Journal of Clinical Monitoring and Computing (2020) 34:715–723
https://doi.org/10.1007/s10877-019-00385-x

ORIGINAL RESEARCH

Preoperative transcranial Doppler and cerebral oximetry as predictors of delirium following valvular heart surgery: a case–control study

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Received: 30 July 2019 / Accepted: 29 August 2019 / Published online: 3 September 2019

Abstract
Delirium is a frequent and serious complication after cardiac surgery with cerebral hypoperfusion as one from the key pathophysiological mechanisms. Middle cerebral artery (MCA) mean blood flow velocity (MFV) measured by transcranial Doppler has been used as a marker of cerebral perfusion, and cerebral oximetry (rSO_2) value as a marker of its adequacy. This prospective observational trial examined the predictive value of MCA MFV and rSO_2, measured immediately before induction of anesthesia, for delirium after valvular heart surgery in elderly patients. In 113 patients, delirium was evaluated for 7 days postoperatively, using the confusion assessment method for the intensive care unit. The primary endpoint was the occurrence of postoperative delirium. Overall, 16 patients (14%) exhibited delirium. MCA MVF values could not predict the development of delirium. Preoperative statin use, geriatric depression scale score, and low preoperative rSO_2 (< 60%) showed association with delirium occurrence in univariable analysis. After multivariable analysis, only the low preoperative rSO_2 (< 60%) (OR 6.748, 95% CI 1.647–27.652, $P=0.008$) remained as an independent predictor of delirium. Preoperative MCA MFV was not significantly associated with delirium after valvular heart surgery in elderly patients, while a low baseline rSO_2 value was associated with a sevenfold increased risk of delirium.

Keywords Cardiac surgical procedures · Delirium · Heart valve diseases · Spectroscopy, Near-infrared · Ultrasonography, Doppler, Transcranial

1 Introduction

Delirium is recognized as a common postoperative complication of cardiac surgery, with serious consequences including morbidity, long-term cognitive dysfunction, and even mortality [1]. Therefore, proper assessment of risk factors related to delirium is of high priority.

Several studies have shed light on risk factors related to delirium following cardiac surgery, which include patient-, surgery-, and cardiopulmonary bypass (CPB)-related factors that converge to indicate the importance of cerebral hypoperfusion and systemic inflammation [2, 3]. Likewise, a decrease in cerebral blood flow, and subsequent conversion to anaerobic glycolysis, has been demonstrated in delirium [4]. Measurements of middle cerebral artery (MCA) mean flow velocity (MFV) by transcranial Doppler (TCD) in non-surgical patients directly confirmed impairment of cerebral perfusion and showed correlations with cognitive dysfunction and delirium [5, 6].

Cerebral blood flow can be assessed non-invasively by TCD and indirectly by cerebral oximetry (rSO_2). Both methods have been applied during cardiac surgery to predict post-operative neurologic complications, with conflicting results [7, 8]. Moreover, studies revealed impracticability of TCD as a continuous monitor [9]. Likewise, calculating the cumulative area or time under an arbitrary cut-off value of rSO_2 during the entire surgery to predict neurocognitive outcome seems to be of limited clinical significance [10]. In contrast, baseline MCA MFV or rSO_2 values may represent the patient's individual reserve against cerebral hypoperfusion

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and offer advantage in terms of clinical practicability when compared to continuous monitoring [11, 12]. Indeed, a previous study in cardiac surgery has shown a close relationship between low baseline MCA MFV and postoperative cognitive decline [11]; however, evidence regarding the correlation with delirium is lacking.

In the current observational trial, we aimed to assess the predictive value of preoperative MCA MFV and rSO_2 value for the occurrence of delirium in elderly patients undergoing valvular heart surgery.

2 Materials and methods

2.1 Patients

This prospective observational study was sanctioned by the Institutional Review Board (4-2015-0319) of the Yonsei University Health System, Seoul, Republic of Korea, and registered at www.ClinicalTrials.gov (identifier: NCT02478736). Informed consent was obtained from all individual participants included in the study. The following methods were carried out in accordance with the relevant regulations. The study included 113 patients, who were enrolled from June 2015 to March 2017. The inclusion criteria were: (1) age ≥ 60 years, (2) scheduled for valvular heart surgery. The exclusion criteria were: (1) inability to undertake the mini-mental state examination (MMSE) and Confusion Assessment Method for the intensive care unit (CAM-ICU) procedures, (2) patients with unstable hemodynamics or who were intubated before surgery, (3) diagnosis of stroke, transient ischemic attack or neurologic diseases, and (4) patients diagnosed with significant (≥ 50%) intracranial stenosis confirmed by angiography.

2.2 Study endpoints and power calculation

The endpoint for this study was the occurrence of delirium. The primary outcome measures were the predictive values of MCA MVF and rSO_2 values for delirium following valvular heart surgery in elderly patients. A sample size calculation was performed under the assumption that MCA MFV could predict the occurrence of delirium with similar efficacy as rSO_2 values reported in a previous study [12]. Thus, the area under the receiver operating characteristic curve (AUROC) for MCA MVF was assumed to be 0.7. Because the expected incidence of delirium in a similar subset of surgical patients was approximately 20% (institutional data), to detect a 0.2 difference in the AUROC at a 2-sided alpha = 0.05 with 80% power, 105 participants were required. Anticipating a dropout rate of 40% due to the high incidence of poor acoustic temporal window in elderly Asian female participants, 175 patients were enrolled.

2.3 Neurologic assessment

Trained research personnel not involved in the study examined all patients for delirium daily, first using the Richmond Agitation Sedation Scale to examine the level of consciousness, then using the Korean CAM-ICU [13] or CAM to detect delirium. A positive CAM-ICU/CAM test result during the first 7 days postoperatively was defined as delirium.

Before anesthetic induction, all patients received a TCD evaluation by the same trained researcher [bilateral MCA blood flow velocity monitoring using power M-mode Doppler (TCD 100 M, Spencer Technologies Inc., Seattle, WA)]. Transtemporal insonation was performed with a 2 MHz pulsed TCD probe, and data on peak systolic velocity (PSV) and end-diastolic velocity (EDV) in the bilateral MCA were collected. MFV and pulsatility indices (PI) [$PI = (PSV - EDV) \div MFV$] provided by automatic calculation. PSV and EDV were measured three times on each side at 2–3 min time intervals, and the mean values of MFV and PI were used for analysis. If the measured MCA MFV exceeded 100 cm/s, the patient was dropped from the study, because significant MCA stenosis could not be ruled out.

In addition, the patients underwent continuous bihemispheric rSO_2 observation. The rSO_2 was measured using the INVOS^{TM} Cerebral/Somatic Oximeter 5100 (Somanetics, Troy, MI, USA) with bihemispheric Near-Infrared Spectroscopy sensors, and the mean of the values from both sides was used for analysis. The baseline value of rSO_2 was obtained in the supine position in room air before anesthesia, and measurement was continued until ICU transfer. The lowest and highest intraoperative rSO_2 values were also obtained.

2.4 Study design and perioperative measurements

The patients were evaluated with the CAM-ICU a day before surgery to assess their eligibility for this study. Likewise, MMSE and geriatric depression scale short form (SGDS) Korean Version [14] were also tested to assess baseline cognitive function and depressive mood. The patient characteristics, logistic EuroSCORE, co-morbid diseases, and chronic medications were documented. Laboratory tests were conducted for levels of hematocrit, albumin, leukocytes, c-reactive protein, creatinine, and estimated glomerular filtration rate. Intraoperative variables included type of surgery, durations of aortic cross clamp and CPB, and transfusion requirement. Postoperative evaluation included transfusion requirement, lengths of ICU and hospital stay, and the incidence of composite morbidity endpoints defined by the Society of Thoracic Surgeons, including acute kidney injury, prolonged ventilator care (> 24 h), permanent stroke, hemostatic reoperation, deep sternal wound infection, and in-hospital mortality. Intraoperative hemodynamic parameters and laboratory variables, including the mean arterial pressure (MAP), cardiac index, PaO_2, $PaCO_2$, and hematocrit levels, were recorded at the following predetermined time points: (1) prior to anesthetic induction, (2) 10 min post-induction, (3) 10 min after CPB initiation, (4–6) 40, 80, and 120 min after CPB initiation, respectively, (7) 10 min after CPB-off, and (8) 5 min after sternum closure.

The predictors including results of TCD, rSO_2, and perioperative variables were blinded to participants and trained personnel who examine participants for postoperative delirium to prevent additional information bias.

2.5 Perioperative management

Perioperative care, including CPB management, was done according to an institutional standardized protocol. In brief, anesthesia was initiated using midazolam (0.05 mg/kg) and sufentanil (1.5 µg/kg), and maintained with sufentanil (0.5 µg/kg/h) and sevoflurane. Anesthetic depth was maintained at a score of 40–60 on the bispectral index (A-200 Bispectral Index® score monitor, Aspect Medical System Inc., Newton, MA). During the operation, MAP was maintained at 60–80 mmHg using norepinephrine first, and if the target MAP could not be maintained with escalating doses of norepinephrine (maximum of 0.3 µg/kg/min), vasopressin was added (2.4–4 unit/h). Milrinone was used in cases of left ventricular ejection fraction < 30%, right ventricular dysfunction, or pulmonary hypertension. During CPB, the non-pulsatile flow rate was maintained at 2.0–2.5 l/min/m^2 using a tepid temperature (32–33 °C) and alpha-stat management. Packed red blood cells were transfused when the hematocrit was < 20% during CPB or < 25% otherwise. Fresh frozen plasma (FFP) and platelets were transfused at the discretion of the attending anesthesiologist and cardiac surgeon during surgery. After surgery, if bleeding exceeded more than 200 ml/h for 2 consecutive hours, FFP or platelets or both were transfused, if the International Normalized Ratio was greater than 1.3 or the platelet count was less than 50×10^3/ml.

During ICU care, postoperative sedation was achieved using propofol at 1 to 2 mg/kg/h and remifentanil at 0.1 µg/kg/min, if required. Postoperative pain was assessed using a 10-cm visual analogue scale (0, pain-free; 10, worst imaginable pain) and controlled with fentanyl-based intravenous patient-controlled analgesia.

2.6 Statistical analyses

SPSS software for windows (version 23, SPSS Inc., Chicago, IL) was used for analyses. Data were expressed as the number of patients (percentage), mean ± standard deviation (SD), or median (interquartile range, IQR). Continuous data were tested for normality and analyzed using the Mann–Whitney *U* test or independent *t* test, as required. Categorical data were analyzed using Fisher's exact test or the Chi square test. Intergroup comparisons of the serially assessed data were done using linear mixed models with an unstructured covariance matrix. Two fixed effects were included, the between-subjects factor of the occurrence of delirium and the within-subject factor of time.

Variables that yielded a *P* value of less than 0.05 from the intergroup comparisons of perioperative data between patients with and without delirium were entered into the univariable logistic regression analysis. Variables with $P < 0.05$ on that analysis were finally included in the multivariable analysis. A *P* value less than 0.05 was deemed statistically significant, except for the serially assessed data, which was subjected to a Bonferroni correction. The optimal cutoff values for the continuous variables were determined by receiver operating characteristics (ROC) analysis.

3 Results

Data from 113 patients were included in the study (Fig. 1). Postoperative delirium was observed in 16 (14%) patients within 7 days after surgery. The percentages of patients receiving statins, and the SGDS score, were significantly different between the groups (Table 1).

The MCA MFV and the percentage of patients with low preoperative MCA MFV (< 30 cm/s) were similar between the groups (Table 2). The preoperative rSO_2 values (56 ± 6 vs. 62 ± 7, $P = 0.007$) and intraoperative highest rSO_2 values [67 (IQR 64–72) vs. 72 (IQR 68–78), $P = 0.005$] were significantly lower in the delirium group than in the non-delirium group, but the lowest intraoperative rSO_2 values were similar between the groups (Table 2).

Intraoperative hemodynamic and arterial blood gas analysis data were comparable between the groups over time. Also, the postoperative hemodynamic data and lowest hematocrit values were similar between the groups over time (Fig. 2).

The number of ICU days [3 (IQR 2–7) vs. 2 (IQR 1–3), $P = 0.02$] and number of hospital days [17 (IQR 12–27) vs. 10 (IQR 8–16), $P = 0.002$] were increased in the delirium group than in the non-delirium group. The incidences of composite of morbidity endpoints (63% vs. 31%, $P = 0.014$) and acute kidney injury (50% vs. 23%, $P = 0.032$) were

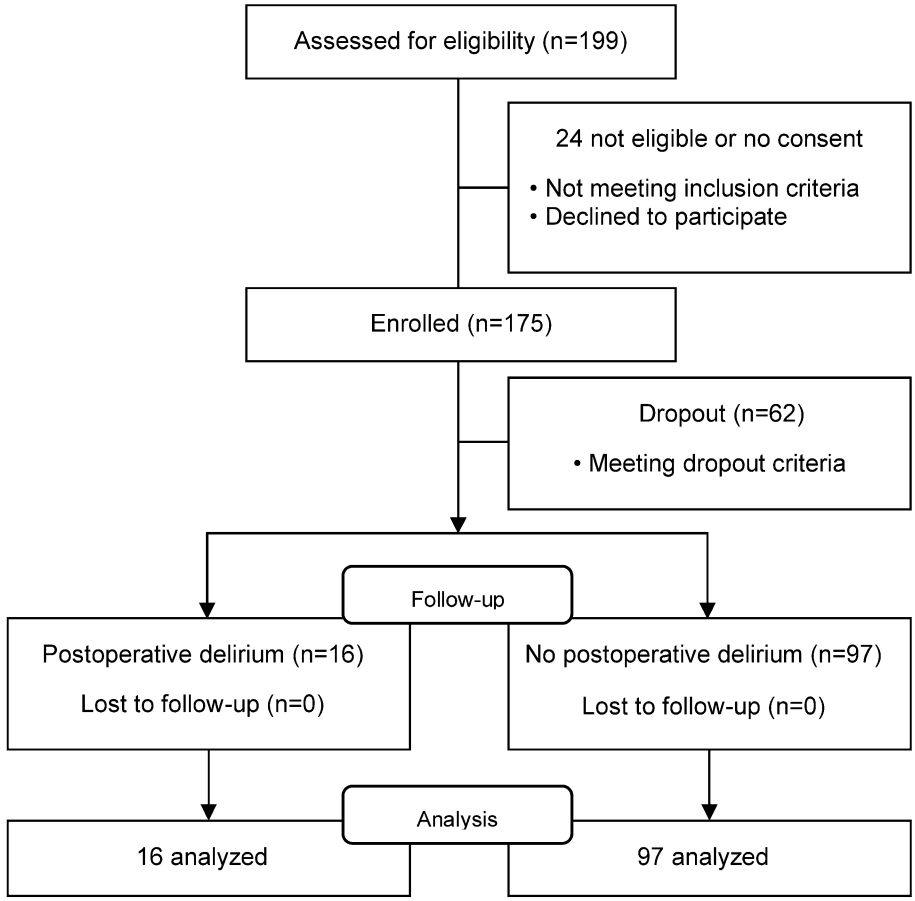

Fig. 1 Patient enrolment into the study

significantly higher in the delirium group than in the non-delirium group (Table 3).

In the multivariable analysis, only low baseline rSO_2 (< 60%) [odds ratio (OR) 6.748, 95% confidence interval (CI) 1.647–27.652, $P = 0.008$] remained as an independent risk factor of delirium. Preoperative statin administration (OR 0.231, 95% CI 0.046–1.155, $P = 0.074$) and SGDS score (OR 1.194, 95% CI 0.987–1.446, $P = 0.069$) were associated with delirium, without statistical significance (Table 4).

The optimal cut-off value of preoperative rSO_2 for predicting delirium after surgery was 59.5% (AUROC 0.739, 95% CI 0.611–0.866, $P = 0.002$), yielding a sensitivity of 81% and specificity of 67% (Fig. 3).

4 Discussion

This prospective observational study found that the preoperative MCA MFV value assessed by TCD could not predict the development of delirium, whereas a low preoperative rSO_2 value (< 60%) was linked to an estimated sevenfold increased occurrence of delirium.

Considering the clinical significance of delirium in cardiac surgery and the role of cerebral hypoperfusion in its pathogenesis [15, 16], a more thorough risk stratification involving the baseline reserve for cerebral perfusion may allow optimization of perioperative management. Preoperative rSO_2 values, indirectly indicating the inadequacy of cerebral perfusion, have been shown to predict delirium after cardiac surgery, although they do not provide direct information on cerebral blood flow [12].

Cerebral blood flow velocity examined with TCD at the MCA has proven to be a valid tool of investigating cerebral perfusion [17]. Many studies exploring the relationship between cerebral hemodynamics measured with TCD and delirium or cognitive dysfunction have reported positive correlations [5, 6]. MCA MFV, PI, and the cerebral autoregulation index, measured by TCD, were found to be useful for diagnosing delirium superimposed on dementia [6], and for predicting sepsis-related delirium [18], although intraoperative TCD monitoring could not forecast delirium [7]. In cardiac surgical patients, TCD has been used mainly to investigate the association among hypoperfusion, microemboli, and postoperative cognitive dysfunction, yielding conflicting results [19, 20]. Also, current anesthetic practice involving routine monitoring with bispectral index and cerebral oximetry in cardiac surgical patients limits the application of TCD as a continuous intraoperative monitor.

Table 1 Baseline characteristics

	Delirium (n = 16, 14%)	Non-delirium (n = 97)	*P* value
Male, %	11 (69)	60 (62)	0.597
Age, years	71 ± 5	70 ± 6	0.674
Body surface area, m^2	1.618 ± 0.149	1.663 ± 0.154	0.276
Educational level, years, IQR	8 (6–12)	11 (6–12)	0.436
MMSE score < 24, %	3 (19)	13 (14)	0.699
Geriatric depression scale (short form) IQR	4 (1–7)	2 (1–4)	0.029
EuroSCORE, IQR	7 (5–9)	6 (4–8)	0.206
Diabetes mellitus, %	3 (19)	27 (28)	0.553
Chronic kidney disease, %	3 (19)	7 (7)	0.15
Pre-operative lung disease, %	2 (13)	8 (8)	0.632
Pre-operative medication			
Statin use, %	2 (13)	43 (44)	0.016
Beta blocker use, %	6 (38)	29 (30)	0.567
Calcium channel blocker use, %	1 (6)	23 (24)	0.186
RAS blocker use, %	8 (50)	58 (60)	0.461
Diuretics use, %	12 (75)	62 (64)	0.388
Pre-operative left ventricular ejection fraction, %	57 ± 13	61 ± 14	0.27
Hematocrit, %	37 ± 5	38 ± 6	0.51
Albumin, g/dl, IQR	3.9 (3.6–4.3)	4.1 (3.7–4.3)	0.476
Leukocytes, /µl	5805 ± 1851	5838 ± 1664	0.942
C-reactive protein, mg/l, IQR	7.8 (1.6–10.4)	2.7 (0.8–6.8)	0.119
Creatinine, mg/dl	1.02 ± 0.25	0.97 ± 0.91	0.8

Data are presented as mean ± standard deviation (SD), median (interquartile range, IQR), or number of patients (%)

IQR interquartile range, *MMSE* the mini–mental state examination, *RAS* renin-angiotensin system

Table 2 Pre-operative values of transcranial Doppler and perioperative values of cerebral oximetry

	Delirium (n = 16)	Non-delirium (n = 97)	*P* value
Mean cerebral blood flow velocity			
Left MCA, cm/s	42 ± 14	44 ± 14	0.523
Right MCA, cm/s	42 ± 15	43 ± 13	0.738
Lower MCA MFV, cm/s	37 ± 13	39 ± 11	0.548
Lower MCA MFV < 30 cm/s, %	4 (25)	21 (22)	0.751
Pulsatility index			
Left MCA, IQR	0.85 (0.75–1.06)	0.89 (0.76–1.03)	0.924
Right MCA, IQR	0.92 (0.82–1.04)	0.88 (0.76–1.02)	0.413
Low MVF combined with high PI, %	1 (7)	0 (0)	0.15
Difference between left and right MCA MFV, cm/s, IQR	7.7 (4.7–12.7)	8.5 (3.3–20.1)	0.531
Pre-operative rSO_2, %	56 (6)	62 (7)	0.007
Lowest rSO_2, %, IQR	43 (37–46)	45 (38–49)	0.267
Highest rSO_2, %, IQR	67 (64–72)	72 (68–78)	0.005

Data are presented as mean ± standard deviation (SD), median (interquartile range, IQR), or number of patients (%)

MCA middle cerebral artery, *MFV* mean blood flow velocity, *IQR* interquartile range, rSO_2 cerebral oximetry

In the context of a single preoperative measurement, reduced MCA MFV was reported as an independent risk factor for short-term postoperative cognitive decline in cardiac surgical patients [11]. However, the connection between delirium and cognitive dysfunction remains elusive [21], and no comprehensive data exist regarding the predictive

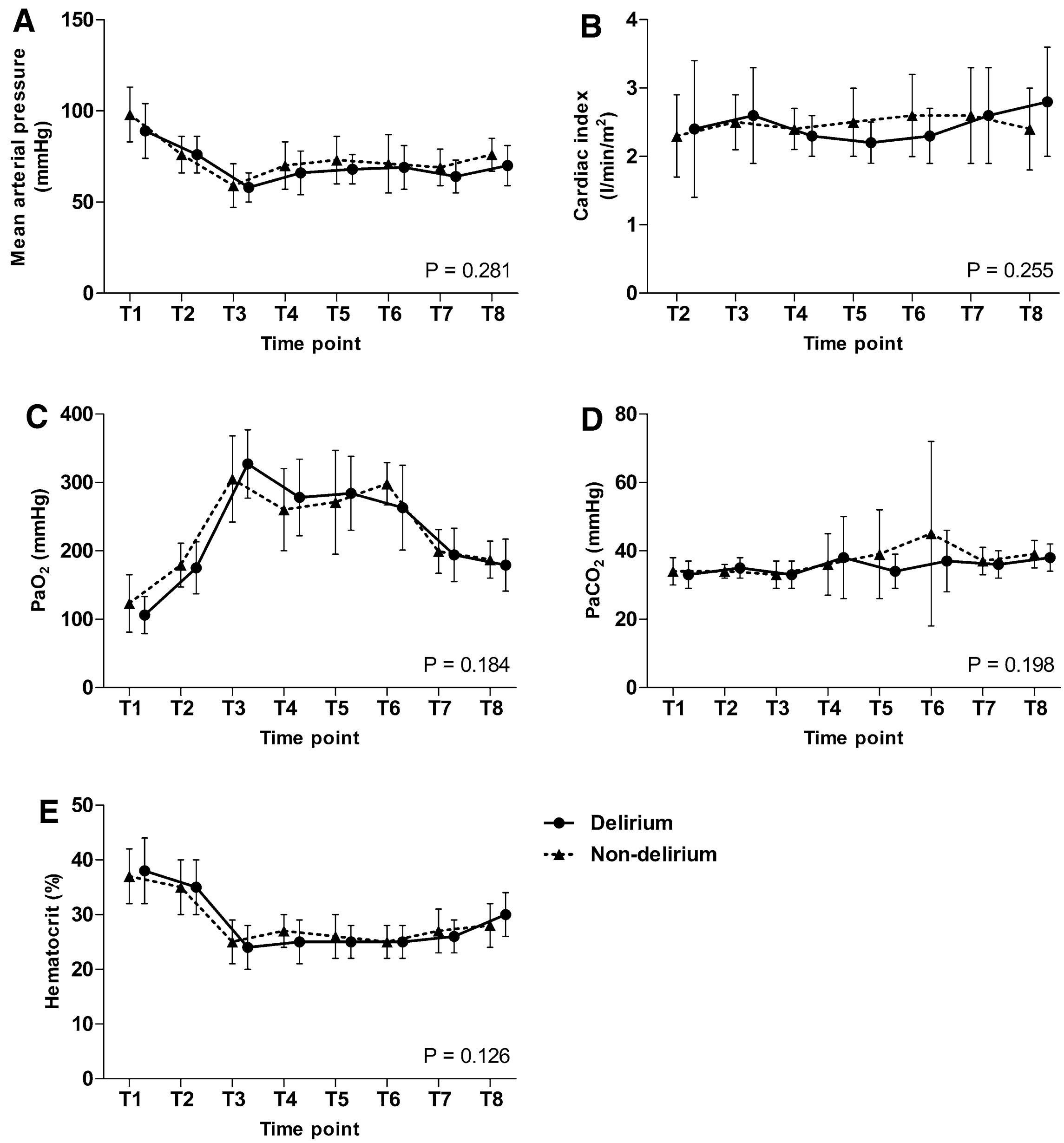

Fig. 2 Perioperative serial changes in hemodynamics and laboratory data. Serial changes in mean arterial pressure (**a**), cardiac index (**b**), the partial pressure of oxygen in the arterial blood (**c**), the partial pressure of CO_2 in the arterial blood (**d**), and hematocrit levels (**e**) of patients with postoperative delirium (circle, solid line) compared with those without (triangle, dotted line). Variables were recorded at the following predetermined time points: (T1) prior to anesthetic induction, (T2) 10 min post-induction, (T3) 10 min after CPB initiation, (T4–6) 40, 80, and 120 min after CPB initiation, respectively, (T7) 10 min after CPB-off, and (T8) 5 min after sternum closure. The values of cardiac index were recorded at same time except timepoint (T1) before anesthetic induction. Error bars represent standard deviations

value of preoperative TCD values for delirium after cardiac surgery. We hypothesized that by providing direct information on cerebral blood flow and because it is able to identify patients with delirium in a non-surgical population, preoperative MCA MFV values could predict high risk for delirium in elderly patients with valvular heart disease. The type of surgery was limited to valvular heart surgery because most previous studies on delirium were focused on coronary artery disease patients, while procedures other than isolated coronary artery bypass surgery were found to be independent predictors of delirium [22].

Contrary to our expectations, a significant relationship between the preoperative MCA MFV value and postoperative delirium could not be detected. One possible explanation is that the direct relationship between MFV and cerebral blood flow may be altered by reduced

Table 3 Intraoperative and postoperative data

	Delirium (n = 16)	Non-delirium (n = 97)	*P* value
Surgical procedure, n (%)			0.13
Mitral valve replacement/repair	3 (19)	9 (9)	
Aortic valve replacement/repair	2 (13)	36 (37)	
Tricuspid valve replacement/repair	3 (19)	5 (5)	
Multiple valve replacement/repair	4 (25)	20 (21)	
Valve replacement/repair + CABG	1 (6)	10 (10)	
Valve replacement/repair + other	3 (19)	17 (18)	
Total circulatory arrest, n (%)	1 (6)	6 (6)	> 0.999
Pre-operative cerebral perfusion pressure, mmHg (MAP–CVP)	63 ± 11	66 ± 10	0.202
Duration of CPB, min, IQR	115 (90–189)	105 (80–133)	0.125
Duration of ACC, min, IQR	88 (51–139)	75 (54–100)	0.28
Perioperative transfusion, n (%)	12 (75)	63 (69)	0.773
Morbidity endpoints, n (%)	10 (63)	30 (31)	0.014
Hemostatic reoperation, n (%)	2 (13)	3 (3)	0.146
Acute kidney injury, n (%)	8 (50)	22 (23)	0.032
Prolonged ventilation > 24 h, n (%)	4 (25)	11 (11)	0.223
Stroke, n (%)	0 (0)	1 (1)	> 0.999
Deep sternal wound infection, n (%)	0 (0)	2 (2)	> 0.999
In-hospital mortality, n (%)	2 (13)	2 (2)	0.095
Intensive care unit days, IQR	3 (2–7)	2 (1–3)	0.02
Hospital days, IQR	17 (12–27)	10 (8–16)	0.002

Data are presented as mean ± standard deviation (SD), median (interquartile range, IQR), or number of patients (%)

CABG coronary artery bypass grafting, *MAP* mean arterial pressure, *CVP* central venous pressure, *CPB* cardiopulmonary bypass, *IQR* interquartile range, *ACC* aortic cross clamp

Table 4 Predictive power of chosen variables including pre-operative cerebral oximetry values for delirium according to logistic regression analyses

Variables	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Pre-operative statin use	0.179 (0.039–0.832)	0.028	0.231 (0.046–1.155)	0.074
Pre-operative geriatric depression scale (short form)	1.214 (1.024–1.439)	0.025	1.194 (0.987–1.446)	0.069
Baseline $rSO_2 < 60\%$	5.919 (1.584–22.122)	0.008	6.748 (1.647–27.652)	0.008
Left MCA MFV	0.986 (0.945–1.029)	0.519		
Right MCA MFV	0.993 (0.954–1.034)	0.735		

CI confidence interval, rSO_2 relative cerebral oxygen saturation, *MCA MFV* middle cerebral artery mean blood flow velocity

vascular compliance with aging [23]. Nonetheless, MCA MFV could accurately discriminate patients with delirium superimposed on dementia, and a reversible increase in MCA MFV could be observed after resolution of delirium in elderly, non-surgical patients [6]. Even so, MCA MFV is only an indicator of cerebral blood flow, and does not provide a direct measure of metabolic demands. Based on our results, it does not seem to provide information regarding the cerebral perfusion reserve and its predictive role on delirium occurrence is not evident.

In contrast to MCA MFV, a low preoperative rSO_2 value (< 60%) was identified as an independent risk factor for delirium. This result is congruent with the results of previous studies [10, 12], in which baseline rSO_2 values have been suggested to reflect cognitive reserve [10, 12]. The cut-off value of preoperative rSO_2 value that best predicted delirium was 59.5% in the present study. This value was comparable to the previously reported cut-off value of 60% that we used for our analysis [12]. Owing to the suboptimal reserve of cerebral perfusion in patients with a low preoperative rSO_2

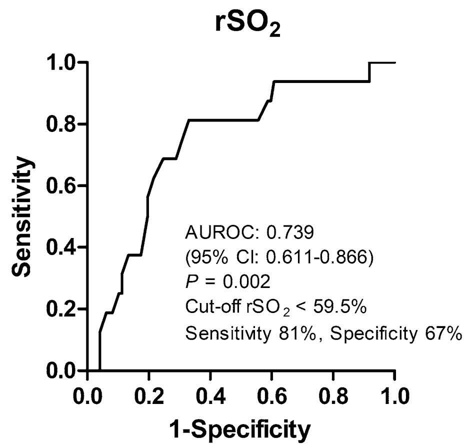

Fig. 3 The receiver operating characteristic curves for baseline rSO_2 value on postoperative delirium. *rSO_2* relative cerebral oxygen saturation, *AUROC* area under the receiver operating characteristic, *CI* confidence interval

value, a small decrease in cerebral perfusion might have led to delirium. In terms of its role as a continuous monitor, monitoring cumulative intraoperative area of decrease in rSO_2 value under various cut-off values, and intraoperative interventions to restore rSO_2 to an arbitrary target value, have been tested with the goal of detecting or reducing neurocognitive decline in cardiac surgery; however, the results have been inconsistent [10, 24].

Of interest, preoperative statin use and SGDS score were shown to be associated with postoperative delirium without statistical significance. The protective effect of statin against the development of delirium was depicted by a large prospective cohort study of cardiac surgical patients [25], which was suggested to be attributable to its endothelial protective action in combination with its anti-inflammatory and immunomodulatory effects [26]. Depressive symptoms have also been identified as risk factors of postoperative delirium in several studies [16, 27]. Cogent mechanisms linking depression with delirium include decreased serotonergic activity in the brain, elevated concentration of cortisol and/or poor physical condition [27].

An interesting observation of the current study is the higher incidence of acute kidney injury in patients who exhibited delirium. A close correlation between these two complications has been implicated previously, which may be attributable to the following reasons. Experimental data indicate that acute kidney injury could lead to inflammation in the brain [28]. Furthermore, kidney dysfunction might reduce the clearance of medications, metabolites, or other potential neurotoxins after cardiac surgery. Although few studies have shown this relationship in patients undergoing cardiac surgery, a study in critically ill patients has shown similar results [29].

The present study is subject to the following limitations. First, the overall delirium incidence was lower than expected (16% vs. 20%), limiting the statistical power. Second, about 30% of enrolled patients dropped out because of poor acoustic temporal window, and this could have produced a selection bias. This incidence, however, was similar to those reported in other previous studies involving Korean patients, and was accounted for in the sample size calculation when the study was designed [30]. Lastly, the postoperative incidence of acute kidney injury was greater in the delirium group, although its exact temporal relationship with delirium cannot be properly analyzed. However, acute kidney injury as a covariate of delirium has been shown not to alter the relationship between rSO_2 and delirium [31].

In conclusion, preoperative MCA MFV measured by TCD failed to provide information regarding the occurrence of delirium after valvular heart surgery in elderly patients, but a low baseline rSO_2 value (< 60%), reflecting inadequacy of the reserve of cerebral perfusion, was associated with a sevenfold increased risk of delirium. Preoperative statin use may be beneficial in the prevention of delirium that merits further studies.

Acknowledgements The current work received exclusive support from departmental resources.

Author contributions Conceptualization: Young-Lan Kwak; Methodology: Young-Lan Kwak, Sarah Soh; Formal analysis and investigation: Sarah Soh, Jong-Wook Song, Nakcheoul Choi; Writing—original draft preparation: Sarah Soh; Writing—review and editing: Jae-Kwang Shim, Young-Lan Kwak; Resources: Jae-Kwang Shim, Young-Lan Kwak; Supervision: Young-Lan Kwak.

Funding The current work received exclusive support from departmental resources.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Institutional Review Board of the Yonsei University Health System, reference number-4-2015-0319) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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