Acta Cardiol Sin 2019;35:468–475
Original Article
doi: 10.6515/ACS.201909_35(5).20190325A

Cardiovascular Surgery

Predictors of Postoperative Atrial Fibrillation after Beating-Heart Coronary Artery Bypass Surgery: Is Cardiopulmonary Bypass a Risk Factor?

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Backgrouand: To determine the risk factors and postoperative outcomes of new-onset atrial fibrillation (AF) following beating-heart coronary artery bypass grafting (CABG) surgery.

Methods: A total of 458 patients who underwent beating-heart CABG without the use of aortic cross clamping and cardioplegic arrest between January 2011 and January 2015 were included in the study, and they were divided into two groups according to the development of new-onset AF as the AF group (n = 143) and non-AF group (n = 315). Both groups were compared in terms of preoperative clinical features and perioperative data, and the risk factors and postoperative outcomes of AF following beating-heart CABG were determined.

Results: The incidence of postoperative AF was 31.2%. Patients in the AF group were significantly older (68.08 ± 7.76 vs. 61.76 ± 9.83 years, $p \leq 0.001$) and had significantly higher use of cardiopulmonary bypass during surgery (69.2% vs. 43.2%, $p \leq 0.001$) than the patients in the non-AF group. The patients with AF also had statistically significantly longer lengths of intensive care unit and hospital stay than those without AF (43.79 ± 32.39 vs. 30.49 ± 33.31 hours, $p \leq 0.001$, and 8.20 ± 4.37 vs. 5.77 ± 2.16 days, $p \leq 0.001$, respectively).

Conclusions: Our study revealed that age and the use of cardiopulmonary bypass during surgery were independent predictors of AF following beating-heart CABG. In addition, postoperative AF was associated with prolonged intensive care unit and hospital stay. Further prospective randomized studies with larger patient series are required to support our research and attain more accurate data.

Key Words: Atrial fibrillation • Beating-heart • Cardiopulmonary bypass • Coronary artery bypass grafting • Predictor • Risk factor

INTRODUCTION

Atrial fibrillation (AF) is an arrhythmia characterized by 350 to 600 atrial depolarizations per minute without effective atrial contractions which are reflected on electrocardiography (ECG) as small irregular and varying atrial amplitudes and morphologies. During atrial depolarization, also called F wave, around 100-160 irregular ventricular responses occur per minute.[1] AF is the most commonly encountered arrhythmia following coronary artery bypass grafting (CABG) surgery. After the operation, it occurs most frequently on the second and third day.[2,3] Although in most cases postoperative AF is self-limiting and has a benign course, it poses some risks such as systemic embolization, cerebrovascular events (CVEs) and hemodynamic deterioration, leading to increases in the length of hospital stay, costs, and mortality.[2-5] Hence, it is very important to determine patients who are at risk of postoperative AF, and to take due precautions in the perioperative period.

Received: October 25, 2018 Accepted: March 25, 2019
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Although there is a lack of consensus among published studies, many risk factors for AF after CABG have been identified, including increased age, male sex, low ejection fraction, chronic obstructive pulmonary disease, chronic renal dysfunction and preoperative withdrawal of beta-blocker drugs.[2,6-10] However, the studies that have identified these risk factors of postoperative AF have mostly been derived from conventional CABG with cardioplegic arrest, and a limited amount of data on the incidence, risk factors and outcomes of postoperative AF after beating-heart CABG are available in the existing literature. Therefore, we designed this study to determine the incidence, risk factors and postoperative outcomes of new-onset AF after beating-heart CABG.

METHODS

Ethical status

The study was started once the Institutional Ethics Committee had approved the study protocol. The study was performed according to the principles of the Helsinki Declaration, and written informed consent forms were obtained from each patient before the surgery.

Patients and study design

The study population consisted of 458 patients who underwent beating-heart CABG surgery without the use of aortic cross clamping and cardioplegic arrest between January 2011 and January 2015 in our institution. Patient data were obtained from hospital records and then reviewed retrospectively. The patients were divided into two groups according to the development of AF during the postoperative period until discharge. Group 1 (AF group) and Group 2 (non-AF group) consisted of 147 and 311 patients, respectively. Both groups were compared in terms of baseline clinical characteristics, intraoperative data, and postoperative outcomes. The risk factors and postoperative outcomes of AF after beating-heart CABG were then determined.

Postoperative AF was defined as new-onset AF of any duration in the postoperative period which required medical treatment (beta-blockers, calcium channel blockers, amiodarone, anticoagulants, etc.).

The exclusion criteria were persistent/permanent AF or a history of paroxysmal AF before the surgery, conventional on-pump CABG with the use of aortic cross clamping and cardioplegic arrest, conversion from off-pump to on-pump CABG or from on-pump beating-heart to conventional CABG during the operation, emergency surgery, redo cardiac surgery, and concomitant valve surgery or surgical procedures other than isolated CABG.

Surgical approach

Both off-pump and on-pump beating-heart CABG techniques were performed by the same surgical team who had a similar level of experience with both procedures. The surgical technique to be performed was assigned a day before the surgery according to the patients' demographics, clinical features, and aortic and coronary vasculature. Nonetheless, the final decision regarding the surgical technique was made following the evaluation of coronary anatomy and ascending aorta during the surgery.

Although demographic and clinical features and especially age, gender, diabetes mellitus and left ventricular dysfunction were taken into account when deciding the surgical technique, the parameter mainly taken into consideration was the patients' angiography images in the preoperative period. According to the diameters of coronary arteries and the diffusiveness of stenotic lesions in the coronary arteries after they had been evaluated with angiography preoperatively, in the cases where the coronary arteries were thin and the lesions were diffuse, on-pump beating-heart CABG technique was considered first as the technique to be performed during the operation. Nevertheless, the coronary arteries were re-evaluated during the surgery and the final decision was mainly made intraoperatively according to the coronary vasculature. In cases where exploration of the target coronary arteries was very difficult and required considerable manipulation of the heart, such as in target coronary arteries with an intramyocardial course or localized in the atrioventricular groove especially for circumflex coronary arteries, the on-pump beating-heart technique was usually preferred. The on-pump technique was also usually preferred in patients with cardiac hypertrophy. On the other hand, the off-pump technique was primarily preferred in patients with severe ascending aorta diseases such as porcelain aorta and disseminated atherosclerotic involvement of the ascending

aorta in order to avoid additional aortic cannulation.

All patients were operated through median sternotomy under general anesthesia. The left internal thoracic artery and vena saphena magna were used as primary bypass grafts in most of the patients. Off-pump CABG was performed in 223 patients, and on-pump beating-heart CABG was performed in 235 patients.

Arrhythmia monitoring

All patients were transferred to the intensive care unit (ICU) at the end of the operation, and monitored continuously using a cardiac rhythm monitor during ICU follow-up. Standard 12-lead ECG recordings were obtained from all patients before the operation, immediately after the operation, and then routinely on a daily basis during postoperative hospital stay both in the ICU and in the acute inpatient ward. During acute inpatient ward follow-up after discharge from the ICU, trained nurses observed the patients' hemodynamic parameters including radial pulse rate every 4 hours. Additional ECG recordings were obtained when there was any clinical suspicion of arrhythmia.

Statistical analysis

Preoperative, intraoperative, and postoperative variables were compared between the patients with and without postoperative AF using different statistical tests. Categorical variables were analyzed using the chi-square test. Normally distributed continuous variables were analyzed using independent samples t-tests. The non-parametric Mann Whitney U test was used for non-normal data. In addition to univariate analysis, multivariate analysis was conducted, and the odds ratio (OR) for each factor was assessed after controlling for other variables. For the multivariate analysis, logistic regression was used. In univariate analysis, the variables with p-values less than 0.50 that were thought to be related to AF were included in the model. Continuous data are expressed as mean $\pm$ standard deviation, and categorical variables as the frequency and percentage for each group. The analyses were performed using the Statistical Package for Social Sciences 25.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The results of the study were evaluated within a 95% reliance, and a p-value < 0.05 was considered to be statistically significant.

RESULTS

The analysis included 143 patients with AF (44 females, 99 males) and 315 patients without AF (109 females, 206 males). The incidence of postoperative AF in this study was 31.2% (143/458). The non-AF group and AF group were compared in terms of demographic and preoperative, intraoperative, and postoperative factors after CABG surgery (Table 1, Table 2 and Table 3, respectively).

The patients with AF were significantly older than those without AF ($p \leq 0.001$). The average age of the non-AF group was 61.76 ± 9.83 years, whereas the average age of the AF group was 68.08 ± 7.76 years. There were no significant differences in any other preoperative and demographic factors between the AF and non-AF groups (all p values > 0.05; Table 1).

When intraoperative factors were considered (Table 2), it was observed that the patients with AF had a significantly higher use of cardiopulmonary bypass (CPB) during the surgery compared to the patients without AF (69.2% vs. 43.2%, $p \leq 0.001$). The patients with postoperative AF had a significantly higher value of distal bypass (3.69 ± 0.773 vs. 3.43 ± 0.866, $p = 0.007$). There were no statistically significant differences between the AF and non-AF groups in the other intraoperative variables.

The patients with and without AF were significantly different in numerous postoperative variables (Table 3). The patients with AF had statistically significantly longer lengths of ICU and hospital stay, and more transfused erythrocyte suspension (ES) units than the non-AF group ($p \leq 0.001$ for the lengths of ICU and hospital stay, and $p = 0.001$ for transfused ES units). The average lengths of ICU and hospital stay in the AF group versus the non-AF group were 43.79 ± 32.39 versus 30.49 ± 33.31 hours, and 8.20 ± 4.37 versus 5.77 ± 2.16 days, respectively; whereas the average number of transfused ES units in the AF group versus the non-AF group were 1.23 ± 1.05 versus 0.94 ± 1.03, respectively. There were no statistically significant differences between the patients with and without postoperative AF with respect to extubation time, hematocrit level, unit of transfused fresh frozen plasma, use of inotropic agents and intra-aortic balloon pumps, major postoperative complications including low cardiac output syn-

Table 1. Demographic and preoperative variables

Variables	Non-AF group (n = 315)	AF group (n = 143)	p value
Age	61.76 ± 9.83	68.08 ± 7.76	< 0.001
Gender (Male)	206 (65.4%)	99 (69.2%)	0.420
Body mass index	27.49 ± 4.00	27.46 ± 3.49	0.926
Obesity	59.28 (18.7%)	28 (19.6%)	0.830
LMCA disease	66 (21%)	28 (19.6%)	0.736
Low LVEF	209 (66.3%)	90 (62.9%)	0.477
LVEF level	50.12 ± 8.82	50.15 ± 8.23	0.814
Hypertension	214 (67.9%)	99 (69.2%)	0.783
Diabetes mellitus	125 (39.7%)	51 (35.7%)	0.413
Hyperlipidemia	124 (39.4%)	60 (42.0%)	0.600
Myocardial infarction	100 (31.7%)	54 (37.8%)	0.207
Chronic renal dysfunction	17 (5.4%)	6 (4.2%)	0.585
Chronic liver disease	1 (0.3%)	2 (1.4%)	0.184
Peripheral arterial disease	39 (12.4%)	18 (12.6%)	0.951
COPD	19 (6.0%)	15 (10.5%)	0.092
Previous CVE	8 (2.5%)	2 (1.4%)	0.439
Previous PCI	33 (10.5%)	17 (11.9%)	0.653
Smoking	85 (27%)	41 (28.7%)	0.708

AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; CVE, cerebrovascular event; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.
Data expressed as mean ± standard deviation for continuous variables or number (%) for categorical variables.
Continuous variables compared using independent samples t-test.
Mann Whitney U test was used for comparing LVEF level variable.
Categorical variables reported as frequency (percent) and compared using chi square tests.

Table 2. Intraoperative variables

Variables	Non-AF group (n = 315)	AF group (n=143)	p value
CPB use	136 (43.2%)	99 (69.2%)	< 0.001
CPB time (min)	87.94 ± 27.98	94.48 ± 35.05	0.116
LITA use	306 (97.1%)	135 (94.4%)	0.151
Complete revascularization	299 (94.9%)	137 (95.8%)	0.682
Number of distal bypass	3.43 ± 0.87	3.69 ± 0.77	0.007

AF, atrial fibrillation; CPB, cardiopulmonary bypass; LITA, left internal thoracic artery.
Data expressed as mean ± standard deviation for continuous variables or number (%) for categorical variables.
Independent samples t-test was used for comparing CPB times.
Mann Whitney U test was used for comparing numbers of distal bypass.
Categorical variables were compared using chi square tests.

drome, myocardial infarction, CVE, mediastinitis, pneumonia, respiratory failure requiring reintubation, severe bleeding requiring re-exploration, acute renal dysfunction requiring hemodialysis, gastrointestinal bleeding, and in-hospital mortality.

After identifying the significant risk factors, multivariate analysis was performed to evaluate the relationships between the development of postoperative AF and its risk factors by adjusting for other independent variables that may also be related to AF. The multivariate analysis was conducted using a logistic regression model, and the results revealed that the risk of developing postoperative AF increased by 7.6% with a one-year increase in the patient's age [OR 1.076 with 95% CI: (1.047, 1.106), p < 0.001], and that the risk of AF was 2.1 times higher when CBP was used during the operation [OR 2.110 with 95% CI: (1.289, 3.456), p = 0.003] (Table 4).

Table 3. Postoperative variables

Variables	Non-AF group (n = 315)	AF group (n = 143)	p value
Extubation time (hour)	7.29 ± 3.01	7.30 ± 3.80	0.416
Length of ICU stay (hour)	30.49 ± 33.31	43.79 ± 32.39	< 0.001
Length of hospital stay (day)	5.77 ± 2.16	8.20 ± 4.37	< 0.001
Hematocrit level	29.02 ± 3.42	28.42 ± 3.51	0.077
Transfused ES (unit)	0.94 ± 1.03	1.23 ± 1.05	0.001
Transfused FFP (unit)	1.91 ± 0.99	1.82 ± 0.99	0.564
Inotrope requirement	32 (10.2%)	10 (7.0%)	0.277
IABP requirement	15 (4.8%)	5 (3.5%)	0.539
Low cardiac output syndrome	15 (4.8%)	4 (2.8%)	0.329
Myocardial infarction	6 (1.9%)	3 (2.1%)	0.890
Cerebrovascular event	9 (2.9%)	1 (0.7%)	0.143
Reintubation	10 (3.2%)	4 (2.8%)	0.828
Pneumonia	7 (2.2%)	3 (2.1%)	0.933
Mediastinitis	5 (1.6%)	2 (1.4%)	0.879
Reexploration for bleeding	7 (2.2%)	5 (3.5%)	0.429
ARD requiring hemodialysis	5 (1.6%)	3 (2.1%)	0.699
Gastrointestinal bleeding	2 (0.6%)	0 (0.0%)	0.340
In-hospital mortality	5 (1.6%)	2 (1.4%)	0.879

AF, atrial fibrillation; ARD, acute renal dysfunction; ES, erythrocyte suspension; FFP, fresh frozen plasma; IABP, intraaortic balloon pump; ICU, intensive care unit.
Data expressed as mean ± standard deviation for continuous variables or number (%) for categorical variables.
Mann Whitney U test was used for continuous variables.
Categorical variables were compared using chi square tests.

Table 4. Results of multivariate analysis for prediction of independent risk factors

Variables	p value	Odds ratio (95% CI)
Age	< 0.001	1.076 (1.047, 1.106)
Gender (Male)	0.201	0.718 (0.432, 1.193)
Low LVEF	0.372	0.797 (0.484, 1.312)
Diabetes mellitus	0.509	0.848 (0.519, 1.384)
Myocardial infarction	0.563	1.159 (0.703, 1.911)
COPD	0.124	1.972 (0.831, 4.679)
CPB use	0.003	2.110 (1.289, 3.456)
Number of distal bypass	0.190	1.225 (0.905, 1.659)
Extubation time	0.675	1.015 (0.947, 1.088)
Length of ICU stay	< 0.001	1.003 (0.996, 1.010)
Length of hospital stay	< 0.001	1.474 (1.292, 1.681)
Hematocrit level	0.943	1.003 (0.931, 1.080)
Transfused ES	0.323	1.130 (0.887, 1.439)
Inotrope requirement	0.148	0.411 (0.123, 1.370)
LCOS	0.602	1.625 (0.262, 10.084)

CI, confidence interval; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; ES, erythrocyte suspension; ICU, intensive care unit; LCOS, low cardiac output syndrome; LVEF, left ventricular ejection fraction.
Results of multivariate logistic regression analysis of postoperative atrial fibrillation as the dependent variable.
The goodness of fit of the model in the logistic regression analysis was confirmed by a p-value of 0.688 in the Hosmer-Lemeshow test.

DISCUSSION

Postoperative atrial fibrillation (POAF) is a frequent complication of cardiac surgery, affecting 10% to 40% of patients undergoing isolated CABG surgery.[2,11-13] Despite improvements in cardiac anesthesia, surgical and myocardial protection techniques, no significant decline in the incidence of POAF has been observed. On the contrary, its incidence has increased paradoxically in recent years because of the older age more comorbidities of the surgical patients, and due to advancements in continuous ECG monitoring technology. In our study population, the overall incidence of POAF was 32.1%, The incidence of POAF after CABG in our study was comparable to the literature.

Ischemia-reperfusion injury occurs following the release of aortic cross clamp during conventional on-pump surgery. It is known that ischemia-reperfusion injury increases the risk of POAF development.[14,15] We aimed to avoid ischemia-reperfusion injury by using the beating-heart CABG technique, and therefore to reduce the incidence of POAF; however, since we included all AF cases (including AF that did not alter hemodynamic parameters, and even very short-lived and transient AF) in

the AF group, we did not obtain a lower POAF incidence in our study population.

Although in earlier studies POAF has been considered to be a self-limiting, temporary, benign and well-tolerated clinical condition, recent studies have suggested that it is more 'malignant' than previously thought, and associated with prolonged ICU and hospital stay, greater usage of healthcare resources, increased perioperative morbidity, and even increased early and late mortality.[2-5,10,16-20] A two-fold increased risk of cardiovascular mortality has also been reported in patients with POAF after CABG.[21,22]

The pathophysiology of POAF following CABG is not completely understood. Current evidence suggests that a combination of several factors plays role in the occurrence of POAF. These factors include enhanced inflammation, ischemia, oxidative stress, atrial fibrosis, excessive delivery of catecholamines to the systemic circulation, imbalance of the autonomic tonus, and changes in the expression of connexins that cause the formation of a predisposing anatomic substrate.[23]

Determining the risk factors of POAF following CABG is important, since it may contribute to the implementation of prevention strategies and prompt management. Although numerous risk factors have been reported in different studies, increased age is the strongest risk factor for POAF, and is almost always identified as a significant predictor in the literature.[2-11,16-18,21,23] The causal relationship between age and AF development has been explained by atrial dilation and myocyte loss due to aging, muscle atrophy, decrease in conduction tissue and fibrosis. These pathophysiological changes in atrium tissue may then lead to multiple pathways for re-entry that induce atrial arrhythmias including AF.[24,25] In our study population, age was the only preoperative risk factor for POAF, and a one-year increase in the patient's age was associated with 7.6% increase in the risk of developing POAF.

We also revealed that the use of CPB during beating-heart CABG surgery was another independent predictor of POAF. Moreover, the risk of POAF was 2.1 times higher when CBP was applied during beating-heart CABG surgery. The effect of using CPB during CABG on the development of POAF is controversial. Some studies have reported that off-pump CABG reduces the development of POAF compared to on-pump CABG.[26-28] Additionally, a recent systematic review and meta-analysis study comprising a total of 16,261 participants from 54 clinical trials comparing the safety and effectiveness of off-pump and on-pump CABG reported that the incidence of POAF was significantly reduced in the off-pump CABG group.[29] On the other hand, some other studies have shown that off-pump CABG does not reduce AF development in postoperative period compared with on-pump technique, and that it is associated with statistically similar incidence of POAF.[11,30-32] As a result, the scientific data from both randomized and observational studies in the existing literature are inconsistent, and many studies investigating this matter have weaknesses in design, conduct or interpretation. However, in the comparative studies, the on-pump technique was mostly attributed to conventional CABG with the use of aortic cross clamping and cardioplegic arrest, and in the literature there are very few studies regarding comparisons of the off-pump technique with on-pump beating-heart CABG (without aortic cross clamping and cardioplegic arrest) in terms of POAF development.

In our study, ES transfusion was associated with POAF development in the univariate analysis, but not in the multivariate analysis. The effect of blood transfusion on POAF development after CABG is another controversial issue. Although a significant association between blood transfusion and POAF development has been reported in many studies,[33-35] other studies have not demonstrated this association.[2,36,37] In accordance with our study, ES transfusion was not considered to a significant predictor of AF that develops in patients undergoing isolated beating-heart CABG.

In almost all studies in the literature, patients with POAF after CABG have been reported to have longer lengths of ICU and hospital stay. Similarly to the literature, our study also revealed that the mean lengths of ICU and hospital stay were significantly longer in the patients with POAF than in those without POAF. Compared to a normal sinus rhythm, AF can worsen the patients' hemodynamic status due to the lack of coordinated atrial function and tachycardia. Moreover, it is a potential cause of several major adverse events such as thromboembolism, CVE and myocardial infarction, and it requires early and appropriate treatment. Hemodynamic instability secondary to AF, possible complications and treatment procedures of AF are the major reasons for

prolonged ICU and hospital stay.

Limitations of the study

This study has several limitations. The main limitation is the retrospective nature of data collection in this study. Patients with complex and diffuse coronary artery disease were more likely to undergo on-pump beating-heart CABG. Therefore, patient selection bias for the surgical procedure was possible. Other important limitations were comparing AF and non-AF groups who underwent off-pump and on-pump beating-heart CABG without subdividing them, and the lack of mid- and long-term outcomes of the patients and thus not establishing a relationship between POAF and late survival. In addition, continuous cardiac rhythm monitoring was not performed after ICU discharge in the acute inpatient ward. Although during acute inpatient ward follow-up standard ECG recordings were obtained routinely every day and whenever there was a clinical suspicion of arrhythmia, it is likely that short episodes of asymptomatic AF may be missed.

CONCLUSIONS

The results of our study demonstrated that age and the use of CPB during surgery were independent predictors of POAF following beating-heart CABG. In addition, POAF was associated with prolonged ICU and hospital stay. However, further prospective randomized studies with a larger sample size are necessary in order to support our research and attain more accurate data.

CONFLICT OF INTEREST

All the authors declare no conflict of interest.

REFERENCES

1. Olgin JE, Zipes DP. Specific arrhythmias: diagnosis and treatment. In: Libby P, Bonow RO, Mann DL, Zipes DP. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 8th ed. Philadelphia: Saunders, 2008:869.
2. Yuksel A, Velioglu Y, Tecimer ME, et al. Is there any relationship of postoperative atrial fibrillation with the use of blood products and postoperative hemoglobin levels in patients undergoing coronary artery bypass grafting? *Med Science* 2018.
3. Filardo G, Damiano RJ Jr, Ailawadi G, et al. Epidemiology of new-onset atrial fibrillation following coronary artery bypass graft surgery. *Heart* 2018;104:985-92.
4. Villareal RP, Hariharan R, Liu BC, et al. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. *J Am Coll Cardiol* 2004;43:742-8.
5. El-Chami MF, Kilgo P, Thourani V, et al. New-onset atrial fibrillation predicts long-term mortality after coronary artery bypass graft. *J Am Coll Cardiol* 2010;55:1370-6.
6. Aranki SF, Shaw DP, Adams DH, et al. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. *Circulation* 1996;94:390-7.
7. Zaman AG, Archbold RA, Helft G, et al. Atrial fibrillation after coronary artery bypass surgery: a model for preoperative risk stratification. *Circulation* 2000;101:1403-8.
8. Mathew JP, Fontes ML, Tudor IC, et al. A multicenter risk index for atrial fibrillation after cardiac surgery. *JAMA* 2004;291:1720-9.
9. Banach M, Rysz J, Drozdz JA, et al. Risk factors of atrial fibrillation following coronary artery bypass grafting: a preliminary report. *Circ J* 2006;70:438-41.
10. Mariscalco G, Klersy C, Zanobini M, et al. Atrial fibrillation after isolated coronary surgery affects late survival. *Circulation* 2008; 118:1612-8.
11. Bohatch Júnior MS, Matkovski PD, Di Giovanni FJ, et al. Incidence of postoperative atrial fibrillation in patients undergoing on-pump and off-pump coronary artery bypass grafting. *Rev Bras Cir Cardiovasc* 2015;30:316-24.
12. Polat A, Şahin İ, Yücel C, et al. Coronary vasculature and postoperative atrial fibrillation: a risk factor analysis. *Turk Gogus Kalp Dama* 2013;21:567-73.
13. Chen SW, Chang CH, Chu Y, et al. Postoperative renal outcomes of on-pump beating-heart versus cardioplegic arrest coronary artery bypass grafting. *Acta Cardiol Sin* 2017;33:542-50.
14. Ercan A, Karal IH, Gurbuz O, et al. A comparison of off-pump and on-pump coronary bypass surgery in patients with low EuroSCORE. *J Cardiothorac Surg* 2014;9:105.
15. Gurbuz O, Kumtepe G, Yolgosteren A, et al. A comparison of off- and on-pump beating-heart coronary artery bypass surgery on long-term cardiovascular events. *Cardiovasc J Afr* 2017;28:30-5.
16. Al-Shaar L, Schwann TA, Kabour A, et al. Increased late mortality after coronary artery bypass surgery complicated by isolated new-onset atrial fibrillation: a comprehensive propensity-matched analysis. *J Thorac Cardiovasc Surg* 2014;148:1860-8.
17. Erdil N, Kaynak M, Dönmez K, et al. Nebivolol in preventing atrial fibrillation following coronary surgery in patients over 60 years of age. *Rev Bras Cir Cardiovasc* 2014;29:581-7.
18. Phan K, Ha HS, Phan S, et al. New-onset atrial fibrillation following coronary bypass surgery predicts long-term mortality: a systematic review and meta-analysis. *Eur J Cardiothorac Surg* 2015; 48:817-24.
19. Yoldas H, Karagoz I, Ogun MN, et al. Novel mortality markers for

critically ill patients. *J Intensive Care Med* 2018:885066617753389.
20. Karagoz I, Aktas G, Yoldas H, et al. Association between hemogram parameters and survival of critically ill patients. *J Intensive Care Med* 2017:885066617703348.
21. Ahlsson A, Bodin L, Fengsrud E, et al. Patients with postoperative atrial fibrillation have a doubled cardiovascular mortality. *Scand Cardiovasc J* 2009;43:330-6.
22. Wu ZK, Iivainen T, Pehkonen E, et al. Fibrillation in patients subjected to coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2003;126:1477-82.
23. Erdil N, Gedik E, Donmez K, et al. Predictors of postoperative atrial fibrillation after on-pump coronary artery bypass grafting: is duration of mechanical ventilation time a risk factor? *Ann Thorac Cardiovasc Surg* 2014;20:135-42.
24. Kitzman DW, Edwards WD. Age-related changes in the anatomy of the normal human heart. *J Gerontol* 1990;45:M33-9.
25. Schauerte P, Scherlag BJ, Patterson E, et al. Focal atrial fibrillation: experimental evidence for a pathophysiologic role of the autonomic nervous system. *J Cardiovasc Electrophysiol* 2001;12:592-9.
26. Ascione R, Caputo M, Calori G, et al. Predictors of atrial fibrillation after conventional and beating heart coronary surgery: a prospective, randomized study. *Circulation* 2000;102:1530-5.
27. Järvinen O, Laurikka J, Tarkka MR. Off-pump versus on-pump coronary bypass. Comparison of patient characteristics and early outcomes. *J Cardiovasc Surg (Torino)* 2003;44:167-72.
28. Chen YB, Shu J, Yang WT, et al. Meta-analysis of randomized trials comparing the effectiveness of on-pump and off-pump coronary artery bypass. *Chin Med J (Engl)* 2012;125:338-44.
29. Dieberg G, Smart NA, King N. On- vs. off-pump coronary artery bypass grafting: a systematic review and meta-analysis. *Int J Cardiol* 2016;223:201-11.
30. Enc Y, Ketenci B, Ozsoy D, et al. Atrial fibrillation after surgical revascularization: is there any difference between on-pump and off-pump? *Eur J Cardiothorac Surg* 2004;26:1129-33.
31. Turk T, Vural H, Eris C, et al. Atrial fibrillation after off-pump coronary artery surgery: a prospective, matched study. *J Int Med Res* 2007;35:134-42.
32. Lewicki L, Siebert J, Rogowski J. Atrial fibrillation following off-pump versus on-pump coronary artery bypass grafting: incidence and risk factors. *Cardiol J* 2016;23:518-23.
33. Koch CG, Li L, Van Wagoner DR, et al. Red cell transfusion is associated with an increased risk for postoperative atrial fibrillation. *Ann Thorac Surg* 2006;82:1747-56.
34. Choi YS, Shim JK, Hong SW, et al. Risk factors of atrial fibrillation following off-pump coronary artery bypass graft surgery: predictive value of C-reactive protein and transfusion requirement. *Eur J Cardiothorac Surg* 2009;36:838-43.
35. Sood N, Coleman CI, Kluger J, et al. The association among blood transfusions, white blood cell count, and the frequency of post-cardiothoracic surgery atrial fibrillation: a nested cohort study from the Atrial Fibrillation Suppression Trials I, II, and III. *J Cardiothorac Vasc Anesth* 2009;23:22-7.
36. Murphy GJ, Reeves BC, Rogers CA, et al. Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. *Circulation* 2007;116:2544-52.
37. Auer J, Weber T, Berent R, et al. Risk factors of postoperative atrial fibrillation after cardiac surgery. *J Card Surg* 2005;20:425-31.