Association between cerebral desaturation and an increased risk of stroke in patients undergoing deep hypothermic circulatory arrest for cardiothoracic surgery

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Abstract

Objective: To determine the relationship between a decrease in cerebral oxygen saturation (rSO_2) – determined by near-infrared spectroscopy – below 80% of preoperative baseline and the incidence of stroke in patients undergoing deep hypothermic circulatory arrest (DHCA) for cardiac and/or thoracic aortic surgery.
Setting: Cardiac anesthesia unit of a University Hospital
Design: Retrospective analysis of the anesthesia charts and the institutional cardiac surgery database for the year 2006.
Patients: 51 patients undergoing DHCA monitored bi-hemispherically with an INVOS 5100 cerebral oxymeter.
Interventions: None
Measurements and main results: Patients were grouped according to an rSO_2 less or greater than 80% of baseline for the left or right hemisphere in a desaturation (n = 11) and a no-desaturation group (n = 40). No between group differences in demographic variables and preoperative baseline rSO_2 were observed. Duration of cardiopulmonary bypass, aortic cross-clamp, DHCA and effective cerebral ischemia were not different between the groups. The minimal absolute and relative rSO_2-levels in the desaturation group were significantly lower than in the no-desaturation group. Two patients in the desaturation group but none in the no-desaturation group presented with a postoperative stroke (18.1% vs. 0%; p = 0.043).
Conclusion: These findings suggest that an rSO_2 lower than 80% of preoperative baseline in patients undergoing cardiac and/or thoracic aortic surgery with DHCA is associated with a significant risk of an adverse neurological outcome. Preventing cerebral desaturation during DHCA procedures may thus help to reduce postoperative neurological deficits.

Introduction

Monitoring of cerebral oxygenation by near-infrared spectroscopy (NIRS) has been suggested to be valuable for the non-invasive determination of cerebral perfusion [1,2]. However, the usefulness of this technology is still controversial due to a lack of data from adequately powered prospective, randomized trials, the unconclusive results of a meta-analysis on this technology published some years ago [3], and disagreement between cerebral oxygen saturation determined by some NIRS monitors in comparison with jugular bulb oxygenation as an invasive gold standard for the determination of cerebral oxygen balance [2].

Limited clinical data are available about the usefulness of rSO_2-monitoring in adult patients undergoing deep hypothermic circulatory arrest (DHCA) for thoracic aortic surgery, since most of the data have been obtained either in animal models or in pediatric cardiac surgery. Orihashi and coworkers have shown that a sustained drop in cerebral oxygen saturation below 55% and prolonged periods of hypoperfusion (cerebral oxygen below 60%) during DHCA with selective cerebral perfusion were associated with adverse neurological events [4]. Olsson and coworkers have shown that patients with a stroke after thoracic cardiovascular surgery with DHCA involving the aortic arch treated with selective antegrade perfusion had a lower cerebral oxygen saturation (rSO2) ratio (actual rSO2 / baseline rSO2) than patients recovering uneventfully [5]. Receiver-operator curve (ROC) analyses revealed that rSO2-ratios below 0.87 to 0.76 were strongly associated with a significant risk of stroke (Odd's ratio: 5.6 to 21).

In 2006 we adopted the technology of NIRS in our cardiac anesthesia unit and started to measure rSO_2 in an increasing number of patients undergoing deep hypothermic circulatory arrest with an INVOS® cerebral oximeter (INVOS 5100; SOMANETICS, Troy, USA). Its use was at the discretion of the attending anesthesiologist and it is important to note that, at that time, no treatment algorithms had been established at our institution, which therapeutic consequences should be drawn from a decrease in rSO_2 levels. In contrast, when starting to measure cerebral oxygen saturation, a relevant number of cardiac anesthetists and surgeons were rather skeptical regarding the reliability of the technology and tended to ignore the data displayed by the rSO_2 monitor.

The present retrospective analysis is designed to determine the relationship between intraoperative cerebral desaturation and postoperative neurological outcome in a heterogeneous population of patients undergoing thoracic vascular surgery with DHCA.

Methods

Following approval by the local ethical committee an analysis of the anesthesia charts and the institutional cardiac surgery database for the year 2006 was performed to determine the intraoperative course of absolute rSO_2 levels, the rSO_2-ratio, the postoperative incidence of stroke, and clinically relevant outcome parameters in patients undergoing cardiac and/or thoracic vascular surgery with DHCA. The rSO_2-ratio was calculated as actual rSO_2 / baseline rSO_2. 51 patients were identified that fulfilled the criteria of DHCA and concomitant, bi-hemispheric rSO_2-monitoring. Patients were grouped according to the occurrence of a rSO_2 ratio less or greater than 0.8 [5] for the left or the right hemisphere in a desaturation (DESAT) and a no-desaturation (NO-DESAT) group and between group differences in cerebral oxygenation, demographic, procedure related, clinical outcome variables, and the incidence of neurological dysfunction were determined.

Surgical procedures

All patients underwent thoracic aortic surgery with cardiopulmonary bypass (CPB) and DHCA at a minimum bladder temperature of 18°C. 12 patients were additionally subjected to cardiac surgery (i.e aortic valve replacement or reconstruction). With the exception of 2 patients undergoing descending aortic surgery and one patient presenting with an aneurysma spurium of the ascending aorta, cardioplegic arrest was induced by blood cardioplegia. Four patients in the DESAT and three patients in the NO-DESAT groups were emergency cases presenting with type A aortic dissection or a ruptured aortic aneurysm; one of the emergency cases in the DESAT-group entered surgery during cardiopulmonary resuscitation. Demographic data and type of surgery in both groups are given in table 1.

Selective antegrade cerebral perfusion during DHCA was used in 12 cases (3 in the DESAT-group, 9 in the NO-DESAT-group); de-airing of cerebral vessels was routinely performed by retrograde perfusion of the vena cava superior.

Anesthesia

General anesthesia was induced with etomidate and sufentanil and maintained with sevoflurane and sufentanil before and after CPB, and with propofol and sufentanil during CPB. Depth of anesthesia was guided by bispectral index (BIS) monitoring aiming to a BIS of 30 to 40 before and after CPB and a BIS of 0 immediately before DHCA. If necessary, midazolam 5 to 20 mg was added to achieve the desired anesthesia depth. Cerebral cooling blankets were routinely applied if oropharyngeal temperature during systemic

Table 1. Demographic and surgical data

	DESAT	NO-DESAT	significance
Age [years]	58 (38-75)	64 (21-84)	n.s.
Height [cm]	180 (160-193)	177 (155-198)	n.s.
Weight [kg]	79 (57-106)	82 (50-103)	n.s.
Euroscore	8 (1-21)	8 (3-16)	n.s.
Bypass time [min]	160 (135-330)	177 (85-310)	n.s.
Aortic crossclamp time [min]	123 (0-248)	140 (42-293)	n.s.
DHCA time [min]	25 (14-74)	20 (15-77)	n.s.
ECI time [min]	17 (15-25)	20 (2-38)	n.s.
DHCA-BT [°C]	18 (16-18)	18 (17-18)	n.s.
Asc. aortic surgery [n]	9	35	n.s.
Aortic arch [n]	3	2	n.s.
Desc. aortic surgery [n]	0	2	n.s.
Miscellaneous [n]	5	19	n.s.

Demographics and surgical data in patients showing a decrease in regional cerebral oxygen saturation ratio (rSO2-ratio) < 0.8 (DESAT-group) or not (NO-DESAT-group) while undergoing deep hypothermic circulatory arrest (DHCA). Data are given as median and range. n.s.: not significant. ECI: effectice cerebral ischemia time; DHCA-BT: body (bladder) temperature during deep hypothermic circulatory arrest. Mann-Whitney-U test or Fisher's exact test.

cooling was below 27°C and maintained until start of rewarming. All patients were treated with 4 MiU aprotinine (2 MiU in the CPB circuit and 2 MiU as a continuous infusion over 2h) during rewarming, when body temperature exceeded 27°C.

Cardiopulmonary bypass management

Blood flow during CPB was adjusted to achieve a mixed venous oxygen saturation – measured at the inflow of the CBP circuit – higher than 70% and a mean arterial blood pressure between 50 to 70 mmHg. If necessary, norepinephrine and nitroglycerin were applied either as a bolus or a continuous infusion to achieve this goal. Hematocrit was adjusted between 26% and 29%. Acid base balance was performed following alpha-stat blood gas principles.

Statistical analyses

Following the observation, that several variables were not normally distributed, statistical analyses were performed non-parametrically by the Mann-Whitney U test for continuous and Fisher's exact test for nominal variables. Data are given as median, minimum, and maximum. Duration of DHCA is given as absolute duration and as effective cerebral ischemia time (DHCA minus duration of selective antegrade perfusion). A $p < 0.05$ indicates statistical significance.

Results

11 patients were identified that had a rSO_2 ratio < 0.8 during the procedure. No between group differences in demographic variables, Euroscore, duration of cardiopulmonary bypass, aortic cross-clamp time, DHCA, and effective cerebral ischemia time were observed (table 1).

Absolute rSO_2 baseline levels were not different between both groups (figure 1). The minimal absolute rSO_2 levels and the minimal rSO_2-ratios in both groups are given in figure 1, showing significant differences between the DESAT and the NO-DESAT group. Two patients in the DESAT-group died during surgery (both emergency cases), 1 patient in the NO-DESAT group died on day 3 after surgery due to intractable cardiac arrhythmia following a severe low cardiac output syndrome.

Two patients, both in the DESAT group, presented with a postoperative stroke leading to an incidence of 18.1 % in the DESAT vs. 0% in the NO-DESAT-group

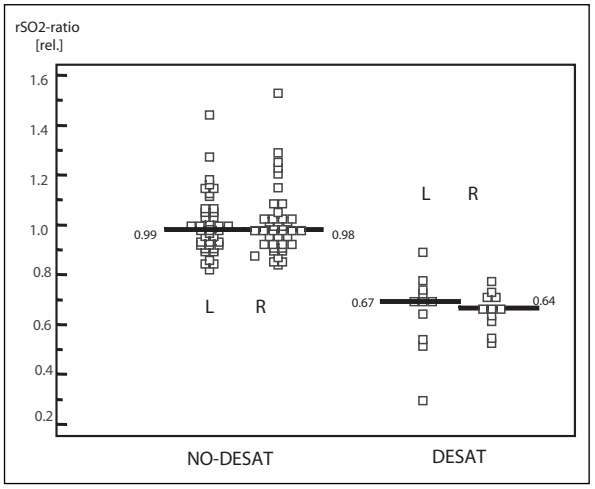

Figure 1a. Minimal regional oxygen saturation (rSO_2) ratio (minimal absolute rSO_2 level / baseline rSO_2) in patients undergoing cardiac and thoracic aortic surgery with deep hypothermic circulatory arrest graded according to rSO_2 - ratio < 0.8 (DESAT-group) or > 0.8 (NO-DESAT-group). Median is given as line with the adjacant value. Mann-Whitney-U test.

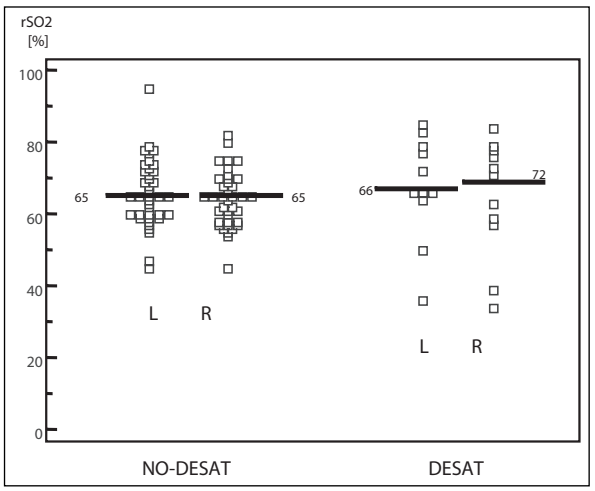

Figure 1b. Baseline absolute regional oxygen saturation (rSO_2) levels in patients undergoing cardiac and thoracic aortic surgery with deep hypothermic circulatory arrest graded according to the lowest intraoperative rSO_2-ratio. DESAT: rSO_2-ratio < 0.8; NO-DESAT: rSO_2 > 0.8. Median is given as line with the adjacant value. Mann-Whitney-U test revealed no significant difference.

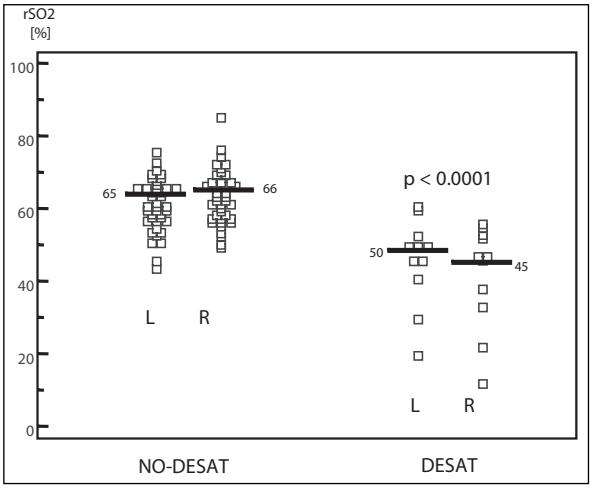

Figure 1c. Minimal absolute regional oxygen saturation (rSO_2) levels in patients undergoing cardiac and thoracic aortic surgery with deep hypothermic circulatory arrest graded according to the lowest intraoperative rSO_2-ratio. DESAT: rSO_2-ratio < 0.8; NO-DESAT: rSO_2 > 0.8. Median is given as line with the adjacant value. Mann-Whitney-U test.

(p = 0.043). Both patients had undergone DHCA of short duration and had not been treated by selective cerebral perfusion. In both patients, the stroke was verified by computer tomography and was found to be in the hemisphere in which cerebral desaturation had been observed. No significant between group differences in other relevant clinical outcome variables were observed (table 2).

Discussion

Despite various measures to maintain cerebral integrity and to reduce neurological complications, thoracic aortic vascular surgery carries a substantial risk of an adverse neurological outcome. Contemporary case series report an incidence of stroke in the range between 6 to 9% [6,7,8].

Deep hypothermic circulatory arrest is frequently used to minimize neurological damage by reducing cerebral oxygen consumption. However, the individual cerebral oxygen balance is difficult to assess during the no flow period. Thus, at least theoretically, rSO_2 monitoring by means of near-infrared spectroscopy may be rather helpful to determine the actual cerebral oxygen status in this situation.

Table 2. Clinically relevant outcomes

	DESAT (n=11)	**NO-DESAT (n=40)**	**significance**
Time to extubation [h]	6 (6-120)	6 (6-192)	n.s.
Stroke [n]	2	0	p = 0.043
Pulmonary compl. [n]	4	11	n.s.
Need for RRT [n]	0	1	n.s.
LCOS [n]	0	2	n.s.
HDU stay [d]	6 (2-13)	3 (1-34)	n.s.
Hospital stay [d]	9 (6-21)	10 (4-45)	n.s.

Clinically relevant outcomes in patients showing a decrease in regional cerebral oxygen saturation ratio (rSO_2-ratio) < 0.8 (DESAT group) or not (NO-DESAT group) while undergoing deep hypothermic circulatory arrest. Data are given as median and range. n.s.: not significant. Pulmonary complications: prolonged ventilation, reintubation, or pleural effusion requiring drainage. RRT: renal replacement therapy. LCOS: low cardiac output syndrom requiring high-dose inotropes and/or postoperative intraaortic balloon counterpulsation; HDU: high-dependency unit (intensive care unit and intermediate care unit). Mann-Whitney-U test or Fisher's exact test.

Cerebral oxygen saturation monitoring by NIRS has been introduced in clinical practice in 1977 [9]. Since then, several observational and small prospective studies have shown that maintaining cerebral oxygenation in the near normal range improves outcome in patients undergoing on-pump cardiac surgery [10,11,12], but also in general surgery patients [13].

The optimal level of cerebral oxygen saturation and which degree of desaturation may be acceptable without increasing neurological risk during cardiac surgery is a matter of ongoing debate and may be dependent on the NIRS device used [2]. Animal data have clearly shown that rSO_2 levels reflect changes in cerebral blood flow and that rSO_2 levels below 40% are reflective of severe cerebral hypoperfusion and anaerobic metabolism [14].

Yao and coworkers observed an increased incidence of postoperative neurological impairment in CABG patients showing rSO_2 levels below 35% absolute [12]. Edmonds et al. suggest a cut-off level of 50% absolute with respect to data gathered outside the cardiac surgery theatre during various measures associated with decreased cerebral perfusion [1].

Very recently this cut-off level was adapted by Slater and coworkers in a prospective study on postoperative cognitive dysfunction in 240 CABG patients, showing that patients with prolonged periods (more than 6000 seconds) of cerebral desaturation (rSO_2 less than 50% absolute) had a significantly increased risk (Odds ratio: 2.69; p = 0.003) of a decline of at least one standard deviation in a cognitive function test after adjustment for various pre- and perioperative risk factors [15].

With respect to the fact that the device used in the present study has technological limitations to determine absolute oxygen saturation reliably in every patient [2] it may be more appropriate to follow trends in rSO_2 levels rather than to focus on absolute rSO_2 levels. To adapt for variations in baseline levels, the rSO_2-ratio – i.e. the ratio between the actual and the baseline saturation – may be calculated. Samra and coworkers showed that a decrease in rSO_2 ratio to 0.8 had a sensitivity of 80% and a specificity of 82.2% to detect a neurological compromise in patients undergoing carotid endarteriectomy with regional anesthesia [16]. Very recently, these findings have been confirmed by Moritz et al. who observed a sensitivity and specifity of 83% in the same setting [17]. In the present study we followed this approach. However, as can be derived from figure 1, the median of the minimal absolute rSO_2 levels in the DESAT-group were 50 (L) and 45% (R). Consequently the patients in this group may be regarded as severely desaturated; independent from the classification used.

Only few clinical studies have focused on the relation between neurological outcome and the results of cerebral oxygenation monitoring in adult patients undergoing circulatory arrest [4,5,18]. No data on the use of rSO_2 monitoring in relation to clinical outcome in patients with isolated DHCA (without concomitant antegrade or retrograde perfusion) are available. To the best of our knowledge the present study is thus the first to describe the effects of cerebral desaturation determined by NIRS in a population in which the majority of patients (74%) underwent thoracic aortic or cardiac surgery without additional perfusion measures. Our

data show that a decrease in the rSO_2-ratio to less than 0.8 in patients is associated with a significantly higher incidence of an adverse neurological outcome, suggesting that preventing cerebral desaturation during DHCA procedures may help to reduce neurological deficits.

It is of note that all patients – besides standard measures like cerebral cooling with ice-packs and a body (bladder) temperature of 18° Celsius – had BIS monitoring and that anesthesia depth during DHCA was titrated to "burst suppression" levels (BIS = 0). The fact that cerebral desaturation occurred despite these precautions is suggestive of a high interindividual variability of oxygen needs that cannot be derived from conventional monitoring. And indeed, with increasing experience in intraoperative rSO_2 monitoring we have repeatedly observed patients showing an extremely rapid decrease in rSO_2 levels while others do not even reach baseline levels even after prolonged DHCAs of 30 min or more. This has led to a change in surgical management, since the surgeons at our institution are now much more liberal in using selective antegrade or – if this is not feasible – retrograde perfusion if rSO_2 tends to fall below baseline.

Limitations

The etiology of perioperative strokes in patients undergoing cardiac surgery is multifactorial and may either be related to hypoperfusion as well as an embolic event. The latter may be related to arteriosclerotic debris or air embolism. With respect to the fact that small amounts of air are often present after open heart and aortic vessel surgery, an embolic nature of the two strokes observed in this series cannot be ruled out. However, the patients that developed a perioperative stroke were not treated by selective perfusion; consequently at least an arteriosclerotic embolic event as the consequence of manipulating cerebral vessels with the perfusion cannula is rather unlikely.

The most important limitation applies to the retrospective nature of this study and the fact that the rSO_2 levels were derived from handwritten anesthesia charts in which only the minimal rSO_2 levels during DHCA were recorded. Consequently we cannot make statements about the duration of these desaturation periods. The duration of desaturation, however, has been reported to be an important aspect for the interpretation of rSO_2 levels since prolonged desaturation periods have been shown to be much more detrimental than short "dips" with subsequent restoration of oxygenation [4]. Another consequence of the retrospective nature of the study is the lack of data on the presence and severity of non-focal neurologic events and the lack of cognitive function tests.

Another limitation applies to the low incidence of stroke – the overall incidence was 3.9% – making statistical analyses liable to potential error. This may be derived from the fact that the significant difference between the DESAT and the NO-DESAT group would have been lost in case of only one patient with stroke in the NO–DESAT group. However, with respect to this relatively low incidence of stroke we have to accept this potential of error in this retrospective analysis and will never be able to set up a prospective trial on this issue, since a study being capable of showing a reduction in stroke rate from 4% to 2% would require inclusion of more than thousand patients.

In conclusion, the results of the present retrospective study suggest that monitoring cerebral oxygen saturation by means of near-infrared spectroscopy is a useful adjunct in patients undergoing cardiac and thoracic aortic surgery with DHCA and that a decrease in the rSO_2-ratio below 0.8 is associated with a significant risk of an adverse neurological outcome. Preventing cerebral desaturation during DHCA procedures may thus help to reduce postoperative neurological deficits.

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