ISSN: 1607-8322, e-ISSN: 2220-5799 Anaesthesia, Pain & Intensive Care
Vol 27(6); December 2023 DOI:10.35975/apic.v27i6.2354

ORIGINAL RESEARCH CARDIAC ANESTHESIA

Incidence and risk factors for delirium after open heart surgery with cardiopulmonary bypass

Thang Toan Nguyen[1], Do Dinh Ta[2], Hai Sy Ho[3], Hung Duc Duong[4]

Author affiliations:

1. Thang Toan Nguyen, Center for Anesthesia and Intensive Care, Bach Mai Hospital / Department of Anesthesia and Intensive Care, Hanoi Medical University, Hanoi, Vietnam; E-mail: nguyentoanthang@hmu.edu.vn; ORCID: {0009-0006-5866-3036}
2. Do Dinh Ta, Viet Nam National Heart Institute, Bach Mai Hospital, Hanoi, Vietnam; E-mail: tadinhdo106@gmail.com; ORCID: {0009-0000-0897-2726}
3. Hai Sy Ho, Center for Anesthesia and Intensive Care, Bach Mai Hospital, Hanoi, Vietnam; E-mail: haigmhshmu@gmail.com; ORCID: {0009-0001-0991-8833}
4. Hung Duc Duong, Viet Nam National Heart Institute, Bach Mai Hospital, Hanoi, Vietnam; E-mail: duongdh38@yahoo.com

Correspondence: Thang Toan Nguyen, Center for Anesthesia and Surgical Intensive Care, Bach Mai Hospital, Hanoi, Vietnam, 78 Giai Phong, Dong Da, Hanoi, 100000, Vietnam; E-mail: nguyentoanthang@hmu.edu.vn

ABSTRACT

Background & objectives: Postoperative delirium is a prevalent complication, particularly following cardiac surgery, and has detrimental effects on patient outcomes, including increased morbidity and mortality and prolonged stays in the intensive care unit. This study aims to estimate the incidence and identify the risk factors for delirium.

Methodology: This prospective observational study was conducted on adult patients undergoing open-heart surgery with cardiopulmonary bypass at the Cardiovascular Surgery Unit at Bachmai Hospital, Vietnam. The Confusion Assessment Method for the ICU (CAM-ICU) was utilized to assess delirium twice daily during the initial four days post-surgery. Perioperative variables were analyzed by univariable and multivariable logistic regression.

Results: Among the 285 patients included in this study, 56 were diagnosed with delirium using the CAM-ICU, representing a prevalence rate of 19.6%. Multivariate regression analysis revealed several independent risk factors for delirium, including advanced age (odd ratio - OR; 95% confidence interval-CI) (1.07; 1.03-1.10), a history of cerebrovascular accident (3.95; 1.31-11.84), prolonged cardiopulmonary bypass duration (1.02; 1.00-1.03), postoperative atrial fibrillation (2.47; 1.15-5.28), and opioid use time (13.65; 5.69-32.75).

Conclusion: The incidence of delirium after open heart surgery with cardiopulmonary bypass was 19.6%. Advanced age and a history of cerebrovascular accidents were identified as non-modifiable risk factors for postoperative delirium. Meanwhile, there were three modifiable risk factors, including cardiopulmonary bypass duration, atrial fibrillation, and the time of opioid administration.

Abbreviations: CAM-ICU: Confusion Assessment Method for the Intensive Care Unit

Key words: Postoperative Delirium; Risk Factors; Incidence; Open-Heart Surgery; Cardiac Surgery

Citation: Nguyen TT, Ta DD, Ho HS, Duong HD. Incidence and risk factors for delirium after open heart surgery with cardiopulmonary bypass. Anaesth. pain intensive care 2023;27(6):639−645; **DOI:** 10.35975/apic.v27i6.2354

Received: Oct 04, 2023; **Revised:** Oct 28, 2023; **Accepted:** Oct 31, 2023

1. INTRODUCTION

According to The American Psychiatric Association's fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5),[1] delirium is defined as a condition with five key features: a disturbance in attention and awareness; this disturbance only occurs from hours to a few days; it represents a change from baseline attention and awareness, and it usually fluctuates in severity depending on the time of the day. Delirium also may express itself as an disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception). These changes in mental status are not explained by other pre-existing, established, or evolving neurocognitive disorders and do not occur in the context of a severely reduced level of arousal, such as a coma. Also, these do not relate to the side effects of other medical conditions, substance intoxication or withdrawal (i.e., due to drug abuse or a medication), exposure to a toxin, or are due to multiple etiologies.[2–4] Delirium after surgery is very common, and has been associated with adverse outcomes, such as prolonged hospitalization, increased mortality, and prolonged cognitive impairment.[5,6]

The gold standard for delirium diagnosis is evaluation by a psychiatrist using DSM-5 criteria, which is not feasible in the ICU. There are many validated instruments to assess delirium in critically ill patients, and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) is one of the most widely studied and recommended instruments by the Society of Critical Care Medicine's 'Pain, Agitation, and Delirium guidelines' for monitoring delirium in ICU patients because of its simplicity, flexibility, and efficacy.[6]

Until now, there have not been any pharmacological interventions that have proven to be effective, so the identification of risk factors for delirium is very important, especially in cardiac surgery patients. This helps doctors and nurses to have a suitable attitude and practice in the perioperative period to reduce the risk of delirium. Therefore, we conducted this study to assess the incidence and identify the risk factors for delirium after open-cardiac surgery with cardiopulmonary bypass.

2. METHODOLOGY

2.1. Study design

This study was conducted at the Cardiac Surgery Unit at Bach Mai Hospital, Vietnam, between December 2020 and May 2021, as an observational prospective study involving adult patients aged 18 y and above, who underwent cardiac surgery with cardiopulmonary bypass. Consent to participate in the study was obtained from each patient. Patients with conditions that hindered delirium assessment using the CAM-ICU, such as dementia or deafness, as well as those with severe complications like stroke or who expired during the study, were excluded from the study. The existence of delirium before surgery also excluded the patient from the study.

2.2. Anesthesia and surgery

All the patients received standard care, including an examination one-day before their surgery to take their history and evaluate their physical, mental, and cognitive status. All patients received general anesthesia; induction by midazolam, etomidate, fentanyl and rocuronium, and maintenance of anesthesia with TCI propofol, fentanyl and rocuronium, in combination with sevoflurane or isoflurane inhalation. They also received tranexamic acid and prophylactic antibiotics. Heparin was used to stop blood clot formation during cardiopulmonary bypass (CPB), and protamine sulphate was used to reverse the heparin's effects after CPB stopped. These drugs were used according to ACT guidelines during surgery. The pump flow rate in running CPB was between 2.4 and 2.8 L/min/m^2; mean blood pressure was maintained between 60 and 90 mmHg, and mild hypothermia was induced at 33 °C and 35 °C. After surgery, the patient was transferred to the recovery room, sedated with midazolam and fentanyl, and extubated when all criteria were met.

Postoperative analgesia included intravenous patient–controlled analgesia using morphine or erector spinae plane (ESP) nerve block using ropivacaine through catheter for the first three days postoperatively, combined with other pain relievers such as paracetamol and nonsteroidal anti-inflammatory drugs.

As part of the study, questionnaires, physical tests, and medical records, were used to get information about the patients. This included demographic information, e.g., age, gender, ASA physical status classification system, NYHA, EuroSCORE II, and medical histories like hypertension, cerebrovascular accident, diabetes, and history of alcohol abuse. Operative time, CPB time, aortic cross-clamp time, and number of drainages were noted. After surgery, number of days using benzodiazepines, opioids, mechanical ventilation duration, occurrence of acute renal failure and blood transfusion after surgery were recorded. Hypotension was defined as mean arterial pressure of less than 60 mmHg.

2.3. Delirium assessment

The diagnostic tool to evaluate delirium after surgery was the CAM-ICU, which allows for the diagnosis of delirium in both mechanically ventilated and extubated patients. The CAM-ICU includes four assessment steps: (1) acute change or fluctuating mental status, (2) decreased attention, (3) disoriented thinking, and (4) altered mental status. A patient was diagnosed with delirium when both features (1) and (2) were present, along with either feature (3) or (4). The evaluation was performed by the investigator or nurses who were trained to assess delirium using the CAM-ICU. Delirium was assessed twice daily at 7:00 and 18:00 hours in the first four days after surgery.

2.4. Statistical analysis

The data were analyzed using SPSS 20.0 software.

Table 1: The characteristics of perioperative variables

Variables		All patients (n = 285)	Delirium (n = 56)	Non-delirium (n = 229)	p value
Age	Years	56.1 ± 12.4	62.1 ± 11.1	54.6 ±12.4	**< 0.001**
Sex	Male	147 (51.6)	32 (21.8)	115 (78.2)	0.055
	Female	138 (48.4)	24 (17.4)	114 (82.6)	
History of arterial hypertension		72 (25.3)	20 (35.7)	52 (22.7)	**0.047**
History of stroke		27 (9.5)	9 (16.1)	18 (7.9)	**0.045**
ASA classification	3-4	66 (23.2)	19 (33.9)	47 (20.5)	**0.033**
EuroSCORE II	≥ 1.6%	152 (53.3)	41 (73.2)	111 (48.5)	**0.001**
Preoperative values	Na+ (mmol/L)	138.4 ± 2.9	137.6 ± 3.1	138.7 ± 2.9	**0.016**
	Albumin (G/L)	41.0 ± 5.1	39.6 ± 6.7	41.37 ± 4.4	0.083
	GFR (mL/m)	68.0 ± 19.3	61.6 ± 17.9	69.6 ± 19.3	**0.005**
	EF (%)	59.4 ± 11.4	57.9 ± 11.9	59.81 ± 11.3	0.280
Type of surgery	VS	220 (77.2)	39 (69.6)	181 (79.0)	0.096
	CABG	52 (18.2)	21 (40.4)	31 (59.6)	
	Other	13 (4.4)	7 (53.8)	4 (47.2)	
CPB time (min)		88.8 ± 30.6	103.4 ± 36.6	85.3 ± 27.8	**< 0.001**
Aortic clamp time (min)		59.7 ± 24.5	70.7 ± 28.1	57.0 ± 22.8	**< 0.001**
Surgery time (min)		185.8 ± 50.2	207.9 ± 51.3	180.4 ± 48.6	**< 0.001**
Ventilator time (days)		1.4 ± 0.9	1,8 ± 1.0	1.3 ± 0.7	**0.005**
Benzodiazepine use (days)		1.4 ± 0.9	1.9 ± 1.4	1.2 ± 0.7	**0.000**
Opioid use (days)		2.4 ± 1.0	3.2 ± 1.3	2.2 ± 0.8	**0.000**
Number of surgeries	≥ 2 types	56 (19.6)	17 (30.1)	39 (17.0)	**0.024**
Number of drainages	≥ 3	84 (29.4)	25 (44.6)	59 (25.8)	**0.005**
Days of drainages	> 3 days	202 (70.9)	48 (85.7)	154 (67.2)	**0.006**
Blood transfusion		239 (83.9)	53 (94.6)	186 (81.2)	**0.014**
Postoperative complications	AF	101 (35.4)	27 (48.2)	74 (32.3)	**0.026**
	AKI	224 (78.6)	50 (89.3)	174 (76.0)	**0.03**
	Hypotension	55 (19.3)	16 (28.6)	39 (17.0)	0.05
	Na+ disorder	211 (74.0)	39 (69.6)	172 (75.1)	0.403

Values are presented as mean ± standard deviation, or number (%). p-values were determined by t-test, chi-square test, or Fisher's exact test; GFR, glomerular filtration rate; EF, ejection fraction; CPB, cardiopulmonary bypass; CABG, coronary artery bypass graft; VS: valve surgery; AF: atrial fibrillation; AKI: acute kidney injury

Quantitative variables were described as mean and standard deviation ($\bar{X}$, SD). The two mean values were compared using the t-test for standard variables and the Mann-Whitney U test for non-standard variables. Qualitative variables were described as numbers (n) and percentages and tested using the chi-squared test. Odds ratios (ORs) were calculated to show the effect size of perioperative risk factors. Then, the statistically significant risk factors after univariate analysis ($P < 0.05$) were entered into a logistic multivariable regression model, which was based on the model's fit (Hosmer & Lemeshow Test $P > 0.05$) to find the most powerful model. The difference was considered statistically significant at $P < 0.05$.

2.5. IRB approval

We conducted this study in compliance with the principles of the Declaration of Helsinki. The study's protocol was reviewed and approved by the Hanoi Medical University Ethical Review Board vide No. 5161/QĐ-ĐHYHN. Written informed consent was obtained from all patients.

3. RESULTS

There were 285 eligible patients enrolled in the study. Among them, 56 (19.6%) had delirium and 229 (80.4%) had no delirium. The average age of the patients was 56.1 ± 12.5 y, and the average EuroSCORE II value was 2.9 ± 3.3. The most common surgery was valve surgery (77.2%). Table 1 shows the main patient characteristics and the results of the univariate analysis.

Patients with delirium were older and had a higher frequency of comorbidities (higher EuroSCORE II, higher ASA physical status, and history of stroke) than the non-delirium group. Regarding the surgical procedure, there were statistical differences in cardiopulmonary bypass time (CPB), surgery duration, and aortic clamp times between patients with delirium and without delirium. Post-operative variables witnessed differences between the two groups including the duration of mechanical ventilation, benzodiazepine use, and opioid use. The rate of post-operative complications was similar in the delirium and non-delirium groups (Table 1).

The majority of delirium cases manifested on the first day after surgery, accounting for 44.6% of the total delirium patients, and the incidence gradually declined over the subsequent days. 46.4% of patients suffered from delirium during the first two days, while only three patients had delirium for more than three days. In terms of recording time, the evening period accounted for the highest proportion at 58.3% (Table 2; Figures 1 and 2).

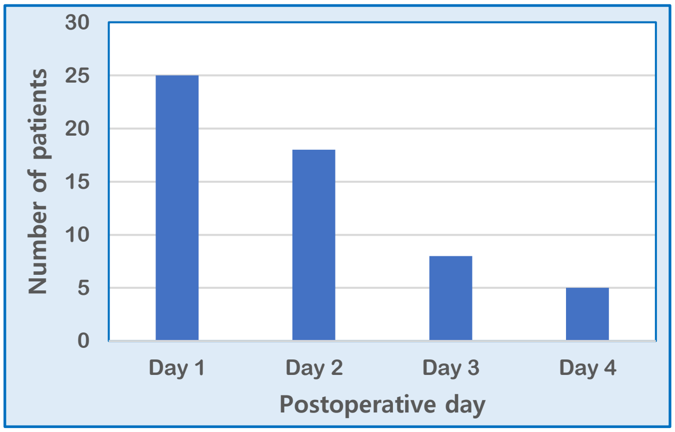

Figure 1: The number of patients with delirium and the postoperative day

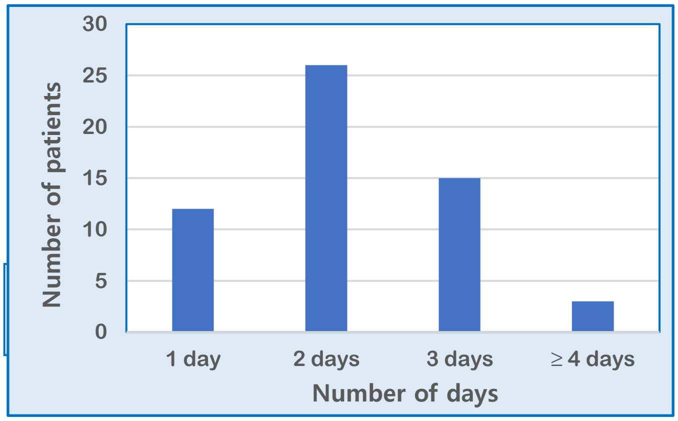

Figure 2: The number of patients with delirium and the number of days of delirium

Table 2: The distribution of patients according to onset time and the duration of delirium

Onset time	Number of cases
Day 1	25 (44.6)
Day 2	18 (32.1)
Day 3	8 (14.2)
Day 4	5 (8.9)
Duration	**Number of cases**
1 day	12 (21.4)
2 days	26 (46.4)
3 days	15 (26.8)
≥ 4 days	3 (5.4)

Values are presented as number and percentage (%).

A multiple logistic regression analysis performed on these risk factors above identified five independent risk factors associated with delirium. Factors associated with delirium are shown in Table 3, including advanced age, a history of cerebrovascular accidents, a prolonged CPB duration, postoperative atrial fibrillation, and time of opioid use, with an adjusted OR of 1.07, 3.95, 1.02, 2.47, and 13.65, respectively.

4. DISCUSSION

Postoperative delirium in our study had an incidence of 19.6%, which falls within the reported range of 4.1 – 54.9% in the literature for cardiac surgery patient.[2,7]

Delirium predominantly occurred during the first three days following surgery and rarely extended beyond four

Table 3: Multivariate analysis factors associated with delirium

Risk factors	OR	95% CI	P-value
Age	1.07	1.03-1.10	**< 0.001**
Stroke history	3.95	1.32-11.84	**0.014**
CPB time	1.02	1.00-1.03	**0.001**
Postoperative atrial fibrillation	2.47	1.15-5.28	**0.02**
Duration of opioid use	13.65	5.68-32.75	**< 0.001**

P < 0.05 considered significant; OR: odd ratio; CI: confidence interval; CPB: cardiopulmonary bypass. This was based on the model's fit (Hosmer & Lemeshow Test).

days, aligning with findings from previous studies.[8] However, in our study, we found other factors that may be related to this problem. Several risk factors such as the length of mechanical ventilation, the level of sodium during surgery, and the EuroSCORE II, showed statistically significant differences between the two groups. However, multivariate regression analysis found that older age, a history of stroke, prolonged cardiopulmonary bypass duration, atrial fibrillation after surgery, and opioid use were the only ones that were independently linked to postoperative delirium.

Advanced age has consistently been recognized as a risk factor for postoperative delirium, with several underlying explanations.[2,3] Ageing is often accompanied by the progression of atherosclerotic plaques in major arteries, predisposing individuals to cerebral hypoperfusion and thromboembolism. Chronic cerebral ischemia resulting from carotid artery stenosis can lead to white matter damage. Intraoperative factors such as reduced cerebral oxygen supply due to narrowed blood vessels, hypotension, and hypoxemia can contribute to postoperative brain dysfunction.[7] Moreover, aging is associated with a decline in the cholinergic pathway, a neurotransmitter system implicated in delirium. Dysregulation in acetylcholine synthesis, involving precursors, enzymes, and receptors, can contribute to delirium. Additionally, brain injury, such as cerebral ischemia and stress, can significantly deplete acetylcholine levels. An imbalance between cholinergic and other neurotransmitters can trigger delirium.[9] Age-related reductions in brain volume, weight, and neuronal density may further account for the heightened susceptibility to delirium in the elderly.

The incidence of delirium has consistently been found to be higher in individuals with a history of stroke compared to those without stroke in numerous international studies.[10-13] Stroke patients often experience impaired brain function and are more likely to have comorbidities such as hypertension, dyslipidemia, and atherosclerosis. Atherosclerosis, characterized by intense inflammatory responses in elderly patients, can result in reduced cerebral perfusion and the formation of microthrombi.[14]

Previous research by Sabol F et al. has demonstrated a correlation between delirium development and prolonged cardiopulmonary bypass (CPB) time as well as extended aortic clamp time.[14] Rudolph JL et al. study further revealed that an aortic clamp time exceeding 68 min was associated with an increased risk of postoperative delirium.[15] One possible explanation for this association is that the combination of cerebral atherosclerosis and postoperative inflammatory changes may impede cerebral blood flow, which is exacerbated by the non-pulsatile nature of CPB during circulatory arrest. The study by Brown WR et al.[16] supported these findings by indicating that longer operative and CPB durations were linked to an elevated risk of air embolism in the brain. Lengthy surgical procedures, often involving complex interventions on the heart and major blood vessels, pose a higher risk of blood clot formation. In a meta-analysis with 14 studies in 2021, Haiyan Chen et al. failed to find the relationship between aortic cross-clamp time and the increase in postoperative delirium rate.[7] So more studies are needed to verify this factor.

Atrial fibrillation has been consistently identified as an independent risk factor for postoperative delirium in various studies.[10,18] It is believed that atrial fibrillation contributes to delirium through mechanisms such as cerebral hypoperfusion resulting from thromboembolic events and the intraoperative or postoperative decrease in arterial blood pressure associated with this arrhythmia.[19] However, our study did not find a relationship between preoperative atrial fibrillation and delirium incidence. Interestingly, we observed a higher rate of delirium in the postoperative atrial fibrillation group compared to the group without postoperative atrial fibrillation (26.7% versus 15.8%), with statistical significance (P = 0.026). The odds ratio (95% CI) was 1.95 (1.08-3.53), indicating postoperative atrial fibrillation as a risk factor for delirium after surgery. This may be attributed to various factors influencing hemodynamics, coagulation disorders, and reduced cerebral perfusion associated with surgery, which are more prominent in postoperative atrial fibrillation cases. Conversely, patients often receive optimal medical therapy and anticoagulation preoperatively, which may explain the lack of association between preoperative atrial fibrillation and delirium.

Benzodiazepines and opioids are commonly used in general anesthesia for their sedative and analgesic effects respectively. Existing literature suggests that these drugs can contribute to the onset of delirium, although there is conflicting evidence.[20] In our study, the duration of benzodiazepine use in the delirium group was significantly longer than that in the non-delirium group. However, multivariate analysis did not identify benzodiazepine use as an independent risk factor for delirium. Conversely, duration of opioid use increases the likelihood of the emergence of delirium with an odds ratio of 13.65 (95% CI 5.69-32.75). Although the evidence of the effect of these drugs on delirium is not clear, caution should be exercised to avoid excessive use of opioid analgesics or minimize it as much as possible.[4,20]

5. LIMITATIONS

Several limitations should be acknowledged in our study. Firstly, the study did not specifically focus on different types of operations, as the rate and underlying mechanisms of delirium can vary among surgical procedures. Secondly, we did not evaluate the impact of vasopressor use, opioid consumption, duration and severity of hypotension on delirium. Thirdly, postoperative analgesia methods varied, and we did not assess postoperative pain, which is a known risk factor for delirium. Lastly, the study did not assess other psychological factors, such as family support and sleep, which may play a significant role in developing postoperative delirium.

6. CONCLUSIONS

The incidence of delirium after open heart surgery with cardiopulmonary bypass was 19.6%. Advanced age and a history of cerebrovascular accidents were identified as non-modifiable risk factors for postoperative delirium. Meanwhile, there were three modifiable risk factors including cardiopulmonary bypass duration, postoperative atrial fibrillation, and opioid use time.

7. Conflict of interest

The authors made no declarations regarding potential conflicts.

8. Funding

No external or industry funding was involved in this study.

9. Acknowledgments

We gratefully thank the colleagues and staff in the operating theater and cardiac intensive care unit for their cooperation in data collection.

10. Authors' contribution

1. NTT: conceptualization, investigation, methodology, project administration, resources, supervision, validation, writing – review and editing
2. TDD: data curation, formal analysis, investigation, methodology, and writing the original draft.
3. HSH: analysis, investigation, software, validation, and writing the original draft.
4. DDH: conceptualization, methodology, resources, supervision, review and editing.

11. REFERENCES

1. American Psychiatric Association D-TF. Diagnostic and statistical manual of mental disorders: DSM-5™ (5th ed.). American Psychiatric Publishing 2013; DOI: 10.1176/appi.books.9780890425596
2. Asghar A, Siddiqui KM, Ahsan K, Chughtai S. Postoperative delirium after cardiac surgery; incidence, management and prevention. INTENSIVE CARE. 2017;21.
3. Gani H, Prifti P, Naco M, et al. The incidence of postoperative delirium in elderly patients undergoing urologic surgery. INTENSIVE CARE. 2012;16. Medical archives (Sarajevo, Bosnia and Herzegovina), 67(1), 45–47. DOI: 10.5455/medarh.2013.67.45-47
4. Järvelä K, Porkkala H, Karlsson S, Martikainen T, Selander T, Bendel S. Postoperative Delirium in Cardiac Surgery Patients. J Cardiothorac Vasc Anesth. 2018;32(4):1597-1602. DOI: 10.1053/j.jvca.2017.12.030
5. Lin, L., Zhang, X., Xu, S., Peng, Y., Li, S., Huang, X., Chen, L., & Lin, Y. (2022). Outcomes of postoperative delirium in patients undergoing cardiac surgery: A systematic review and meta-analysis. Frontiers in cardiovascular medicine, 9, 884144. DOI: 10.3389/fcvm.2022.884144
6. Needham, D. M., Slooter, A. J. C., Pandharipande, P. P., Watson, P. L., Weinhouse, G. L., Nunnally, M. E., Rochwerg, B., Balas, M. C., van den Boogaard, M., Bosma, K. J., Brummel, N. E., Chanques, G., Denehy, L., Drouot, X., Fraser, G. L., Harris, J. E., Joffe, A. M., … Alhazzani, W. (2018). Clinical Practice Guidelines for the Prevention and Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU. Critical care medicine, 46(9), e825–e873. DOI: 10.1097/CCM.0000000000003299
7. Chen H, Mo L, Hu H, Ou Y, Luo J. Risk factors of postoperative delirium after cardiac surgery: a meta-analysis. J Cardiothorac Surg. 2021;16(1):113. DOI: 10.1186/s13019-021-01496-w
8. Cereghetti C, Siegemund M, Schaedelin S, et al. Independent Predictors of the Duration and Overall Burden of Postoperative Delirium After Cardiac Surgery in Adults: An Observational Cohort Study. J Cardiothorac Vasc Anesth. 2017;31(6):1966-1973. DOI:10.1053/j.jvca.2017.03.042
9. Hshieh TT, Fong TG, Marcantonio ER, Inouye SK. Cholinergic Deficiency Hypothesis in Delirium: A Synthesis of Current Evidence. J Gerontol A Biol Sci Med Sci. 2008;63(7):764-772. DOI: 10.1093/gerona/63.7.764
10. Deiner S, Silverstein JH. Postoperative delirium and cognitive dysfunction. Br J Anaesth. 2009;103:i41-i46. DOI:10.1093/bja/aep291

11. Ordonez-Velasco L, Hernández-Leiva E. Factors associated with delirium after cardiac surgery: A prospective cohort study. Ann Card Anaesth. 2021;24(2):183. DOI: 10.4103/aca.ACA_43_20

12. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. The Lancet. 2014;383(9920):911-922. DOI: 10.1016/S0140-6736(13)60688-1

13. Pol RA, Van Leeuwen BL, Reijnen MM, Zeebregts CJ. The relation between atherosclerosis and the occurrence of postoperative delirium in vascular surgery patients. Vasc Med. 2012;17(2):116-122. DOI: 10.1177/1358863X11429723

14. Sabol F, Bilý B, Artemiou P, et al. Incidence and risk factors of delirium in patients after cardiac surgery: Modifiable and non-modifiable factors. Cor Vasa. 2015;57(3):e168-e175. DOI: 10.1016/j.crvasa.2015.01.004

15. Rudolph JL, Jones RN, Levkoff SE, et al. Derivation and Validation of a Preoperative Prediction Rule for Delirium After Cardiac Surgery. Circulation. 2009;119(2):229-236. DOI: 10.1161/CIRCULATIONAHA.108.795260

16. Brown WR, Moody DM, Challa VR, Stump DA, Hammon JW. Longer Duration of Cardiopulmonary Bypass Is Associated With Greater Numbers of Cerebral Microemboli. Stroke. 2000;31(3):707-713. DOI: 10.1161/01.STR.31.3.707

17. Smulter N, Lingehall HC, Gustafson Y, Olofsson B, Engström KG. Delirium after cardiac surgery: incidence and risk factors. Interact Cardiovasc Thorac Surg. 2013;17(5):790-796. DOI: 10.1093/icvts/ivt323

18. Banach M, Mariscalco G, Ugurlucan M, Mikhailidis DP, Barylski M, Rysz J. The significance of preoperative atrial fibrillation in patients undergoing cardiac surgery: preoperative atrial fibrillation--still underestimated opponent. Europace. 2008;10(11):1266-1270. DOI: 10.1093/europace/eun273

19. Zaal IJ, Devlin JW, Peelen LM, Slooter AJC. A Systematic Review of Risk Factors for Delirium in the ICU*: Crit Care Med. 2015;43(1):40-47. DOI: 10.1097/CCM.0000000000000625

20. Hori Y, Mihashi M. Relationship Between Delirium Development and Its Causative Factors in the Intensive Care Unit After Cardiac Surgery. Yonago Acta Med. 2023;66(2):214-222. DOI: 10.33160/yam.2023.05.003

