BMC Cardiovascular Disorders

RESEARCH

Open Access

Amiodarone use and prolonged mechanical ventilation after cardiac surgery: a single-center analysis

Xin Li[1†], Haitao Zhang[1†], Yuanxi Luo[1†], Jiqing Zhu[3*], Dongjin Wang[1*] and Li Xu[2*]

Abstract

Background Prolonged mechanical ventilation (PMV) after cardiac surgery increases the risk of complications such as pulmonary atelectasis and ventilator-associated pneumonia. This study aims to investigate the risk factors associated with delayed extubation, including the impact of cardiovascular medication.

Method This retrospective, single-center study analyzed 1,976 patients who underwent open heart surgery at Nanjing Drum Tower Hospital from October 2020 to January 2023. Patients were categorized into early extubation ($n=1071$) and delayed extubation ($n=905$) groups. Multivariate logistic regression was employed to identify risk factors for delayed extubation. Amiodarone were indicated to be associated with delayed extubation. To further address bias, we derived a propensity score predicting the function of Amiodarone on delayed extubation, and matched 228 cases to 684 controls with similar risk profiles.

Results Multivariate analysis confirmed that hypertension, stroke, amiodarone use, age, LVEF, CPB time, and DHCA were significant predictors of delayed extubation. Postoperative use of amiodarone was significantly associated with delayed extubation (OR:1.753, 95%CI: 1.287–2.395, $P<0.001$). PSM analysis further confirmed that patients receiving amiodarone had longer ventilation times, prolonged hospital stays, and higher in-hospital mortality.

Conclusion Postoperative use of amiodarone is a significant predictor of delayed extubation, warranting careful consideration in clinical practice. Further research is needed to clarify the causal relationship between amiodarone use and extubation outcomes.

Keywords Cardiac surgery, Amiodarone, Delayed extubation

†Xin Li, Haitao Zhang and Yuanxi Luo contributed equally to this work.

*Correspondence:
Jiqing Zhu
zhu13814061145@163.com
Dongjin Wang
dongjin_wang@126.com
Li Xu
iamxuli@163.com
[1] Department of Cardiac Surgery, Nanjing Drum Tower Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Graduate School of Peking Union Medical College, Beijing, China
[2] Clinical Trial Institution, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Number 321 Zhongshan Road, Nanjing 210008, China
[3] Department of Anesthesia, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing, China

Background

Prolonged mechanical ventilation (PMV) increases the likelihood of pulmonary atelectasis and ventilator-associated pneumonia [1]. With no doubt that, PMV after heart surgery was associated with an increased risk of morbidity and mortality [2, 3]. Early extubation is a critical component of the cardiac surgical pathway to enhance recovery, allowing for early mobility and oral nutrition. Successful early extubation strategies have also been associated with reduced intensive care unit and hospitalization lengths [4]. There are different definitions of early extubation times, with early extubation occurring between 4–11 h postoperatively and delayed extubation occurring between 15–96 h postoperatively [5–7]. Currently, early extubation is not always possible for all patients.

Studies have analyzed risk factors for delayed extubation. Lynn V. Doering et al. found that patients aged 70 years or older were 11.25 times more likely to be intubated for more than 8 h postoperatively than younger patients, regardless of the surgeon or anesthesiologist [8]. According to Gianfranco Sanson et al., it is not advisable to extubate a patient until they have achieved safe respiratory, oxygen saturation, and hemodynamic conditions, as well as good neurocognitive function [9]. Several post- and peri-operative variables have been purposed as risk factors of delayed extubation, including preoperative cardiac tamponade, central arterial cannulation for cardiopulmonary bypass (CPB), postoperative stroke, postoperative renal dysfunction that required temporary hemodialysis, and re-exploration to stop bleeding [10]. However, there are still some shortcomings that need to be addressed: the relatively small sample size, the singularity of surgery type, and the lack of clarity regarding the definition of delayed extubation time.

As the population ages, patients are more likely to experience postoperative arrhythmias that require control with medications such as amiodarone [11]. Study showed that every 10-year increase in age is associated with a 75% increase in the odds of developing atrial fibrillation [12]. A retrospective study of over 15,000 patients revealed that the prevalence of postoperative atrial fibrillation following cardiac surgery was as high as 58.1% in individuals aged 60 and above, in comparison to 14% in those below 50 years of age [13]. Studies have shown that amiodarone is pulmonary toxic and may induce pulmonary fibrosis, and that postoperative use of amiodarone may affect time on the ventilator. Up until now, there is a lack of studies discussing the impact of postoperative amiodarone use on extubation time.

Based on data from nearly 2,000 cardiac surgery patients in our center, this study aimed to investigate the risk factors for delayed extubation after cardiac surgery. The findings would assist clinicians in predicting postoperative surgical complications and optimizing the use of limited medical resources.

Methods

Study design

This retrospective, single-center study was conducted at Nanjing Drum Tower Hospital, including 1976 consecutively selected patients who underwent open heart surgery from October 2020 to January 2023. This study was approved by the Ethics Committee of Nanjing Drum Tower Hospital (approval number: 2020–249-01).

The study included patients who had open heart surgery under general anesthesia with tracheal intubation. The following patients were excluded: 1) preoperative temperature $\geq$ 38 °C, 2) those who underwent cardiovascular surgery due to trauma, infective endocarditis, tumors, and malignant tumors, 3) preoperative infected patients, 4)patients diagnosed with inflammatory immune disorders or connective tissue disorders, 5) pregnant or breastfeeding patients, 6)without informed consent, 7)patients who died in the ICU, 8) patients who required secondary intubation.

Patient management

All patients were transferred to the ICU of the cardiac surgery department for postoperative monitoring and treatment. Patients were considered ready for an initial spontaneous-breathing trial if they met the following weaning criteria: a respiratory rate of 35 breaths per minute or lower; adequate oxygenation, defined as either an oxygen saturation of at least 90% (obtained during ventilation with a fraction of inspired oxygen [Fio2] of $\leq$ 40% and a positive end-expiratory pressure (PEEP) of $\leq$ 8 cm of water) or a ratio of partial pressure of arterial oxygen (Pao2) (measured in mm Hg) to Fio2 of at least 150 (obtained during ventilation with a PEEP of $\leq$ 8 cm of water); adequate cough; an awake state; no use of continuous sedation; and no use of vasopressors (or use of minimal doses).

Spontaneous breathing for 30 min through a ventilator in continuous positive airway pressure (CPAP) mode with a PEEP of 5 cm H2O.Then the following seven items are checked: (1) Respiratory rate (RR) > 35/min for 5 min or more. (2) Rapid shallow breathing index (RSBI) > 100 cycles/min/L. (3) SaO2 < 90% for 5 min or more. (4) Heart rate (HR) > 120/min, or sustained increase 20% greater than baseline. (5) Systolic blood pressure < 90 mm Hg or > 180 mm Hg for 5 min or more. (6) Emergence of a chest pain or a new electrocardiogram change. (7) Dyspnea, increased anxiety, and diaphoresis. In the event that none of the aforementioned conditions is met, the SBT test is deemed a success and the extubation assessment is

initiated [14–16]. Uniform use of mask oxygenation was applied after tracheal extubation. The patients were classified into two groups based on the duration of mechanical ventilation: the early extubation group (mechanical ventilation time ≤ 12 h) and the delayed extubation group (mechanical ventilation time > 12 h). This creates a balanced match in terms of numbers. In this study, nearly 90% of the patients had ventilation times of less than 26 h. When using 48 h postoperatively as the criterion for delayed ventilation grouping, the delayed ventilation group may be more skewed towards critically ill patients, with only a small number of cases.

Statistical analysis

R version 4.3.1 was used for statistical analysis. Quantitative variables were assessed for normality using the Shapiro–Wilk test. Those conforming to a normal distribution were expressed as mean ± standard deviation (SD), and t-tests were used to compare between groups. Nonparametric continuous variables were expressed as median (interquartile range (IQR)) and compared using the Mann–Whitney U test. Qualitative variables are expressed as percentages (%) and compared using the chi-square test or Fisher's exact test. Multifactor logistic regression incorporating indicators that reached statistical significance in univariate analysis ($P < 0.1$).

It was found that the use of amiodarone after cardiac surgery ($p < 0.001$) was significantly associated with delayed extubation. To reduce confounding factors, we used a propensity matching score (PSM) for 1:3 matching. We selected variables with standardized mean difference (SMD) > 0.2 in the univariate analysis, including age (SMD = 0.198), hypertension, emergency, surgery type, LVEF, CPB, ACC, DHCA, plasma, and platelet, with the use of amiodarone after the current operation as the dependent variable. SMD < 0.20 between matching pairs indicates acceptable balance. All reported P values are two-sided, and values of $P < 0.05$ were considered statistically significant.

Result

Baseline and univariate analysis

A total of 1976 patients were included in the study. The patients were divided into two groups based on the duration of postoperative mechanical ventilation: those ventilated for ≤ 12 h (1071 patients) and those ventilated for > 12 h (905 patients). Age, gender, drink, hypertension, stroke, CKD, MI, history of cardiac surgery, LVEF, emergency surgery, surgery type, CPB, ACC, DHCA, RBC, plasma, platelet, amiodarone are correlated with duration of mechanical ventilation. The baseline data for both groups are detailed in Tables 1 and 2.

Multivariate analysis

To further explore the risk factors for prolonged ventilator time, variables with $P \leq 0.10$ in the univariate analysis were included in the multivariate logistic regression analysis. Those that were statistically significant included: hypertension (OR:1.389, 95%CI: 1.133–1.701, $P = 0.002$), stroke (OR1.701:, 95%CI: 1.135–2.562, $P = 0.010$), amiodarone (OR:1.753, 95%CI: 1.287–2.395, $P < 0.001$), age (OR:1.015, 95%CI: 1.007–1.024, $P < 0.001$), LVEF (OR:0.971, 95%CI: 0.958–0.983, $P < 0.001$), CPB (OR:1.005, 95%CI: 1.001–1.008, $P = 0.005$), DHCA(OR:1.023, 95%CI: 1.010–1.038, $P = 0.001$), plasma(OR:1.001, 95%CI: 1.001–1.001, $P < 0.001$). Detailed results of the multifactor logistic analysis are shown in Fig. 1.

Propensity matching analysis

Study revealed that the postoperative use of amiodarone was a risk factor for delayed extubation. To better control for confounding factors, we matched patients who never use amiodarone postoperatively with those who used it in a 3:1 ratio. Before matching, the SMD values of age, hypertension, emergency, surgery type, LVEF, CPB, ACC, DHCA, plasma, and platelet were 0.198, 0.284, 0.429, 0.459, 0.227, 0.503, 0.455, 0.490, 0.644 and 0.427, respectively. After matching, the SMD values were 0.019, 0.015, 0.004, 0.151, 0.010, 0.004, 0.010, 0.011, 0.031 and < 0.001. SMD before and after matching was shown in Fig. 2. The balance between the two groups was good, and the information of perioperative baseline and characteristics in PSM cohort is shown in Online supplement Table 1. Patients who were administered postoperative amiodarone had a higher proportion of cardiac surgery history (3.5% vs 7.9%, $P = 0.011$), an increased probability of postoperative ventilator time exceeding 12 h (49.1% vs 60.5%, $P = 0.004$), prolonged LOS (17.00 [13.00,21.00] vs 19.00 [16.00,24.00], $P < 0.001$), and increased in-hospital mortality (0.9% vs 4.4%, $P = 0.001$). However, there was no statistically significant difference in ICU length of stay (3.00 [2.00,4.00] vs 3.00 [2.00,5.00], $P = 0.125$) (Online supplement Table 2). The multifactorial logistic regression analysis of matched patients is shown in Table 3.

Subgroup analysis

To better reveal differences in outcomes based on the type of cardiac surgery, we performed a subgroup analyses and the results are shown in Fig. 3. The findings indicated that amiodarone was a risk factor for delayed extubation for all surgical types, after adjusting for confounding variables (hypertension, stroke, amiodarone, age, LVEF, CPB, DHCA and plasma). Subgroup analysis revealed that Isolated CABG (OR: 2.42, 95%CI: 1.01–5.82, $P = 0.047$), AVR or MVR (OR: 2.13, 95%CI:

Table 1 Perioperative baseline and characteristics

Variable	Early Extubation= (*n*=1071)	Delayed Extubation (*n*=905)	*P*
Preoperative variable			
Age (year)	58.00 [50.00, 67.00]	61.00 [52.00, 69.00]	<0.001
Gender (male)	611 (57.0)	564 (62.3)	0.020
BMI $(kg/m)^2$	23.80 [22.00, 26.30]	24.20 [21.90, 26.60]	0.256
Smoke	124 (11.6)	106 (11.7)	0.982
Drink	80 (7.5)	95 (10.5)	0.023
Hypertension	434 (40.5)	494 (54.6)	<0.001
Diabetes	136 (12.7)	109 (12.0)	0.711
Stroke	51 (4.8)	70 (7.7)	0.008
COPD	5 (0.5)	4 (0.4)	1
CAD	238 (22.2)	186 (20.6)	0.398
MI	20 (1.9)	29(3.2)	0.079
CKD	14 (1.3)	28(3.1)	0.010
History of cardiac surgery	43 (4.0)	59(6.5)	0.016
PCI	19 (1.8)	22(2.4)	0.389
LVEF (%)	55.00 [53.00, 58.00]	55.00 [48.00, 58.00]	<0.001
Operative variable			
Emergency	42 (3.9)	151(16.7)	<0.001
Surgery type			<0.001
Isolated CABG	167 (15.6)	131 (14.5)	
AVR or MVR	476 (44.4)	277 (30.6)	
AVR+MVR	122 (11.4)	112 (12.4)	
Valvular surgery + CABG	46 (4.3)	74 (8.2)	
Thoracic aortic surgery	165 (15.4)	271 (29.9)	
Others	95 (8.9)	40 (4.4)	
CPB (min)	114.00 [77.00, 148.00]	149.00 [106.00, 192.00]	<0.001
ACC (min)	78.00 [44.00, 108.00]	104.00 [69.00, 140.00]	<0.001
DHCA (min)	0.00 [0.00, 0.00]	0.00 [0.00, 14.00]	<0.001
RBC (unit)	0.00 [0.00, 3.00]	3.00 [0.00, 6.00]	<0.001
Plasma (ml)	0.00 [0.00, 500.00]	450.00 [0.00, 750.00]	<0.001
Platelet (unit)	0.00 [0.00, 0.00]	0.00 [0.00, 1.00]	<0.001

*COPD:*Chronic obstructive pulmonary disease, *CAD* Coronary Artery Disease, *MI* Myocardial infarction, *CKD* Chronic kidney disease, *PCI* Percutaneous coronary intervention, *LVEF* Left ventricular ejection fraction, *CABG* Coronary artery bypass grafting, *AVR* Aortic valve replacement, *MVR* Mitral valve replacement, *CPB* Cardiopulmonary bypass, *ACC* Aortic cross clamp, *DHCA* Deep hypothermic circulatory arrest, *RBC* Red blood cell

Table 2 Postoperative characteristics

Variable	Early Extubation=(*n*=1071)	Delayed Extubation(*n*=905)	P
Postoperative variable			
Amiodarone	90 (8.4)	138(15.2)	<0.001
Mechanical ventilation Time (hour)	6.00 [4.00, 7.50]	20.00 [16.00, 26.00]	<0.001
LOS (day)	16.00 [13.00, 19.00]	17.00 [14.00, 23.00]	<0.001
ICU (day)	2.00 [2.00, 3.00]	3.00 [2.00, 5.00]	<0.001
Death in hospital	3 (0.3)	31 (3.4)	<0.001

LOS Length of stay, *ICU* Intensive care unit

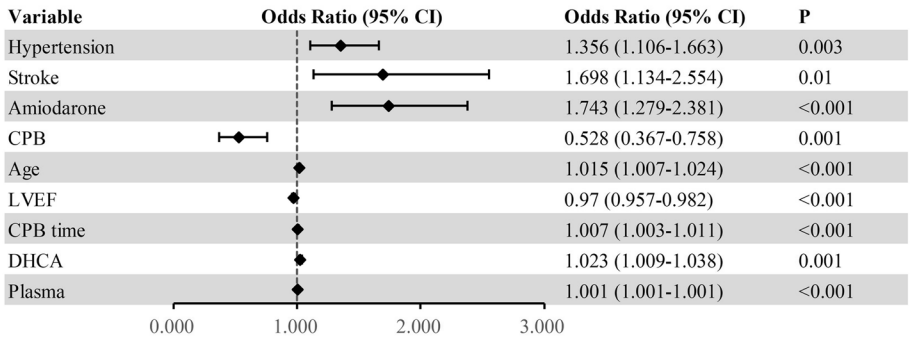

Fig. 1 Multivariate analysis of factors associated with delayed extubation, with 95% confidence intervals (CI), showed that amiodarone was associated with delayed extubation (1.753, 95%CI:1.287–2.395, $P < 0.001$)

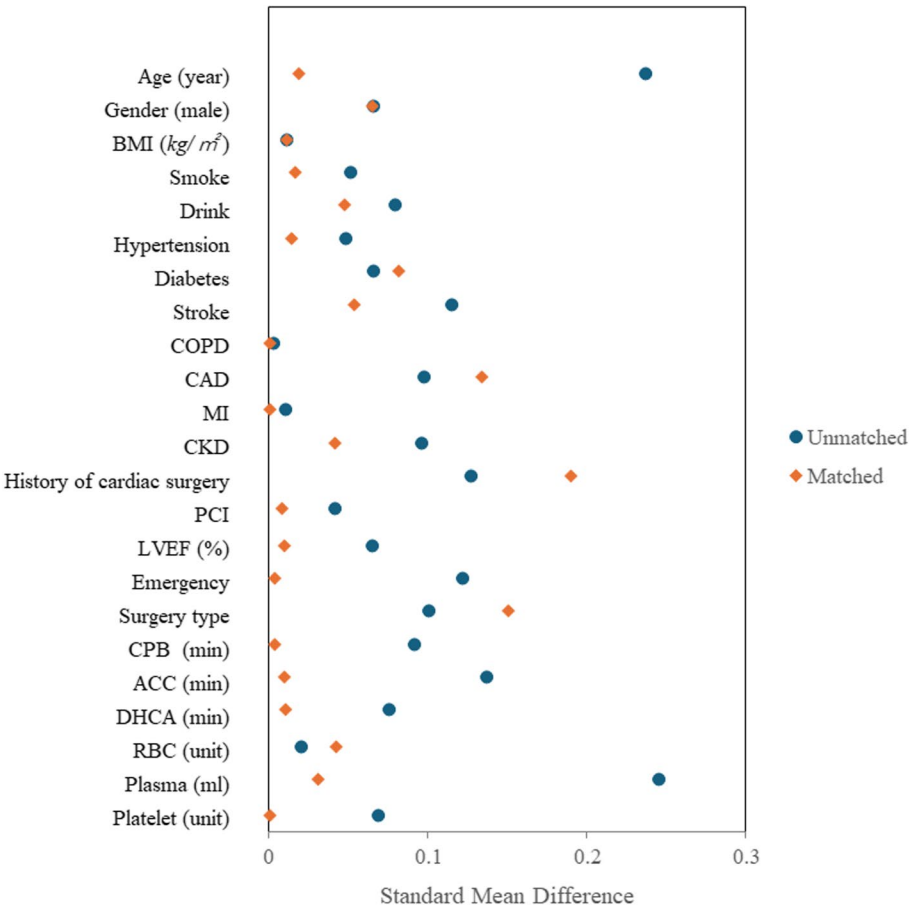

Fig. 2 Standardized mean difference (SMD) before and after matching, showed that there was a decrease in the SMD values

1.33–3.42, $P = 0.002$), and Others (OR: 4.44, 95%CI: 1.26–15.6, $P = 0.020$), suggesting that amiodarone were identified as risk factors for delayed extubation in these three surgical categories. In the case of AVR + MVR (OR: 0.63, 95%CI: 0.25–1.59, $P = 0.333$), Valvular surgery + CABG (OR: 0.64, 95%CI: 0.16–2.59, $P = 0.532$), and thoracic aortic surgery (OR: 1.54, 95%CI: 0.72–3.29, $P = 0.260$), no statistically significant associations were identified.

Discussion

This investigation elucidates that hypertension, stroke, postoperative use of amiodarone, performance of cardiopulmonary bypass (CPB), increasing age, decreased LVEF,

Table 3 Multivariate analysis of factors associated with delayed extubation in propensity-matched cohort

Variable	Odds Ratio	95% Confidence Interval	*P* Value
amiodarone	1.797	1.278-2.536	0.001
age	1.025	1.010-1.039	0.001
LVEF	0.968	0.948-0.987	0.001
CPB	1.010	1.002-1.018	0.016
DHCA	1.033	1.012-1.058	0.003
RBC	1.213	1.117-1.323	<0.001

prolonged CPB and DHCA, and increased plasma usage have been identified as risk factors for delayed ventilator time. After adjusting for potential biases, the multifactorial analysis still indicated that amiodarone administration was still associated with delayed extubation.

Multivariate regression modeling showed that hypertension, stroke, amiodarone, CPB, age, LVEF, CPB time, and DHCA were independent predictors of PMV. As age, LVEF, CPB time, and DHCA were analyzed as continuous variables, an increase of one unit corresponds to an increase in the odds ratio (OR). CPB alters hepatic and renal clearance mechanisms, thereby affecting the pharmacokinetics of opioids following extracorporeal circulation. These changes may increase the occurrence of neurological abnormalities, such as somnolence and delirium, particularly in elderly patients. Additionally, extubation may be delayed due to the corresponding demands on the patient's mental state. Older age, increased tissue brittleness, and surgical complexity can all increase CPB time. This is supported by Wong DT et al.'s study [17]. Previous studies have often used a specific age as a threshold for increased risk of delayed extubation. However, our study analyzed age as a continuous variable and found that the risk of delayed extubation increases with age. This approach provides a more nuanced understanding of the relationship between age and delayed extubation. The use of amiodarone postoperatively may indicate the presence of cardiac arrhythmia in the patient. At the same time, amiodarone can also cause pulmonary fibrosis, which affects pulmonary ventilation and gas exchange, leading to decreased oxygenation and prolonged extubation time. Studies indicate that treatment with amiodarone for more than 48 h may increase the risk of acute pulmonary toxicity [18–20].

Francesca Cislaghi et al. identified several independent predictors of PMV, including CCS or NYHA score higher than 2, LVEF of 30% or less, COPD, CKD, undergoing redo or emergency surgery, CPB time more than 77 min, and RBC or FFP transfusion more than 4 units[2]. All variables included in the univariate analysis were also included in the multivariate analysis. Our study found no statistical differences between COPD and CKD in the univariate analysis. This may be due to patient population heterogeneity. However, studies have shown that creatinine or estimated glomerular filtration rate (eGFR) is a strong predictor of failure to extubate in operating room. This suggests the possibility of further subdividing CKD to facilitate the detection of intergroup differences [21–23]. Three studies didn't identify stroke as a risk factor for delayed extubation [17, 23, 24]. Our analysis did not find emergency, RBC, and plasma infusion to be risk factors for delayed extubation. The absence of emergency surgery can be attributed to the expertise of our cardiac surgery team. However, our findings regarding RBC and plasma infusion contradict several previous studies, and we were unable to provide a plausible explanation for this discrepancy.

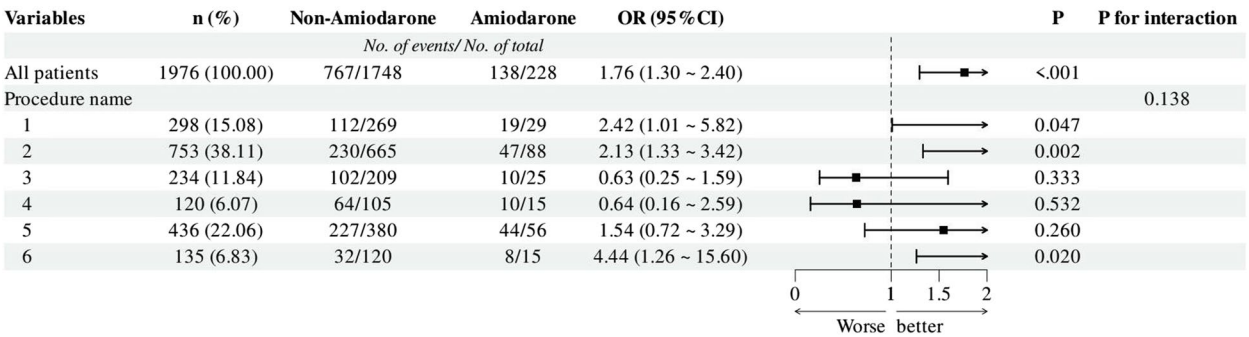

Fig. 3 Treatment effect on delayed extubation by subgroup, showed that amiodarone was a risk factor for delayed extubation for all surgical types, after adjusting for confounding variables (hypertension, stroke, amiodarone, age, LVEF, CPB, DHCA and plasma). Subgroup analysis revealed that Isolated CABG (OR: 2.42, 95%CI: 1.01–5.82, $P=0.047$), AVR or MVR (OR: 2.13, 95%CI: 1.33–3.42, $P=0.002$), and Others (OR: 4.44, 95%CI: 1.26–15.6, $P=0.020$), suggesting that amiodarone were identified as risk factors for delayed extubation in these three surgical categories. In the case of AVR + MVR (OR: 0.63, 95%CI: 0.25–1.59, $P=0.333$), Valvular surgery + CABG (OR: 0.64, 95%CI: 0.16–2.59, $P=0.532$), and thoracic aortic surgery (OR: 1.54, 95%CI: 0.72–3.29, $P=0.260$), no statistically significant associations were identified

The propensity-matched cohort study indicated that patients who received postoperative amiodarone had longer ventilator use, longer hospital stays, and higher in-hospital mortality rates, all else being equal. Multifactorial regression analysis also identified amiodarone as the most significant risk factor. Therefore, caution should be exercised when using amiodarone postoperatively.

Subgroup analyses indicated that amiodarone was a risk factor for delayed extubation for all surgical types and revealed that amiodarone were identified as risk factors for delayed extubation in these three surgical categories (Isolated CABG, AVR or MVR and Others). It is acknowledged that the serial effects of relatively complex types of surgery have the capacity to affect the effect of amiodarone on delayed extubation to a certain extent. This is evidenced by the observed OR less than 1 and non-significant p-values. Consequently, further studies will be conducted with the objective of analysing the data on a larger sample.

Our study has several limitations. First, our study was limited by its single-center and retrospective design, which may have resulted in regional specificity. Although inclusion indicators such as anesthetic drug use and preoperative albumin status could have improved accuracy, their inclusion would have required a significant amount of work and may have introduced unknown bias. We anticipate that future studies will continue to improve upon these limitations. Secondly, we collected data on other medications at the beginning, including diuretics, anticoagulants, antiplatelet agents, and antihypertensive medications. They were not included in the formal statistics due to bias caused by the influence of the patient's history and the type of surgery, which may neglect their impact on the ventilator time. Thirdly, the analysis considered amiodarone, a drug used for arrhythmia, as a potential risk factor for prolonged ventilator time. However, it is important to note that the study did not establish a causal link between delayed extubation and amiodarone use. It is unclear whether the use of amiodarone led to impaired lung function and therefore the need for prolonged ventilation, or if the prolonged extubation was due to hemodynamic instability and other factors in patients with arrhythmia. The next step is to collect information on preoperative amiodarone use and preoperative cardiac rhythm variability. Additionally, it is important to clarify whether the observed arrhythmia is a new postoperative occurrence for further analysis.

Conclusion

Risk factors for prolonged ventilator time after cardiac surgery include hypertension, stroke, amiodarone use, CPB, age, LVEF, CPB time, DHCA, and plasma. Postoperative use of amiodarone may be a significant predictor of delayed extubation, but the intrinsic link needs to be further investigated.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04576-0.

Supplementary Material 1.

Supplementary Material 2.

Acknowledgements
Not applicable.

Clinical trial number
Not applicable.

Authors' contributions
L.X and D.J.W designed the overall study with contributions from X.L and Y.X.L designed and carried out experiments, collected and analyzed data, and cowrote the paper. H.T.Z assembly protocol, and analyzed data with J.Q.Z. All authors read and approved the final manuscript.

Funding
Fundings from the Affiliated Drum Tower Hospital, Medical School of Nanjing University (No. 2023-LCYJ-ZD-03) and National Natural Science Foundation of China (82300459, 82241212).

Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the ethical committee of Drum Tower Hospital (approval number: 2020–249-01). Because of the retrospective nature of the study, the patient's consent for inclusion was waived.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 24 October 2024 Accepted: 14 February 2025
Published online: 24 February 2025

References

1. Vieillard-Baron A, Naeije R, Haddad F, et al. Diagnostic workup, etiologies and management of acute right ventricle failure : A state-of-the-art paper. Intensive Care Med. 2018;44(6):774–90. https://doi.org/10.1007/s00134-018-5172-2. [publishedOnlineFirst:2018/05/11].
2. Cislaghi F, Condemi AM, Corona A. Predictors of prolonged mechanical ventilation in a cohort of 5123 cardiac surgical patients. Eur J Anaesthesiol. 2009;26(5):396–403. https://doi.org/10.1097/EJA.0b013e3283232c69.
3. Heringlake M, Nowak Y, Schön J, et al. Postoperative intubation time is associated with acute kidney injury in cardiac surgical patients. Critical care (London, England). 2014;18(5):547. https://doi.org/10.1186/s13054-014-0547-4. [publishedOnlineFirst:2014/10/04].
4. McCarthy C, Fletcher N. Early Extubation in Enhanced Recovery from Cardiac Surgery. Crit Care Clin. 2020;36(4):663–74. https://doi.org/10.1016/j.ccc.2020.06.005. [publishedOnlineFirst:2020/09/08].

5. Engelman DT, Ben Ali W, Williams JB, et al. Guidelines for Perioperative Care in Cardiac Surgery. JAMA Surgery 2019;154(8) https://doi.org/10.1001/jamasurg.2019.1153
6. McCarthy C, Fletcher N. Early Extubation in Enhanced Recovery from Cardiac Surgery. Crit Care Clin. 2020;36(4):663–74. https://doi.org/10.1016/j.ccc.2020.06.005.
7. Rajakaruna C, Rogers CA, Angelini GD, et al. Risk factors for and economic implications of prolonged ventilation after cardiac surgery. J Thorac Cardiovasc Surg. 2005;130(5):1270–7. https://doi.org/10.1016/j.jtcvs.2005.06.050. [publishedOnlineFirst:2005/11/01].
8. Doering LV. Relationship of age, sex, and procedure type to extubation outcome after heart surgery. Heart & lung : the journal of critical care. 1997;26(6):439–47. https://doi.org/10.1016/s0147-9563(97)90037-6. [publishedOnlineFirst:1998/02/12].
9. Sanson G, Sartori M, Dreas L, et al. Predictors of extubation failure after open-chest cardiac surgery based on routinely collected data. The importance of a shared interprofessional clinical assessment. European journal of cardiovascular nursing 2018;17(8):751–59. https://doi.org/10.1177/1474515118782103. [published Online First: 2018/06/09].
10. Maisat W, Siriratwarangkul S, Charoensri A, et al. Perioperative risk factors for delayed extubation after acute type A aortic dissection surgery. J Thorac Dis. 2020;12(9):4796–804. https://doi.org/10.21037/jtd-20-742.
11. Bessissow A, Khan J, Devereaux PJ, et al. Postoperative atrial fibrillation in non-cardiac and cardiac surgery: an overview. Journal of thrombosis and haemostasis : JTH. 2015;13(Suppl 1):S304–12. https://doi.org/10.1111/jth.12974. [publishedOnlineFirst:2015/07/08].
12. Mathew JP, Fontes ML, Tudor IC, et al. A multicenter risk index for atrial fibrillation after cardiac surgery. JAMA. 2004;291(14):1720–9. https://doi.org/10.1001/jama.291.14.1720. [publishedOnlineFirst:2004/04/15].
13. Shirzad M, Karimi A, Tazik M, et al. Determinants of postoperative atrial fibrillation and associated resource utilization in cardiac surgery. Rev Esp Cardiol. 2010;63(9):1054–60. https://doi.org/10.1016/s1885-5857(10)70209-7. [publishedOnlineFirst:2010/09/02].
14. Nitta K, Okamoto K, Imamura H, et al. A comprehensive protocol for ventilator weaning and extubation: a prospective observational study. J Intensive Care. 2019;7:50. https://doi.org/10.1186/s40560-019-0402-4. [publishedOnlineFirst:2019/11/14].
15. Thille AW, Gacouin A, Coudroy R, et al. Spontaneous-Breathing Trials with Pressure-Support Ventilation or a T-Piece. N Engl J Med. 2022;387(20):1843–54. https://doi.org/10.1056/NEJMoa2209041. [publishedOnlineFirst:2022/10/27].
16. Boles JM, Bion J, Connors A, et al. Weaning from mechanical ventilation. Eur Respir J. 2007;29(5):1033–56. https://doi.org/10.1183/09031936.00010206. [publishedOnlineFirst:2007/05/02].
17. Wong DT, Cheng DC, Kustra R, et al. Risk factors of delayed extubation, prolonged length of stay in the intensive care unit, and mortality in patients undergoing coronary artery bypass graft with fast-track cardiac anesthesia: a new cardiac risk score. Anesthesiology. 1999;91(4):936–44. https://doi.org/10.1097/00000542-199910000-00012. [publishedOnlineFirst:1999/10/16].
18. Boriani G, Ferruzzi L, Corti B, et al. Short-term onset of fatal pulmonary toxicity in a patient treated with intravenous amiodarone for post-operative atrial fibrillation. Int J Cardiol. 2012;159(1):e1–4. https://doi.org/10.1016/j.ijcard.2011.10.134. [publishedOnlineFirst:2011/12/02].
19. Camus P, Martin WJ 2nd, Rosenow EC 3rd. Amiodarone pulmonary toxicity. Clin Chest Med. 2004;25(1):65–75. https://doi.org/10.1016/s0272-5231(03)00144-8. [publishedOnlineFirst:2004/04/06.
20. Donaldson L, Grant IS, Naysmith MR, et al. Acute amiodarone-induced lung toxicity. Intensive Care Med. 1998;24(6):626–30. https://doi.org/10.1007/s001340050627. [publishedOnlineFirst:1998/07/29].
21. Constantinides VA, Tekkis PP, Fazil A, et al. Fast-track failure after cardiac surgery: development of a prediction model. Crit Care Med. 2006;34(12):2875–82. https://doi.org/10.1097/01.Ccm.0000248724.02907.1b. [publishedOnlineFirst:2006/11/01].
22. Lee A, Zhu F, Underwood MJ, et al. Fast-track failure after cardiac surgery: external model validation and implications to ICU bed utilization. Crit Care Med. 2013;41(5):1205–13. https://doi.org/10.1097/CCM.0b013e31827711ad. [publishedOnlineFirst:2013/02/08].
23. Youssefi P, Timbrell D, Valencia O, et al. Predictors of Failure in Fast-Track Cardiac Surgery. J Cardiothorac Vasc Anesth. 2015;29(6):1466–71. https://doi.org/10.1053/j.jvca.2015.07.002. [publishedOnlineFirst:2015/10/04].
24. Sato M, Suenaga E, Koga S, et al. Early tracheal extubation after on-pump coronary artery bypass grafting. Annals of thoracic and cardiovascular surgery : official journal of the Association of Thoracic and Cardiovascular Surgeons of Asia 2009;15(4):239–42. [published Online First: 2009/09/19]

Publisher's Note