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

Introduction

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

Accepted: October 23, 2018: Published: October 25, 2018
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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 (PaO₂), partial pressure of arterial carbon dioxide (PaCO₂), 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 respiration (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 ± 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 = 1.0004-1.0004], 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
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 postoperative delirium were included in the multivariate logistic regression model.

Post-extubation factors

Table 5: Multivariate logistic regression analyses.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio 95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>1.0449 1.0056-1.0919</td>
<td>0.024</td>
</tr>
<tr>
<td>BMI</td>
<td>0.9857 0.8874-1.0950</td>
<td>0.789</td>
</tr>
<tr>
<td>Brinkman index</td>
<td>1.0006 0.9999-1.0013</td>
<td>0.068</td>
</tr>
<tr>
<td>EF, %</td>
<td>1.0071 0.9729-1.0424</td>
<td>0.688</td>
</tr>
<tr>
<td>Sex (M), N (%)</td>
<td>1.5278 0.7321-3.181</td>
<td>0.259</td>
</tr>
<tr>
<td>Alcohol, N (%)</td>
<td>0.7222 0.2490-2.0945</td>
<td>0.541</td>
</tr>
<tr>
<td>Diabetes, N (%)</td>
<td>1.7189 0.7841-3.7684</td>
<td>0.176</td>
</tr>
<tr>
<td>Hypertension, N (%)</td>
<td>0.5252 0.2336-1.1809</td>
<td>0.119</td>
</tr>
<tr>
<td>Hypercholesterolemia, N (%)</td>
<td>0.7119 0.2936-1.7263</td>
<td>0.452</td>
</tr>
<tr>
<td>Cerebral vascular disease, N (%)</td>
<td>1.8003 0.8042-4.0304</td>
<td>0.158</td>
</tr>
<tr>
<td>Dementia, N (%)</td>
<td>1.3717 0.1210-15.5554</td>
<td>0.802</td>
</tr>
<tr>
<td>AF, N (%)</td>
<td>2.6857 1.1269-6.4010</td>
<td>0.026</td>
</tr>
<tr>
<td>Hemodiafiltration, N (%)</td>
<td>1.4028 0.3983-4.9408</td>
<td>0.604</td>
</tr>
<tr>
<td>Living alone, N (%)</td>
<td>0.8922 0.3268-2.4359</td>
<td>0.824</td>
</tr>
</tbody>
</table>

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

BMI: Body mass index; EF: Ejection fraction; AF: Atrial fibrillation.
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
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, Ceregelli 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 = 1.11-1.5], 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 increase in/in balance during surgery may be caused gas exchange disturbances, electrolyte balance disturbances, and low output. 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 gather preoperative and intraoperative information, manage appropriate postoperative potassium levels, and provide 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 (APACHE), 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 sediment 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.

Acknowledgments

We thank the nursing staff in the ICU of Rinku General Medical Center for their valuable comments and support of the study.

References


