



ORIGINAL ARTICLE

Risk Factors for Postoperative Delirium after Cardiac Surgery

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Abstract

Introduction: Postoperative delirium affects prognosis and the probability of survival. It is important for medical professionals to predict and prevent delirium, as well as implement appropriate interventions, early in the course of care. This study sought to reveal the risk factors for postoperative delirium based on general characteristics such as circulatory dynamics in patients admitted to the ICU after cardiac surgery.

Methods: Patients who underwent cardiac surgery were included in this study (n = 149). Trained nurses assessed postoperative delirium using the intensive care delirium screening checklist (ICDSC) from immediately after extubation to 2 days after extubation. Postoperative delirium was defined as the presence of at least four ICDSC items or diagnosed by a psychiatrist. Research variables were selected from preoperative, intraoperative, and postoperative factors. We performed univariate and multivariate logistic regression analysis using these variables.

Results: Postoperative delirium developed in 40 patients (26.8%). Delirium was independently associated with a history of atrial fibrillation (odds ratio = 3.9109 [95% confidence interval = 1.3578-11.2643], p = 0.011), surgical time (1.0039 [1.0008-1.0069], p = 0.009), in/out balance during the surgery (1.0002 [1.0000-1.0004], p = 0.041), potassium levels immediately after surgery (0.3061 [0.1111-0.8435], p = 0.018), and systemic vascular resistance index immediately after extubation (1.0013 [1.0001-1.0025], p = 0.033).

Discussion & conclusion: Medical professionals, especially nurses, can potentially predict and prevent delirium by observing the identified risk factors.

Keywords

Postoperative delirium, Cardiac surgery, Risk factor, Prediction care

or perception, and it has an acute onset fluctuating course [1]. Risk factors for delirium include patient characteristics, chronic pathology, environmental variables, and acute illness [2]. Delirium is a common complication in the intensive care unit (ICU). It is considered delirium is caused by multiple associated factors. Pathophysiologically, delirium has been associated with gamma-aminobutyric acid-ergic (GABAergic) and cholinergic neurotransmitter system activity and dopamine excess [3-5]. Consequently, delirium is considered to be caused by various factors such as structural brain changes and neurotransmitters. In particular, in the ICU, it is important to provide care for patients in consideration of these factors, as postoperative patients admitted to the ICU are more likely to experience changes in their general condition. It is difficult to monitor neurotransmitters in the clinic; however, monitoring various parameters such as circulatory dynamics and vital signs related to neurotransmitters and comprehending the general condition can facilitate assessments of the risk factors for delirium. In particular, it has profound significance for nurses to predict to occurrence of postoperative delirium using these parameters because ICU nurses have regularly observed these parameters.

The currently reported incidence of delirium in the ICU is 20-50% [6-10]. Furthermore, there are reports that the incidence of delirium in patients after cardiac surgery ranges from 21% to 46% [11-13]. Delirium is linked to higher mortality and increased lengths of stay in the hospital or ICU [14-16], a higher frequency of medical accidents caused by dangerous behavior, and greater medical costs [17]. For these reasons, it is important for medical professions to prevent and detect delirium early in the clinical course and implement appropriate interventions.

Introduction

Delirium is a common clinical syndrome characterized by deviations of consciousness, cognitive function,



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Tools for diagnosing delirium include the confusion assessment method for the ICU (CAM-ICU) and intensive care delirium screening checklist (ICDSC). These tools are useful for diagnosis [18,19]. However, it is difficult to assess delirium using these tools in patients who cannot communicate because of sedation and intubation. Furthermore, it will also be difficult for medical professionals to predict and prevent delirium using these tools. Therefore, this study aimed to reveal the risk factors for postoperative delirium based on general characteristics such as circulatory dynamics in patients admitted to the ICU after cardiac surgery.

Materials and Methods

Study design

Retrospective cohort study.

Patients' selection

Patients who underwent cardiac surgery between January 1, 2014, and March 31, 2016, participated in this study. We excluded patients who underwent re-intubation or underwent tracheotomy because of prolonged ventilator use.

Delirium assessment

Trained nurses assessed postoperative delirium using ICDSC from immediately after extubation to 2 days after extubation. The assessment was performed every 8 h and when the patients' condition varied. Moreover, postoperative delirium was defined as a patient with ICDSC score ≥ 4 , or a patient diagnosed with delirium by a psychiatrist.

Data collection

Research variables were selected from those identified in previous studies and those typically monitored by nurses and divided into four categories, namely, preoperative, intraoperative, postoperative, and post-extubation factors. All data were acquired from the patients' medical records. Preoperative factors included the patients' medical histories (diabetes, hypertension, hypercholesterolemia, cerebral vascular disease, dementia, and atrial fibrillation [AF]) and living environment. In addition, the following variables were selected as preoperative factors: age, sex, body mass index, ejection fraction, alcohol use, Brinkman's index, and residential status. The intraoperative variables include surgical time, type of surgery, in/out balance during the surgery, cardiopulmonary bypass time, blood loss, and emergency operation. Postoperative factors were defined as those evaluated immediately after ICU admission following surgery, and the following variables were assessed: cardiac index, systemic vascular resistance index (SVRI), and central venous pressure (CVP) measured using a pulmonary artery catheter (Swan-Ganz thermodilution catheter, Edwards, USA); pH, partial pressure of arterial oxygen (PaO_2), partial pressure of arterial car-

bon dioxide (PaCO_2), and potassium measured via blood gas analysis; doses of propofol and fentanyl; continuous hemodiafiltration/hemodialysis (CHD); and family visitation. Moreover, the post-extubation variables, which were monitored immediately after extubation, were respiratory time and noninvasive positive pressure respirator (NPPV), in addition to factor assessed immediately after surgery. We performed the assessment following extubation and change of the reservoir or oxygen mask. The study was approved by the ethics review board of Rinku General Medical Center.

Data analysis

The primary outcome was the occurrence of delirium, and classified the patient according to whether the presence of delirium or absence. In the statistics analysis, we first performed univariate logistic regression analysis among the four categories. The significance level was $p < 0.1$. Concerning type of surgery, Pearson's chi-square test was used. Data were presented as the mean \pm standard deviation or number (percent). Second, multivariate logistic regression analysis was used to analyze factors that satisfied the statistical significance level in the previous analysis to estimate odd ratios (ORs) and 95% confidence intervals [CIs]. The significance level was $p < 0.05$. Finally, we analyzed sensitivity and specificity by calculating the area under the curve (AUC) from the obtained receiver operating characteristic curve (ROC). JMP Pro Version 13 (SAS Institute Inc., USA) was used for all statistical analyses.

Results

Of 149 patients included in the study, 40 (26.8%) developed delirium with 2 days of ICU admission.

Preoperative factors

We examined the associations of each preoperative factor with postoperative delirium using univariate logistic regression models. As a result, age was independently associated with postoperative delirium (OR = 1.0449 [95% CI = 1.0056-1.0919], $p = 0.024$; Table 1). In addition, among 27 patients with histories of AF (18.1%), 12 developed postoperative delirium. A history of AF was significantly associated with postoperative delirium (OR = 2.6857 [95% CI = 1.1269-6.4010], $p = 0.026$).

Intraoperative factors

Table 2 shows the result of univariate logistic regression for intraoperative factors. Postoperative delirium was significantly associated with surgical time and in/out balance during the surgery (surgical time: OR = 1.0023 [95% CI = 1.0003-1.0045], $p = 0.025$; in/out balance during the surgery: OR = 1.002 [95% CI = 1.00004-1.0004], $p = 0.016$). Because we considered that surgical time interacted with the balance during surgery, we examined the correlation between them using Spearman's correlation coefficient. A significant

Table 1: Preoperative factors.

	All patients (n = 149)	No delirium (n = 109)	Delirium (n = 40)	Odds ratio	95% CI	P-value
Age, years	70.94 ± 10.88	69.79 ± 11.89	74.08 ± 6.61	1.0449	1.0056-1.0919	0.024
BMI	22.97 ± 3.47	23.02 ± 3.57	22.84 ± 3.23	0.9857	0.8874-1.0950	0.789
Brinkman index	297.91 ± 517.74	249.51 ± 475.72	429.80 ± 605.11	1.0006	0.9999-1.0013	0.068
EF, %	59.13 ± 11.17	58.88 ± 10.80	59.74 ± 12.15	1.0071	0.9729-1.0424	0.688
Sex (M), N (%)	78 (52.3)	54 (49.5)	24 (60.0)	1.5278	0.7321-3.181	0.259
Alcohol, N (%)	23 (15.4)	18 (16.5)	5 (12.5)	0.7222	0.2490-2.0945	0.541
Diabetes, N (%)	40 (26.8)	26 (23.9)	14 (30.0)	1.7189	0.7841-3.7684	0.176
Hypertension, N (%)	114 (76.5)	87 (79.8)	27 (67.5)	0.5252	0.2336-1.1809	0.119
Hypercholesterolemia, N (%)	37 (25.0)	29 (26.6)	8 (20.0)	0.7119	0.2936-1.7263	0.452
Cerebral vascular disease, N (%)	36 (24.2)	23 (21.1)	13 (32.5)	1.8003	0.8042-4.0304	0.158
Dementia, N (%)	3 (2.0)	2 (1.8)	1 (2.5)	1.3717	0.1210-15.5554	0.802
AF, N (%)	27 (18.1)	15 (13.8)	12 (30.0)	2.6857	1.1269-6.4010	0.026
Hemodiafiltration, N (%)	12 (8.1)	8 (7.3)	4 (10.0)	1.4028	0.3983-4.9408	0.604
Living alone, N (%)	24 (16.1)	18 (16.5)	6 (15.0)	0.8922	0.3268-2.4359	0.824

Data are presented as the mean ± SD or number (%); Univariate logistic regression analyses with $p < 0.10$.

BMI: Body mass index; EF: Ejection fraction; AF: Atrial fibrillation.

Table 2: Intraoperative factors.

	All patients (n = 149)	No delirium (n = 109)	Delirium (n = 40)	Odds ratio	95% CI	P-value
Type of surgery						
CABG, N (%)	22 (14.8)	14 (12.8)	8 (20)			
AVR, N (%)	23 (15.4)	20 (18.3)	3 (7.5)			
MVP or MVR, N (%)	8 (5.4)	7 (6.4)	1 (2.5)			
Aorta replacement, N (%)	38 (25.5)	27 (24.8)	11 (27.5)			
Two type of valve replacement or reconstruction, N (%)	7 (4.7)	3 (2.8)	2 (5.0)			
CABG + valve surgery, N (%)	5 (3.4)	5 (4.6)	0 (0)			
Aorta replacement + valve surgery, N (%)	10 (6.7)	8 (7.3)	2 (5.0)			
Other (one type), N (%)	7 (4.7)	5 (4.6)	2 (5.0)			
Other (multiple types), N (%)	31 (20.8)	20 (18.3)	11 (27.5)			0.4411
Surgical time, min	500.31 ± 175.88	480.90 ± 161.20	555.48 ± 203.12	1.0023	1.0003-1.0044	0.025
In/out balance during the surgery, mL	5074.73 ± 2109.39	4824.85 ± 2094.88	5755.65 ± 2020.51	1.0002	1.00004-1.0004	0.016
Blood loss, mL	1102.98 ± 1366.5	1083.45 ± 1489.34	1156.2 ± 968.12	1.0000	0.9997-1.0003	0.776
CPB time, minute	210.50 ± 105.90	58.88 ± 10.80	59.74 ± 12.15	1.0071	0.9729-1.0424	0.198
Emergency operation, N (%)	33 (22.15)	23 (21)	10 (25)	1.2464	0.5154-2.8675	0.612

Data are presented as the mean ± SD or number (%); Pearson's chi-square test with $p < 0.1$. Univariate logistic regression analyses with $p < 0.10$.

CPB: Cardiopulmonary bypass; CABG: Coronary artery bypass graft; AVR: Aortic valve replacement; MVR: Mitral valve replacement; MVR: Mitral valve reconstruction.

statistical correlation was not observed ($r = 0.08$, $p = 0.334$). Therefore, these two factors were included in the multivariate logistic regression models.

Postoperative factors

Table 3 presents the results of univariate logistic regression analysis of postoperative factors. Postoperative delirium was significantly associated with the cardiac index (OR = 0.4200 [95% CI = 0.2292-0.7234], $p = 0.001$) and potassium levels (OR = 0.4131 [95% CI = 0.1665-0.9698], $p = 0.042$).

Post-extubation factors

Univariate logistic regression analysis revealed significant associations of postoperative delirium with SVRI (OR = 1.0011 [95% CI = 1.0001-1.0021], $p = 0.030$) and respiratory time (OR = 1.0001 [95% CI = 1.0000-1.0003], $p = 0.049$) (Table 4).

Multivariate logistic regression analyses

Table 5 shows the result of multivariate logistic regression, in which the 8 factors (age, AF, surgical time, balance during operation, immediately postoperative cardiac index, postoperative potassium levels, post-extubation SVRI, and respiratory time) associated with

Table 3: Postoperative factors.

	All patients (n = 149)	No delirium (n = 109)	Delirium (n = 40)	Odds ratio	95% CI	P-value
CI, L/min/m ²	2.85 ± 0.78	2.98 ± 0.81	2.53 ± 0.62	0.4200	0.2292-0.7234	0.001
SVRI, dyne.sec.cm ⁻⁵ .m ²	1940.42 ± 638.98	1925.44 ± 635.01	1978.23 ± 655.52	1.0001	0.9996-1.0007	0.659
CVP, mmHg	10.20 ± 3.14	10.21 ± 3.06	10.18 ± 3.39	0.9969	0.8874-1.1207	0.958
pH	7.35 ± 0.06	7.35 ± 0.05	7.35 ± 0.07	0.1870	0.0003-112.493	0.608
PaO ₂ , mmHg	198.30 ± 88.16	195.65 ± 85.37	205.51 ± 96.18	1.0012	0.9971-1.0052	0.548
PaCO ₂ , mmHg	42.78 ± 5.68	42.62 ± 0.41	43.22 ± 6.33	1.0011	0.9329-1.0833	0.975
Potassium, mmoL/L	3.98 ± 0.44	4.03 ± 0.41	3.87 ± 0.50	0.4131	0.1665-0.9698	0.042
Propofol, mg/kg	2.30 ± 1.11	2.27 ± 1.18	2.36 ± 0.97	1.0779	0.7510-1.5531	0.683
Fentanyl, µg/kg	0.38 ± 0.15	0.37 ± 0.15	0.38 ± 0.15	1.5746	0.1368-18.1208	0.717
CHD, N (%)	2 (1.3)	1 (0.9)	1 (2.5)	2.7692	0.1079-71.1044	0.484
Family visitation, N (%)	118 (79.2)	87 (79.8)	31 (77.5)	0.8710	0.3704-2.1781	0.759

Data are presented as the mean ± SD or number (%); Univariate logistic regression analyses with p < 0.10.

CI: Cardiac index; SVRI: Systemic vascular resistance index; PaO₂: Partial pressure of arterial oxygen; PaCO₂: Partial pressure of arterial carbon dioxide.

Table 4: Post-extubation factors.

	All patients (n = 149)	No delirium (n = 109)	Delirium (n = 40)	Odds ratio	95% CI	P-value
Cardiac index, L/min/m ²	3.18 ± 0.65	3.22 ± 0.70	3.08 ± 0.48	0.6869	0.3524-1.2677	0.236
SVRI, dyne.sec.cm ⁻⁵ .m ²	1775.60 ± 399.28	1729.05 ± 403.56	1900.63 ± 364.18	1.0011	1.0001-1.0021	0.030
CVP, mmHg	8.76 ± 3.18	8.6 ± 3.07	9.18 ± 3.46	1.0584	0.9430-1.1886	0.332
pH	7.42 ± 0.05	7.42 ± 0.05	7.43 ± 0.05	240.64	0.1353-428048.7	0.143
PaO ₂ , mmHg	123.79 ± 35.48	126.06 ± 34.01	117.49 ± 39.06	0.9926	0.9809-1.0034	0.184
PaCO ₂ , mmHg	39.73 ± 5.60	39.85 ± 5.93	39.41 ± 4.62	0.9859	0.9211-1.0537	0.670
Potassium, mmoL/L	4.23 ± 0.35	4.25 ± 0.34	4.19 ± 0.38	0.6125	0.2090-1.7448	0.359
Fentanyl, µg/kg	0.34 ± 0.16	0.35 ± 0.15	0.33 ± 0.18	0.4343	0.0421-4.4802	0.480
CHD, N (%)	14 (9.4)	8 (7.3)	6 (15)	2.2279	0.6902-6.8677	0.164
Family visitation, N (%)	26 (17.5)	18 (16.5)	8 (20)	1.2639	0.4790-3.1120	0.620
Ventilator time, min	2707.86 ± 2433.10	2460.07 ± 2263.83	3383.08 ± 2763.00	1.0001	1.0000-1.0003	0.049
Pain, N (%)	29 (19.5)	22 (20.2)	7 (17.5)	0.8388	0.3077-2.0679	0.714
NIPPV, N (%)	4 (2.7)	2 (1.8)	2 (5)	2.8158	0.3288-24.1274	0.318

Data are presented as the mean ± SD or number (%); Univariate logistic regression analyses with p < 0.10.

SVRI: Systemic vascular resistance index; PaO₂: Partial pressure of arterial oxygen; PaCO₂: Partial pressure of arterial carbon dioxide; NIPPV: Noninvasive positive pressure ventilator.

Table 5: Multivariate logistic regression analysis.

	Coefficient	Standard error	Odds ratio	95% CI	P-value
Intercept	-2.0696	3.5417			
Age, years	0.0257	0.0267	1.0261	0.9738-1.0811	0.314
AF, N (%)	0.6819	0.2699	3.9109	1.3578-11.2643	0.011
Surgical time, min	0.0039	0.0016	1.0039	1.0008-1.0069	0.009
Balance during operation, mL	0.0002	0.0001	1.0002	1.0000-1.0004	0.041
Cardiac index, L/min/m ²	-0.5174	0.3568	0.5961	0.2962-1.1995	0.131
Potassium, mmoL/L	-1.184	0.5171	0.3061	0.1111-0.8435	0.018
SVRI, dyne.sec.cm ⁻⁵ .m ²	0.0013	0.0006	1.0013	1.0001-1.0025	0.033
Ventilator time, min	0.00004	0.0001	1.0000	0.9998-1.0003	0.683

Multivariate logistic regression analyses with p < 0.05.

CI: Cardiac index; SVRI: Systemic vascular resistance index; PaO₂: Partial pressure of arterial oxygen, PaCO₂: Partial pressure of arterial carbon dioxide; NIPPV: Noninvasive positive pressure ventilator.

postoperative delirium in univariate logistic regression were examined. As a result, a history of AF (OR = 3.9109 [95% CI = 1.3578-11.2643], p = 0.011), surgical time (OR = 1.0039 [95% CI = 1.0008-1.0069], p = 0.009), In/out balance during the surgery (OR = 1.0002 [95%

CI = 1.0000-1.0004], p = 0.041), potassium levels (OR = 0.3061 [95% CI = 0.1111-0.8435], p = 0.018), and SVRI (OR = 1.0013 [95% CI = 1.0001-1.0025], p = 0.033) were significantly associated with postoperative delirium. Moreover, the AUC calculated from the ROC, which was

obtained via multivariate logistic regression, was 0.809. Consequently, the sensitivity and specificity were 82.9% and 67.0%, respectively.

Discussion & Conclusion

Preoperative atrial fibrillation

Preoperative AF may contribute to postoperative delirium by inducing cerebral emboli, brain hypoperfusion, and periods of atrial hypotension [20,21]. Conversely, hypoperfusion increases the probability of cerebral hypoxia, which reduces the synthesis of acetyl coenzyme A, glutamate, and acetylcholine in the citric acid cycle. Decreased brain cholinergic and glutaminergic activity could be responsible for delirium [22]. Cholinergic neurons, which inhibit the excitation of neurons extensively, projected into a large of the cerebral cortex and hippocampus. Furthermore, cholinergic neurons in the pedunculopontine tegmental nucleus and laterodorsal tegmental nucleus project to the thalamus, which is associated with the adjustment of arousal [23,24].

In a previous study, Zhang revealed associations between postoperative delirium and perioperative risk factors after CABG surgery. Consequently, he reported that preoperative AF was an independent risk factor for postoperative delirium (OR = 3.96 [95% CI = 1.727-9.066]) [25]. Furthermore, Cereghetti raha in a cohort study identified preoperative as an independent risk factor for delirium after cardiac surgery (OR = 2.30 [95% CI = 1.30-4.09], $p = 0.004$) [26]. Thus, our findings aligned with previous results.

Surgical time

Afonso, et al. reported in a prospective observation study that assessed delirium using RASS or CAM-ICU for patients after cardiac surgery that the duration of surgery was independently associated with delirium (OR = 1.3 [95% CI = 1.1-1.5], $p = 0.0002$) [27]. Prolonged surgical times may lead to increased invasion and immune reactions. The levels of inflammatory cytokines that control biological defense reactions, such as interleukin (IL)-6, IL-8, and tumor necrosis factor (TNF), are increased by invasive treatment such as surgery. These reactions can act individually or as part of a network system [28]. These pro-inflammatory cytokines act on the brain via a fast neural pathway and a slower humoral pathway [29]. Delirium can possibly occur because of abnormal neurotransmitter production and balance [30]. An elevated cerebrospinal fluid IL-6 concentration is observed in patients undergoing cardiac surgery [31]. Furthermore, a positive correlation was noted between inflammatory cytokine levels and surgical time [32]. In previous studies of the relationships between delirium and inflammatory cytokines, the IL-6 concentration was positively correlated with the Memorial Delirium Assessment Scale (MDAS), which assesses the severity of delirium ($r = 0.449$, $p < 0.001$) [33]. In addition, Rooij, et al. reported associations of IL-6 (OR = 2.39 [95% CI =

1.03-5.56], $p = 0.044$) and IL-8 (OR = 2.57 [95% CI = 1.06-6.26], $p = 0.038$) levels with delirium in hospitalized patients [28]. Therefore, increased inflammatory cytokine production might increase the risk of delirium.

In/out balance during the surgery

Invasive reactions caused by the surgery include enhanced vascular permeability, resulting in the movement of extracellular fluid to the third space; thus, patients undergoing cardiac surgery require large quantities of transfused during the operation to maintain the circulating blood volume. Consequently, an increased in/out balance during surgery may be caused gas exchange disturbances, electrolyte balance disturbances, and low output. The in/out balance during surgery is possibly associated with postoperative delirium [34]. Smelter, et al. reported that the in/out balance during surgery is an independent risk factor for delirium in patients who underwent cardiac surgery, (OR = 2.77 [95% CI = 1.51-5.11], $p = 0.001$) [35], in line with our findings.

Postoperative potassium

In prior research, Jang reported that a decreased potassium concentration is independently associated with delirium in patients admitted to rehabilitation wards (OR = 0.144 [95% CI = 0.064-0.327], $p < 0.001$) [36]. In addition, disturbance of the balance of electrolytes such as sodium and potassium or glucose increases the risk of delirium after surgery [37,38]. In a prospective cohort study of patients after cardiac surgery, Zhang, et al. identified electrolyte disturbance as a risk factor for delirium for patients who underwent CABG [25]. In research about the correlation between delirium and potassium levels, increased potassium concentrations were positively correlated with delirium [39]. However, the mechanism by which electrolyte disturbances, in particular those of potassium, lead to delirium remains unclear. In addition, only a few reports have identified a link between potassium disturbances and delirium. It is possible that decreases of the potassium concentration prolong the action potential duration, leading to overexcited neurons and delirium.

SVRI after extubation

The causes of increased SVRI include hypertension, peripheral vascular constriction, shock, and low output. Immediately after extubation, factors linked to respiration and hemodynamics, such as the cardiac index, CVP, and PaO₂, were not associated with delirium.

Conversely, it is suggested that variation of hemodynamic variables such as systemic vascular resistance and heart rate are caused by stimulation to cardiovascular system during intubation [40,41]. Additionally, the increase of SVRI may have been caused by stimulation associated with extubation. Cardiovascular stimulation enhances sympathetic nerve activity, resulting in elevated adrenaline and dopamine release [42]. These changes could explain the association of SVRI with delirium.

We identified five factors that were associated with delirium following cardiac surgery. It is important that medical professionals, especially nurses, gather preoperative patient information before ICU admission and share intraoperative information with the surgical staff. During postoperative management, potassium levels must be measured at appropriate times such as when increasing or decreasing diuresis and when electrocardiographic abnormalities such as arrhythmia are observed, and adequate corrective measures must be employed. Concerning SVRI, sympathetic hyperactivity caused by acute stress and invasion should be reduced. It may be possible to prevent delirium by preventing these changes.

In conclusion, we identified significant associations of postoperative delirium with AF, surgical time, in/out balance during the surgery, postoperative potassium levels, and post-extubation SVRI. These results suggest that medical professionals, especially nurses, can predict and prevent delirium by observing and correcting these risk factors. In addition, to prevent postoperative delirium, nurses have to need to gather preoperative and intraoperative patient information, manage appropriate postoperative potassium levels, and provide to care as reduce SVRI.

Limitations

This study had several limitations. First, we could not completely exclude the effect of bias because this study analyzed a retrospective cohort. In particular, we could not assess the Acute Physiology and Chronic Health Evaluation score (APACH), which evaluates the severity of illness in patients admitted to the ICU. Second, because the study was conducted at a single institute, there may have been bias regarding intraoperative factors and intubation times. Third, we did not use CAM-ICU because of many of the patients were very severe and sedated by RASS -3 to -4 not to be burden on hemodynamics. However duration of mechanical ventilation have been too longer by deep sedation. We needed to consider that sedation levels and assessment of delirium during sedation. Fourth, the specificity was low in this study, indicating that the occurrence of delirium was overestimated. As an explanation, skill in evaluating delirium possibly differed among nurses because the work experience of the nursing staff ranged 1-20 years. Finally, we could not assess the subtype of delirium. Risk factors for delirium possibly differ by subtype. These issues must be analyzed in the future.

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References

1. National Institute for Health and Clinical Excellence: Guidance (2010) Delirium: Diagnosis, prevention and management. London: Royal College of Physicians.
2. Van Rompaey B, MM Elseviers, MJ Schuurmans, LM Shortridge-Baggett, S Truijien, et al. (2009) Risk factors for delirium in intensive care patients: A prospective cohort study. *Crit Care* 13: 77.
3. Reade MC, S Finfer (2014) Sedation and delirium in the intensive care unit. *N Engl J Med* 370: 444-454.
4. Yoshitaka S, M Egi, T Kanazawa, Y Toda, K Morita (2014) The association of plasma gamma-aminobutyric acid concentration with postoperative delirium in critically ill patients. *Crit Care Resusc* 16: 269-273.
5. Yilmaz S, E Aksoy, AI Diken, A Yalcinkaya, ME Erol, et al. (2016) Dopamine administration is a risk factor for delirium in patients undergoing coronary artery bypass surgery. *Heart Lung Circ* 25: 493-498.
6. Shi CM, DX Wang, KS Chen, XE Gu (2010) Incidence and risk factors of delirium in critically ill patients after non-cardiac surgery. *Chin Med J (Engl)* 123: 993-999.
7. Lin SM, CD Huang, CY Liu, HC Lin, CH Wang, et al. (2008) Risk factors for the development of early-onset delirium and the subsequent clinical outcome in mechanically ventilated patients. *J Crit Care* 23: 372-379.
8. Kanova M, P Sklienka, K Roman, M Burda, J Janoutova (2017) Incidence and risk factors for delirium development in ICU patients - A prospective observational study. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 161: 187-196.
9. Mori S, JR Takeda, FS Carrara, CR Cohrs, SS Zanei, et al. (2016) Incidence and factors related to delirium in an intensive care unit. *Rev Esc Enferm USP* 50: 587-593.
10. van den Boogaard M, L Schoonhoven, JG van der Hoeven, T van Achterberg, P Pickkers (2012) Incidence and short-term consequences of delirium in critically ill patients: A prospective observational cohort study. *Int J Nurs Stud* 49: 775-783.
11. Koster S, AG Hensens, J van der Palen (2009) The long-term cognitive and functional outcomes of postoperative delirium after cardiac surgery. *Ann Thorac Surg* 87: 1469-1474.
12. Rudolph JL, SK Inouye, RN Jones, FM Yang, TG Fong, et al. (2010) Delirium: An independent predictor of functional decline after cardiac surgery. *J Am Geriatr Soc* 58: 643-649.
13. Saczynski JS, ER Marcantonio, L Quach, TG Fong, A Gross, et al. (2012) Cognitive trajectories after postoperative delirium. *N Engl J Med* 367: 30-39.
14. Ely EW, S Gautam, R Margolin, J Francis, L May, et al. (2001) The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Med* 27: 1892-1900.
15. Ouimet S, BP Kavanagh, SB Gottfried, Y Skrobik (2007) Incidence, risk factors and consequences of ICU delirium. *Intensive Care Med* 33: 66-73.
16. Koster S, AG Hensens, MJ Schuurmans, J van der Palen (2012) Consequences of delirium after cardiac operations. *Ann Thorac Surg* 93: 705-711.
17. Milbrandt EB, S Deppen, PL Harrison, AK Shintani, T Speroff, et al. (2004) Costs associated with delirium in mechanically ventilated patients. *Crit Care Med* 32: 955-962.
18. Serpa Neto A, AP Nassar Júnior, SO Cardoso, JA Manetta, VG Pereira, et al. (2012) Delirium screening in critically ill patients: A systematic review and meta-analysis. *Crit Care Med* 40: 1946-1951.

19. Flores DG, JIF Salluh, RÁ Chalhub, LC Quarantini (2012) The confusion assessment method for the intensive care unit (CAM-ICU) and intensive care delirium screening checklist (ICDSC) for the diagnosis of delirium: A systematic review and meta-analysis of clinical studies. *Crit Care* 16: 115.
20. Kazmierski J, M Kowman, M Banach, T Pawelczyk, P Okonski, et al. (2006) Preoperative predictors of delirium after cardiac surgery: A preliminary study. *Gen Hosp Psychiatry* 28: 536-538.
21. Kazmierski J, M Kowman, M Banach, W Fendler, P Okonski, et al. (2008) Clinical utility and use of DSM-IV and ICD-10 Criteria and The Memorial Delirium Assessment Scale in establishing a diagnosis of delirium after cardiac surgery. *Psychosomatics* 49: 73-76.
22. Shadvar K, F Baastani, A Mahmoodpoor, E Bilehjani (2013) Evaluation of the prevalence and risk factors of delirium in cardiac surgery ICU. *J Cardiovasc Thorac Res* 5: 157-161.
23. Dautan D, I Huerta-Ocampo, IB Witten, K Deisseroth, JP Bolam, et al. (2014) A major external source of cholinergic innervation of the striatum and nucleus accumbens originates in the brainstem. *J Neurosci* 34: 4509-4518.
24. Steriade M, S Datta, D Pare, G Oakson, RC Curro Dossi (1990) Neuronal activities in brain-stem cholinergic nuclei related to tonic activation processes in thalamocortical systems. *J Neurosci* 10: 2541-2559.
25. Zhang WY, WL Wu, JJ Gu, Y Sun, XF Ye, et al. (2015) Risk factors for postoperative delirium in patients after coronary artery bypass grafting: A prospective cohort study. *J Crit Care* 30: 606-612.
26. Cereghetti C, M Siegemund, S Schaedelin, J Fassl, MD Seeberger, et al. (2017) Independent predictors of the duration and overall burden of postoperative delirium after cardiac surgery in adults: An observational cohort study. *J Cardiothorac Vasc Anesth* 31: 1966-1973.
27. Afonso A, C Scurlock, D Reich, J Raikhelkar, S Hossain, et al. (2010) Predictive model for postoperative delirium in cardiac surgical patients. *Semin Cardiothorac Vasc Anesth* 14: 212-217.
28. de Rooij SE, BC van Munster, JC Korevaar, M Levi (2007) Cytokines and acute phase response in delirium. *J Psychosom Res* 62: 521-525.
29. Konsman JP, P Parnet, R Dantzer (2002) Cytokine-induced sickness behaviour: Mechanisms and implications. *Trends Neurosci* 25: 154-159.
30. Cerejeira J, H Firmino, A Vaz-Serra, EB Mukaetova-Ladinska (2010) The neuroinflammatory hypothesis of delirium. *Acta Neuropathol* 119: 737-754.
31. Kalman J, A Juhasz, G Bogats, B Babik, A Rimanoczy, et al. (2006) Elevated levels of inflammatory biomarkers in the cerebrospinal fluid after coronary artery bypass surgery are predictors of cognitive decline. *Neurochem Int* 48: 177-180.
32. Antonelli M, G Testa, L Tritapepe, RR D'Errico, D Costa, et al. (1999) IL-8, IL-6 and ICAM-1 in serum of paediatric patients undergoing cardiopulmonary bypass with and without cardiocirculatory arrest. *J Cardiovasc Surg (Torino)* 40: 803-809.
33. Kuswardhani RAT, YS Sugi (2017) Factors related to the severity of delirium in the elderly patients with infection. *Gerontol Geriatr Med* 3.
34. Mailhot T, S Cossette, J Lambert, W Beaubien-Souligny, A Cournoyer, et al. (2018) Delirium after cardiac surgery and cumulative fluid balance: A case-control cohort study. *J Cardiothorac Vasc Anesth*.
35. Smulter N, HC LingeHall, Y Gustafson, B Olofsson, KG Engström (2013) Delirium after cardiac surgery: Incidence and risk factors. *Interact Cardiovasc Thorac Surg* 17: 790-796.
36. Jang S, KI Jung, WK Yoo, MH Jung, SH Ohn (2016) Risk factors for delirium during acute and subacute stages of various disorders in patients admitted to rehabilitation units. *Ann Rehabil Med* 40: 1082-1091.
37. Wang LH, DJ Xu, XJ Wei, HT Chang, GH Xu (2016) Electrolyte disorders and aging: Risk factors for delirium in patients undergoing orthopedic surgeries. *BMC Psychiatry* 16: 418.
38. Yildizeli B, MO Ozyurtkan, HF Batirel, K Kuscu, N Bekiroglu, et al. (2005) Factors associated with postoperative delirium after thoracic surgery. *Ann Thorac Surg* 79: 1004-1009.
39. Horacek R, B Krnacova, J Prasko, K Latalova (2016) Delirium as a complication of the surgical intensive care. *Neuropsychiatr Dis Treat* 12: 2425-2434.
40. Wohlner EC, LJ Usubiaga, BM Jacoby, GE Hill (1979) Cardiovascular effects of extubation. *Anesthesiology* 51: S195.
41. Nishina K, K Mikawa, M Shiga, N Maekawa, H Obara (1996) Prostaglandin E1 attenuates the hypertensive response to tracheal extubation. *Can J Anaesth* 43: 678-683.
42. van Munster BC, S de Rooij, M Yazdanpanah, PJ Tienari, KH Pitkala, et al. (2010) The association of the dopamine transporter gene and the dopamine receptor 2 gene with delirium, a meta-analysis. *Am J Med Genet B Neuropsychiatr Genet* 153: 648-655.