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Impact of preoperative persistent or permanent atrial fibrillation on in-hospital mortality after coronary artery bypass graft surgery

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ABSTRACT

Introduction: Atrial fibrillation (AF) is an arrhythmia that has a well-established impact on cardiovascular and cerebrovascular morbidity and mortality. However, the role of this arrhythmia plays on surgical risk remains uncertain. **Objective:** To evaluate the impact of preoperative persistent or permanent AF on in-hospital mortality after isolated coronary artery bypass graft surgery (CABG). **Methods:** Prospective cohort with 2,377 patients submitted to isolated CABG between January 2014 and December 2021. Sixty-two variables, including baseline factors, operative characteristics, and outcomes, were analyzed. Patients were divided into two study groups: No preoperative AF (n=2,287) and preoperative persistent or permanent AF (N=n=90). The comparison between the groups was performed initially by descriptive and univariate analysis. Subsequently, the analysis of mortality predictors was performed using binary logistic regression - multivariate adjusted analysis. **Results:** Patients with preoperative AF were older, had a higher prevalence of pulmonary hypertension and anemia, had lower ejection fraction and had higher surgical risk scores when compared with patients with no history of atrial fibrillation. The in-hospital death was more frequent in patients with a history of AF (3.2% vs 8.9%, P=0.010). Through the multivariate analysis, it was possible to verify that preoperative AF is independently associated with the occurrence of in-hospital mortality after CABG (OR 2.68; 95% CI 1.21-5.94, P=0.015). **Conclusion:** Preoperative persistent or permanent AF has been shown to have a significant impact on in-hospital mortality rates after CABG even after adjusted multivariate analysis, being an independent risk predictor for the occurrence of postoperative death.

KEYWORDS: Physiological cardiac stimulation; His-bundle ventricular stimulation; Ventricular dysfunction.

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INTRODUCTION

Atrial fibrillation (AF) is a supraventricular arrhythmia that impairs cardiac function and increases the risk of stroke. The condition is characterized by uncoordinated electrical activation of the atrium resulting in an irregular ventricular response[1]. As a result of atrial fibrillation, blood is temporarily retained in the atrium, which can lead to thrombus formation in the atrial appendage, increasing the risk of thromboembolic stroke. The occurrence of AF is associated with a five-fold increased chance of stroke[2].

AF is the most frequent sustained cardiac arrhythmia, and its prevalence is increased with age, being an important factor of morbidity and mortality[3,4]. This arrhythmia affects more than 18% of individuals over 60 years and about 50% of those over the age of 80 years after CABG surgery. Hypertension is also considered an important predictor, since it is associated with cardiac structural alterations such as fibrosis and dilation, as well as other AF related comorbidities[5].

In addition, AF is a frequent arrhythmia in the postoperative period of cardiac surgery. In this context, it is associated with the presence of comorbidities, a longer hospitalization time and a higher cost related to surgery[6]. AF usually occurs more frequently in the first five postoperative days, with a peak between 24 and 72 hours, being infrequent after the first week[7].

Since it was established in 1964, coronary artery bypass graft surgery (CABG) is the standard treatment for complex coronary artery disease. It is, since the most performed cardiac surgery in the world. In Brazil, the number of annual interventions is around 20 thousand procedures[8]. Thus, the study of preoperative risk factors has become indispensable for an accurate assessment of patients. Some of these factors constitute the surgical risk scores established in cardiology practice, but which, despite the wide use, present important limitations, which are capable of underestimating or overestimating the risk according to the population studied[9,10]. One of these scores is the EuroSCORE, that in its two versions does not consider preoperative AF as a relevant risk factor for cardiac surgery. On the other hand, the STS Score considers AF in the risk assessment associated with cardiac surgery[11,12].

These findings reinforce that the study of risk factors for heart surgery remains relevant and necessary[9,10]. In addition, the absence of AF in one of the main cardiovascular risk scores used in clinical-surgical practice evidences the need for studies that evaluate the influence of preoperative AF in relation to the results obtained with the accomplishment of cardiovascular surgical procedures. Therefore, the present study aimed to evaluate the impact of preoperative persistent or permanent AF on in-hospital mortality after CABG.

METHODS

Prospective cohort study with consecutive inclusion of all patients undergoing isolated CABG between January 2014 and December 2021 in a reference surgical center in southern Brazil. All patients were operated by the same surgical team and were submitted to the same care protocol. The present study was approved by the local Ethical Committee and was based on the guidelines and norms of good practices in clinical research.

A total of 2377 patients were included, 70.5% were males and the mean age was 63 years. Sixty-two variables, including comorbidities, previous history, operative characteristics and outcomes, were analyzed. Based on the preoperative diagnosis of persistent or permanent AF, the patients were then divided into two study groups: No preoperative AF (n=2287/96.2%) and preoperative AF (n=90/3.8%). For the preoperative AF group, we considered only very well documented persistent and long standing persistent (permanent) diagnosis by 24 hours Holter and registers of periodic electrocardiograms.

The data used to perform the study are part of the prospective registry of cardiovascular surgeries of the institution. All patients undergoing cardiovascular surgery are included in the registry and their data are tabulated in a coded form compatible with statistical analysis software. For the present study, all patients submitted to isolate CABG were selected and it was created a new data set for these specific patients.

The descriptive analysis was performed to evaluate qualitative data frequencies and to evaluate measures of central tendency of quantitative data. Subsequently, the normality of the numerical variables was evaluated through kurtosis, asymmetry, and Kolmogorov-Smirnov test. Through this analysis we could observe that all the numerical variables of the study were compatible with the use of parametric statistical tests.

The comparison between groups in relation to preoperative, surgical and outcome variables was initially performed by univariate analysis (Pearson's Chi-square and T-Test for independent samples). Subsequently, the identification and confirmation of possible predictors of mortality were performed through multivariate analysis - binary logistic regression. The primary outcome for this study was in hospital mortality.

The variables that composed the regression model for in hospital mortality were selected through univariate statistical tests, Chi-square for categorical variables and T-Test for Independent Samples for continuous variables. The predictive accuracy of the regression model was measured by ROC curve of the probabilities estimated by the multivariate model. The significance level adopted was 5% and the software used was SPSS V23.

RESULTS

The univariate analysis showed that patients with persistent or permanent AF were older, had a higher prevalence of pulmonary hypertension and anemia, had lower left ventricular ejection fraction, and had higher surgical risk scores when compared with patients with no diagnosis of atrial fibrillation (Table 1).

Table 1. Baseline characteristics of study groups.

Preoperative status	No AF (n=2287)	Persistent or permanent AF (n=90)	*P*
Age (years)	62.8±9.4	67.9±8.1	<0.001
Female	683 (29.9%)	20 (22.2%)	0.119
Systemic hypertension	1936 (84.7%)	79 (87.8%)	0.418
Diabetes	922 (40.3%)	33 (36.7%)	0.489
AMI	837 (36.6%)	36 (40%)	0.511
Renal impairment	267 (11.7%)	14 (15.6%)	0.265
Clearence of creatinine	73±28	70±26	0.309
Renal replacement therapy	53 (2.3%)	3 (3.3%)	0.534
Smoking	1130 (49.4%)	45 (50%)	0.913
COPD	164 (7.2%)	10 (11.1%)	0.159
Pulmonary hypertension	38 (1.7%)	8 (8.9%)	<0.001
Stroke	162 (7.1%)	9 (10%)	0.294
Extracardiac arteriopathy	150 (6.6%)	7 (7.8%)	0.649
Ejection fraction of LV	60±13	55±15	0.001
Heart Failure (NYHA III/IV)	459 (20.1%)	17 (18.9%)	0.784
Anemia	736 (32.2%)	38 (42.2%)	0.046
Unstable angina	187 (8.2%)	6 (6.7%)	0.607
Previous CV surgery	58 (2.5%)	4 (4.4%)	0.265
Previous PCI	459 (20.1%)	14 (15.6%)	0.293
Left main stenosis > 50%	535 (23.4%)	23 (25.6%)	0.635
EuroSCORE I	3.4±3.9	5.2±5.9	0.005
EuroSCORE II	1.7±1.5	2.4±2.6	0.011
STS Score	1.05±1.04	2.14±2.62	<0.001

Source: Elaborated by the authors.

In the analysis of the operative characteristics, we verified that the urgency and emergency surgeries did not present difference between the study groups, as well as the use of the left internal mammary artery (LIMA) as graft, complete revascularization, aortic clamping time and total time of cardiopulmonary bypass. The only surgical variable that presented a significant difference was the use of cardiopulmonary bypass, which was significantly more frequent in patients with atrial fibrillation (Table 2).

Table 2. Surgical characteristics of study groups.

Surgical variables	No AF (n=2287)	Persistent or permanent AF (n=90)	*P*
Urgency/Emergency	149 (6.5%)	5 (5.6%)	0.717
CABG on pump	1428 (62.4%)	72 (80%)	0.001
Graft of LIMA	2061 (90.1%)	80 (88.9%)	0.702
Complete revascularization	2198 (96.2%)	85 (94.4%)	0.413
Aortic clamping time (minutes)	63±19	65±27	0.533
CPB time (minutes)	79±23	85±37	0.223

Source: Elaborated by the authors.

The incidence of some outcomes was significantly higher in the group with AF prior to surgery. Myocardial infarction, sepsis, major cardiovascular and cerebrovascular events (MACCE) and in-hospital death from any cause (Fig. 1) were significantly more frequent in the postoperative period of patients with AF.

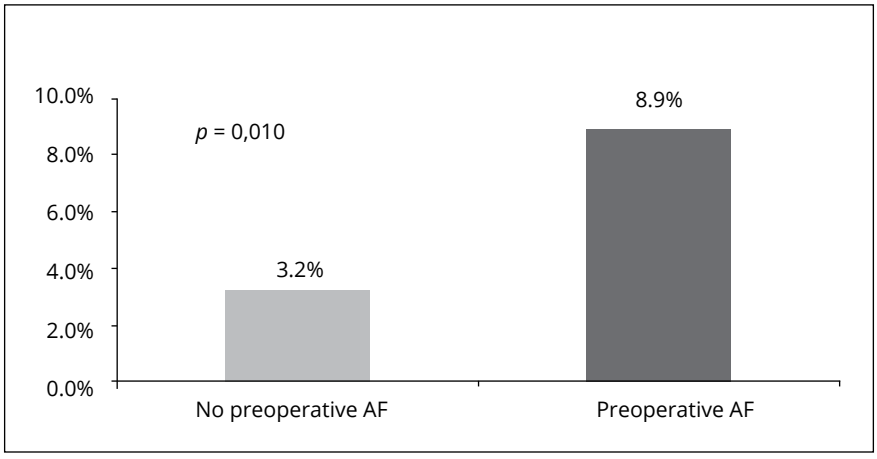

Figure 1. In-hospital mortality by prevalence of atrial fibrillation
Source: Elaborated by the authors.

The other outcomes analyzed did not present an important statistical difference between the study groups (Table 3).

Through the multivariate analysis adjusted for the variables that demonstrated differences in the preliminary univariate analysis considering mortality as the primary outcome, it was possible to verify that preoperative AF is independently associated with the occurrence of in-hospital death after CABG (OR 2.68, 95% CI, 1.21 - 5.94, *P*=0.015). The presence of preoperative AF resulted in a significant increase of 68% in the relative risk of in-hospital death after CABG. In addition to persistent or permanent AF, female gender, kidney damage, anemia and not using LIMA as a graft had a significant p-value in the adjusted multivariate analysis, also being characterized as independent predictors for the occurrence of in-hospital death (Table 4).

Table 3. Post-operative incidences of outcomes.

Outcomes	No AF (n=2287)	Persistent or permanent AF (n=90)	*P*
Conversion to on-pump CABG	3 (0.1%)	0 (0%)	0.743
Reoperation for any cause	69 (3.0%)	6 (6.7%)	0.062
New revascularization	19 (0.8%)	0 (0%)	1.000
Stroke	109 (4.8%)	4 (4.4%)	1.000
Myocardial infarction	45 (2.0%)	6 (6.7%)	0.011
Major bleeding	33 (1.4%)	3 (3.3%)	0.153
Heart failure	68 (3.0%)	1 (1.1%)	0.302
Pleural effusion	34 (1.5%)	0 (0%)	0.638
Pacemaker implantation	8 (0.3%)	1 (1.1%)	0.294
Saphenectomy site infection	32 (1.4%)	3 (3.3%)	0.144
Sternal infection	92 (4.0%)	2 (2.2%)	0.390
Sepsis	19 (0.8%)	3 (3.3%)	0.048
MACCE	221 (9.7%)	17 (18.9%)	0.004
Length of hospital stay (days)	10.7±14.4	12.6±11.8	0.238
In-hospital death	73 (3.2%)	8 (8.9%)	0.010

Source: Elaborated by the authors.

Table 4. Logistic regression model for in-hospital mortality.

Variables	Wald	OR	IC 95%	*p*
Female	5.71	1.77	1.10 – 2.83	0.017
Diabetes *mellitus*	0.43	1.17	0.73 – 1.86	0.510
Renal impairment	12.5	2.58	1.52 – 4.36	<0.001
Heart failure (NYHA III/IV)	2.78	1.54	0.92 – 2.58	0.095

Source: Elaborated by the authors.

DISCUSSION

With the accomplishment of this study, we could observe that the persistent or permanent atrial fibrillation in the preoperative period is associated with the occurrence of in-hospital death after the isolated CABG. While hospital mortality was 3.2% in the group with no diagnosis of AF, the mortality in the group with persistent or permanent AF was 8.9%. Although the study groups showed differences regarding baseline characteristics, these differences were stabilized through the adjusted multivariate analysis, which confirmed the association between preoperative atrial fibrillation and mortality, characterizing this sustained arrhythmia as an independent predictor of death.

The logistic regression model had a predictive accuracy of 75%, which is a good predictor considering that preoperative and intraoperative variables were considered, following the pattern of surgical risk scores. In this way, postoperative factors were not considered. Nevertheless, the logistic regression model was able to explain a significant part of the variability of the outcome.

These findings about in-hospital mortality corroborate what studies have shown in recent years. Patients referred for cardiovascular surgery and who have a history of atrial fibrillation have reduced survival after performing the cardiovascular surgical procedure. In 2004, Quader et al.[13] published a study that analyzed 46,984 patients undergoing isolated CABG with follow-up of ten years. The authors concluded that AF is a marker of high-risk patients and found that the 10-year

survival rate reaches 24% in favor of the group with no preoperative history of AF. In addition, in 2007, Ngaage et al.[14] concluded that preoperative AF represents an increase of 40% in the relative risk of death after CABG.

More recently, in 2018, Malaisrie et al.[15] conducted a large study using data from the Medicare-Linked Society of Thoracic Surgeons. A total of 361,138 patients undergoing to isolated CABG between 2006 and 2013 were analyzed. The researchers found that preoperative AF was strongly associated with the occurrence of in-hospital death and that the presence of this arrhythmia before the surgery was an independent predictor of mortality (OR 1.5, $P<0.001$)[15]. Other important study about preoperative AF and CABG was performed on the Swedish Heart Surgery Registry, Batra et al.[16], analyzed data from 9,107 patients undergoing isolated CABG. The researchers found that patients with preoperative atrial fibrillation are at high risk for death from any cause (HR 1.27 / CI 95% 1.01 – 1.60) and cardiovascular death (HR 1.52 / CI 95% 1.10 – 2.11) after surgery[16].

In addition, some studies have shown that surgical ablation reduces mortality in 30 days, significantly reducing the incidence of stroke and transient ischemic attacks[17,18]. These findings resulted in an update of STS guidelines in 2017, which recommended surgical ablation at the same time as baseline surgery – mitral valve surgery, aortic valve surgery or CABG[18,19]. In resume, the guideline suggests that the intervention in patients with preoperative AF increases the patient chances of survival after cardiovascular surgery.

The mechanism that leads patients with coronary artery disease to develop atrial fibrillation is still not well defined and may be different from the mechanisms involved in valvular patients or other cardiovascular condition. Studies have shown that atrial ischemia can cause atrial fibrillation through changes in conduction and repolarization of the atrium[20,21].

Risk factors such as high age, hypertension and obesity are shared by atrial fibrillation and coronary artery disease[22]. In our study, the age of patients with a history of preoperative AF was higher, averaging five years longer than patients without AF. Pulmonary hypertension, anemia, and lower ejection fraction were also more frequent in patients with AF.

Estimates referring to the prevalence of AF in the preoperative period suggest that up to 10% of patients undergoing to CABG have a history of AF[15]. The prevalence observed in our study was 3.8%, below most of the prevalence of AF verified in previous studies. This data suggests that part of the patients may be underreporting or that is a portion of the population without a diagnosis of atrial arrhythmia.

Unfortunately, the outcomes comparison of patients with sinus rhythm and patients with history of AF can be difficult because the characteristics of coronary artery disease that affects the patients can be quite heterogeneous[23,24]. However, in our study, the only operative variable that presented difference between the groups was the use of cardiopulmonary bypass, which, in turn, did not present a significant association with in-hospital death in the adjusted multivariate analysis. The others operative's variables did not present significant differences, suggesting a similar pattern of CABG performed.

CONCLUSION

Preoperative persistent or permanent AF is a frequent condition and has a significant impact on the increase in the occurrence of in-hospital death after CABG in our population. The results presented reinforce the importance of careful preoperative evaluation of AF and the analysis of the treatment options for reversible cases of AF before the elective surgeries. Other important aspect is the inclusion of the AF in the surgical risk models, considering that this arrhythmia is not considered to estimate mortality in the two versions of the European surgical risk score, which are widely diffused and used in medical practice all over the world.

CONFLICT OF INTEREST

Not applicable.

AUTHOR'S CONTRIBUTION

Conceptualization: Rosler AM, Sales MC; **Methodology:** Rosler AM, Sales MC; **Investigation:** Ferreira G, Prediger VW, Nascimento JP, Rosler AM; **Writing – Original Draft:** Rosler AM, Sales MC; **Writing – Review and Editing:** Rosler AM, Sales MC, Lucchese FA; **Funding Acquisition:** Lucchese FA; **Resources:** Lucchese FA; **Supervision:** Lucchese FA.

DATA AVAILABILITY STATEMENT

All data sets were generated or analyzed in the current study.

FUNDING

Not applicable.

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