valve insufficiency, and/or bleeding, direct aortic cannulation was performed in 37 (49%) patients, more recently after primary venous drainage into an enlarged CBP reservoir and cannulation of the true aortic lumen under visual inspection [16,17]. After aortic crossclamping cardioplegic arrest was initiated early by intracoronary cold, crystalloid cardioplegia (1500-2000ml Custodiol solution, Köhler Chemie GmbH, Bensheim, Germany). Antegrade selective cerebral perfusion was started via the right subclavian artery cannula after crossclamping the proximal brachiocephalic trunk and additional cannulation of the left common carotid artery was performed for BASCP, while the left subclavian artery was blocked proximally using a 6 F Fogarty catheter. A blood pressure cuff around the right arm was inflated to supraarterial pressures to minimize blood run-off into the arm. In case of primary direct aortic cannulation, the brachiocephalic trunk was cannulated separately.

HCA was initiated at a blood temperature of approx. 18°C when a bladder temperature of 25-26°C had been reached and cerebrovascular perfusion was performed with 18-20°C cold blood, using a flow of approximately 10ml.kg^{-1}.min^{-1} so as to maintain a cerebral arterial pressure of 40-60mmHg. Cooling blankets were routinely placed around the head.

Measurements

Near-infrared spectroscopy (NIRS): The principles of NIRS are described elsewhere [18-20]. We used a NIRO-200™ (Hamamatsu Photonics, Hamamatsu, Japan) for TOI measurements, i.e., the ratio of oxyhaemoglobin to total

haemoglobin (consisting of oxyhemoglobin and deoxyhemoglobin) [21,22], believed to be unaffected by optical path length factors [22], hemoglobin concentration, skull thickness, or cerebrospinal fluid layer diameter [23]. The sensors contain a laser diode and two detectors placed at 3.7 and 4.3cm from the light emitting source. Following anesthetic induction sensors were placed on the right and the left foreheads, with their caudad border approximately 1cm above the eyebrow and their median edge at the midline [24,25]. Bifrontal TOI measurements were started before sternotomy using these values as each invidividual's baseline for subsequent measurements. Desaturation was defined as an absolute TOI of <50% or a decrease to <80% from each individual's respective baseline since a TOI of less than 50% or its relative decrease by greater than 20% from baseline are considered intervention triggers [26]. Such a decrease in TOI to <80% of baseline has a sensitivity of 80% and a specificity of 82.2% to detect neurological compromise in awake patients undergoing carotid endarterectomy [27,28]. Measurements were continued until chest closure. Surgeons and anesthetists saw the displayed NIRS-values but no interventions were made based on NIRS readings. The anesthetists attending the patients could enter time markers for clinical events and/or the anesthetic records.

A computer with dedicated NIRO-2000L software was later connected to the NIRS monitor to download data. Data were analyzed without prior knowledge of the patients' postoperative course. Data reduction occurred for typical surgical time point, i.e., sternotomy, start of CPB, aortic clamping, start of HCA, start and end of BASCP, end of HCA, aortic declamping, end of CPB, and after chest closure, respectively.

Duration of HCA and BASCP and body temperatures were also documented. The hospital data base was used to document the length of ICU and hospital stay, and for follow-up until discharge or in-hospital death.

Cerebral complications: Cerebral events were defined as newly evident cerebral deficits such as regional cerebral ischemia including infarction or generalized brain edema, as identified by brain CT and/or magnetic resonance imaging, as diagnosed by a neuroradiologist. Imaging was performed with clinical abnormalities such as pupillary difference, hemiplegia, inappropriate wake-up, or neurological abnormalities. Apparently older, preoperative cerebral pathologies, if present on images and so explicitly defined by neuroradiologists, were not considered a new event.

Data analysis

Data from 76 subsequent patients were analyzed off-line in this prospective observational study by the first author independent of the radiologist. Normally distributed data (as tested by Kolmogorov-Smirnov test) such as patients' characteristics and TOI values are reported as numbers, frequencies, and means ± standard deviation (SD). Normally distributed data were compared using the Student's two-sided t-test for unpaired samples and/or one-way or 2-way-repeated measures ANOVA. The Chi^2-test was used to compare categorical variables. An a priori alpha error p of less than 0.05 was considered statistically significant.

The potential relationship between NIRS desaturation to a TOI <50% and of a TOI decrease to <80% of the patients' baseline and postoperative cerebral events, in particular regional cerebral ischemia including infarction, was analyzed using univariate and multivariate analysis, and with TOI at different time points, and the durations of HCA and BASCP as independent risk factors. For multivariate analysis, we used a binary logistic regression model to calculate odds ratios, 95% confidence intervals (CI), and p-values for the risk of TOI desaturation or cerebral events/ regional ischemia in a stepwise backward fashion including all variables that were significant at a level p<0.1 in univariate analysis and variables which are assumed to be associated with cerebral events (HCA, BASCP). The following a priori null hypotheses were tested using new cerebral events as primary criterion:

1) There is no difference in the incidence of the primary criterion (cerebral events, in particular regional cerebral ischemia including infarction) in patients with and without NIRS oxygen desaturation (absolute TOI decrease to <50% or <80% of the individual patients' baseline TOI), and 2) in patients with cerebral events, there is no difference in the incidence of TOI desaturation compared to those without cerebral events.

RESULTS

NIRS tissue oxygenation index during anesthesia and surgery

Figure 1 shows the course of average TOI, both as absolute TOI values (A) and those relative to each patients' respective individual baseline (B). Baseline TOI averaged 70.4% ± 10.8 and 67.9% ± 9.1 over the left and right foreheads, respectively, and did not change significantly thereafter. TOI values at the start of CPB averaged 66.6% ± 11.3 (left) and 64.4% ± 10.2 (right), 66.9% ± 9.5 (left) and 65.3% ± 11.3 (right) at aortic crossclamping, and 66.7% ± 11.7 (left) and, right 66.1% ± 11.9 (right) before HCA, respectively. Despite a tendency to decrease, average TOI did not decrease significantly at the start and end of HCA and BACSP (left: 61.2% ± 13.5, right: 62.3% ± 12). After reestablishment of CPB and rewarming TOI averaged 67.1% ± 13.2 (left) and 64.8% ± 11.2 (right) at chest closure and this also did not differ from baseline. The same held true for changes in TOI relative to the patients' individual baseline (Figure 1(B)). With respect to the left and right recording sites mean absolute and relative TOI values ran in parallel and there were no significant changes between values derived from the right and left recording sites at any time (Figure 1).

Incidence of cerebral events in patients with and without NIRS tissue desaturation (forward analysis)

A) Tissue oxygenation index <50%

26 of 76 NIRS monitored patients (34%) had a TOI <50% sometime during surgery and 50 had not. Twenty-six of these 76 patients (34%) had a postoperative cerebral event, 11 (42%) in the TOI desaturation group and 15 (58%) in the no-desaturation group. The incidence of cerebral events in patients showing a TOI desaturation and those not showing a TOI desaturation did not differ (p=0.206, Table 1).

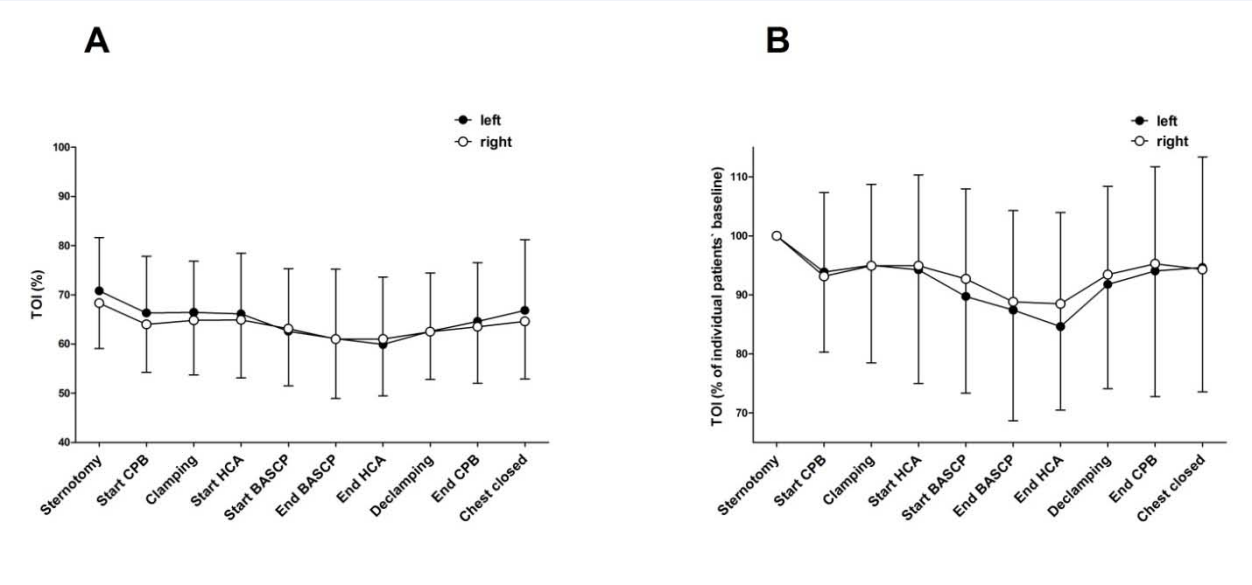

Figure 1 Tissue oxygenation index as measured by NIRS on the left (full blue circles) and right (open red circles) forehead expressed as absolute TOI values (A, left panel) and as a percentage of each individual patient's baseline (B, right panel) over the surgical course in patients undergoing aortic arch surgery with hypothermic circulatory arrest and bilateral antegrade selective cerebral perfusion hemisphere. Data are means ± SD.

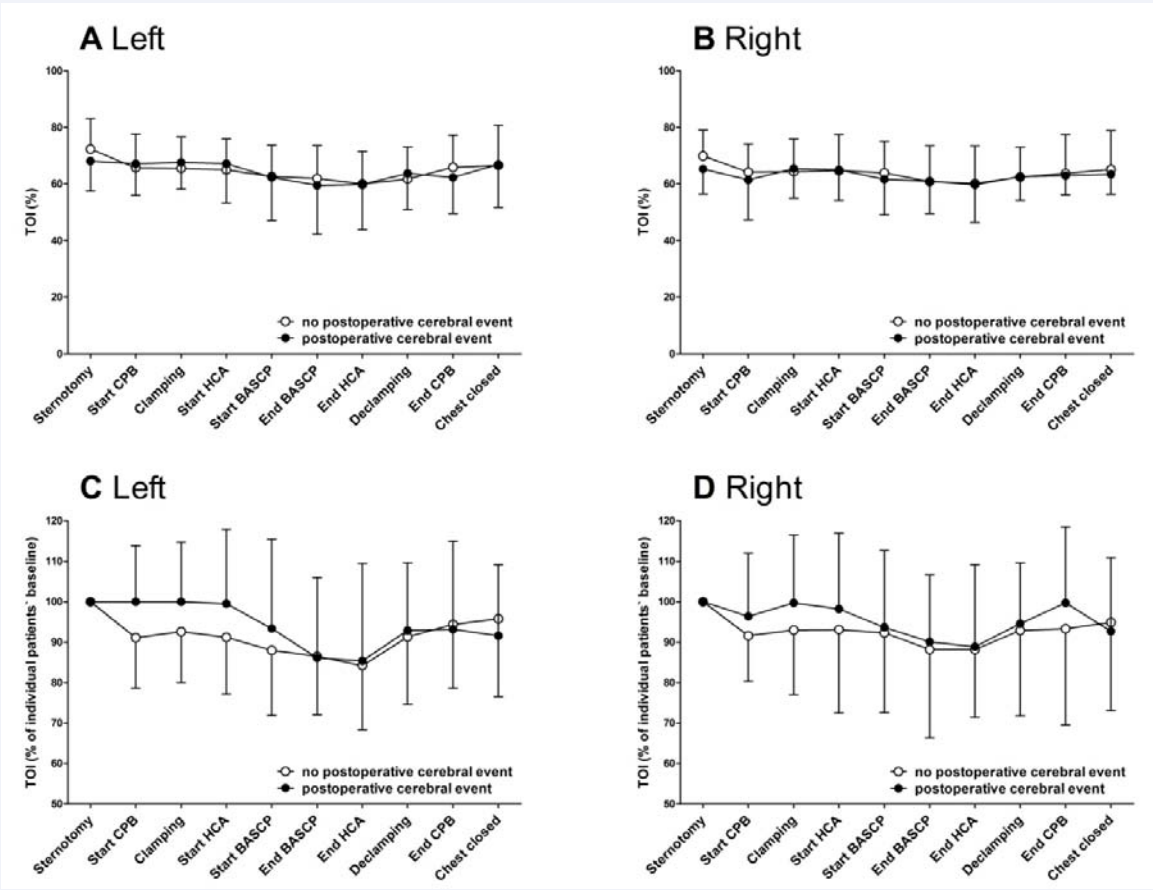

Figure 2 Tissue oxygenation index (TOI) as measured by NIRS on the left (A) and right (B) forehead in patients with (full blue circles) and without (open red circles) postoperative cerebral events when expressed as absolute TOI values (A,B) and as a percentage of each individual patient's baseline (C,D) over the course of surgery in patients undergoing aortic arch surgery with hypothermic circulatory arrest and bilateral antegrade selective cerebral perfusion hemisphere. Data are means ± SD.

Postoperatively, 22 of 76 patients (29%) presented new regional ischemia including infarction, 9 (41%) in the TOI desaturation group and 13 patients (59%) in the no-desaturation group (p=0.299, Table 1).

In multivariate analysis, we found no significant association when gender, global regional ischemia, and perfusion variables (HCA, BASCP) were included, and TOI was not an independent risk factor for cerebral events.

No differences in demographic and other variables such as duration of HCA or BASCP were observed between patients who showed TOI desaturation and those who did not (Table 1).

B) TOI desaturation to <80% of the patients' individual baseline

55 of 76 patients (72%) had a TOI decrease to less than 80% of their respective individual baseline and 21 patients had not. Twenty-six of 76 patients (34%) had a perioperative cerebral event, 19 (73%) in the desaturation group and 7 (27%) in the no-desaturation group. The incidence of cerebral events in patients with and without a decrease of TOI to <80% of their individual baseline was not different (p=0.573, Table 1).

Twenty-two of 76 patients (29%) presented new regional ischemia including cerebral infarction, 16 (73%) in the desaturation group and 6 patients (27%) in the no-desaturation group (p=0.6) (Table 1).

Again, a TOI decrease to <80% of the individual patients' baseline was not an independent risk factor, as analysed by multiple regression analysis, and no differences in demographic variables or duration of DHCA or BASCP were observed between the desaturation and the no-desaturation patients (Table 1).

Incidence of decreased NIRS tissue oxygenation index in patients with and without cerebral events (backward analysis)

A) Cerebral events

To examine the potential relevance of TOI the incidence of decreased intraoperative TOI was compared between 26 of 76 patients (34%) in whom cerebral events had occurred and 50 patients (66%) not showing a postoperative cerebral event. There was neither a significant difference in the incidence of desaturation (TOI<50%) between patients with (11 of 26 patients [42%]) and without (15 of 26 patients [58%], p=0.206, Table 2) cerebral events nor in the incidence of a TOI decrease to <80% of each individual patients' baseline (cerebral events: 19 of 55 patients [35%] vs. no events: 36 of 55 patients [65%]), p=0.573, Table 2).

Furthermore, the time course of TOI during surgery did not differ between patients with and without postoperative cerebral events, neither when considering absolute TOI nor its relative decrease (p=0.216, fig. 2).

In contrast, in patients with cerebral events the duration of both HCA (59 min ± 34 vs. 43 ± 33, p=0.049) and of BASCP (66 min ± 27 vs. 50 ± 26, p=0.013) were substantially and significantly increased.

Not unexpected, the length of hospital stay (51 days ± 37 vs. 21 ± 17, p=0.001), length of ICU stay (46 days ± 39 vs. 12 ± 13, p=0.001), and also of in-hospital mortality (p=0.014) were all increased in patients with cerebral events when compared to those without (Table 2).

In multivariate analysis, we also found a significant association of cerebral events with duration of BASCP (p=0.023, CI: 1.004-1.049). The incidence of emergency surgery did not differ (p=0.34) between patients with and without cerebral events.

B) Regional ischemia including infarction

Regional cerebral ischemia including infarction was documented in 22 (29%) of 76 patients. To examine its potential association with TOI the incidence of decreased TOI was compared between patients in whom regional ischemia had occurred and 54 patients (71%) not showing regional cerebral ischemia. There was no difference in the incidence of intraoperative desaturation (TOI<50%) between patients with and without (9 of 26 patients [35%] vs. 17 of 26 patients [65%], p=0.299, Table 2) ischemia nor in the incidence of a TOI decrease to less than 80% of each individual patients' baseline (16 of 55 patients [29%] vs. 39 of 55 patients [71%]), p=0.6, Table 2).

Again, however, in patients with regional cerebral ischemia duration of both HCA (61 min ± 35 vs. 43 ± 33, p=0.041) and BASCP (65 min ± 27 vs. 51 ± 26, p=0.032) were substantially increased. Length of hospital stay (53 days ± 38 vs. 22 ± 19, p=0.001), length of ICU stay (48 days ± 40 vs. 14 ± 16, p=0.001), and also of in-hospital mortality (p=0.042) were all significantly increased compared to patients without regional cerebral ischemia (Table 2).

In multivariate analysis, we found a significant association with regional ischemia when duration of BASCP (p=0.03, 95% CI: 1.003-1.051) was included as a variable. The incidence of emergency operations did not differ.

DISCUSSION

In this prospective study, we measured bifrontal TOI by state-of-the-art NIRS in patients undergoing aortic arch surgery with BASCP and HCA, i.e., in a cohort at high risk for cerebral complications. To our knowledge, this study is the first to assess the association of TOI desaturation with cerebral events in such patients. Using two different, strict, and well-defined cut-off criteria for TOI decrements, previously validated in patients undergoing awake common carotid artery clamping [26-28], we assessed the association of NIRS desaturation with cerebral events and vice versa.

Not unexpected, cerebral complications were frequent with an overall incidence of 34%, and associated with increased ICU and hospital stay as well as mortality. This underlines the grave sequelae of such complications.

NIRS desaturation below predefined cut-off values was common. However, neither was decreased TOI associated with cerebral events nor could postoperative cerebral events be traced back to intraoperative desaturation episodes. In fact, while both duration of HCA and BASCP were significant predictors of cerebral complications intraoperative TOI was not, regardless of whether

TOI was expressed as an absolute TOI decrease or as changes from each individual's baseline. Thus, NIRS monitoring appears to have few merits in predicting cerebral events following aortic arch surgery.

While one may take for granted that NIRS is useful intraoperatively and measures brain oxygenation in adults few data support this notion. Cerebral complications after aortic arch surgery likely arise from multiple mechanisms, e.g., large-vessel embolism [29], atheromatous-related cerebrovascular thrombosis, cerebral microemboli [30], ischemic malperfusion, and/or a long duration of BASCP and not all of these mechanisms may immediately impact on TOI. However, BASCP duration but not TOI significantly correlated with cerebral events. Thus, our data do not support the view that intraoperative bifrontal TOI is predictive for cerebral events or may guard against brain damage even in this high risk setting.

This may or may not be explained by several considerations. First, there is no clinical gold standard measuring true brain oxygen saturation. Frontal NIRS, at best, examines a focal and superficial brain area within a depth of about 1-1.5cm and deeper brain remote from the light path, e.g., hippocampus and medial temporal lobes, primary cortex, visual pathways, and brainstem, may all be injured without evoking TOI changes. Anecdotally, this is illustrated by a patient with right middle cerebral artery occlusion with TOI readings remaining at 60-65% [31]. Furthermore, TOI might reflect only changes in the scalp rather than brain tissue. Although dedicated algorithms might minimize signal contamination from extracranial sources [25] this is controversial [18,24,32-34]. Scalp ischemia evoked a TOI decrease from 72% to 59% [33] and clamping the carotid arteries a decrease of only 7-12% [34]. A normal or near normal TOI was even shown in (brain) dead patients with absent brain blood flow [10,35-37], and human corpses dead for hours [10,38]. This may relate to technical difficulties, unclear algorithms, and/or unrealistic methodological assumptions [31,39].

Another question is whether TOI provides information enabling outcome relevant decisions. Despite the high incidence of cerebral events in our patients, the frequency of such events was not greater in patients with NIRS desaturation than in those without. This suggests that TOI, at least as assessed with the NIRO-200™ device, is not useful for predicting and hence possibly avoiding intraoperative cerebral events in the vast majority of such patients while duration of HCA was predictive.

Our findings contrast with another study in 51 patients reporting that postoperative stroke was significantly more common in patients with a TOI <80% of baseline than in those without desaturation [14]. Furthermore, in 46 patients undergoing aortic arch surgery with deep HCA but only unilateral selective antegrade cerebral perfusion stroke were more likely in those with a TOI decrease to 65-80% of baseline [15]. Possibly, different results relate to different endpoints and/or techniques, i.e., degree of HCA and various techniques for brain perfusion methodology [14,40], and/or to different NIRS devices.

Our study has limitations. First, patients were not randomized to receive NIRS or no NIRS but such a randomization might be considered unethical. Second, our results, i.e., no association of cerebral events with TOI desaturation and vice versa, may relate to a small sampling size or event frequency and thus type II statistical error. While it appears difficult to make a reasonable a priori power analysis for the hypotheses addressed based on previous data and specific surgical techniques always prevail locally, the number of patients in our study was rather large considering the low prevalence of such cases. Furthermore, the overall incidence of new cerebral events, i.e., the manifestation of the study end point, in our cohort was high. Thus, if a clear cut association between all-cause cerebral events and decreased NIRS-TOI would exist with this specific surgery, we are confident that our study should have revealed it.

CONCLUSION

In conclusion, in this cohort at high risk for cerebral complications, intraoperative NIRS desaturation (as defined by two established criteria) was not associated with an increased incidence of cerebral events. Conversely, patients with postoperative cerebral events could not be traced back to reveal a greater incidence in intraoperative desaturation. While duration of HCA and BASCP was predictive of postoperative cerebral events, an absolute or relative TOI decrease as measured by NIRS was not.

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