Sociedade Brasileira de Anestesiologia

Brazilian Journal of ANESTHESIOLOGY

ORIGINAL INVESTIGATION

The association of hemoglobin with postoperative delirium and atrial fibrillation after cardiac surgery: a retrospective sub-study

Sinem Sari[a,b], Jack Brooker[a], Mateo Montalvo-Campana[a], Peter Shehata[c], Xuan Pu[d], Steven Insler[e], Kurt Ruetzler[a,c], Christopher A. Troianos[f], Alparslan Turan[a,c,*]

[a] *Cleveland Clinic, Anesthesiology Institute, Department of Outcomes Research, Cleveland, Ohio*
[b] *Adnan Menderes University, Department of General Anesthesiology, Aydın, Turkey*
[c] *Cleveland Clinic, Anesthesiology Institute, Department of General Anesthesiology, Cleveland, Ohio*
[d] *Cleveland Clinic, Department of Quantitative Health Sciences, Cleveland, Ohio*
[e] *Cleveland Clinic, Anesthesiology Institute, Department of Intensive Care & Resuscitation, Cleveland, Ohio*
[f] *Cleveland Clinic, Anesthesiology Institute, Cleveland, Ohio*

Received 2 May 2022; accepted 26 February 2023
Available online 8 March 2023

KEYWORDS
Anemia;
Delirium;
Atrial fibrillation;
General anesthesia;
Cardiac surgery

Abstract

Background: Most cardiac surgery patients experience postoperative anemia. Delirium and Atrial Fibrillation (AF) are common and independent predictors of morbidity and mortality. Few reports examine their association with postoperative anemia. This study aims to quantify the association between anemia and these outcomes in patients undergoing cardiac surgery.

Methods: This post-hoc analysis of the DECADE randomized controlled trial ran at six academic US hospitals. Patients aged 18—85 years with heart rate > 50 bpm undergoing cardiac surgery who had daily hemoglobin measurements in the first 5 Postoperative Days (POD) were included. Delirium was assessed twice daily with the Confusion Assessment Method for the ICU (CAM — ICU), preceded by the Richmond Agitation and Sedation Scale, with patients excluded from assessment if sedated. Patients had daily hemoglobin measurements, continuous cardiac monitoring plus twice-daily 12-lead electrocardiograms, up to POD4. AF was diagnosed by clinicians blinded to hemoglobin levels.

Results: Five hundred and eighty-five patients were included. Mean postoperative hemoglobin Hazard Ratio (HR): 0.99 (95% CI 0.83, 1.19; p = 0.94) per 1 g.dL^{-1} hemoglobin decrease. 197 (34%) developed AF, mainly on POD = 2.3. Estimated HR = 1.04 (95% CI 0.93, 1.17; p = 0.51) per 1 g.dL^{-1} hemoglobin decrease.

Conclusions: Most patients undergoing major cardiac surgery were anemic in the postoperative phase. AF and delirium occurred in 34% and 12% of patients, respectively, but neither were significantly correlated with postoperative hemoglobin.

* Corresponding Author.
E-mail: turana@ccf.org (A. Turan).

https://doi.org/10.1016/j.bjane.2023.02.003

Introduction

Over 900,000 cardiac procedures are performed annually in the United States and with an ageing population this number is projected to rise considerably.[1] Delirium and Atrial Fibrillation (AF) are common complications of cardiac surgery with an incidence of up to 87% for delirium and 65% for AF.[2,3] Delirium is an acute onset of disturbed consciousness and cognitive ability, and is associated with an increased risk of death, Intensive Care Unit (ICU) length of stay, and hospital length of stay. Postulated mechanisms for the development of postoperative delirium include inflammation and hypoxia during the surgery itself as well as anesthetic and analgesia side effects (particularly volatile anesthetic gases and opioids).[4,5]

The incidence of anemia ranges from 5% to 75.8% in patients undergoing non-emergent surgical procedures with variation attributed to the particular study population and diagnostic criteria.[6-8] According to the World Health Organization (WHO) definition of anemia (< 13 g.dL^{-1} for males, $<$ 12 g.dL^{-1} for females), the incidence can be as high as 80 −90%.[9] Factors contributing to anemia include surgical blood loss, hemodilution from intravenous infusions and blunted postsurgical erythropoiesis due to inflammation.[10] Additionally, many surgical patients may have preoperative anemia due to nutritional deficiencies, hemorrhage in the case of trauma or due to chronic disease states.[10] Anemia leads to end organ dysfunction, presumably due to poor tissue perfusion arising from the reduced oxygen carrying capacity of blood when in the anemic state. Anemia is associated with poor postoperative outcomes including increased mortality, acute kidney injury, stroke, and infection.[11] The association between delirium and perioperative anemia is intuitive and biologically plausible, but presently the association remains unclear with relatively little published literature.

Postoperative AF is associated with increased in-hospital and long-term mortality, stroke, hospital length of stay and increased healthcare costs.[2,12,13] Possible mechanisms include myocardial inflammation, perioperative catecholamine release as part of the surgical stress response, mechanical injury, atrial dilation due to intraoperative volume overload and ischemia.[2,14-16] Given the possible role of atrial or global cardiac ischemia in the development of postoperative AF, there is a plausible link between perioperative anemia and postoperative AF. However, as with perioperative delirium, there is a lack of published evidence quantifying this link and current evidence is inconsistent.

This retrospective post-hoc analysis of a completed Randomized Controlled Trial (RCT) is designed to further quantify and characterize the association between perioperative anemia and the development of postoperative delirium and AF. Specifically, we tested the primary hypothesis that low hemoglobin levels are associated with postoperative delirium. Secondarily, we tested the hypothesis that low hemoglobin levels are associated with atrial fibrillation during the five postoperative days after cardiac surgery.

Methods

Study design and participants

This retrospective post-hoc analysis is a sub-study of the published DECADE trial (NCT02004613), which enrolled 798 participants at six academic centers in the United States.[17] Centers included three Cleveland Clinic centers including the main campus, Ohio State Wexner Medical Center, Northwestern University Medical Center, and UCLA Medical Center. The primary objective of the DECADE study was to assess the efficacy of dexmedetomidine in preventing AF and delirium in patients undergoing cardiac surgery. Patients aged 18−85 years who were scheduled for cardiac surgery with cardiopulmonary bypass and who had heart rates $\geq$ 50 beats per min were included.

Only patients in the DECADE trial treated in the Cleveland Clinic system were considered and only patients who had daily hemoglobin measurement after the surgery were enrolled in this analysis. Since 10 (1.7%) patients were missing on delirium and 2 (0.3%) patients missing on confounders after complete case analysis, we simply excluded them from our study population (Fig. 1). The study protocol and data utilization were approved by the Cleveland Clinic Foundation's Institutional Review Board.

Measurements

Patients in the cardiac ICU had continuous electrocardiographic monitoring. The diagnosis of atrial fibrillation in the cardiac ICU was made by clinicians masked to group allocation. Additionally, patients had twelve-lead Electrocardiograms (ECG) morning and evening for the first five postoperative days or until hospital discharge if sooner. A cardiologist or anesthesiologist masked to randomized group allocations diagnosed AF based upon the ECG. Atrial fibrillation was defined by: clinician diagnosis with documented arrhythmia lasting at least 5 min in monitored patients or the presence of arrhythmia on ECGs in unmonitored patients.

Delirium assessments were preceded by a Richmond Agitation and Sedation Scale to assess sedation.[18] Delirium was only assessed if Richmond Agitation and Sedation Scale scores were not −4 or −5, indicating insufficient alertness. Confusion Assessment Method for the ICU (CAM-ICU) evaluations were done in person by formally trained masked research physicians for the initial 5 postoperative days as long as patients remained hospitalized. Morning assessments were done before 10:00, and evening assessments after 17:00. Nurses, independent of research physicians' evaluation, also assessed CAM-ICU daily and described patients' mental status in their notes. Patients were considered to have had delirium if one or more CAM-ICU assessments by investigators or nurses were positive, or if there was clear indication of delirium in written nursing evaluations.

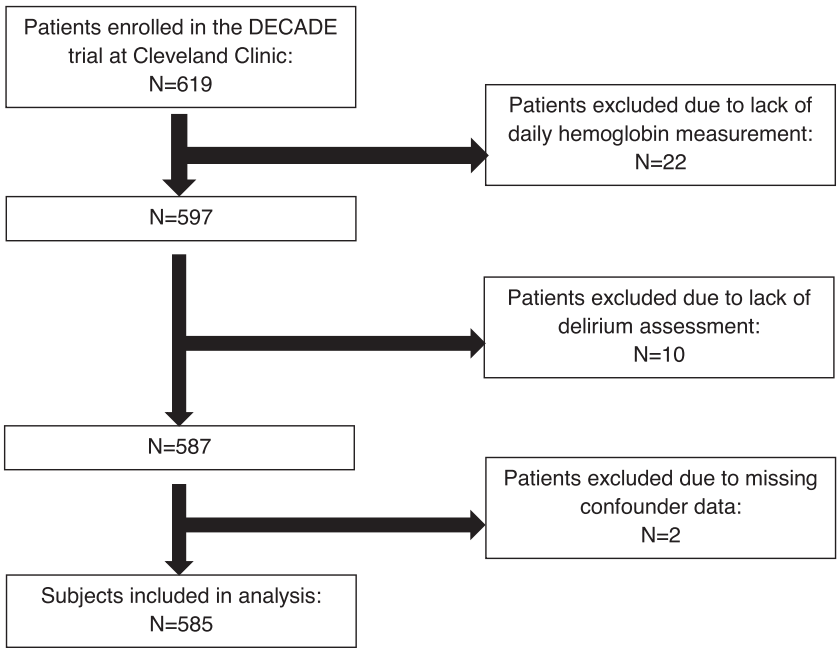

Figure 1 Description of the screening and subject selection process for this post-hoc analysis of the DECADE trial.

Exposure and confounders

Our exposure of interest was daily lowest hemoglobin from day of surgery until hospital discharge or postoperative day 4, whichever came first. Confounders were adjusted in all multivariable analyses including demographic, medical history, intraoperative and surgery characteristics (Table 1).

All the data was available in the original trial and only one medical history variable was obtained from our database.

Table 1 Baseline and demographic characteristics by postoperative lowest Hgb levels before event (n = 585).

Factor	< 8 g.dL^{-1} (n = 153)	8–11 g.dL^{-1} (n = 378)	≥ 11 g.dL^{-1} (n = 54)	ASD
Age, year	63 ± 11	63 ± 11	59 ± 11	0.36
Female	63 (41)	112 (30)	7 (13)	0.67
ASA physical status				0.06
I–III	30 (20)	76 (20)	12 (22)	
IV–V	123 (80)	302 (80)	42 (78)	
White	138 (90)	362 (96)	51 (94)	0.22
BMI, kg.m^{-2}	29 ± 10	29 ± 5	30 ± 10	0.15
Comorbidities				
History of stroke or TIA	14 (9.2)	12 (3.2)	3 (5.6)	0.25
Diabetes	49 (32)	74 (20)	5 (9.3)	0.59
Pulmonary disease	21 (14)	49 (13)	4 (7.4)	0.21
Kidney disease	25 (16)	23 (6.1)	4 (7.4)	0.33
Surgery duration, hour	6.2 [5.2, 7.5]	5.5 [4.7, 6.6]	4.9 [4.4, 5.8]	0.89
Surgical type				0.68
Valve/Aorta only	59 (39)	230 (61)	38 (70)	
CABG only	2 (1)	5 (1)	0 (0)	
CABG + Valve/Aorta	92 (60)	143 (38)	16 (30)	
Blood loss, mL	250 [0, 250]	250 [0, 250]	250 [0, 250]	0.09
Intraoperative RBC, mL	0 [0, 300]	0 [0, 0]	0 [0, 0]	0.61
RBC transfusion within postoperative 5 days, mL	350 [0, 700]	0 [0, 0]	0 [0, 0]	1.49

ASD, Absolute Standard Deviation; ASA physical status, American Society of Anesthesiologists physical status; BMI, Body Mass Index; TIA, Transitional Ischemic Attack; CABG, Coronary Artery Bypass Grafting; RBC, Red Blood Cell; Hgb, Hemoglobin.
Summary statistics are presented as mean ± SD (standard deviation), median [Q1, Q3], or n (%) by the lowest hemoglobin across postoperative days.
The ASD describes the difference of variables by groups. The higher the ASD, the more imbalanced it is.
Usually, ASD < 0.1 is considered as a good balance.

Statistical analysis

The association between postoperative hemoglobin and delirium was assessed using a multiple time-varying Cox proportional hazards model adjusting for all potential confounders in Table 1. The daily lowest hemoglobin measurement before onset of delirium was used as the time-varying exposure. We used a survival model to analyze the association between anemia and outcome to address the potential bias that can occur from the different follow-up times for each patient: patients who were discharged earlier or had earlier postoperative delirium had shorter exposure period than patients without the outcome.

The relationships between postoperative hemoglobin and atrial fibrillation were assessed in the Cox proportional hazard survival model in the same manner as in the primary analysis, adjusted for all confounders listed in Table 1.

The significance criterion was 0.05 for both primary and secondary analysis. SAS statistical software version 9.4 (SAS Institute, Cary, NC, USA) was used for data retrieval and statistical analysis.

Power considerations

A *priori*

Of the 798 originally enrolled patients in the DECADE trial, only those treated at the primary study center were intended for inclusion (619). After participants were excluded due to missing hemoglobin measurements, outcomes, and confounders there was a residual sample of 585. The incidence of delirium was 15% and was simplified into a binary outcome. We simplified the power statement, treating delirium as a binary outcome, because the survival analysis planned is more powerful than logistic regression analysis assumed for the purpose of power assessment. We provided a power of 85% to detect an odds ratio of developing delirium 1.2 or greater for a one-unit increase in hemoglobin at the 0.05 significance level, assuming a normal distribution of hemoglobin with mean of 10 and standard deviation of 2 $mg.mL^{-1}$.

Post-hoc

Similar to a *priori* power calculation, delirium was simplified to a binary outcome and logistic regression was used to calculate power. With a sample size of 585, there was a power of over 0.9 to detect an odds ratio of 1.35 or greater with the observed delirium incidence of 0.13 and a normal distribution of hemoglobin with mean of 9.8 and standard deviation of 1.5 $mg.mL^{-1}$.

Results

Six-hundred nineteen Cleveland Clinic patients in the DECADE trial were considered for inclusion. After excluding patients with missing hemoglobin measurements, outcomes, and confounders, 585 patients were included in the final analysis (Fig. 1).

The baseline and confounder characteristics are listed in Table 1 by hemoglobin groups. On average, there were 4, 6, 3, 2, and 1 postoperative hemoglobin measurements from postoperative day 0 to postoperative day 4, respectively. Mean postoperative hemoglobin was 10 $g.dL^{-1}$ on postoperative day 0 and 1. Hemoglobin level was 9 $g.dL^{-1}$ from postoperative day 2 to postoperative day 4, inclusively. Patients whose mean hemoglobin was < 8 $g.dL^{-1}$ during the hospital stay had a median RBC transfusion (Q1, Q3) of 350 (0, 700) mL during the 5-day study period, while patients with mean hemoglobin ≥ 8 $g.dL^{-1}$ had a median RBC transfusion of 0 (0, 0) mL.

Postoperative delirium was present in 72 (12%) patients. Postoperative hemoglobin was not found to be significantly associated with delirium with an estimated Hazard Ratio (HR) of 0.99 (95% CI 0.83, 1.19; $p = 0.94$) associated with each 1 $g.dL^{-1}$ decrease in hemoglobin concentration (Table 2, Supplemental Table 2). This corresponds to 1% lower chance of experiencing delirium at next time point given the patient has not yet experienced the event.

One hundred ninety-seven patients (34%) developed atrial fibrillation with approximately 83% atrial fibrillation occurring during the first 3 postoperative days, primarily postoperative days 2 or 3. Postoperative atrial fibrillation was not found to be associated with hemoglobin level with an estimated HR of 1.04 (95% CI 0.93, 1.17; $p = 0.51$) with each 1 $g.dL^{-1}$ decrease in hemoglobin concentration (Table 2, Supplemental Table 3). This corresponds to a 4% higher chance of experiencing atrial fibrillation at the next time point given that the patient has not yet experienced the event.

No significant association between delirium and either intraoperative RBC transfusion volume or RBC transfusion volume within the first postoperative 5 days was found: estimated HR = 1.00 (95% CI 1.00, 1.001; $p = 0.22$) associated with each ml increase in intraoperative RBC transfusion and 1.00 (95% CI 1.00, 1.001; $p = 0.70$) associated with each ml increase in RBC transfusion within postoperative 5 days.

Additionally, there was no significant association between AF and intraoperative RBC transfusion amount ($p = 0.18$) or RBC transfusion amount within postoperative 5 days ($p = 0.79$).

Table 2 Association between hemoglobin and primary and secondary outcome (n = 585).

	HR associated with each $g.dL^{-1}$ decrease in Hgb (95% CI)[a]	*p*-value
Primary outcome		
Delirium	0.99 (0.83, 1.19)	0.94
Secondary outcome		
Atrial fibrillation	1.04 (0.93, 1.17)	0.51

HR, Hazard Ratio; Hgb, Hemoglobin; CI, Confidence Interval.

[a] The estimates were obtained from a time-varying covariate Cox-proportional hazards model with each corresponding outcome and daily hemoglobin concentration before the event/censoring time as the time-varying exposure, adjusting for confounders in Table 1.

Discussion

We did not find an association between low hemoglobin levels and either postoperative delirium or atrial fibrillation. Relatively little literature pertaining to postoperative delirium and anemia exists. Kunz et al., in a post-hoc analysis, included 183 patients undergoing a range of elective surgical procedures.[6] Ten out of 93 (10.9%) patients without postoperative anemia developed postoperative delirium. In the group with postoperative anemia, 28 (38.4%) out of 90 patients suffered postoperative delirium.[18] The difference from our results could be related to the type of surgeries included and/or the delirium assessment itself, which utilized a different tool, the Nursing Delirium Screening Scale. This tool, whilst validated, has been reported to have low sensitivity.[19] Combined with the lower frequency of delirium assessment compared to our study, it is possible that study design features can explain the difference in results between this study and that reported by Kunz et al.

A study of 415 patients aged over 65 years with hip fractures presenting for surgery found that hemoglobin less than 9.7 $mg.dL^{-1}$ was associated with delirium.[20] This level of anemia was examined as it is the level below which transfusion is generally considered in the locality of the study (The Netherlands). Assessment of delirium was done daily on the first 8 postoperative days using criteria from the Diagnostic and Statistical Manual 5 (DSM5) but a specific screening tool was not described. Higher levels of hemoglobin classified as anemic per WHO criteria were not assessed, so a definitive odds ratio for anemic and non-anemic patients cannot be compared to this study. The study included a more age-restricted study population which specifically excluded those who were anticipated to require ICU or coronary care unit placement. These factors, combined with a different surgical intervention, less frequent assessment of delirium (daily compared to twice daily in this study), and the lack of a validated assessment tool implies that a comparison of results with this study is not appropriate.

A prospective study of 472 patients undergoing major non-cardiac surgery using the CAM assessment (non-ICU equivalent of the assessment used in current study) found that preoperative hemoglobin < 13 $g.dL^{-1}$ was significantly associated with the incidence of postoperative delirium, however a correlation with postoperative anemia was not reported.[21] Patients included in this study were more than 65 years of age and the delirium assessment was performed only once per day during the first two postoperative days. The authors noted that intraoperative blood transfusion was the leading risk factor for the development of postoperative delirium, but the hemoglobin criteria for transfusions were not noted nor was the incidence of postoperative anemia.

A possible confounding factor is the impact of transfusion itself on the risk for delirium since those patients with more severe anemia are more likely to receive a greater volume of packed Red Blood Cells (RBC). No significant relationship between postoperative delirium and either the intraoperative RBC transfusion volume nor the volume of RBC transfused in the first five postoperative days was identified. The same was true of postoperative AF. This finding conflicts with the results of a secondary analysis of older patients undergoing major non-cardiac surgery.[21] However, this study found that postoperative delirium was only associated with transfusion volumes over 1 liter, which is significantly larger than transfusion volumes administered in our study population. Kwon and colleagues failed to find any correlation between intraoperative or early postoperative transfusion and delirium.[22] Transfusion does appear to be related to postoperative AF, possibly due to the effects of volume overload or inflammation.[23,24] The fact that no significant correlation between postoperative AF and transfusion volume in the intraoperative and early postoperative was identified in our study may be due to the generally low volumes of RBC administered in our patient sample.

Evidence linking postoperative atrial fibrillation with anemia is limited and conflicting. A systematic review and meta-analysis including 22 studies comprising 6098 patients identified multiple hematological abnormalities as established predictors of postoperative AF, however hemoglobin was not among them.[25] Another retrospective study of 1191 patients undergoing open cardiac surgery found that hemoglobin < 12.5 $g.dL^{-1}$ and hematocrit $< 35\%$ were associated with AF on univariate analysis, however on multivariate analysis, only hematocrit was significantly associated.[26] This study utilized a preoperative (48 hours before surgery) blood draw to assess anemia and excluded all patients with previously diagnosed atrial arrhythmias, but unlike this study, postoperative hemoglobin levels were not taken into consideration. Goldman reported that anemia (based on hematocrit $< 30\%$) is not a primary risk factor the development of AF in non-cardiac surgery.[27] This prospective study included 916 patients undergoing major non-cardiac surgery who were over 40 years of age and did not display a rhythm other than sinus rhythm during surgery. There are distinct differences in type of surgery and the assessment of both anemia and AF compared to our study.

Kim et al. evaluated 2627 patients undergoing catheter ablation for AF and found that pre-procedure anemia was independently predictive of the recurrence of AF, although post-procedure anemia was not considered.[28] We are not aware of additional studies examining the link between anemia and postoperative AF, however the plausible biological link between hypoxia (and thus, presumably, anemia) and postoperative AF has been discussed.[16] Studies have demonstrated that chronically hypoxic patients, such as those with obesity, Obstructive Sleep Apnea (OSA) or Chronic Obstructive Pulmonary Disease (COPD), have a higher incidence of postoperative AF.[29,30] The possibility that an adrenergic response to anemia is implicated in the development of postoperative AF has also been postulated.

Limitations of this study include its retrospective nature. Although the results did not demonstrate an association between anemia and either delirium or AF, the study design would not have been able to establish causation even if an association was demonstrated. Given the focus of interest in this study was major cardiac surgery requiring cardiopulmonary bypass, results may not be generalizable to other surgical procedures.[31]

Conclusion

This is the only study examining the association between postoperative hemoglobin, AF, and delirium in major cardiac surgery. Anemia was very common among patients

undergoing major cardiac surgery requiring cardiopulmonary bypass, with mean hemoglobin levels falling below WHO criteria for anemia throughout the period between surgery and POD4. Both delirium and atrial fibrillation were common in the postoperative phase. However, there was no significant association with postoperative hemoglobin and either delirium or AF identified.

Funding/Support

The study was funded by departmental funds. None of the authors has a personal financial interest related to this research.

Register number

Institutional Review Board (IRB): 21-399. This is a retrospective sub study of the DECADE trial (IRB 12-1379, NCT02004613).

Conflicts of interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjane.2023.02.003.

References

1. How Many Cardiac Surgeries Are Performed Each Year? – New Study by iData Research – iData Research [Internet]. [cited 2022 Jun 2]. Available from: https://idataresearch.com/over-900000-cardiac-surgeries-performed-every-year-in-the-united-states/.
2. Maisel WH, Rawn JD, Stevenson WG. Atrial fibrillation after cardiac surgery. Ann Intern Med. 2001;135:1061—73.
3. Demeure MJ, Fain MJ. The elderly surgical patient and postoperative delirium. J Am Coll Surg. 2006;203:752—7.
4. Beloosesky Y, Hendel D, Weiss A, et al. Cytokines and C-reactive protein production in hip-fracture-operated elderly patients. J Gerontol A Biol Sci Med Sci. 2007;62:420—6.
5. Deiner S, Silverstein JH. Postoperative delirium and cognitive dysfunction. Br J Anaesth. 2009;103:i41—6. Suppl 1.
6. Kunz JV, Spies CD, Bichmann A, Sieg M, Mueller A. Postoperative anaemia might be a risk factor for postoperative delirium and prolonged hospital stay: A secondary analysis of a prospective cohort study. PLoS One. 2020;15:e0229325.
7. Haljamäe H, Stefánsson T, Wickström I. Preanesthetic evaluation of the female geriatric patient with hip fracture. Acta Anaesthesiol Scand. 1982;26:393—402.
8. Shander A, Knight K, Thurer R, Adamson J, Spence R. Prevalence and outcomes of anemia in surgery: a systematic review of the literature. Am J Med. 2004;116:58—69. Suppl 7A(7 SUPPL. 1).
9. Gómez-Ramirez S, Jericó C, Muñoz M. Perioperative anemia: Prevalence, consequences, and pathophysiology. Transfus Apher Sci. 2019;58:369—74.
10. Fowler AJ, Ahmad T, Phull MK, Allard S, Gillies MA, Pearse RM. Meta-analysis of the association between preoperative anaemia and mortality after surgery. Br J Surg. 2015;102:1314—24.
11. Creswell LL, Schuessler RB, Rosenbloom M, Cox JL. Hazards of postoperative atrial arrhythmias. Ann Thorac Surg. 1993;56:539—49.
12. Yadava M, Hughey AB, Crawford TC. Postoperative Atrial Fibrillation: Incidence, Mechanisms, and Clinical Correlates. Heart Fail Clin. 2016;12:299—308.
13. Villareal RP, Hariharan R, Liu BC, Kar B, Lee VV, Elayda M, et al. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. J Am Coll Cardiol. 2004;43:742—8.
14. Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVliet M, et al. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. Circulation. 1996;94:390—7.
15. Tchervenkov CI, Wynands JE, Symes JF, Malcolm ID, Dobell ARC, Morin JE. Persistent atrial activity during cardioplegic arrest: a possible factor in the etiology of postoperative supraventricular tachyarrhythmias. Ann Thorac Surg. 1983;36:437—43.
16. Palin CA, Kailasam R, Hogue CW. Atrial fibrillation after cardiac surgery: pathophysiology and treatment. Semin Cardiothorac Vasc Anesth. 2004;8:175—83.
17. Turan A, Duncan A, Leung S, Karimi N, Fang J, Mao G, et al. Dexmedetomidine for reduction of atrial fibrillation and delirium after cardiac surgery (DECADE): a randomised placebo-controlled trial. Lancet. 2020;396:177—85.
18. Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal Pv, Keane KA, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. Am J Respir Crit Care Med. 2002;166:1338—44.
19. Hargrave A, Bastiaens J, Bourgeois JA, Neuhaus J, Josephson SA, Chinn J, et al. Validation of a Nurse-Based Delirium-Screening Tool for Hospitalized Patients. Psychosomatics. 2017;58:594—603.
20. van der Zanden V, Beishuizen SJ, Scholtens RM, de Jonghe A, de Rooij SE, van Munster BC. The Effects of Blood Transfusion on Delirium Incidence. J Am Med Dir Assoc. 2016;17:748—53.
21. Behrends M, Depalma G, Sands L, Leung J. Association between intraoperative blood transfusions and early postoperative delirium in older adults. J Am Geriatr Soc. 2013;61:365—70.
22. Kwon YS, Kim JH, Lee JJ, Seo EM. The relationship between perioperative blood transfusion and postoperative delirium in patients undergoing spinal fusion surgery: Clinical Data Warehouse Analysis. Medicina (Kaunas). 2022;58:268.
23. Alameddine AK, Visintainer P, Alimov VK, Rousou JA. Blood transfusion and the risk of atrial fibrillation after cardiac surgery. J Card Surg. 2014;29:593—9.
24. Liu S, Li Z, Liu Z, Hu Z, Zheng G. Blood transfusion and risk of atrial fibrillation after coronary artery bypass graft surgery: A meta-analysis of cohort studies. Medicine. 2018;97:e9700.
25. Weymann A, Ali-Hasan-Al-Saegh S, Popov AF, Sabashnikov A, Mirhosseini SJ, Liu T, et al. Haematological indices as predictors of atrial fibrillation following isolated coronary artery bypass grafting, valvular surgery, or combined procedures: a systematic review with meta-analysis. Kardiol Pol. 2018;76:107—18.
26. Turkkolu ST, Selçuk E, Köksal C. Biochemical predictors of postoperative atrial fibrillation following cardiac surgery. BMC Cardiovasc Disord. 2021;21:167.
27. Goldman I. Supraventricular tachyarrhythmias in hospitalized adults after surgery. Clinical correlates in patients over 40 years of age after major noncardiac surgery. Chest. 1978;73:450—4.
28. Kim M, Hong M, Kim JY, Kim IS, Yu HT, Kim TH, et al. Clinical relationship between anemia and atrial fibrillation recurrence

after catheter ablation without genetic background. Int J Cardiol Heart Vasc. 2020;27:100507.
29. Yamashita K, Hu N, Ranjan R, Selzman CH, Dosdall DJ. Clinical risk factors for postoperative atrial fibrillation among patients after cardiac surgery. Thorac Cardiovasc Surg. 2019;67:107—16.
30. Mooe T, Gullsby S, Rabben T, Eriksson P. Sleep-disordered breathing: a novel predictor of atrial fibrillation after coronary artery bypass surgery. Coron Artery Dis. 1996;7:475—8.
31. Chelazzi C, Villa G, de Gaudio AR. Postoperative atrial fibrillation. ISRN Cardiol. 2011;2011:203179.