

Improved perioperative neurological monitoring of coronary artery bypass graft patients reduces the incidence of postoperative delirium: the Haga Brain Care Strategy

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Abstract

OBJECTIVES: Postoperative delirium is a major cause of morbidity and mortality after cardiovascular surgery. Risk factors for postoperative delirium include poor cerebral haemodynamics and perioperative cerebral desaturations. Our aim was to reduce the postoperative delirium rate by using a new prevention strategy called the Haga Brain Care Strategy. This study evaluates the efficacy of the implementation of the Haga Brain Care Strategy to reduce the postoperative delirium rate after elective coronary artery bypass graft (CABG) procedures. The primary endpoint was the postoperative delirium rate, and the secondary endpoint was the length of stay in the intensive care unit.

METHODS: The Haga Brain Care Strategy consisted of the conventional screening protocol for delirium with the addition of preoperative transcranial Doppler examinations, perioperative cerebral oximetry, modified Rankin score, delirium risk score and (if indicated) duplex examination of the carotid arteries. In case of poor preoperative haemodynamics, the cerebral blood flow was optionally optimized by angioplasty or the patient was operated on under mild hypothermic conditions. Perioperative cerebral desaturations >20% outside the normal range resulted in intervention to restore cerebral oxygenation. Cerebral oximetry was discontinued when patients regained consciousness. Patients undergoing elective CABG procedures in 2010 were compared with patients scheduled for coronary bypass graft procedures in 2009 who had not been exposed to additional Haga Brain Care Strategy assessment.

RESULTS: A total of 233 and 409 patients were included in 2009 and 2010, respectively. The number of patients subjected in 2010 to transcranial Doppler examinations, cerebral oximetry or both (Haga Brain Care Strategy) were 262 (64.1%), 201 (49.1%) and 139 (34.0%), respectively. The overall rate of postoperative delirium decreased from 31 (13.3%) in 2009 to 30 (7.3%) in 2010 ($P=0.019$). A binary logistic regression model showed that the Haga Brain Care Strategy was an independent predictor of a reduced risk of developing a postoperative delirium (odds ratio = 0.37, $P=0.021$).

CONCLUSIONS: With the implementation of the Haga Brain Care Strategy in 2010, a reduction of the incidence of postoperative delirium in patients undergoing elective CABG procedures was observed. In addition, the length of stay in the intensive care unit showed an overall tendency to decline. The limited number of observations and the current study design do not allow a full evaluation of the Haga Brain Care Strategy but the data support the idea that a sophisticated preoperative assessment of cerebral haemodynamics and perioperative monitoring of cerebral oximetry reduce the incidence of the postoperative delirium in CABG surgery.

Keywords: Postoperative delirium • Cerebral oximetry • Transcranial Doppler • Coronary artery bypass grafting

INTRODUCTION

Delirium is an important cause of morbidity, mortality and prolonged hospital stay after cardiovascular surgery. Important risk factors for developing delirium after cardiovascular surgery are pre-existing cognitive disorders, cerebral pathology, age older than 70 years, poor preoperative cerebral haemodynamics and perioperative cerebral desaturations [1–3]. The reported

incidence of postoperative delirium (POD) after cardiovascular surgery ranges from 3.1 to 32% depending on the criteria used to define POD, study design, and type of cardiovascular procedure [2, 4].

Murkin's randomized prospective study pointed out that untreated perioperative cerebral hypoxia is an important cause of poor outcome and that perioperative interventions that restore cerebral saturations within normal limits are associated with a

good outcome. Moreover, Slater *et al.* showed that the severity and duration of cerebral hypoxemia during coronary artery bypass graft (CABG) surgery are a strong independent risk factors for POD. In other words, POD is to a certain extent an 'ischaemic encephalopathy'. Various events lead to cerebral desaturations, including systemic hypotension, blood loss, cerebral air embolisms and mismatch between cerebral perfusion and metabolism. Early detection and treatment of cerebral desaturations during CABG procedures will provide the opportunity to optimize the cerebral haemodynamics, and therefore reduce the chance of developing POD [3, 5].

The conventional brain care strategy at our institution to reduce the risk of a POD consisted of the documentation of pre-existing cognitive brain disorders and cerebrovascular events, auscultation of the carotid arteries and, if indicated according to established guidelines, duplex scanning of the carotid arteries [6]. The conventional brain care strategy included elective pre-CABG carotid surgery limited to patients with either symptomatic, unilateral, high-grade artery stenosis or to patients with asymptomatic, bilateral, high-grade carotid artery stenosis.

The above-mentioned conventional brain care strategy was replaced by a new strategy, called the Haga Brain Care Strategy (HBCS). The HBCS presumed that the POD rate could be reduced by subjecting patients to preoperative transcranial Doppler (TCD) screening and perioperative cerebral oximetry monitoring. With TCD, we were able to evaluate the adequacy of cerebral blood flow and identify patients with poor cerebral haemodynamics. By acting on the (silent) desaturations observed by cerebral oximetry, we were able to prevent the occurrence of deep and long-lasting periods of cerebral ischaemia during and after CABG surgery. The HBCS included pre-CABG angioplasty of the carotid artery in either patients with a unilateral symptomatic carotid artery high-grade stenosis or elective angioplasty in patients with poor cerebral haemodynamics.

Therefore, there were theoretically three options to pursue if a patient was identified with poor preoperative cerebral haemodynamics: (i) waiving surgery (in case of very poor cerebral flow due to multilevel occlusions in the cardio-cerebral arterial tree); (ii) restoration of cerebral flow in case of single level carotid artery stenosis by angioplasty or carotid endarterectomy or (iii) protecting the vulnerable brain during surgery using mild hypothermia in combination with close monitoring of cerebral flow with cerebral oximetry.

After the implementation of the HBCS in 2010, we examined patient outcomes with an observational study. The primary endpoint was the POD rate, and the secondary endpoint was the length of stay in the intensive care unit (ICU).

METHODS

Study design and inclusion/exclusion criteria

From January 2009 until November 2010, The Haga Teaching Hospitals (The Hague, The Netherlands) enrolled 642 patients on the basis of the following inclusion criteria: age >18 years and elective CABG or CABG plus procedure. CABG plus procedures included revascularization of the coronary arteries combined with a valve reconstruction procedure, Maze procedure or aorta ascendens replacement. Patients undergoing a redo-CABG or off-pump CABG procedure were excluded. From January 2010, we prospectively observed the patients while the HBCS was implemented. For

logistical reasons, we were unable to subject every patient to both TCD and cerebral oximetry. Approximately, four patients were scheduled each day for CABG/CABG plus procedures: two in the morning and two near noon. In general, patients with high-risk procedures and/or with greater risk of complications were scheduled in the morning. For both logistical and medical reasons, the surgical team decided that the patients scheduled in the morning would be more likely subjected to cerebral oximetry. To compare our results, we retrospectively collected data from patients who had an elective CABG or CABG plus procedure in 2009 with the conventional brain care strategy.

Data management

The following data were collected preoperatively using electronic Case Record Forms (CRFs): background demographics, type of surgery, modified Rankin Score (mRS), delirium risk score, results of TCD and duplex examinations, preoperative neurological consultations, preoperative carotid surgery or angioplasty and the use of cerebral oximetry. Postoperative outcome parameters were neurological complications (such as delirium and stroke rate), length of stay in the ICU and mRS at discharge. The CRFs were the input of a downloadable internet-based data management system that allowed online statistical analysis of all CRF data. This data management system was developed by Mediwebdesign[®] in The Netherlands (<http://www.mediwebdesign.nl/spi/cabg/loginreal.php>).

Modified Rankin scale

The mRS is a numeric scale used to measure the amount of dependence or disability in daily activities. It ranges from 0 to 6, where 0 means no disability or discomfort and 6 means the death of the patient [7]. Every patient had a preoperative mRS of at least 2, as angina negatively influenced all patients' daily activities. Patients who were more disabled (e.g. due to heart failure) were classified with a higher mRS. All discharged patients had an mRS ≥ 2 , as they all experienced discomfort and impairment due to sternotomy. If postoperative complications occurred and/or patients needed extra care after discharge, the postoperative mRS increased depending on how severely the daily activities were affected.

Preoperative delirium risk score

The preoperative delirium risk score is a tool to assess whether the patient has an increased risk of developing delirium after surgery. This assessment is based on the following risk factors: a history of delirium, pre-existing cognitive disorders, age, substance abuse, visual or auditory impairment and self-sufficiency. Although this predictive model has yet to be validated, it is based on the predictive model for delirium from Inouye and Charpentier [8]. The model is a generally accepted tool for estimating the risk of developing POD.

Delirium assessment

Simple bedside tests are usually used to detect delirium, however, a recent review of the literature showed that 'there is

not unanimity about which scale is the best' [9]. Therefore, we chose to use the Delirium Observation Screening (DOS) scale which was developed by a group of seven experts in the field of delirium. Internal consistency, predictive validity and concurrent and construct validity of the DOS scoring scale were tested in two prospective studies with high-risk groups of patients: geriatric medicine patients and as well a surgical patients [10].

The DOS scale, a 25-item scale, was developed to facilitate early recognition of delirium, according to the Diagnostic and Statistical Manual-IV criteria [11]. These clinical criteria of delirium consist of the following factors: disturbances of consciousness (i.e. reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention. A change in cognition (such as memory deficit, disorientation and language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established or evolving dementia. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.

The parameters of the DOS are tested three times daily, based on nurses observations during regular care.

If delirium was suspected by the medical staff, a geriatrician or internist was consulted to confirm POD and/or to exclude depression or dementia as an alternative cause of cognitive dysfunction. A neurologist was consulted if coma, epilepsy or stroke was suspected.

Ultrasound

Cerebral haemodynamics was evaluated preoperatively using a TCD examination (2-MHz pulsed bidirectional TCD, Delica 9-series, Delicate Manufacturer, Shenzhen, China). If this examination was not possible because of absent temporal windows, the patients cerebral haemodynamics were analysed by duplex scanning of the carotid arteries (Toshiba Xario[®], Ultrasound Imaging System, SSA-680A). The TCD examinations were performed by nurse practitioners as part of the routine work-up for these patients. Good cerebral haemodynamics were defined as a pulsatility index (PI) >0.6 in both middle cerebral arteries (MCAs) (or carotid siphon) or carotid arteries, with no stenotic lesions or stenotic lesions <70%. Poor haemodynamics were defined by a PI <0.6. We chose the PI measured at the origin of the MCA to determine the adequacy of cerebral blood flow for several reasons. Our first reason is that the MCA provides 80% of the hemispheric blood flow. Secondly, studies of occlusive cerebrovascular diseases have demonstrated that the pulsatility of the flow accurately reflects the adequacy of the collateral flow in case of an occluded or haemodynamically significant stenosed carotid artery [12]. The third argument for studying the PI measured by TCD is that this index is independent of the angle of insonation, and is therefore a much better parameter to evaluate the adequacy of collateral circulation than MCA blood flow velocities, which are dependent on the angle of insonation.

Cerebral oximetry

Non-invasive cerebral oximetry was performed by near-infrared spectroscopy (NIRS) (INVOS 5100; Somanetics Corporation, Troy, MI, USA). The NIRS procedure started in the operation room before the administration of anaesthesia, and was continued

during cardiac surgery and the postoperative phase until the patient was awake and haemodynamically stable in the ICU. Infrared light sensors were placed over both fronto-temporal areas. Resting baseline rSO₂ values were obtained after waiting at least 1 min after placement of sensors once values had stabilized, with patients resting quietly. Continuous rSO₂ values were stored on a disk with a 15s update for the duration of the intraoperative period. Cerebral desaturations were defined as oxygenation values >25% below the preoperative baseline value. When oxygenation values dropped to 20% below the preoperative baseline value, interventions were performed. A number of different possible interventions could be chosen apart from increasing the depth of anaesthesia and reducing the temperature: (i) raising systemic BP (using inotropes), (ii) raising pump flow (when on cardiopulmonary bypass) or raising flow (use of vasodilators fluid), (iii) elevating PaCO₂, (iv) raising FiO₂ (inspired oxygen concentration) and (v) raising blood haematocrit.

The choice of which interventions to take depended on the different circumstances in which cerebral deoxygenation occurred. The anaesthesiologist in charge took these circumstances into account in making decisions which action to take, as well as the fact that some actions (e.g. raising FiO₂, raising pump flow) are achieved faster than others (e.g. reducing temperature).

Because of different alleged causes for cerebral deoxygenation, no strict sequence of interventions was used. The effects of the actions taken were monitored and could lead to possible further or other steps mentioned above.

Cardiovascular procedures

The surgical team (four surgeons and five anesthesiologists) utilized uniform anaesthesia, surgical and perfusion techniques. All of the CABG and CABG plus procedures were performed with a cardiopulmonary bypass. Standard flow rates of 2.2–2.4 l/min were utilized to maintain a mean arterial pressure >60 mmHg, partial pressure of carbon dioxide (arterial) maintained at ≥40 mmHg by alpha-stat management, and haematocrit maintained above 22%.

A standardized balanced anaesthetic technique was used, combining hypnotics, analgesics and muscle relaxants. Induction of anaesthesia was performed by using etomidate (0.3 mg/kg ideal body weight (IBW)), sufentanyl (0.5 mg/kg IBW) and rocuronium (0.6 mg/kg). Maintenance of anaesthesia and postoperative sedation in the ICU was achieved by using propofol and sufentanyl infusion, with perioperative use of sevoflurane as a volatile anaesthetic. Depth of anaesthesia during surgery was measured using BIS (bispectral index) monitoring (BIS, Aspect industries), using a target value of 30–60 (in normothermic conditions). Standard haemodynamic monitoring was performed using invasive systemic blood pressure (cannulation of radial artery), central venous pressure (cannulation of right internal jugular vein) and 5 lead electrocardiography. Respiratory monitoring consisted of measurement of peripheral oxygen saturation and ventilatory end-tidal CO₂ measurement. Periodical bloodgas analysis provided extra information about haemodynamic and ventilatory conditions. Assessment of cardiac function and output using echocardiography and pulmonary artery catheter was optional.

Statistical analyses

Categorical values are presented as numbers (percentages) and were analysed using chi-square tests or Fisher's exact tests. The

Fisher's exact test was used instead of the chi-squared test when the expected frequencies calculated from the marginal totals were (considerably) less than five in cross tables (as the normal approximation of the binomial distribution will then be less appropriate). For numerical data whose distributions approximate normality, an independent *t*-test was used for comparisons. To evaluate the independent effects of age, sex, preoperative delirium risk score, type of surgery and additional screening (none vs HBCS) on the development of POD, a binary logistic regression model was used. Statistical significance was considered at $P < 0.05$. SPSS (v 17.0) statistical software was used for statistical analysis.

RESULTS

The cohort of CABG/CABG plus patients included 233 patients in 2009 and 409 patients in 2010. Comparison of the baseline demographics and preoperative clinical parameters are listed in Table 1. These data demonstrate no significant differences between the baseline demographics of patients who had surgery in 2009 vs 2010. However, the population of 2010 had a near significant ($P = 0.055$) higher preoperative delirium risk score compared with the population of 2009.

As expected, there was an increase in the number of patients receiving TCD examinations and cerebral oximetry due to the active implementation of the HBCS. The number of patients who underwent the full HBCS work-up increased from 4 (1.7%) in 2009 to 139 (34.0%) in 2010. Poor preoperative cerebral haemodynamics (uni- or bilateral PI < 0.6) were observed in 2.7% of all patients who were investigated with TCD. In 2010, one of these patients underwent an uncomplicated preoperative restoration of cerebral flow by carotid angioplasty; the other patients had carotid artery occlusions and were subjected to mild hypothermia during surgery. Moreover, these patients were closely monitored perioperatively using cerebral oximetry. None of these patients experienced either POD or stroke. One patient underwent an uncomplicated carotid endarterectomy in 2009 because of a symptomatic carotid artery stenosis. None of the patients in this cohort were refused for surgery because of poor cerebral flow due to multilevel occlusions in the cardio-cerebral arterial

Table 1: Comparison of baseline demographics and preoperative clinical parameters of patients included in 2009 and 2010

Factors	2009 (n = 233)	2010 (n = 409)	P-value
Age	68.21 ± 10.1	68.68 ± 10.0	0.568
Sex (male/female)	74.2%/25.8%	68.2%/31.8%	0.128
Type of surgery (CABG/CABG plus)	80.3%/19.7%	75.8%/24.2%	0.229
Preoperative delirium risk score	0.71 ± 1.3	0.94 ± 1.5	0.055
Preoperative mRS	2.08 ± 0.3	2.13 ± 0.4	0.094
TCD examination	9.0%	64.1%	
Cerebral oximetry (NIRS)	1.7%	49.1%	
HBCS (TCD + NIRS)	1.7%	34.0%	
Duplex examination	13.3%	13.0%	

Table 2: Comparison of postoperative clinical parameters of patients included in 2009 and 2010

Factors	2009 (n = 233)	2010 (n = 409)	P-value
Length of ICU stay			
Mean	2.11 ± 3.0	1.83 ± 2.9	0.228
1 day	70.0%	79.2%	
>1 day	30.0%	20.8%	0.011
Mean length of hospital stay	7.15 ± 6.3	7.27 ± 6.1	0.441
Neurological complications			
POD	13.3%	7.3%	0.019
Stroke	1.3%	1.5%	1.000
Postoperative mRS	2.52 ± 0.7	2.56 ± 0.8	0.537
Mortality	1.3%	1.2%	1.000

Table 3: Comparison of baseline demographics and clinical parameters of patients included in 2009 and 2010 with and without POD

Factors	No POD (n = 581)	POD (n = 61)	P-value
Age	67.79 ± 9.8	75.31 ± 9.7	<0.001
Sex (male/female)	69.9%/30.1%	75.4%/24.6%	0.520
Type of surgery (CABG/CABG plus)	79.9%/20.1%	54.1%/45.9%	<0.001
Preoperative risk of POD	0.74 ± 1.3	1.92 ± 2.1	<0.001
Preoperative mRS	2.10 ± 0.369	2.20 ± 0.5	0.043
Mean length of ICU stay	1.65 ± 2.3	4.64 ± 6.0	<0.001
Mean length of hospital stay	6.56 ± 4.1	13.51 ± 14.1	<0.001
Stroke	0.9%	6.6%	<0.001
Postoperative mRS	2.52 ± 0.8	2.82 ± 0.9	0.002
Mortality	1.2%	1.6%	0.640

tree. Preoperative neurological consultations were performed in ~7.5% of patients. During the implementation phase of this study, the percentage of neurological consultations tended to decline (9.8% in 2009 vs 6.1% in 2010).

Comparison of the postoperative clinical parameters demonstrates a significant reduction of the incidence of POD (Table 2). The percentage of patients developing POD declined from 13.3% in 2009 to 7.3% in 2010 ($P = 0.019$).

When comparing the mean ICU stay of the patients included in 2009 (2.11 days) and 2010 (1.83 days), there is no significant difference ($P = 0.228$), the median ICU stay in both years is one day. However, the lack of significant difference was due to a few outliers in 2010. To correct for these outliers, we dichotomized the ICU stay into the following groups: patients who were admitted to the ICU for one day, and those who were admitted for more than one day. We found a significant increase ($P = 0.011$) in the percentage of patients who were admitted to the ICU for only one day in 2010 (79.2%) compared with those in 2009 (70.0%).

Comparison of the baseline demographics and clinical parameters of patients with and without POD confirmed our

Table 4: Binary logistic regression model listing the ORs of developing POD in selected cohort (patients with HBCS and without additional intervention)

Factor	% or mean	OR	CI (95%)	P-value
Age	68.34	1.06	(1.02–1.11)	0.007
Sex (male/female)	70.5%	0.68	(0.31–1.50)	0.336
Preoperative delirium risk score	0.81	1.41	(1.17–1.71)	<0.001
Type of surgery (CABG vs CABG plus)	76.4%	3.68	(1.77–7.66)	<0.001
Additional screening (none vs HBCS)	67.5%	0.37	(0.16–0.86)	0.021

supposition that risk factors of POD include high age, CABG plus procedure and a high-preoperative risk of delirium (Table 3). Furthermore, Table 3 demonstrates that the patients developing POD had a significantly longer stay in the ICU and hospital. Moreover, the data reveal an increased number of strokes in patients who experience POD.

A binary logistic regression model was used to determine the independent effects of age, sex, preoperative delirium risk score, type of surgery and the use of HBCS on the development of POD after CABG/CABG plus procedures (Table 4). To fully evaluate the effect of the HBCS, we included only the patients who either had both TCD and cerebral oximetry or no additional evaluation at all, thus excluding the patients who had only the duplex or cerebral oximetry. Table 4 shows that patients who underwent the HBCS in 2009 and 2010 had a significantly lower risk of developing POD [odds ratio (OR) = 0.37, $P = 0.021$] compared with the patients who had no additional evaluation. Furthermore, a higher preoperative delirium risk score imparts a significantly increased risk of developing POD (OR = 1.41, $P < 0.001$). As mentioned previously, age and type of surgery are significant risk factors for developing POD.

DISCUSSION

This retrospective follow-up study was designed to evaluate the efficacy of the HBCS in reducing the POD rate after elective CABG/CABG plus procedures. The data demonstrated a reduction of the delirium rate after implementation of the HBCS. Although the study design was retrospective and observational, and not randomized, the observed reduction of the delirium rate is impressive given the almost-similar baseline demographics of the 2009 and 2010 cohorts (Table 1). If one takes a closer look at the baseline demographics in Table 1, it shows a near-significant higher preoperative risk of POD in 2010. Thus, even though there is an almost significant higher risk of developing POD in 2010 compared with 2009, we still see a significant reduction of the POD rate in 2010 with the implementation of the HBCS. This could mean that the actual risk reduction of the HBCS is even greater than described in the results. This observation and the results of Table 4 which show that the HBCS is an independent factor that contributes to a significant lower POD rate, mean that our aim to reduce the POD rate with the implementation of the HBCS was successful. It is important to realize

that the HBCS was not implemented in all patients treated in 2010. Therefore, we hope to report further reduction of the delirium rate in the future, when the HBCS is implemented in a greater proportion of patients.

The reduction of the POD rate has a great impact on the level of care: fewer patients experienced a delirium which is often a frightening and dangerous condition. Table 3 clearly shows that patients who experience delirium are admitted longer in the ICU, stay longer in the hospital and experience more strokes. The current study confirms the well known often devastating consequences of experiencing delirium in the postoperative phase of CABG surgery. However, apart from the patient's perspective, the cost of care for CABG surgery is expected to decline because of the observed reduced delirium rate. Although this study did not address the cost-benefit ratio of CABG, it is clear that the reduced delirium rate and the reduced length of stay in the ICU will save money and prevent loss of the quality of life [13].

Another observation of the current data is that the preoperative delirium risk score, which is not validated for CABG surgery patients, was closely associated with the POD incidence. Higher preoperative delirium risk scores are associated with a significant increase in the likelihood of developing POD. As the validation of the DOS score was not the primary goal of this study, additional studies are needed to establish the validity of this test in CABG surgery.

The observation that patients with POD have an increased stroke rate deserves some explanation (Table 3). In some patients, the coexistence of stroke and delirium may be explained by the fact that certain types of strokes (e.g. right parietal infarctions) may present with delirium-like symptoms. Alternatively, the observed stroke and delirium relationship may be explained by the fact that both entities share a common pathophysiology. For instance, multiple showers of solid and/or gaseous embolism and/or long-lasting systemic and cerebral hypoperfusion states may be responsible for the combination of stroke and delirium, and may explain the clinical observation that patients with poor bilateral haemodynamics due to carotid artery occlusions are susceptible to both haemodynamic stroke and ischaemic cerebral POD. These considerations regarding the common causes of stroke and POD suggest that peri-CABG stroke prevention regimes may reduce the incidence of POD, and *vice versa*. For example, pre-CABG restoration of cerebral flow may prevent both haemodynamic strokes and ischaemic cerebral POD. Unfortunately, because of the low incidence of poor preoperative haemodynamics in patients scheduled for CABG surgery, very large, multicenter studies are needed to prove the aforementioned hypothesis.

The efficacy of cerebral oximetry during CABG surgery has been demonstrated by Murkin *et al.* [5], who observed significantly fewer incidences of major organ dysfunction. The Murkin study design was a randomized prospective study that did not mention data on delirium rate; however, Murkin did observe a reduced stroke rate in patients who were treated in the intervention group vs the control group. In the context of Murkin's findings and the present data, one might logically conclude that the use of NIRS accounts for the observed reduction in delirium rate in the present study. To what extent preoperative TCD contributes to the observed delirium reduction rate is less clear; the number of patients in the present study is too small to draw a firm conclusion.

The implementation of NIRS perioperatively had an effect on anaesthetic management. Without using NIRS, adequate cerebral blood flow and oxygen delivery was assumed by monitoring and correction of indirect parameters, such as blood pressure, peripheral oxygen saturation and circulating volume/cardiac output. When using NIRS, more direct information about cerebral tissue oxygenation *c.q.* cerebral tissue perfusion became available. Not only do we think this provides essential information about when cerebral blood flow is compromised, it also gives an optimal feedback on 'how effective' the cerebral blood flow has been restored. Moreover, NIRS gives direct feedback on the efficacy of 'different types' of interventions that have been executed. Our clinical impression is that due to the use of NIRS technology, we tended more to choose flow-guided therapeutical interventions (e.g. increasing pump flow) than pressure-guided interventions (e.g. the use of vasopressors).

Several limitations of this study must be taken into consideration. First, the study design was a single centre retrospective follow-up and not randomized, which implies that the results are a good reflection of the efficacy of the HBSC strategy in this cohort of patients, but are not clinical proof that this HBSC strategy will work for other cohorts. Furthermore, in the present study, the follow-up was limited to the discharge of the patient, which is obviously a very short time frame in which to determine outcomes. As an additional drawback, the hospital admission time is not an accurate standard with which to define patients' recoveries after surgery. This parameter does not distinguish between patients who are going home after discharge and patients who are transferred to another hospital for further recovery. Therefore, we measured the overall length of ICU stay as an indicator of the overall recovery rate of each patient after surgery.

There are a number of potential confounding factors that are not measured in this study and which could potentially contribute to the risk of developing POD. We did not estimate, for instance, the dislodgement of aortic atheroma, or the quality of de-airing of the heart during open heart procedures nor did we measure acute reperfusion injury. However, the cardiovascular surgeons did not change perioperative strategies and protocols during 2009 and 2010. Therefore, we deemed it not likely that these were major confounding factors.

However a more relevant confounding factor could be introduced by the fact that in 2010 the cardio-anaesthesiologist became more aware of preserving an adequate cerebral flow rather than just aiming at a stable blood pressure to preserve the cerebral haemodynamic by the use of NIRS. It might well be the case that using the NIRS might have a beneficial effect on patients who are monitored with the instrument, but also on those patients who are not monitored by the NIRS once the anaesthesiologist becomes more aware of the close relationship between the cerebral saturation and the level of the pump flow. This might be an important factor that one needs to take into account when evaluating the value of NIRS in surgery.

Addressing the issue of bias one can argue that because the HBSC was implemented in 2010, not all patients underwent the full work-up. The selection of patients who underwent the HBSC could be considered as a bias. This selection was because of a limited number of NIRS devices at our disposal. The two main reasons for monitoring patients more often in the morning were the following. These patients were scheduled in

the morning because they had a higher risk of developing complications compared with those operated on the afternoon, therefore we deemed it necessary that they get additional monitoring. Also it was not always possible logistically to start cerebral oximetry in the afternoon because of a lack of available devices, mostly because they were still monitoring the patients in the ICU.

In conclusion, in conjunction with the implementation of the HBSC in 2010, a reduction of POD incidence has been observed in patients after CABG and CABG plus procedures. The length of ICU stay has been reduced. The data support the idea that sophisticated preoperative assessment of cerebral haemodynamics and perioperative monitoring of cerebral oximetry reduce the incidence of the POD in CABG surgery. However, the study design and the current number of observations do not allow a full evaluation of the HBSC. It is for instance unclear to what extent ultrasound and NIRS contribute to the current observations. A randomized, controlled trial is needed to fully evaluate the efficacy of the HBSC.

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