의학석사 학위논문

The relationship between intraoperative cerebral oximetry and postoperative delirium in patients undergoing off-pump coronary artery bypass graft surgery

무심폐기 관상동맥 우회술을 받는 환자의 수술 중 대뇌 산소 포화도와 수술 후 섬망 발생의 상관관계

2020년 2월

서울대학교 대학원

의학과 마취통증의학전공

임 이 랑

Abstract

The relationship between intraoperative cerebral oximetry and postoperative delirium in patients undergoing off-pump coronary artery bypass graft surgery

Leerang Lim
Colleage of Medicine
Department of Anesthesiology and Pain Medicine
The Graduate School
Seoul National University

Introduction: Cerebral oximetry has been widely used to measure regional oxygen saturation in brain tissue, especially during cardiac surgery. Despite its popularity, there have been inconsistent results on the use of cerebral oximetry during cardiac surgery, and few studies have evaluated cerebral oximetry during off pump coronary bypass graft surgery (OPCAB).

Methods: Between October 2004 and December 2016, 1,439 patients underwent OPCAB. Among them, 815 patients with sufficient data on regional cerebral oxygen saturation (rSO_2) were enrolled in this study. Retrospectively, we analysed perioperative variables and the reduction in rSO_2 below cut-off values of 75%, 70%, 65%, 60%, 55%, 50%, 45%, 40%, and 35%. Furthermore, we evaluated the relationship between the reduction in rSO_2 and postoperative delirium.

Results: Delirium occurred in 105 of 815 patients. In both univariable and multivariable analyses, the duration of rSO_2 reduction was significantly longer in patients with delirium at cut-offs of <50% and 45% (for every 5min, adjusted odds ratio (OR) 1.007, 95% confidence interval [CI] 1.001-1.014; and adjusted OR 1.012, 95% CI, 1.003-1.021; p=0.024 and 0.011, respectively). The proportion of patients with an rSO_2 reduction <45% was significantly higher among those with delirium (adjusted OR 1.737, 95% CI 1.064-2.836, p=0.027).

Conclusions: In patients undergoing OPCAB, intraoperative rSO_2 was associated with postoperative delirium. The cut-off values for intraoperative rSO_2 were 50% for the total patient population and 55% for patients younger than 68 years.

Keywords Cardiac surgery, Cerebral oximetry, Delirium, Near-infrared spectroscopy, Off-pump coronary artery bypass graft

Student Number: 2018-23158

Contents

Abstract i

Contents iv

List of tables and figures v

Introduction 1

Methods

Study population and anesthetic methods ...3

Data collection and definition 4

Statistical analysis 6

Results 7

Discussion 11

Reference 16

Tables 21

Figures 38

Abstract in Korean 40

LIST OF TABLES AND FIGURES

Tables

Table 1. Baseline and perioperative characteristics of patients with or without delirium 21
Table 2. Comparison of intraoperative regional cerebral oxygen saturation between delirium and no delirium group 24
Table 3. Comparison of intraoperative hemodynamic variables between delirium and no delirium group 26
Table 4. Odds ratios of intraoperative reduction of regional cerebral oxygen saturation for each cut-offs and delirium after surgery 27
Table 5. Odds ratios of predictors of postoperative delirium 29
Table 6. The relationship between intraoperative regional cerebral oxygen saturation and postoperative Acute kidney injury, ICU and hospital length of stay 31
Table 7. Baseline and perioperative characteristics of patients age under 68 32
Table 8. Comparison of intraoperative regional cerebral oxygen saturation between delirium and no delirium group in age under 68 34
Table 9. Odds ratios of intraoperative reduction of regional cerebral oxygen saturation for each cut-offs and delirium after surgery in patients under 68 36

Figures

Figure 1. Flow chart for patient selection 38
Figure 2. The ROC curves of multivariable prediction model of patients under age 68 39

INTRODUCTION

Since Jobsis [1] first published an approach for monitoring cerebral circulation and thereby oxygen sufficiency using near-infrared light in 1977, cerebral oximetry has been widely used to measure regional oxygen saturation in brain tissue continuously and non-invasively, especially during general anesthesia. Using near-infrared spectroscopy (NIRS), cerebral oximetry measures regional cerebral oxygen saturation (rSO_2) by analysing the different intensities of light at specific wavelengths transmitted and received [2,3]. Probes, consisting of a light source and two light detectors, are applied to the bilateral forehead, and monitor regional oxygen saturation of the underlying frontal lobes, which are vulnerable to hypoxic and hypotensive brain injury [4].

Because the neurological outcome is still a matter of concern in cardiac surgery, cerebral oximetry-based resuscitation during cardiac surgery has been increasingly adopted by anesthesiologists [5]. Among post-cardiac surgery neurologic complications, the reported prevalence of delirium is from 3.1% up to 52% by population and diagnostic methods, respectively [6-9]. Moreover, delirium is known to prolong intensive care unit and hospital stays, increase morbidity and mortality, and reduce cognitive and functional recovery [10-12]. Thus, among neurologic complications, delirium is a serious and relatively common neurologic complication.

Despite the widespread use of cerebral oximetry, there have been inconsistent results regarding the relationship between the intraoperative use of cerebral oximetry and improved postoperative neurologic outcomes in cardiac surgery patients [13-17]. There have been few trials designed to identify the optimal cut-off values for cerebral oximetry, resulting in various criteria being used by different studies. Moreover, few studies on cerebral oximetry in patients undergoing off-pump coronary artery bypass graft surgery (OPCAB) have been carried out.

To evaluate the relationship between the intraoperative cerebral oximetry and postoperative delirium and identify the optimal cut-off values for intraoperative cerebral oximetry during OPCAB, we retrospectively analysed data of intraoperative cerebral oximetry values and postoperative delirium from patients who underwent OPCAB.

METHODS

Study population and anesthetic methods

This was a retrospective single-center study approved by the Institutional Review Board of Seoul National University Hospital (IRB no. 1702-114-833). The requirement for written informed consent was waived. After IRB approval, we reviewed the electronic medical records of all patients aged over 18 years who had undergone coronary artery bypass graft surgery (CABG) between October 2004 and December 2016. During this period, 2,333 patients underwent CABG. Among them, we included only patients who had isolated OPCAB. Patients who had been supported with perioperative intra-aortic balloon pump and/or extracorporeal membrane oxygenation were also excluded. Finally, 1,439 patients were included in the study. After data pre-processing, 624 patients were excluded because of insufficient rSO_2 records less than 10 times, the -2 standard deviations (SDs) of the times of rSO_2 measurement, and 815 patients in total were included. The flow chart for patient selection is shown in Figure 1.

During the period, anesthesia for OPCAB was performed as per the institutional routine protocol at that period. When the patients entered the operating room, bi-hemispheric rSO_2 was measured by NIRS from the forehead in the supine position, with other types of monitoring used for vital signs. We used INVOS Cerebral Oximeters (Medtronic, MN, USA) for rSO_2 measurement. Every drug used during anesthesia was given intravenously. Patients were also monitored with a Swan-Ganz catheter (Edwards Lifesciences, Irvine, CA, USA) for mixed venous oxygen saturation (SvO_2) and cardiac index (C.I.). Patients were transferred to the cardio-pulmonary intensive care unit (CPICU) after surgery being sedated and intubated.

Data collection and definition

Baseline characteristics and perioperative variables known to be related to delirium after cardiac surgery were collected [6,9,18-23]. Baseline characteristics included ASA class, order of surgery, emergency, underlying diseases such as hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation and dementia, history of myocardial infarction, stroke and drinking, and laboratory variables like left ventricle ejection fraction (EF), hematocrit, serum creatinine, estimated glomerular filtration ratio (eGFR), serum albumin, and C-reactive protein. Postoperative medical status, including the Acute Physiologiy and Chronic Health Evaluation (APACHE) II score when admitting the CPICU after surgery, ICU and hospital lengths of stay, occurrence of acute kidney injury or new-onset atrial fibrillation, reintubation rate, and in-hospital death, was also collected.

Intraoperatively, total anesthesia and operation time were gathered. From anesthetic records, we extracted the mean arterial pressure (MAP), SvO_2, C.I., and bi-hemispheric rSO_2, independently, every 5 min. The resting MAP before anesthesia induction and initially measured SvO_2 and C.I. were used as baseline values. The MAPs were recorded automatically by the anesthetic monitor, while other variables were recorded manually every 5 to 15 min. We conducted data pre-processing on these variables according to the following steps using R (R3.5.1; The R Foundation for Statistical Computing). First, we excluded patients who had rSO_2 records that included fewer than ten measurements. Second, all data exceeding -2

SDs and +2 SDs for each variable were considered abnormally recorded and removed. Third, empty values for data recorded at 5-min intervals were substituted by the mean of the nearest two records.

After these substitutions, we calculated the total time for which the rSO_2 values decreased below each cut-off (75%, 70%, 65%, 60%, 55%, 50%, 45%, 40%, and 35% of the absolute values). We also treated the reduction in rSO_2 for at least one measurement below each cut-off written above as a categorical variable. The same substitutions and time calculations were carried out for C.I., SvO_2, and MAP, and mean values were used for receiver operating characteristic (ROC) analysis.

Postoperative delirium was determined by institutional neuropsychiatrists (C-W Yeom and colleagues) on the basis of electronic medical records. Neuropsychiatrists reviewed the doctors' and nursing records, including the CAM-ICU [24-26] score evaluated by the attending nurse in the ICU, consultations with neuropsychiatrists and neurologists, and prescriptions for drugs that could be used for delirium (e.g., haloperidol or quetiapine). According to Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [27] and Short-CAM [28] criteria, the neuropsychiatrists evaluated the signs and symptoms recorded and determined whether or not the patient had undergone postoperative delirium. The first onset time and site of delirium after surgery were also collected.

Statistical analysis

All statistical analyses were performed using SPSS, version 23.0, for Windows (IBM Corp., Armonk, NY, USA). We hypothesized a normal distribution for all variables. All categorical variables, except

ASA class, were analyzed using chi-square tests or Fisher's exact test. All continuous variables and ASA class were analysed using Student's t-test and logistic regression analysis. A p-value <0.05 was considered statistically significant.

First, we conducted a univariable analysis for all variables collected. A p-value <0.10 was used to select significant predictors for multivariable analysis. Next, a multivariable logistic regression analysis was performed with selected variables, and total times and occurrence of rSO_2 under each cut-off using a backward stepwise method. We compared the predictive ability of each prediction model to identify significant cut-offs for rSO_2 related to delirium after off-pump coronary artery bypass.

RESULTS

The baseline and perioperative characteristics of the patients are shown in Table 1 (no delirium group vs. delirium group, 710 [87.1%] vs. 105 [12.9%] patients). The range of the first onset time of delirium was from postoperative day 0 to 21, with the median day of postoperative day 3. Among 105 delirium cases, 49 (46.7%) cases occurred in ICU for the first time whereas 56 (53.3%) cases occurred after transferred to general wards. The delirium group had a higher average age and C-reactive protein level, more underlying hypertension and dementia, lower hematocrit, eGFR, and albumin readings, and less drinking history. The group also had higher APACHE II score when admitting the ICU after surgery, longer ICU and hospital stays and more frequent postoperative acute kidney injury and new onset atrial fibrillation and reintubation. In-hospital deaths numbered 3 (2.9%) in the delirium group and 0 in the no delirium group, but this did not reach the level of statistical significance.

The duration and number of intraoperative rSO_2 measurements below each cut-off are shown in Table 2. The duration of rSO_2 reduction was significantly longer in patients with delirium for the cut-offs of <50% and 45% ($p=0.031$ and 0.027, respectively). There was a significantly higher proportion of patients with an rSO_2 reduction <45% among those with delirium ($p=0.048$).

Intraoperative hemodynamic variables are shown in Table 3. Based on the results of an ROC analysis for the mean values of each variable, the cut-off was determined as 68 mmHg, 2.2 $L.min^{-1}m^{-2}$, and 64% for MAP, C.I., and SvO_2, respectively. The total durations of reduction below the cut-off and minimum values were calculated. For all three variables, the total duration of reduction below each cut-off was significantly longer in the delirium group than the no delirium group ($p=0.001$), and these cut-off values were selected for a multivariable analysis as categorical variables.

The odds ratio (OR), 95% confidence interval (CI), and p-values of rSO_2 for each cut-off are shown in Table 4. The OR and 95% CI were calculated for every 5 min of rSO_2 reduction below each cut-off value. Age, sex, hypertension, dementia, preoperative hematocrit, eGFR, serum albumin and C-reactive protein level, intraoperative MAP, C.I. and SvO_2 reduction below each cut-off of ROC analysis were considered as covariables. The APACHE II score was not considered as a covariable because there's some factors in this patient group that influencing independently to the score such as mechanical ventilation, sedation and temporary pacemaker. There was no multicollinearity between the variables included in the analysis, especially between the intraoperative hemodynamic variables and rSO_2 for the occurrence of postoperative delirium. Multivariable logistic regression analysis revealed that the duration of rSO_2 below the 50% and 45% cut-offs was significantly associated with postoperative delirium (for every 5 min, adjusted OR 1.007 [95% CI 1.001-1.014] and 1.012 [1.003-1.021]; $p=0.024$ and 0.011, respectively). Each model showed good fitness (Hosmer-Lemeshow's goodness-of-fit: $p=0.729$ and 0.962, respectively). The rSO_2 values below 45% for at least one measurement were significantly associated with postoperative delirium, and the model fitness was good (adjusted OR 1.737, $p=0.027$; Hosmer-Lemeshow's goodness-of-fit: $p=0.923$; Table 5). The duration of rSO_2 below 50% and 45% was also associated with postoperative acute kidney injury, a longer ICU stay, and longer hospital stay (Table 6).

Based on the ROC analysis, the cut-off age for postoperative delirium occurrence was 68. We conducted a subgroup analysis based on this cut-off. Among 815 patients, 398 (48.8%) were under age 68, and delirium occurred in 19 patients (4.8%). Baseline and perioperative characteristics, including intraoperative hemodynamic variables, are shown in Table 7. Based on a univariable analysis, preoperative EF, and albumin and C-reactive protein levels were selected for a multivariable analysis. Table 8 shows the duration and number of intraoperative rSO_2 values below each cut-off in patients under 68 years of age. The mean and minimum rSO_2 values were significantly lower in the delirium group. The duration of rSO_2 reduction was significantly longer in patients with delirium for the cut-offs of <55%, 50%, and 45%, and the proportion of patients with an rSO_2 reduction below 50% and 45% was significantly higher among those with delirium. These cut-offs were higher than those of the overall group in Table 2. In the multivariable logistic regression analysis, the duration of rSO_2 lower than 55%, 50%, and 45% was significantly associated with postoperative delirium (for every 5 min, adjusted OR 1.012, 1.015, and 1.015, p=0.035, 0.006, and 0.024, respectively), as shown in Table 9. However, the model fitness for the cut-off of 55% was not good (Hosmer-Lemeshow's goodness-of-fit: p=0.022), whereas those for the other cut-offs were good. The AUROCs for prediction models for patients under 68 years of age are shown in Figure 2. The AUC for the model without rSO_2 was 0.688 (95% CI 0.565 – 0.816, p=0.007), and improved with rSO_2 measurement, up to 0.752 (95% CI 0.640 – 0.865, p<0.001) with the duration of rSO_2 <50%.

Among 417 patients over 68 years of age, the incidence of delirium was 20.6% (86/417). In the univariable analysis, older age, hypertension, dementia and low preoperative eGFR were significantly associated with postoperative delirium in the old age group. However, there was no significant association between intraoperative reduction in rSO_2 and postoperative delirium for all cut-offs in either the univariable or the multivariable logistic regression analysis.

DISCUSSION

The results of this study suggest that decreases in intraoperative rSO_2 below 50% are associated with postoperative delirium after OPCAB. This was also associated with postoperative atrial fibrillation and longer ICU and hospital stays. Among patients less than 68 years of age, rSO_2 lower than 55% was associated with postoperative delirium. However, in patients more than 68 years old, intraoperative rSO_2 was not associated with postoperative delirium.

The incidence of delirium in this study was 12.9%, slightly lower than reported by previous studies using similar diagnostic methods (23% to 52%) [9]. One of the reasons for this difference may be the age of the included patients, half of whom were under 68 years of age. Conversely, previous studies have included mostly patients over 60 years of age [9]. Age is one of the most powerful risk factors for delirium after cardiac surgery [29]. Furthermore, we selected only patients who had underwent OPCAB, while in previous studies both on-pump and off-pump cardiac surgery were included, with on-pump surgery being more common [9,18,19,29]. Although the topic remains controversial, some studies have suggested that beating heart surgery can lower the risk of delirium caused by solid microemboli or the alteration of cerebral autoregulation during the cardiopulmonary bypass (CPB) period [18,23,30].

Considering the cut-off values for intraoperative rSO_2 during cardiac surgery, Yao and colleagues [17] set multiple thresholds indicating different degrees of hypoxic brain injury. They used 50%, 45%, 40%, 35%, and 30% as absolute values, corresponding to the baseline value minus 1, 1.5, 2, 2.5, and 3 SDs. An rSO_2 reduction below 40% was significantly associated with postoperative neurologic dysfunction after cardiac surgery with CPB based on a multivable analysis. In several studies, including randomized control trials, prolonged cerebral desaturation below 50% as an absolute value or more than 20% of baseline was associated with postoperative cognitive decline [31-34]. However, these studies were mostly conducted on cardiac surgery with CPB, and evaluated only one or two thresholds rather than various cut-off ranges.

We aimed to determine whether there is a certain cut-off value for intraoperative rSO_2 during OPCAB associated with increased postoperative delirium. Previously, it has been shown that rSO_2 values measured by cerebral oximetry reflect a balance between oxygen consumption and supply in the frontal lobe, especially in the “water-shed” area in the junction between the anterior and middle cerebral arteries [3,16]. Intraoperative cerebral hypoperfusion is also known to be related to postoperative neurological dysfunction after cardiac surgery [17,30-32]. However, several randomized controlled trials showed inconsistent results regarding the relationship between intraoperative rSO_2 reductions during cardiac surgery and postoperative neurologic outcomes. Two meta-analyses focusing on the use of cerebral oximetry and postoperative outcomes after cardiac surgery concluded that there was a low level of evidence linking intraoperative reductions in rSO_2 with postoperative neurologic outcomes [13,35].

There may be several reasons for the inconsistent results regarding the usefulness of cerebral oximetry during cardiac surgery. First, heterogeneous patients were enrolled in previous studies. These studies involved various types of cardiovascular surgeries, including valvar surgery, coronary artery bypass surgery, cardiac tumor surgery, and aortic surgery, which involve different applications of intraoperative CPB and hypothermia. Transient but significant dysfunction in cerebral autoregulation and cerebral desaturation due to hemodilution or microemboli may occur with CPB. Cerebral oxygen consumption is also altered during CPB and hypothermia [14,15,17,18,36,37]. Thus, with or without CPB, these heterogeneous populations may have led to inconsistent results. In the current study, to increase the homogeneity of patients, we included only patients who had undergone OPCAB without CPB.

In addition, previous studies including several randomized controlled trials, used various protocols and rSO_2 cut-off values to trigger intervention to restore rSO_2. This may also have contributed to the inconsistent results. Conversely, we evaluated the relationship between rSO_2 reductions and postoperative delirium at various cut-off values. By analyzing not only the occurrence but also the total duration of rSO_2 reduction, we aimed to identify the threshold of hypoxia exceeding the compensating capacity of the brain relating to the duration of cerebral desaturation.

We also included intraoperative MAP, C.I., and SvO_2 as risk factors for postoperative delirium occurrence. Although these hemodynamic variables can affect intraoperative cerebral perfusion and consequently postoperative delirium, they have not been included in many previous studies. In our study, by conducting a regression analysis, we attempted to rule out the possibility of multicollinearity between these hemodynamic variables and rSO_2.

In the subgroup analysis of patients under age 68, only preoperative EF, level of albumin, and C-reactive protein were associated with postoperative delirium by univariable analysis. The cut-off value of rSO_2 associated with postoperative delirium was 55%, which was slightly higher than the 50% cut-off for the entire study group. Moreover, in patients over age 68, rSO_2 was not associated with postoperative delirium. The pathophysiology of postoperative delirium is complex, and age is one of the most powerful risk factors, along with history of hypertension [6,9,19,21]. Thus, in old patients, other factors associated with old age may more strongly influence the occurrence of postoperative delirium than intraoperative brain oxygenation.

This study has several limitations. First, because this study was retrospective in nature, risk factors that could affect postoperative delirium could not be perfectly controlled. Similarly, the anesthetic management to maintain or restore rSO_2 was not controlled. Second, this study involved cardiac surgery cases from 2004 to 2016, and surgical and anesthetic methods and techniques evolved over this period. These changes may have influenced the occurrence of postoperative delirium. Third, preoperative neurologic function was not assessed, and postoperative delirium was estimated using medical records and prescription history. The incidence of postoperative delirium may therefore have been underestimated. Finally, we could not assess the baseline rSO_2 values. Previous studies consistently found that preoperative baseline rSO_2 was associated with postoperative delirium in cardiac surgery [13,15,35]. However, since this was a retrospective study, the impact of baseline rSO_2 on postoperative delirium could not be evaluated. Consequently, the decrease in rSO_2 relative to the baseline was not estimated. Considering the limitations of this study, prospective, randomized controlled studies may be needed to evaluate the effect of intervention to maintain rSO_2 over 50% (or 55% for patients under 68 years of age) during OPCAB.

In conclusion, in patients undergoing OPCAB, intraoperative rSO_2 below 50% was associated with postoperative delirium. Among patients younger than 68 years, rSO_2 below 55% was associated with postoperative delirium. Therefore, rSO_2 should be maintained at over 50%, or over 55% among patients less than 68 years old, during OPCAB.

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Table 1. Baseline and perioperative characteristics of patients with or without delirium. The values are expressed as mean (SD) or number (proportion).

Characteristics	No delirium (n=710)	Delirium (n=105)	*P*-values
Patients characteristics			
Age; y	65.2 (9.6)	71.9 (8.2)	<0.001
Sex; male	556(78.3%)	74(70.5%)	0.075
BM (kg.m^{-2})	24.6(3.3)	24.1(3.1)	0.128
Preoperative medical status			
ASA physical status			0.322
1	19(2.7%)	1(1.0%)	
2	200(28.2%)	25(23.8%)	
3	478(67.3%)	75(71.4%)	
4	13(1.8%)	4(3.8%)	
History of drinking	233(31.4%)	19(18.3%)	0.006
Hypertension	456(64.2%)	83(79.0%)	0.003
Diabetes mellitus	349(49.2%)	57(54.3%)	0.327
Dyslipidemia	268(37.7%)	35(33.3%)	0.383
Myocardial infarction	80(11.3%)	15(14.3%)	0.37
Atrial fibrillation	50(7.0%)	7(6.7%)	0.888
Chronic kidney disease	275(38.7%)	43(41.0%)	0.663
Dementia	4(0.6%)	5(4.8%)	0.003
History of stroke	452(63.7%)	64(63.3%)	0.591
Left ventricle ejection	55.1(11.1)	53.9(12.5)	0.3

fraction; %			
Hematocrit; %	34.8(4.0)	33.9(4.1)	0.027
Creatinine; $mg.dL^{-1}$	1.4(1.7)	1.5(1.7)	0.3
Estimated GFR; $ml.min^{-1}.1.73^{-1}.m^{-2}$	73.9(27.3)	63.5(26.7)	<0.001
Albumin; $g.dL^{-1}$	4.0(0.4)	3.8(0.4)	<0.001
C-reactive protein; $mg.dL^{-1}$	0.7(1.4)	1.1(2.3)	0.006
Intraoperative variables			
Operation duration; min	362.2(53.4)	362.6(61.7)	0.954
Re-do operation	7(1.0%)	1(1.0%)	0.974
Emergency	76(10.7%)	12(11.4%)	0.823
Operation year			0.602
-2009	54	6	
2010-2014	433	69	
2015-	223	30	
Postoperative medical status			
APACHE II score	23.8(4.9)	26.1(4.9)	<0.001
ICU length of stay; days	2.3(1.7)	5.8(7.1)	<0.001
Hospital length of stay; days	9.9(7.1)	22.1(25.3)	<0.001
Acute kidney injury	133(18.7%)	34(32.4%)	0.001
New onset atrial fibrillation	146(20.6%)	31(29.5%)	0.039

Reintubation	27(3.8%)	18(17.1%)	<0.001
In-hospital death	0	3(2.9%)	0.99

BMI, body mass index; ASA, American Society of \Anesthesiologists; GFR, glomerular filtration rate; APACHE, Acute Physiology and Chronic Health Evaluation.

Table 2. Comparison of intraoperative regional cerebral oxygen saturation (rSO_2) between delirium and no delirium group. The values are expressed as mean (SD) for mean, minimum rSO_2 and mean duration of rSO_2 reduction, number (%) for the incidence of rSO_2 reduction.

rSO_2	No delirium (n=710)	Delirium (n=105)	*P*-values
Mean; %	55.5(6.8)	54.8(7.74)	0.32
Minimum; %	47.6(8.1)	46.7(8.33)	0.298
Mean duration of rSO_2 reduction; min			
<75%	451.0(141.7)	468.0(175.7)	0.267
<70%	442.0(147.9)	459.9(182.1)	0.275
<65%	402.3(167.4)	418.9(195.4)	0.355
<60%	318.2(193.4)	341.9(230.9)	0.254
<55%	204.1(196.1)	231.0(230.3)	0.201
<50%	100.9(159.6)	138.7(202.7)	0.031
<45%	39.3(100.6)	64.6(141.5)	0.027
<40%	11.7(49.2)	18.3(82.1)	0.256
<35%	4.0(28.9)	7.1(50.7)	0.376
Number of patients with rSO_2 reduction			
<70%	709(99.9%)	105(100%)	1
<65%	703(99.0%)	104(99.0%)	0.974
<60%	669(94.2%)	98(93.3%)	0.717
<55%	573(80.7%)	84(80.0%)	0.865
<50%	407(57.3%)	69(65.7%)	0.105

<45%	228(32.1%)	44(41.9%)	0.048
<40%	108(15.2%)	17(16.2%)	0.795
<35%	41(5.8%)	6(5.7%)	0.98

rSO_2, regional cerebral oxygen saturation.

Table 3. Comparison of intraoperative hemodynamic variables between delirium and no delirium group. The values are expressed as mean (SD).

Hemodynamic variables	No delirium (n=710)	Delirium (n=105)	*P*-values
MAP			
Reduction below 68mmHg; min	128.5(112.8)	169.5(134.8)	0.001
Minimum; mmHg	54.2(7.6)	52.5(6.5)	0.026
C.I.			
Reduction below $2.2 L.min^{-1}.m^{-2}$;min	181.9(158.9)	240.2(180.4)	0.001
Minimum; $L.min^{-1}.m^{-2}$	1.7(0.3)	1.6(0.3)	0.05
SvO_2			
Reduction below 64%; min	50.7(91.1)	90.6(146.4)	0.001
Minimum; %	62.3(7.4)	60.5(8.9)	0.032

MAP, mean arterial pressure; C.I., cardiac index; SvO_2, mixed venous oxygen saturation.

Table 4. Odds ratios of intraoperative reduction of regional cerebral oxygen saturation (rSO_2) for each cut-offs and delirium after surgery.

Intraoperative rSO_2	Unadjusted OR (95% CI)	*P*-values	Adjusted OR (95% CI)	*P*-values
Mean	0.985(0.957-1.014)	0.32	0.976(0.942-1.011)	0.175
Minimum	0.987(0.962-1.012)	0.298	0.977(0.948-1.006)	0.124
Duration of rSO_2 reduction (for every 5min)				
<75%	1.004(0.997-1.010)	0.267	1.006(0.999-1.013)	0.118
<70%	1.004(0.997-1.010)	0.275	1.005(0.998-1.012)	0.137
<65%	1.003(0.997-1.009)	0.355	1.004(0.997-1.011)	0.241
<60%	1.003(0.998-1.008)	0.254	1.004(0.998-1.010)	0.155
<55%	1.003(0.998-1.008)	0.201	1.004(0.999-0.010)	0.145
<50%	1.006(1.001-1.011)	0.031	1.007(1.001-1.014)	0.024
<45%	1.009(1.001-1.017)	0.027	1.012(1.003-1.021)	0.011
<40%	1.009(0.994-1.025)	0.256	1.013(0.995-1.030)	0.154
<35%	1.011(0.986-1.037)	0.376	1.021(0.990-1.053)	0.194
Occurrence of rSO_2 reduction				

<70%	.	1	.	1
<65%	1.036(0.126-8.502)	0.974	.	1
<60%	0.858(0.374-1.966)	0.717	1.460(0.423-5.044)	0.549
<55%	0.956(0.572-1.598)	0.865	0.935(0.492-1.777)	0.838
<50%	1.427(0.929-2.192)	0.105	1.599(0.965-2.649)	0.069
<45%	1.525(1.003-2.317)	0.048	1.737(1.064-2.836)	0.027
<40%	1.077(0.616-1.882)	0.795	1.236(0.657-2.326)	0.511
<35%	0.989(0.409-2.390)	0.98	0.839(0.306-2.299)	0.732

OR, odds ratio; rSO_2, regional cerebral oxygen saturation.

Table 5. Odds ratios of predictors of postoperative delirium.

Variables	Multivariable logistic regression - OR (95% CI)	Univariable logistic regression - OR (95% CI)
Age (y)	1.093(1.058-1.129)	1.097(1.066-1.128)
Sex (Female)	-	1.512(0.959-2.386)
Preoperative		
Hypertension	1.908(1.062-3.428)	2.101(1.282-3.445)
Hematocrit (%)	-	0.943(0.896-0.993)
estimated GFR ($ml.min^{-1}.1.73^{-1}.m^{-2}$)	-	0.987(0.980-0.994)
Albumin ($g.dL^{-1}$)	0.485(0.276-0.852)	0.384(0.244-0.605)
C-reactive protein ($mg.dL^{-1}$)	-	1.163(1.044-1.295)
Intraoperative		
MAP < 68mmHg	-	1.002(1.001-1.004)
C.I .< 2.2 $L.min^{-1}.m^{-2}$	-	1.002(1.001-1.003)
SvO_2 < 64%	-	1.003(1.001-1.005)

Occurrence of rSO_2 <45%	1.737(1.064-2.836)	1.525(1.003-2.317)

OR, odds ratio; GFR, glomerular filtration rate; MAP, mean arterial pressure; C.I., cardiac index; SvO_2, mixed venous oxygen saturation; rSO_2, regional cerebral oxygen saturation.

Table 6. The relationship between intraoperative regional cerebral oxygen saturation (rSO_2) and postoperative Acute kidney injury (AKI), ICU and hospital length of stay(LOS). For AKI, the values are expressed as mean (SD) and for LOS, Pearson correlations between two values.

	No AKI (n=648)	AKI (n=167)	P-values	Pearson correlation	ICU_LOS 2.8±3.24(d)	Hospital_LOS 11.5±11.96(d)
rSO_2;%				rSO_2		
Mean	56.2(6.3)	52.3(8.2)	<0.001	Mean	−0.07*	−0.077*
Minimum	48.1(7.8)	45.0(8.6)	<0.001	Minimum	−0.086*	−0.048
Mean duration of rSO_2 reduction; min				Mean duration of rSO_2 reduction		
<50%	88.3±152.4	173.5±197.5	<0.001	<50%	0.146†	0.115†
<45%	30.6±85.9	88.9±156.9	<0.001	<45%	0.203†	0.139†

* P-value<0.05, † P-value <0.01. rSO_2, regional cerebral oxygen saturation; AKI, acute kidney injury; ICU, intensive care unit; LOS, length of stay.

Table 7. Baseline and perioperative characteristics of patients age under 68. The values are expressed as mean (SD) and number (%) for categorized variables.

Characteristics	No delirium (n=379)	Delirium (n=19)	*P*-values
Patients characteristics			
Age; y	58.3(7.3)	58.4(6.6)	0.96
Sex; male	312(82.3%)	16(84.2%)	0.833
BM ($kg.m^{-2}$)	25.0(3.4)	25.3(3.3)	0.727
Preoperative medical status			
ASA physical status			0.686
1	11(2.9%)	0	
2	118(31.1%)	7(36.8%)	
3	244(64.4%)	11(57.9%)	
4	6(1.6%)	1(5.3%)	
History of drinking	144(36.2)	8(42.1)	0.719
Hypertension	228(60.2%)	14(73.7%)	0.245
Diabetes mellitus	198(52.2%)	12(63.2%)	0.356
Dyslipidemia	143(37.7%)	9(47.4%)	0.401
Myocardial infarction	45(11.9%)	3(15.8%)	0.611
Atrial fibrillation	23(6.1%)	1(5.3%)	0.886
Chronic kidney disease	142(37.5%)	10(52.6%)	0.19
Dementia	2(0.5)	0	1
History of stroke	238(62.8%)	9(47.4%)	0.182
Left ventricle	56.6(11.5)	49.7±13.9	0.078

ejection fraction; %			
Hematocrit; %	35.1(4.0)	33.8±3.7	0.171
Creatinine; mg.dL^{-1}	1.5(2.0)	2.0±2.6	0.262
Estimated GFR; ml.min^{-1}.1.73^{-1}.m^{-2}	75.2(28.6)	69.7(32.7)	0.334
Albumin; g.dL^{-1}	4.1(0.4)	3.9±0.4	0.041
C-reactive protein; mg.dL^{-1}	0.6(1.4)	1.8±4.0	0.015
Intraoperative variables			
Operation duration; min	365.0(53.8)	371.0(58.6)	0.636
Re-do operation	1(0.3)	0	1
Emergency	38(10.0)	2(10.5)	0.944
MAP			
Mean; mmHg	74.7(5.5)	73.8(5.8)	0.495
Minimum; mmHg	55.4(7.4)	56.0(9.4)	0.744
C.I.			
Mean ; L.min^{-1}.m^{-2}	2.4(0.4)	2.4(0.4)	0.94
Minimum; L.min^{-1}.m^{-2}	1.7(0.3)	1.8(0.4)	0.881
SvO_2			
Mean; %	71.9(5.6)	71.0(6.5)	0.502
Minimum; %	63.0(7.15)	61.8(8.06)	0.486

BMI, body mass index; ASA, American Society of Anesthesiologists; Americal GFR, glomerular filtration rate; MAP, mean arterial pressure; C.I., cardiac index; SvO_2, mixed venous oxygen saturation.

Table 8. Comparison of intraoperative regional cerebral oxygen saturation (rSO_2) between delirium and nod elirium group in age under 68. The values are expressed as mean (SD) for baseline, mean, minimum rSO_2 and mean duration of rSO_2 reduction, number (%) for the incidence of rSO_2 reduction.

rSO_2	No delirium (n=710)	Delirium (n=105)	P-values
Mean; %	55.60(7.3)	50.6(7.7)	0.004
Minimum; %	47.7(8.2)	42.7(7.4)	0.009
Mean duration of rSO_2 reduction; min			
<75%	450.5(141.7)	445.0(122.9)	0.867
<70%	438.9(151.1)	441.3(126.2)	0.945
<65%	394.6(172.0)	422.9(136.2)	0.48
<60%	316.4(198.7)	381.6(169.3)	0.161
<55%	207.1(196.5)	311.8(196.6)	0.024
<50%	102.5(159.7)	219.7(200.5)	0.002
<45%	43.5(110.3)	114.0(162.4)	0.008
<40%	12.4(54.7)	26.8(94.6)	0.282
<35%	5.3(37.7)	14.0(60.8)	0.35
Number of patients with rSO_2 reduction			
<70%	378(99.7%)	19(100%)	1
<65%	375(98.9%)	19(100%)	1
<60%	355(93.7%)	19(100%)	0.258

<55%	297(78.4%)	18(94.7%)	0.086
<50%	213(56.2%)	16(84.2%)	0.016
<45%	130(34.3%)	11(57.9%)	0.036
<40%	56(14.8%)	6(31.6%)	0.049
<35%	18(4.7%)	1(5.3%)	0.918

rSO_2, regional cerebral oxygen saturation.

Table 9. Odds ratios of intraoperative reduction of regional cerebral oxygen saturation (rSO_2) for each cut-offs and delirium after surgery in patients under 68.

Intraoperative rSO_2	Unadjusted OR (95% CI)	*P*-values	Adjusted OR (95% CI)	*P*-values
Mean	0.920(0.869-0.975)	0.004	0.927(0.874-0.984)	0.012
Minimum	0.934(0.886-0.984)	0.01	0.940(0.891-0.992)	0.025
Duration of rSO_2 reduction (for every 5 min)				
<75%	0.999(0.982-1.016)	0.867	0.997(0.979-1.016)	0.778
<70%	1.001(0.985-1.016)	0.945	0.999(0.982-1.016)	0.887
<65%	1.005(0.992-1.018)	0.479	1.003(0.988-1.017)	0.729
<60%	1.008(0.997-1.019)	0.161	1.005(0.993-1.018)	0.359
<55%	1.011(1.001-1.022)	0.027	1.012(1.001-1.022)	0.035
<50%	1.015(1.005-1.025)	0.004	1.015(1.004-1.025)	0.006
<45%	1.016(1.003-1.029)	0.015	1.015(1.002-1.029)	0.024
<40%	1.014(0.987-1.042)	0.3	1.010(0.982-1.039)	0.492
<35%	1.017(0.980-1.057)	0.372	1.011(0.972-1.052)	0.592

Occurrence of rSO_2 reduction				
<75%	.	1	.	1
<70%	.	1	.	1
<65%	.	1	.	1
<60%	.	1	.	1
<55%	4.970(0.654-37.782)	0.121	4.231(0.551-32.480)	0.165
<50%	4.156(1.191-14.503)	0.025	4.013(1.112-14.482)	0.034
<45%	2.634(1.034-6.709)	0.042	2.283(0.906-6.266)	0.078
<40%	2.662(0.971-7.295)	0.057	2.757(0.980-7.757)	0.055
<35%	1.114(0.141-8.817)	0.918	0.989(0.118-8.300)	0.992

OR, odds ratio; rSO_2, regional cerebral oxygen saturation.

Figure 1. Flow chart for patient selection

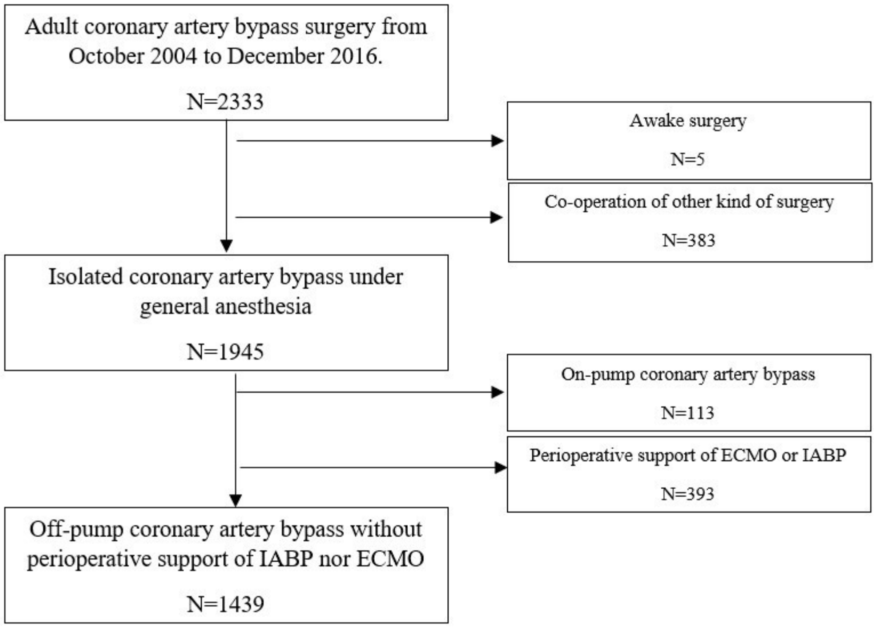
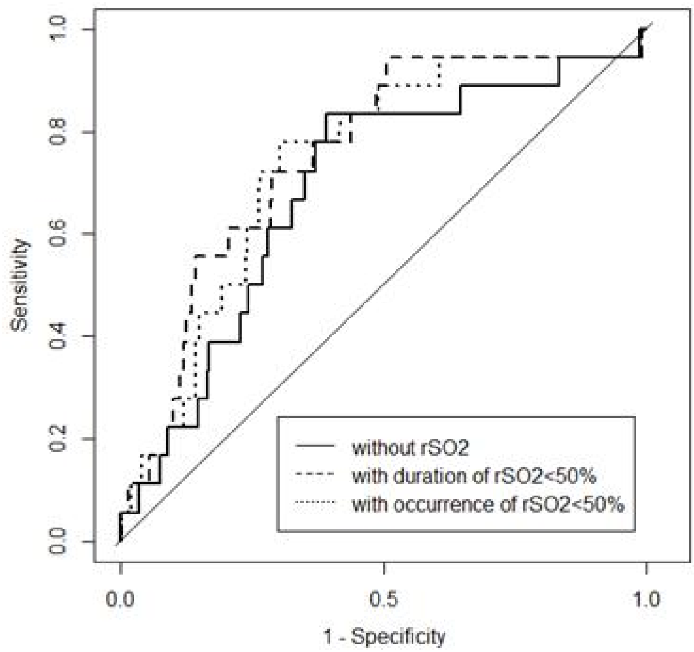


Figure 2. The ROC curves of multivariable prediction model of patients under age 68



국문 초록

서론: 대뇌 산소 포화도는 뇌 조직의 국소적 산소 포화도를 측정하기 위해, 특히 심장수술에서, 광범위하게 사용 되어 왔다. 그러나 그 대중성에도 불구하고, 심장 수술 중 대뇌 산소 포화도의 사용에 대한 결과는 일관되지 않았고, 무심폐기 관상동맥 우회술 중의 대뇌 산소 포화도를 평가한 연구는 거의 없었다.

방법: 2004년 10월부터 2016년 12월까지, 1,439명의 환자가 무심폐기 관상동맥 우회술을 시행받았다. 그 중, 국소 대뇌 산소 포화도에 대한 충분한 양의 데이터를 가진 815명의 환자가 연구에 포함되었다. 후향적으로, 주술기 변수들과 국소 대뇌 산소 포화도의 75%, 70%, 65%, 60%, 55%, 50%, 45%, 40%, 그리고 35% 의 컷오프 값 이하로 감소한 총 시간을 분석하였다. 또한, 국소 대뇌 산소 포화도의 감소와 수술 후 섬망 발생 간의 상관관계를 평가하였다.

결과: 815명의 환자 중 105명에서 섬망이 발생하였다. 단변수 및 다변수 분석 모두에서, 섬망이 발생한 환자 군에서 컷오프 값 50%, 그리고 45% 이하로의 국소 대뇌 산소 포화도의 감소가 유의하게 길었다(매 5분마다, 교정된 오즈비와 95% 신뢰구간은 각각 1.007, 1.001-1.014, 그리고 1.012,

1.003-1.021, p-value는 각각 0.024, 0.011). 국소 대뇌 산소 포화도의 45% 이하로의 감소 비율은 섬망이 발생한 환자군에서 유의하게 높았다 (교정된 오즈비 1.737, 95% 신뢰구간은 1.064-2.836, p-value는 0.027).

결론: 무심폐기 관상동맥 치환술을 받는 환자에서, 수술 중 국소 대뇌 산소 포화도는 수술 후 섬망의 발생과 관련이 있었다. 수술 중 국소 대뇌 산소 포화도의 컷오프 값은 전체 환자군에서는 50%, 68세 이하의 환자군에서는 55% 였다.

주요어: 심장 수술, 대뇌 산소 포화도, 섬망, 근적외선 분광법, 무심폐기 관상동맥 우회술

학 번: 2018-23158