Incidence and Risk Factors of Sub-syndromal Delirium in Patients after Cardiac Surgery

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Abstract [**Objectives**] This study aimed to investigate the incidence and risk factors associated with SSD in patients following cardiac surgery. [**Methods**] A total of 378 patients who underwent cardiac surgery in Taihe Hospital were recruited and screened. Diagnosis of delirium was made using evaluation methods and DSM-5 criteria. SSD was defined as the presence of one or more core features of delirium without meeting the full diagnostic criteria. Statistical analysis included independent samples *t*-test for group comparisons and binary logistic regression analysis to identify independent risk factors for SSD after cardiac surgery. [**Results**] Among the 378 subjects, 112 (29.63%) had SSD, 28 (7.41%) had delirium, and the remaining 238 patients (62.96%) did not present with delirium. Univariate analysis revealed that age, APACHE II score, duration of aortic clamping, length of ICU stay, duration of sedation use, and daily sleep time were significant risk factors for the occurrence of SSD ($P<0.05$). Logistic regression analysis identified age >70 years old, APACHE II score >20 points, length of ICU stay >5 d, and duration of sedation use >24 h as independent risk factors for SSD after cardiac surgery ($P<0.05$). A functional model was fitted based on the analysis results of the binary logistic regression model, yielding the equation logit $P=1.472X_1+2.213X_2+3.028X_3+1.306X_4$. [**Conclusions**] Comprehensive clinical assessment is crucial for patients undergoing cardiac surgery, and appropriate preventive measures should be taken for patients with identified risk factors. Close monitoring of the patient's consciousness should be implemented postoperatively, and timely interventions should be conducted. Further research should focus on model validation and optimization.

Key words Subsyndromal delirium, Cardiac surgery, Patient, Confusion assessment method for intensive care units version (CAM-ICU)

1 Introduction

Delirium is an acute onset of consciousness disorders that affect all higher cerebral cortical function. It exists along the continuum between normal awakening and stupor or coma[1-3], with an incidence of up to 73% during the postoperative period and 14% - 24% during hospital admission[4]. Delirium is an important burden for intensive care units (ICU) associated with ICU mortality, longer durations of mechanical ventilation, and lengths of stay both of ICU and hospital[5-6]. It is difficult to determine the resulting mortality of delirium, and there is no evidence exists that shortening the duration may reduce short-term mortality[1].

Sub-syndromal delirium (SSD) is a more mild form of delirium rather than a different disease in a partial delirium syndrome or "previous delirious" aspect[1-2,5]. Certainly, patients with SSD display only a few delirium symptoms (*e.g.*, inattention, thought disturbances, irritability, anxiety, restlessness, and/or sleep disturbances) without satisfying the full criteria of delirium[1,5]. SSD is clinically interested from the beginning of the 21st century. Same as delirium, SSD is associated with negative patient outcomes, such as lengthened hospital stays, worse cognitive and functional outcomes, and higher mortality rates[6-7].

Despite its clinical significance, detecting SSD is difficult for its variable course and mild symptoms. The incidence of SSD is highly variable, extending from 0.9% to 36.5%. Moreover, risk factors for delirium are identified, including old age, extensive surgical procedure, long term operation, higher number of comorbidities, blood transfusion, longer management in intensive care unit, and decreased serum albumin concentration[2-3,6]. Several studies have examined the factors associated with SSD, although Cole MG[7] have suggested that the risk factors of SSD are similar to those associated with delirium. Nonetheless, SSD may be considered to be their endogenous factors in delirium because SSD may be a marker of basic disease that is not severe enough to cause complete delirium[8-9]. Systematic reviews and meta-analysis about SSD highlight the need for further research to deepen the understanding of risk factors and outcomes associated with SSD, and differentiate patients who present risk factors and results in SSD and delirium[10]. Therefore, the purpose of this study was to evaluate and describe the differences in risk factors and outcomes associated with the different trajectories related to the presence or absence of SSD, delirium and non-delirium among patients hospitalized in a cardiac surgery intensive care unit[11-13].

2 Materials and methods

2.1 Selection The study was approved and the need for patients informed consent was abandoned by the local Ethics Committee of Taihe Hospital, Shiyan City, Hubei Province. Between January 2020 and December 2021, all 395 patients who underwent cardiac surgery in Taihe Hospital were screened after postoperative admission to the ICU. Exclusion criteria: (i) concurrently with other types of cardiovascular diseases, such as aortic dissection; (ii) previous severe mental system diseases, such as schizophrenia; (iii) intraoperative or postoperative complications of intracranial hemorrhage, cerebral Patients with infarction or any disease that can cause disturbance of consciousness; (iv) patients with cardiac arrest during or after surgery; (v) patients with tumors,

Received: October 15, 2023 Accepted: December 2, 2023

Supported by Philosophy and Social Science Research Project of Hubei Education Department in 2022 (22D092); Guiding Scientific Research Project of Shiyan Science and Technology Bureau in 2022 (22Y34).

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blood diseases or autoimmune diseases. Drop-out criteria: (i) in-hospital death due to any cause after surgery; (ii) drop-off of investigators midway. As the result, 17 patients on the first 5 postoperative days were excluded. The relationship between their risk factors and harmful outcomes have already been analyzed[14].

2.2 Screening for subsyndromal delirium We screened patients for symptoms of delirium on a daily basis during the first 7 days of hospitalization. To assess core delirium features, a dedicated postoperative SSD assessment team was established, consisting of 1 doctor and 2 nurses, and all members received the ICU confusion assessment method for the intensive care unit (CAM-ICU)[15] combined with intensive care delirium screening checklist (ICDSC)[16] related training to the level of proficient use. The study showed that the sensitivity and specificity of CAM-ICU and ICDSC for the diagnosis of SSD were 84%, 95% and 83%, 87%[17], respectively. Among them, CAM-ICU includes four contents: sudden change of mental state, distraction, disorder of thinking and change in degree of consciousness. ICDSC includes changes in level of consciousness, inattention, disorientation, hallucination-fantasic psychotic state, psychomotor type, agitation or block, inappropriate speech and emotions, sleep-wake cycle disturbances, and fluctuating symptoms. Assessments were performed every 8 h postoperatively. In the evaluation method, CAM-ICU was used to evaluate patients in the first step, and ICDSC was used to evaluate CAM-ICU-negative patients in the second step, with 0 being negative and 1 – 3 being subdelirium. Two nurses made the assessment respectively. The corresponding results were taken when the two judgments were consistent, or a doctor made the final judgment when the two were inconsistent. We excluded from SSD group patients in whom delirious symptoms could be better explained by neurological deficit due to stroke. Patients without core features of delirium were defined as ND/NSSD.

2.3 Patient characteristics and outcome The following parameters were extracted from the existing database: age, gender, education level, alcoholism, smoking, hypertension, diabetes disease. In addition, patients who reached ICU using acute physiology and chronic health evaluation II (APACHE II) score were evaluated. The primary outcomes of interest included the length of ICU stay, the duration of mechanical ventilation (by standardized criteria of extubation), duration of sedation use and daily sleep time.

2.4 Statistical analysis SPSS 25.0 statistical software was used for data analysis. Continuous variables were presented as means (SDS), and categorical variables were presented as frequencies and percentages. The α significance level was set at 0.05 for all tests. Independent samples t test was used for comparison between two groups; count data were expressed by frequency or percentage (%) was expressed, and the chi-square test was used for comparison between groups. Binary logistic regression analysis was performed on variables with statistically significant differences in univariate analysis to find independent risk factors for SSD after cardiac surgery.

3 Results and analysis

3.1 Characteristics of patient samples As shown in Table 1, 112 (29.63%) of 378 patients had subsyndromal delirium (SSD, and 28 (7.41%) had delirium, while the remaining 238 patients (62.96%) were without delirium.

Univariate analysis showed that age, APACHE II score, duration of aortic clamping, length of ICU stay, duration of sedation use and daily sleep time were the risk factors for the occurrence of SSD.

3.2 Binary logistic regression analysis of the influencing factors of SSD after cardiac surgery As shown in Tables 2 – 3, the variables with statistically significant differences in univariate analysis were assigned, and binary logistic regression analysis was performed. By the logistic regression analysis, age > 70 years old, APACHE II score > 20 points, length of ICU stay > 5 d and duration of sedation use > 24 h were independent risk factors for SSD after cardiac surgery ($P < 0.05$).

3.3 Construct a functional model for predicting SSD after cardiac surgery In accordance with the analysis results of the binary logistic regression model, it was fitted to a functional model to predict SSD after cardiac surgery, namely logit $P = 1.472X_1 + 2.213X_2 + 3.028X_3 + 1.306X_4$, where X_1 is the age (> 70 years old), X_2 is the APACHE II score (> 20 points), X_3 is the length of ICU stay (> 5 d), and X_4 is the duration of sedation use (> 24 h).

Table 1 Univariate analysis between non-delirium, subsyndromal delirium and delirium groups

Variable	Non-delirium (n = 238)	SSD (n = 112)	Delirium (n = 28)	*Omnibus test* (P)	Non-delirium *vs* SSD (P)	Non-delirium *vs* delirium (P)	SSD *vs* delirium (P)
Gender, n (%)				0.106	0.682	0.814	1.000
Male	139 (58.40)	68 (60.71)	17 (60.71)				
Female	99 (41.60)	44 (39.29)	11 (39.29)				
Age // years							
< 70	189 (79.41)	73 (65.18)	11 (39.29)	< 0.001	0.004	< 0.001	0.012
≥ 70	49 (20.59)	39 (34.82)	17 (60.71)				
Education level, n (%)				0.956	0.868	0.783	0.865
≤ 9 years	134 (56.30)	62 (55.36)	15 (53.57)				
> 9 years	104 (43.70)	50 (44.64)	13 (46.43)				

(To be continued)

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Variable	Non-delirium (n = 238)	SSD (n = 112)	Delirium (n = 28)	*Omnibus test* (P)	Non-delirium *vs* SSD (P)	Non-delirium *vs* delirium (P)	SSD *vs* delirium (P)
Alcoholism, n (%)							
Yes	142 (59.66)	73 (65.18)	18 (64.29)	0.586	0.323	0.637	0.929
No	96 (40.34)	39 (34.82)	10 (35.71)				
Smoking, n (%)							
Yes	115 (48.322)	56 (50.00)	12 (42.86)	0.795	0.769	0.584	0.499
No	123 (51.68)	56 (50.00)	16 (57.14)				
Hypertension, n (%)							
Yes	46 (19.33)	28 (25.00)	8 (28.57)	0.319	0.225	0.250	0.699
No	192 (80.67)	84 (75.00)	20 (71.43)				
Diabetes disease, n (%)							
Yes	44 (18.49)	31 (27.68)	9 (32.14)	0.066	0.051	0.087	0.640
No	194 (81.51)	81 (72.32)	19 (67.86)				
APACHE II score//points	19.71 ±5.12	22.09 ±4.87	23.07 ±5.08	0.038	0.034	0.032	0.046
Duration of aortic clamping//h	2.82 ±1.37	3.37 ±1.12	4.46 ±1.53	0.036	0.041	0.028	0.043
Length of ICU stay//d	3.21 ±1.02	5.02 ±2.42	6.16 ±1.81	0.026	0.029	0.016	0.032
Duration of ventilation//h	10.86 ±6.82	12.62 ±8.41	13.15 ±7.29	0.168	0.148	0.245	0.181
Duration of sedation use//h	18.63 ±8.92	24.77 ±9.25	28.96 ±7.78	0.008	0.006	0.004	0.018
Daily sleep time//h	9.72 ±3.29	7.87 ±1.27	5.26 ±2.08	0.037	0.037	0.045	0.041

Note: APACHE II: Acute Physiology and Chronic Health Evaluation II; ICU: intensive care unit; SSD: subsyndromal delirium; h: hour; d: day.

Table 2 Assignment of independent variables in binary logistic regression analysis of factors affecting the occurrence of SSD after cardiac surgery

Independent variable	Assignment method	
Age//years	0 = <70	1 = ≥70
APACHE II score//points	0 = <20	1 = ≥20
Duration of aortic clamping//h	0 = <3	1 = ≥3
Length of ICU stay//d	0 = <5	1 = ≥5
Duration of sedation use//h	0 = <24	1 = ≥24
Daily sleep time//h	0 = >5	1 = ≤24

Note: APACHE II: Acute Physiology and Chronic Health Evaluation II; ICU: intensive care unit; h: hour; d: day.

Table 3 Binary logistic regression analysis of influencing factors of SSD after cardiac surgery

Variable	B	SE	Wald	P value	OR value	95% CI
Constant term	1.682	0.448	5.682	–	–	–
Age//years	1.472	0.387	8.489	0.017	4.328	2.113 – 8.982
APACHE II score//points	2.213	0.341	6.352	0.026	3.271	1.114 – 5.672
Length of ICU stay//d	3.028	0.285	5.182	0.034	3.876	1.037 – 5.247
Duration of sedation use//h	1.306	0.368	7.269	0.021	3.118	1.282 – 4.736

Note: APACHE II: Acute Physiology and Chronic Health Evaluation II; ICU: intensive care unit; h: hour; d: day. B: beta; SE: standard error; OR: odds ratio; CI: confidence interval.

4 Discussion

Cardiac surgery often requires the help of extracorporeal circulation technology, which has the characteristics of long operation time, heavy intraoperative bleeding, and large trauma, and will cause greater stress to the body[1-2,8]. This stress effect will even persist for a period of time after surgery, increasing postoperative complications. As patients undergoing cardiac surgery get older, it is found that more and more patients are prone to postoperative SSD, which increases the length of hospital stay and costs for patients, and imposes a heavy mental burden on patients and their families[18].

SSD is a type of postoperative delirium, which is different from postoperative delirium and has a higher incidence in the ICU[19]. This study found that the incidence of SSD after cardiac surgery was 29.63% (112/378), which was consistent with most reports in the literature. Through univariate and logistic regression analysis, this study found that age > 70 years, APACHE II score > 20 points, length of ICU stay > 5 d and duration of sedation use > 24 h were independent risk factors for SSD after cardiac surgery (P < 0.05). It is suggested that preventive work should be done in the treatment of such patients, the state of consciousness should be closely observed after surgery, and timely intervention should be carried out.

With the development of cardiac surgery techniques, age is no longer a contraindication to major cardiac surgery. In recent years, more and more people over the age of 70 have undergone

heart surgery, which makes medical personnel must pay attention to the influence of age[5,8,11,20]. With the increase of age, the function of various organs gradually declines, especially many elderly patients have a variety of underlying diseases, and the probability of accidents during and after surgery for these patients is greatly increased[21]. Studies have found that advanced age is very likely to cause postoperative delirium, which is mainly related to factors such as neuronal apoptosis, imbalance of white matter and substantianigra, decreased cerebral blood flow, and changes in neurotransmitters. Therefore, we need to pay more attention to the psychological status of elderly patients before surgery, and take relevant measures to alleviate the changes in cognitive function caused by environmental changes, surgery and other factors after surgery.

The APACHE II score is a reliable indicator for judging the severity of the disease in patients, and is closely related to the severity and prognosis of the disease[22]. Patients with APACHE II score >20 are critically ill, often accompanied by unstable vital signs and organ function, which greatly increases the risk of surgery. In addition, the APACHE II score, which includes two factors, age and emergency surgery, has been shown to be closely related to the occurrence of postoperative SSD, suggesting that the APACHE II score can be used as a reliable means to predict the occurrence of postoperative SSD[23]. Periodically assess the severity of the patient's disease, aggressively treat the primary disease, and reduce the severity of the patient's disease, thereby reducing the risk of delirium[24].

The results of this study suggest that the use of sedatives for more than 24 h is an independent risk factor for the development of SSD. Sedative drug therapy is a common treatment measure for ICU patients, which can relieve the pain of the patient, relieve the pain of the patient, and help the patient to fall asleep[25]. However, after the patient uses more sedative drugs, it will affect the transmission of the body's pain signals, affect the body's sensitivity to internal and external environmental stimuli, and cause the patient to respond slowly, fatigue, and impaired cognitive function, which may easily induce the occurrence of delirium syndrome[26]. Therefore, healthcare providers should assess the patient's sedation status from time to time and minimize the dose and duration of sedatives to reduce the risk of sedative-induced subdelirium.

The results of this study showed that the longer the ICU stay, the higher the degree of delirium, which is consistent with the findings before[6,8,10]. The reason for this may be related to the fact that the ICU treats patients at different times and provides continuous and uninterrupted treatment[27]. Light and noise severely affect the patient's rest and sleep, leading to disturbances in the sleep-wake cycle. The patient suffers both physically and mentally, which exacerbates the anxiety, and affects the function of the cerebral cortex, leading to the occurrence of psychiatric symptoms[1-2,5,12]. In addition, due to physical discomfort caused by intubation during treatment, uncertain treatment prognosis, heavy economic burden, social isolation and other reasons, it is easy to cause psychological tension and discomfort in patients after cardiac surgery[10-11]. Depression, burnout, inattention, emotional instability and other symptoms appear in SSD. Therefore, it is necessary to actively identify the causes, improve the ICU environment, reduce noise and light stimulation, promote patients' sleep, and shorten the ICU stay time, thereby reducing the risk of delirium.

5 Conclusions

In conclusion, the incidence of subdelirium was 29.63%, age > 70 years, APACHE II score > 20, ICU stay > 5 d, and sedative drug use > 24 h were independent risk factors for SSD after cardiac surgery in adults. Patients undergoing cardiac surgery should be comprehensively evaluated in clinical work, and appropriate preventive measures should be taken for patients with these risk factors to reduce the incidence of SSD. However, there are still shortcomings in this study: only a prediction model was constructed, and no further model validation was carried out. Subsequent research will focus on the validation of the model and further optimize the model.

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heart failure, did not show a significant advantage. Considering the small sample size and short follow-up time associated with this study, it is necessary to increase the sample size and prolong the follow-up time for further exploration in the future.

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