

Unilateral versus bilateral cerebral oximetry in delirium prevention during CABG and valve surgery

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Abstract

Background: Cerebral oximetry is a non-invasive tool for identifying silent desaturation during cardiac surgery. Peri-operative desaturation may require rapid interventions to avoid adverse events, including delirium. Most desaturations during cardiac surgery occur in both hemispheres. Our objective was to evaluate the difference in applying a single cerebral oximetry sensor versus a dual sensor for preventing delirium in coronary artery bypass grafting and valve surgery.

Methods: We conducted a single-center, retrospective study of all patients undergoing coronary artery bypass grafting and valve surgery between January 2016 and December 2017. Before surgery, we identified any cerebral low flow state by transcranial Doppler ultrasound and either restored cerebral flow prior to surgery or, if that was not possible, waived surgery and offered the patient alternative non-surgical therapies, such as coronary angioplasty. In 2016, patients undergoing cardiac surgery were monitored with bilateral oximetry sensors (control group), whereas a single sensor was used in 2017 (study group).

Results: Bilateral sensors were used in 508 patients and a single oximetry sensor in 498 patients. The use of a unilateral sensor did not influence the delirium rate. Regression analysis confirmed our null hypothesis. The primary outcome delirium rate was not significantly different between the control (bilateral sensors) group (6.4%) and the study (unilateral sensor) group (5.4%) ($p = 0.472$, OR 1.21 [95%CI 0.72 – 2.05]).

Conclusions: Using a single cerebral oximetry sensor instead of bilateral sensors may reduce both the cost of monitoring and the threshold for applying cerebral oximetry during cardiac surgery without influencing the delirium rate.

Keywords: Cerebral oximetry, Cardiac surgery, Delirium.

Presented at the Annual Meeting of the Belgian Society of BeSARPP, November 19, 2022, The Square, Belgium. Internal Review Board approval: Prior to recruitment, we submitted our study for medical ethical review to the accredited Medical Research Ethics Committee Zuid-West Holland (MREC-ZWH). The MREC-ZWH concluded that our study did not fall under the scope of the Medical Research Involving Human Subjects Act (WMO) because participants were not subject to procedures and/or were not required to follow rules of behavior.

Our study did not require permission from the MREC. This study was subsequently assessed by the Science and Research Committee of Haga Teaching Hospital. The Board of Directors approved the execution of this research in its institution on May 4, 2017. This study was archived under file number Haga T16-122 NL and by the MREC-ZWH under number 16-125.

Introduction

Stroke and delirium are potential and feared complications during on-pump cardiac surgery. The etiology underlying delirium is multifactorial, with the biggest risk factor being pre-existing cognitive impairment¹. However, both stroke and delirium can be caused by peri-operative cerebral ischemia^{2,3}. Longstanding peri-operative silent desaturation is associated with increased post-operative delirium rates^{4,5}. Furthermore, peri-operative low-flow states induce watershed strokes in patients with occlusive cerebrovascular disease⁶. In addition, post-operative embolic strokes tend to be more severe in poorly perfused brain areas compared to emboli dislodged in well-perfused brain areas⁷. In other words, the incidence and severity of stroke, and to a certain extent delirium, can be regarded as clinical markers of peri-operative cerebral ischemia.

At our institution, we have developed a dual strategy for detecting cerebral ischemia during cardiac surgery, the Haga Braincare Strategy (HBS). In all patients, prior to cardiac surgery, we perform a transcranial Doppler ultrasound (TCD) to evaluate asymmetric cerebral flow states and identify patients at high risk for stroke. In cases showing a cerebral low-flow state, we attempted to restore the flow deficit by selective carotid angioplasty. If this is not possible, we recommend the second-best options for cardiac disease resolution, such as percutaneous coronary intervention or transcatheter aortic valve implantation (TAVI) procedures.

In the second step of the HBS, we monitor every patient during on-pump cardiac surgery with bilateral oximetry. We previously demonstrated the safety and effectiveness of the HBS in our patient cohort⁸. Since 2009, use of the HBS has consistently reduced the incidence of post-operative delirium > 50% and nearly eliminated severe hemodynamic strokes related to cardiac surgery^{9,10}. However, multiple recent studies have questioned whether goal-directed patient management during cardiopulmonary bypass (CPB) using near infrared spectroscopy (NIRS) monitoring improves outcomes^{11,12}. In our effort to critique our practice, we discussed whether universal bilateral NIRS monitoring is still appropriate. Vretzakis et al. reported that bilateral sensors are required in cardiac surgery because asymmetric recordings can be caused by a number of clinical states, including high-grade carotid artery stenosis, incomplete circle of Willis, and procedure-related factors, such as unilateral or bilateral antegrade cerebral perfusion during aortic surgery¹³. On the other hand, asymmetrical persistent desaturation during cardiac surgery is a highly infrequent event. In addition,

when applying the HBS, we identify patients with poor collaterals prior to cardiac surgery and subsequently reduce the likelihood of peri-operative asymmetric oximetry recordings. Furthermore, if a single sensor is as effective as dual sensors, the cost of cerebral oximetry could be reduced. However, despite these arguments supporting the use of a single sensor, no studies have addressed the issue of delirium prevention in the use of one versus two cerebral sensors during cardiac surgery. Therefore, we investigated whether the delirium rate is similar in cardiac surgery monitored with a single oximetry sensor and bilateral sensors.

Methods

Study design

We performed a retrospective case control study during the period from 1 January 2016 until 31 December 2017 at Haga Hospital. The study compared two groups of patients. The control group comprised patients scheduled for cardiac surgery in 2016, who were monitored peri-operatively with bilateral oximetry sensors. The study group included patients scheduled for cardiac surgery in 2017, who were monitored with unilateral sensors. The oximetry sensors were located on the left and/or right side of the forehead at the discretion of the cardio-anesthesiologist. All patients in both groups were subjected to the HBS. The inclusion criteria were age >18 years and being scheduled for coronary artery bypass grafting (CABG) and/or valve surgery. Exclusion criteria were aortic surgery, MAZE procedures, endocarditis, prior heart surgery, or ventricular septal rupture.

The primary endpoint of the study was the incidence of delirium. Secondary endpoints were stroke incidence, the combined incidence of stroke and delirium, stroke severity, duration of intensive care unit (ICU) stay, duration of hospital stay, and peri-procedural neurological and non-neurological complications.

Identification of patients with poor collaterals prior to surgery

To determine the status of the collateral arteries, we investigated the cerebral hemodynamics at the base of the middle cerebral artery (MCA) using a 2-MHz pulsed bidirectional TCD system (Delica 9-series; Delicate Manufacturer, Shenzhen, China). If the cerebral hemodynamics distal to the carotid artery stenosis revealed a reduced pulsatility index (PI < 0.8) or asymmetrical PI value (PI asymmetry > 50%), then the collateral circulation was considered poor.

If TCD was not possible or the PI was reduced or asymmetrical, we performed duplex scanning of

the carotid arteries with a Toshiba Xario Ultrasound Imaging System (SSA-680A). If duplex scanning revealed patent carotid arteries, the patient was considered to not be at risk of hemodynamic strokes. If duplex scanning showed a high-grade stenosis, CT angiography (CTA) was performed to establish the status of the intracranial collaterals. If both anterior and posterior communicating arteries were present ipsilateral to the hypoperfused MCA, the collateral circulation was graded as 'good'. However, if the anterior and/or posterior communicating arteries were absent, the collateral circulation was graded as 'poor'. Further details of the HBS, including the indications for pre-operative selective carotid angioplasty and/or waiving surgery have been extensively published by Duynstee et al.¹⁰.

Surgical procedures

All patients were treated according to standard surgical, anesthetic, and perfusion protocols as described previously^{9,10}. The standardized balanced anesthetic technique used a combination of hypnotics, analgesics, and muscle relaxants. A bispectral index monitoring system (BIS) was used for every surgical procedure for the titration of sedative hypnotic drugs. CPB was performed with blood flow rates of 2.2–2.4 L/min to maintain a mean arterial pressure >60 mmHg, partial pressure of arterial carbon dioxide \geq 40 mmHg by alpha-stat management, and hematocrit above 22%.

Cerebral oximetry during cardiac surgery

To measure brain oxygenation, all patients were monitored during and after surgery with NIRS (INVOS 5100; Somanetics Corporation, Troy, MI, USA). NIRS monitoring placed on the left and right hemisphere started prior to intubation and was continued until the patient was awake and hemodynamically stable. Details of the NIRS monitoring have been published previously by Palmbergen et al.⁹. Cerebral oxygenation was secured during surgery by application of an algorithm published by Denault et al.¹⁴.

Surveillance for stroke and delirium

At Haga Hospital, early stroke and delirium detection after cardiac surgery has a high priority. Patients are universally screened prior to surgery for cognitive dysfunction, TIA, and stroke. Three times daily, post-surgery patients are subjected to the Delirium Observation Score (DOS)¹⁵. In cases of suspected delirium, an intensive care specialist or geriatric physician was consulted. A neurologist was consulted upon suspicion of seizures, coma, TIA, or stroke. The National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin Score

(mRS) were used to quantify the stroke severity and dependence in daily activities, respectively^{16,17}. The Apache III score was used in the ICU to provide an initial risk classification at admission¹⁸.

Data collection and statistical analysis

All data, including complications, were collected from electronic patient files and documented in a separate downloadable internet-based data management system that allowed statistical analysis. We investigated significant differences between single cerebral oximetry sensor use and dual sensor use in preventing stroke and delirium in CABG and valve surgery, starting with simple univariate analysis. The null hypothesis was that the combined incidence of stroke and delirium was not different between the control group (bilateral sensors) and study group (unilateral sensor). A P-value <0.05 was considered to indicate significance.

We calculated the sample size as follows. Earlier observations at the Haga Brain Initiative found a delirium frequency of 5% with dual sensors^{8,9,10}. We expected no notable differences between the use of a dual sensor and a single sensor. We defined a notable difference as a delirium frequency >10%. In combination with a power of 80% and an alpha of 5%, this means we needed at least 436 persons in each group.

To lower our uncertainty about the primary outcome, we performed several sensitivity analyses. Because the incidence is low, it would be wise to confirm the main hypothesis through this method and test the robustness of the results¹⁹. The sensitivity analyses included a subgroup analysis with only male subjects and an analysis excluding the patients with a hospital stay longer than 21 days.

Statistical analyses were performed using SPSS (v 24.0). Categorical values were analyzed using chi-squared or Fisher's exact tests. For numerical data with distributions approximating normality, we used an independent t-test for comparisons. For comparisons between three groups, we used a one-way ANOVA. When the null hypothesis of an analysis of variance (ANOVA) model was rejected, Bonferonni post-hoc tests were used to identify the population means that were different. When necessary, in order to more broadly investigate certain variables, regression analyses were performed to correct for possible confounders.

Internal Review Board approval

Prior to recruitment, we submitted our study for medical ethical review to the accredited Medical Research Ethics Committee Zuid-West Holland (MREC-ZWH). The MREC-ZWH concluded that our study does not fall under the scope of the

Medical Research Involving Human Subjects Act (WMO) because participants were not subject to procedures and/or were not required to follow rules of behavior.

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Results

This retrospective study included a total of 1006 patients, 777 of whom were scheduled for CABG, 153 for valve surgery, and 76 for CABG and valve surgery. Table I shows the outcome data for the control and study groups. The groups were similar in terms of age, type of surgery, and pre-operative mRS. However, compared to the control group, the study group included a significantly higher male to female ratio. In the statistical analysis of outcome data, we corrected for this difference whenever necessary. In addition, in the sensitivity analyses, we included an additional analysis with only males.

Among all patients, the overall stroke rate was 0.8%, the delirium rate 5.9%, and the combined stroke and delirium rate 6.6%. Regression analysis confirmed our null hypothesis. The primary outcome

delirium rate was not significantly different between the control (bilateral sensors) group (6.4%) and the study (unilateral sensor) group (5.4%) ($p = 0.472$, OR 1.21 [95%CI 0.72 – 2.05]).

The groups also did not significantly differ in stroke rate, mortality rate, or mean mRS at discharge. Compared to the control group, the study group had significantly shorter hospital stays. The latter could partly be explained by the fact that hospital stays lasting over 21 days, caused by postoperative complications, such as multi-organ failure, were recorded for 6 patients in the control group compared to 4 in the study group (Table I). In the sensitivity analyses described below, we excluded these outliers.

On average, patients scheduled for CABG with valve surgery were approximately 4 years older than patients scheduled for CABG, which was a significant difference. We also found that the cumulative stroke and delirium rate significantly differed according to type of surgery (Table II). This relationship was completely based on the delirium rate and not related to the impact of stroke. Patients scheduled for valve surgery or CABG with valve surgery exhibited a significantly increased delirium rate and mean hospital stay compared with patients scheduled for CABG. The incidence of delirium was relatively low in patients scheduled for CABG (4.2%) but increased to 18.4% among patients scheduled for combined CABG and valve surgery. Because of the increased delirium rate, patients who underwent CABG and valve surgery had longer hospital stays. Mortality

Table I. — Sociodemographic variables and outcome data.

Data	Control group	Study group	P-value
Sensor	bilateral	unilateral	
Year	2016	2017	
Number	508	498	
Male-to-female ratio	2.79	4.41	0.003
Mean age, years (SD)	67 (9.5)	67 (9.5)	0.738
CABG	79.7%	74.6%	0.060
Valve surgery	13.9%	16.4%	0.292
Combined CABG/valve surgery	6.3%	8.9%	0.152
Mean pre-operative mRS (range)	1.99 (0-4)	2.04 (1-3)	0.009*
Cumulative stroke & delirium rate	7.4%	5.8%	0.375
Stroke rate	1.2%	0.4%	0.287
Delirium rate	6.4%	5.4%	0.507
mRS at discharge (range)	3.00 (2-6)	3.03 (2-6)	0.168
Mortality rate	1.2%	1.2%	1.000
Apache III (range)	47 (16–120)	46 (16–123)	0.147
Mean ICU stay, days (range)	1.09 (1-27)	1.04 (1-6)	0.355
Mean hospital stay, days (range)	6.63 (1–93)	5.89 (1–21)	0.020
CABG, coronary artery bypass graft; mRS, modified Ranking Scale; ICU, Intensive Care Unit. *Baseline values are with a few exceptions exactly similar.			

Table I. — Complication rates according to type of surgery among all patients.

Data	CABG	Valve surgery	CABG with valve surgery	P-value (CABG/CABG with valve surgery)
Number	777	153	76	
Mean age, years (SD)	66.2 (9.6)	67.8 (9.3)	70.4 (7.3)	<0.001
Cumulative stroke & delirium rate	6%	9%	23%	<0.001
Stroke rate	0.6%	0.6%	2.6%	0.173
Delirium rate	4.2%	8.5%	18.4%	<0.001
Mean hospital stay, days (range)	6.0 (1–93)	6.7 (4–21)	8.2 (1–82)	<0.001
Mortality rate	1.4%	0%	1.3%	0.336

rates were equal across the different types of surgery.

Post-operative stroke severity was mild in patients who experienced combined stroke and delirium, with a mean NIHSS score <5 (Table III). However, stroke patients still had significantly longer hospital stays than patients without neurological complications. The same relationship was found for the delirium rate, in that patients with delirium had significantly longer stays in the ICU and hospital than patients without delirium. Patients who experienced delirium also exhibited a higher mortality rate than reference patients without stroke or delirium, though this difference was not significant.

Sensitivity analysis

As described earlier, we checked the robustness of the results of our outcomes by including only male patients and excluding patients with a hospital stay longer than 21 days. The male-only sensitivity analysis resulted in a cumulative rate of 6.4% for the control group and 6.1% for the study group (P = 0.884; OR 0.96, 95% CI 0.54 – 1.71). For the second sensitivity analysis (without hospital stay outliers), the cumulative rate for the control group was 5.5%

and for the study group 5.9% (P = 0.795; OR 1.07, 95% CI 0.63 – 1.84).

Discussion

In this study, we showed that the status of cerebral oximetry monitoring (1 versus 2 sensors) did not influence the primary outcome of delirium rate in on-pump open heart surgery. Cerebral oximetry in cardiac surgery provides real-time detection of cerebral oxygen saturation, which cannot be estimated from standard hemodynamic monitoring. Observational studies have shown that silent desaturations detected by cerebral oximetry predict the onset of cognitive dysfunction and post-operative delirium^{4,5}. However, recent systematic reviews do not support universal application of cerebral oximetry in patients scheduled for cardiac surgery^{11,12,19,20,21}. Therefore, many cardiac surgical centers in the Netherlands do not use cerebral oximetry at all because they are not convinced that this monitoring enhances peri-operative outcomes. Nevertheless, at Haga, we have had a 50% reduction in delirium rates after implementing cerebral oximetry as part of

Table III. — Patient outcomes according to type of neurological complication.

Data	Stroke	Delirium	Combined stroke & delirium	Reference (all patients without delirium or stroke)	P-value, stroke vs. reference group	P-value, delirium vs. reference group
Number	6 (0.6%)	58 (5.8%)	2 (0.2%)	940		
Mean age, years (SD)	68.7 (7.3)	74.0 (7.1)	68.0 (12.7)	66.3 (9.5)	0.999	<0.001
Mean stroke severity, NIHSS (range)	4.2 (1-13)		6.0			
Mean ICU stay, days (range)	1.00 (1-1)	1.63 (1-27)	4.5 (1-8)	1.02 (1-6)	0.999	<0.001
Mean hospital stay, days (range)	23.3 (6-93)	10.5 (1-82)	12.0 (6-18)	5.9 (1-38)	<0.001	<0.001
Mortality rate	0%	1.7%	1.7%	1.2%	1.000	0.515

NIHSS, National Institutes of Health Stroke Scale; ICU, Intensive Care Unit.

the HBS⁹. We abolished hemodynamic strokes distal to occluded carotid arteries with implementation of the HBS, and Dutch benchmark studies have shown reduced stroke rates after CABG and valve surgery at Haga over the 2014-2018 era¹⁰. Therefore, we are still using cerebral oximeters at our institution. However, the current policy of unilateral oximeter sensor use at the Haga may change if future Dutch benchmark observations show that the delirium rate at our institution is significantly higher than at other Dutch medical cardiac surgery centers.

Here, we showed that using a single sensor did not result in a different primary outcome from using dual sensors in our present patient cohort, which included patients subjected to CABG, valve surgery, or a combined procedure and who exhibit normal cerebral hemodynamics prior to surgery. We conclude that, in this context, the use of a single sensor is sufficient and comparable to using dual sensors, as we observed no increases in the stroke or delirium rate, length of hospital or ICU stay, or mortality rate when using a single sensor compared to a dual sensor. This result would reduce health-related costs for applying cerebral oximetry during cardiac surgery.

The current data confirm our earlier observations that the combined CABG and valve surgery puts patients at a greater risk for ischemic events compared to a separate CABG or valve surgery^{9,10}. These patients had greater risk for both stroke and delirium. This difference is not remarkable because more complex cardiac procedures generate more vessel wall lesions and are more time consuming and, therefore, carry greater risks for complications.

Fortunately, our cohort exhibited mild stroke severity, likely because the cerebral flow and oxygenation were verified by application of the HBS. Earlier observations found that HBS application reduced the post-operative hemodynamic stroke risk, indicating that most post-operative strokes were embolic in nature¹⁰. As adequate flow conditions were secured by cerebral oximetry, we presume that optimal flow states clear emboli, which could explain the mild stroke severity in our present cohort⁷.

In the current study, we only measured the delirium rate and did not directly measure delirium severity. However, the length of stay is a surrogate marker of delirium severity. We found that both ICU and hospital stays were longer among patients who experienced delirium. In 2012, we published similar data regarding the impact of delirium in patients scheduled for cardiac surgery. In 2008, prior to implementation of the HBS, the delirium rate was nearly 13%, and the hospital stay was 14 days for patients who experienced delirium. The present

delirium incidence is approximately 6%, and the length of hospital stay for patients who experience delirium is 11 days. Again, one could hypothesize that this change is related to implementation of the HBS, as it may have prevented the onset of deep hypoxic delirium through the use of perioperative cerebral oximetry. The relatively low delirium incidence and good delirium outcomes in our current study could also be related to the fact that every patient was monitored using a BIS monitor. A recent systemic review showed that BIS monitoring during major surgery is associated with a significantly reduced risk of POD and long-term cognitive dysfunction²².

The present study has limitations. First, it is a single-center study with a limited number of observations. Second, the study is retrospective, which does not have the power of evidence of a randomized controlled trial. Third, the data reflect the real-life data of patients scheduled for cardiac surgery. We did not qualify for subtle changes in cognitive decline or perform MRI of the brain to detect signs of silent cerebral ischemia. Thus, despite the Haga stroke and delirium detection regimen, we could have underestimated the real incidences of stroke and delirium. Fourth, the current data do not allow any conclusion related to the question of whether the use of cerebral oximetry during cardiac surgery is warranted.

In summary, our current results demonstrate that using a single sensor does not result in a different delirium rate than using dual sensors in on-pump cardiac surgery, provided that the HBS is applied. This observation reduced the cost of cerebral oximetry monitoring during CABG and valve surgery at our institution.

Acknowledgments: The authors would like to thank professor Michel van Putten MD, PhD, head of the Department of Clinical Neurophysiology of Medisch Spectrum Twente, for his comments and suggestions.

Funding: None.

Disclosures: The authors declare no conflict of interest.

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doi.org/10.56126/75.2.42