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New risk score for predicting postoperative atrial fibrillation after cardiac surgery

João Lins de Araújo Neto[1], Eduardo Arrais Rocha[1,*]

ORCID ID

Araujo Neto JL https://orcid.org/0000-0001-8185-7142 Rocha EA https://orcid.org/0000-0001-8975-1182

ABSTRACT

Introduction: Postoperative atrial fibrillation is the most common sustained arrhythmia after cardiac surgeries that occurs in approximately 30-50% of patients postoperatively. Because of the substantial evidence recommending prophylactic treatment and the lack of clear indications for commencing treatment, this study aimed to develop a new predictive score for atrial fibrillation after cardiac surgery that represents well the pathophysiology of the disease. **Methods:** This is a retrospective cohort study, involving two public teaching hospitals. The study included 989 adult patients who underwent cardiac surgery, except for heart transplantation or the implantation of a ventricular assist device. Patients with previous atrial fibrillation or those requiring amiodarone were excluded. The variables (age ≥60 years, echocardiographic LA enlargement, inotrope use within 24 hours of surgery, and the need for reoperation) were subjected to univariate analysis of the occurrence of postoperative atrial fibrillation and multivariate analysis using logistic regression. This was then used for developing a risk score. **Results:** Statistically significant variables in the multivariate analysis were age ≥60 years (P<.001), left atrial enlargement based on echocardiography (P=.025), inotrope use within 24 hours after surgery (P=.002), and the need for reoperation within 24 hours after surgery (P=.016). The score comprises these four variables and has an accuracy of 77% for predicting outcomes. Scores ≥3 were related to a 34% risk of postoperative atrial fibrillation. **Conclusions:** The proposed score represents the disease pathophysiology well and has good accuracy for predicting the main outcome.

KEYWORDS: Atrial fibrillation; Postoperative Complications; Cardiac surgery; Risk score.

INTRODUCTION

Atrial fibrillation (AF), the most prevalent sustained arrhythmia globally, has a great impact on the quality of life of affected individuals and places a heavy burden on the public health systems. The incidence of this condition gradually increases with age and has become more prevalent as the life expectancy of the population increases[1,2].

Postoperative AF (POAF) is common after cardiac surgery, with reported rates of 40%–50% after valve surgery and approximately 30% after coronary artery bypass graft (CABG) surgery[3]. It is associated with an increased risk of early stroke and mortality, late stroke and mortality, and prolonged hospital and intensive care unit (ICU) stay, thereby

1. Universidade Federal do Ceará – Programa de Pós-graduação em Ciências Cardiovasculares – Fortaleza-CE, Brazil.
***Correspondence author:** eduardo@cardiol.br
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resulting in higher costs[4-6]. Although often transient and easily reversible to sinus rhythm, POAF can recur after hospital discharge in up to 28% of cases, leading to higher associated mortality[7-9].

The pathogenesis of POAF is not completely known; however, it is believed that intraoperative and early postoperative events (such as inflammation, exacerbated sympathetic activity, and atrial ischemia) add to the presence of pre-existing factors (such as older age, left atrial (LA) enlargement, and left ventricular (LV) dysfunction) and trigger arrhythmia[6].

In terms of prevention of the arrhythmia, the medical societies of cardiologists and anesthesiologists, professionals who usually care for cardiac operated patients, agree that beta-blockers and the antiarrhythmic drug amiodarone are the available options for prevention, with ample scientific evidence proving their effectiveness[10–14]. Therefore, the most recent international guidelines recommend the use of these aforementioned drugs during the perioperative period for the prevention of AF after cardiac surgery[15-17]; however, there is a gap in the scientific literature regarding which patients should receive prophylactic therapy. Furthermore, a simple score that is representative of the pathophysiology of the disease is needed.

The principal objective of this study was to develop a novel predictor score for AF following cardiac surgery, with the aim of facilitating the stratification of patients according to their risk scores. Secondary objectives included assessing the odds ratio of predictors for the occurrence of POAF after cardiac surgery, estimating the incidence of POAF for patients undergoing cardiac surgery, and evaluate the association of POAF with mortality and stroke during hospitalization.

METHODS

Ethics

This research was approved by the research ethics committees of two public teaching hospitals (numbers 28775120.6.3001.5039, July 9, 2020 and 28775120.6.0000.5045, July 8, 2020).

The study was developed in accordance with the ethical standards set forth by resolution 466/12 of the National Health Council. The research ethics committees waived the need for informed consent because of the retrospective and observational nature of the study, during which there was no contact between the researcher and the research participants, and data were obtained only through medical records.

Design and setting

This retrospective, multicenter cohort study was conducted at two public teaching hospitals and analyzed 1139 medical records of patients who underwent cardiac surgery.

Inclusion and exclusion criteria

The inclusion criteria were age ≥ 18 years and open-heart surgery (except for heart transplantation and ventricular assist device implantation) between January 2017 and December 2019. The exclusion criteria were a previous diagnosis of AF, preoperative or intraoperative amiodarone use, incomplete medical data (e.g. lack of echocardiogram), and death in the operating room.

Sampling

A sample size of 501 participants was calculated using G*Power version 3.1.9.7 to achieve a statistical power of 80% and a significance level of 95% in predicting the primary outcome. A non-probabilistic convenience sample was selected for the study. All medical records of patients who met the inclusion criteria and were available for consultation were analyzed.

Data collection procedure, analyzed variables, and outcomes

The data were collected over the course of 12 months, between November 2020 and October 2021. During the actual analysis of the medical records, a form was completed for each patient, containing the relevant information, the variables subjected to analysis, and the resulting outcomes. The variables analyzed were age, sex, systemic arterial hypertension, diabetes mellitus, dyslipidemia, chronic obstructive pulmonary disease or bronchial asthma, beta-blocker use before surgery, acute myocardial infarction within 90 days, smoking, previous cardiac surgery, diagnosis of infective endocarditis, LA and LV enlargement, LA volume index (LAVI), LV remodeling (eccentric or concentric), Left Ventricular Ejection Fraction (LVEF), type of surgery performed, inotrope use (dobutamine or milrinone) within 24 hours after surgery, and the need for reoperation within 24 hours after surgery.

LA enlargement was considered if a P wave had a duration of >120 ms in lead D2 and/or a negative portion of the P wave with a duration of ≥40 ms and an amplitude of ≥1 mm in lead V1. Left ventricular enlargement was considered when the Cornell and Sokolow–Lyon criteria were met or the R wave in the aVL lead was ≥11 mm.

The primary outcome analyzed was AF lasting for a minimum of 30 seconds or requiring the intravenous administration of antiarrhythmics agents. POAF was considered when it occurred within the first 30 days after surgery and its diagnosis was confirmed by 12-lead electrocardiography. To be specific, POAF detection was made twice: first, by the ICU medical team, through assessment of medical records; and then, by the investigators (two cardiologists, one of them an arrythmia specialist), analyzing the electrocardiogram. Outcomes related to POAF were death and stroke during hospitalization after surgery and the lengths of ICU and hospital stay after surgery.

Statistical analysis

The numerical variables analysed included age, LAVI, LVEF, ICU admission, and length of hospital stay. The other variables were analyzed as categorical variables. To facilitate the composition of the score, the age variable was transformed into a categorical variable (<60 and ≥60 years). Moreover, the LAVI variable was transformed into a categorical variable (echocardiographic LA enlargement) because of the paucity of recordings of LAVI values during the analyzed echocardiographic examination (this measure was available in only 324 medical records, representing 32.8% of the sample). The LAVI was considered normal if ≤34 mL/m^2 and increased if >34 mL/m^2. Data were analyzed using SPSS version 23 and Jamovi version 1.6 (IBM Corp., New York, NY, USA). For the purposes of the data analysis, a statistical significance level (α) of 5% was assumed[18].

Initially, the numerical variables were evaluated using the normality test (Shapiro–Wilk test), and all were non-normal variables. Descriptive statistics were performed based on sample data, with numerical variables expressed as medians and interquartile ranges and categorical variables expressed as frequencies and percentages. Then, the variables were examined for their associations with the primary outcome (POAF) during the univariate analysis. The numerical variable LVEF was evaluated using a non-parametric test (Mann–Whitney U test) to verify the association with the primary outcome. The remaining variables (categorical) were evaluated using an association analysis (Chi-square test) to determine their correlation with the primary outcome.

During the multivariate analysis, a logistic regression model involving variables that had a significant association in the univariate analysis was developed. In order, to be included in the score, points were assigned to each predictor variable, in accordance with the odds ratio of each component. To calibrate the logistic regression model, the Hosmer–Lemeshow test was performed. To determine the predictive ability of the model, the accuracy was calculated, and a receiver-operating characteristic (ROC) curve was constructed to assess the discrimination ability of the score.

The variable POAF was analyzed in relation to the outcomes of death and stroke using the Chi-square test and in relation to the length of ICU and hospital stay using the Mann–Whitney U test.

RESULTS

Of the 1139 patients who underwent cardiac surgery, 150 participants were excluded from the study for various reasons. These included a previous diagnosis of AF (n=92), preoperative or intraoperative amiodarone use (n=38), incomplete data in the medical records (n=18), and death during surgery (n=2). Finally, a non-probabilistic sample of 989 medical records of patients who underwent cardiac surgery was included in the study (Fig. 1). The incidence of POAF in this study was 23%. The characteristics of the participants are presented in Table 1.

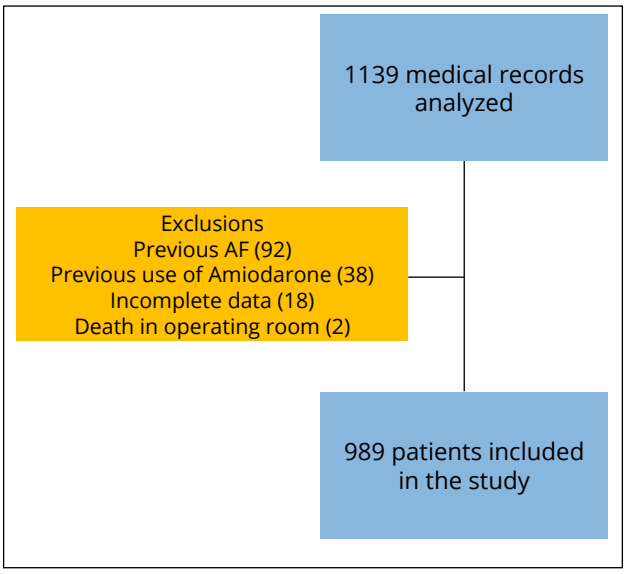

Figure 1. Study sample
Source: Elaborated by the authors.

Table 1. Sample characteristics (N=989)

Variables	Results
Age – median (interquartile range)	63 years (53-69 years)
Age ≥ 60 years old – n (%)	581 (58.7%)
Gender: male – n (%)	617 (62.4%)
Comorbidities – n (%)	
Arterial hypertension	701 (70.9%)
Diabetes Mellitus	345 (34.9%)
Dyslipidemia	328 (33.2%)
Acute myocardial infarct < 90 days	184 (18.6%)
Previous use of beta blocker	838 (84.7%)
Chronic obstructive pulmonary disease/Asthma	27 (2.7%)
Previous cardiac surgery	37 (3.7%)
Smoking	495 (50.1%)
Infective endocarditis	36 (3.6%)
Electrocardiographic variables – n (%)	
Left atrial enlargement	183 (18.5%)
Left ventricular enlargement	263 (26.6%)

Continue...

Table 1. Continuation...

Variables	Results
Echocardiographic variables – n (%)	
Left atrial enlargement and/or LAVI > 34ml/m²	548 (55.4%)
Left ventricular remodeling	473 (47.8%)
LVEF < 40%	120 (12.8%)
LVEF – median (interquartile range)	60% (46-68%)
LAVI – median (interquartile range)	40ml/m² (35-52ml/m²)
Intraoperative and postoperative variables – n (%)	
Mitral valve surgery	141 (14.3%)
Inotropic use	626 (63.3%)
Need for reoperation	55 (5.6%)
Postoperative atrial fibrillation – n (%)	227 (23%)
Outcomes related to postoperative atrial fibrillation – n (%)	
Stroke	16 (1.6%)
Death	56 (5.7%)
Intensive Care Unit stay – median (interquartile range)	4 (3-6 days)
Hospital stay – median (interquartile range)	13 (9-19 days)

LAVI: Left atrium volume index. LVEF: Left ventricular ejection fraction. Source: Elaborated by the authors.

The most frequently performed surgical procedures were isolated CABG (n=570; 57.6%), isolated aortic valve replacement (n=114; 11.5%), mitral valve replacement or repair alone (n=49; 4.9%), and ascending aorta surgery with or without aortic valve surgery (n=45; 4.5%). POAF occurred within a median of 2 days postoperatively (interquartile range, 1–3 days postoperatively).

During the univariate analysis, the variables with a statistically significant association were age ≥60 years, previous cardiac surgery, LA enlargement (according to electrocardiography), echocardiographic LA enlargement, LV remodeling (concentric or eccentric hypertrophy; according to the echocardiogram), surgery of the mitral valve, inotrope use within 24 hours after surgery, and the need for reoperation within 24 hours after surgery.

During the multivariate analysis, age ≥60 years, echocardiographic LA enlargement, inotrope use within 24 hours of surgery, and the need for reoperation were included in the logistic regression model (Table 2). The variables of LA enlargement and echocardiographic LA enlargement both pertain to the same cardiac chamber. Given the greater sensitivity and specificity of the echocardiogram for detecting alterations, this latter variable was included in the risk score. LV remodeling was not included in the multivariate analysis because it was significantly associated with another item of the score (inotrope use during the postoperative period). Furthermore, the variable surgery of the mitral valve, when added to the logistic regression model, determined loss of statistical significance of the variables echocardiographic LA enlargement and need for reoperation. Similarly, the addition of the variable previous cardiac surgery was added to the regression model led to a loss of statistical significance for this variable and the aforementioned echocardiographic LA enlargement variable. Consequently, the variables surgery of the mitral valve and previous cardiac surgery were excluded from the logistic regression model.

In order to be included in the score, a point was assigned to each predictor variable, given that the odds ratio of each component was similar in the logistic regression model. A score of 3 or above was found to be associated with a POAF risk of approximately 34% (Fig. 2).

Table 2. Results of univariate and multivariate analysis

Analyzed variable	Univariate analysis			Multivariate analysis		
	Odds ratio	*p*-value	CI 95%	Odds ratio	*p*-value	CI 95%
Age ≥ 60 years	1.99	*p*<0.001	1.44-2.74	1.97	*p*<0.001	1.42-2.72
Gender	1.23	*p*=0.191	0.90-1.68			
Arterial hypertension	1.09	*p*=0.606	0.78-1.52			
Diabetes Mellitus	1.05	*p*=0.774	0.76-1.43			
Dyslipidemia	1.07	*p*=0.663	0.78-1.47			
Acute myocardial infarct < 90 days	1.28	*p*=0.189	0.88-1.85			
Previous use of beta blocker	1.03	*p*=0.890	0.68-1.56			
Chronic obstructive pulmonary disease/Asthma	0.95	*p*=0.927	0.38-2.40			
Previous cardiac surgery	2.11	*p*=0.028	1.07-4.18			
Smoking	1.01	*p*=0.954	0.75-1.36			
Infective endocarditis	1.12	*p*=0.766	0.52-2.43			
Left atrial enlargement	1.87	*p*<0.001	1.31-2.66			
Left ventricular enlargement	1.35	*p*=0.069	0.97-1.87			
Echocardiographic left atrial enlargement	1.50	*p*=0.009	1.11-2.04	1.43	*p*=0.025	1.04-1.95
Left ventricular remodeling	1.56	*p*=0.003	1.16-2.11			
LVEF < 40%	1.24	*p*=0.106	0.79-1.91			
Mitral valve surgery	1.93	*p*<0.001	1.31-2.84			
Inotropic use	1.88	*p*<0.001	1.35-2.62	1.70	*p*=0.002	1.21-2.38
Reoperation	2.18	*p*=0.006	1.24-3.84	2.04	*p*=0.016	1.14-3.63

CI: Confidence interval. LVEF: Left ventricular ejection fraction. Source: Elaborated by the authors.

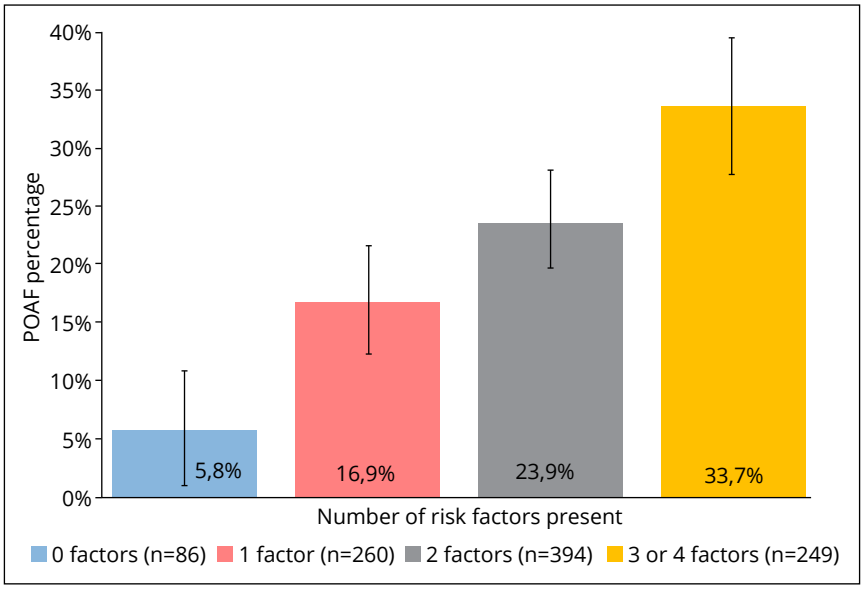

Figure 2. POAF percentage according to the presence of risk factors
Note 1: Error bars represent 95% confidence interval (CI) for POAF percentage values. Note 2: 95% CI for 0 factors (0.83 to 10.79%). 1 factor (12.33 to 21.47%). 2 factors (19.69 to 28.11%) and 3 or 4 factors (27.82 to 39.58%). Source: Elaborated by the authors.

Regarding the calibration of the logistic regression model, the Hosmer–Lemeshow test detected that the score was adequate for the data and was able to satisfactorily predict the outcome (P=.914), that is, the score was found to have good calibration. The proposed score had an accuracy of 77% for predicting POAF. Regarding model discrimination, the area under the ROC curve was 0.633 (Fig. 3).

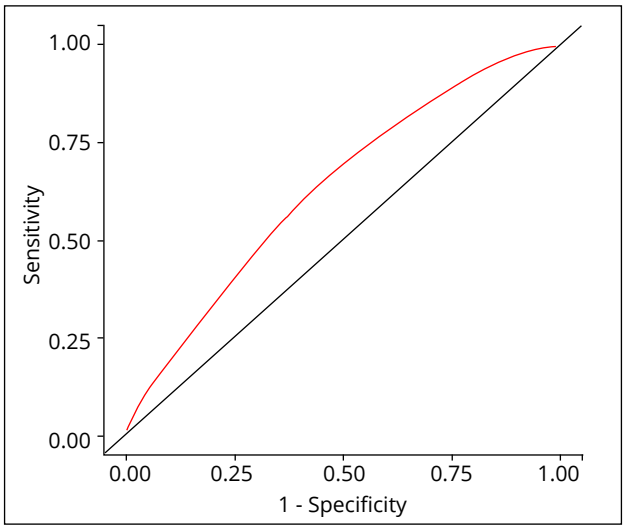

Figure 3. ROC curve of the logistic regression model for POAF prediction
Source: Elaborated by the authors.

Regarding the outcomes related to POAF, the development of arrhythmia was associated with higher rates of death and stroke and longer lengths of ICU and hospital stay (Table 3).

Table 3. Results of the univariate analysis regarding the occurrence of outcomes related to POAF

Outcome related to POAF	Univariate analysis		
	Odds ratio	*p*-value	CI 95%
Death	3.41	*p*<0.001	1.97-5.90
Intensive Care Unit length stay		*p*<0.001	
Hospital length stay		*p*<0.001	
Stroke	2.66	*p*=0.046	0.98-7.23

Note: The outcomes Intensive Care Unit length stay and hospital length stay were submitted to the Mann-Whitney U test. and it was not possible to calculate the odds ratio and 95% CI. POAF: Postoperative atrial fibrillation. CI: Confidence interval. Source: Elaborated by the authors.

DISCUSSION

Since the year 2000, a number of international research centers have attempted to stratify the risk of POAF using risk scores. In 2000, one study involving CABG surgery (n=326) concluded that three variables were related to a high risk of POAF: increased P wave duration; advanced age; and male sex[19]. In 2004, a study of 4657 patients who underwent CABG surgery created and validated a predictor score for AF during the cardiac postoperative period. The identified risk factors were advanced age, history of AF or chronic obstructive pulmonary disease, valve surgery, and withdrawal of beta-blockers or angiotensin-converting enzyme inhibitors during the postoperative period[20]. In 2014, a risk stratification score for POAF was developed using a retrospective cohort that included 17,262 patients from three European centers. The authors concluded that age, chronic obstructive pulmonary disease, emergency surgery, preoperative intra-aortic balloon use, LV ejection fraction (LVEF) <30%, glomerular filtration rate <15 mL/min/m^2 or dialysis, and any valve surgery were independently implicated in the increased risk of POAF[21]. The various scores already proposed in the international literature have been extensively tested to predict the risk of AF, but limited results have been obtained[22,23].

Nevertheless, in the context of the developing world, there has been a paucity of risk scores created for the purpose of predicting POAF. This is important to mention because the population of developing nations comprise the majority of the world population; and, in these countries, many times patients undergo cardiac surgery late in the disease course, frequently with reduced LVEF. In this regard, a Brazilian risk score for POAF was created in 2010 using a prospective cohort of 452

patients. The score was found to be associated with a high risk of arrhythmia in patients aged over 70 years with mitral valve disease, non-use or interruption of beta-blockers, and fluid balance greater than 1500 mL[24].

The incidence of POAF during this study was lower than the reported incidence of arrhythmia; and so was the mortality rate than that reported in the literature. The first was justified by the exclusion of patients with a previous diagnosis of paroxysmal AF, who were not excluded in the other studies. The latter can be explained by the exclusion of patients with previous diagnosis of persistent or permanent AF, because they are known to have higher mortality than those without arrhythmia.

The analyzed variables (age ≥60 years, echocardiographic LA enlargement, inotrope use within 24 hours of surgery, and the need for reoperation) correlated with the outcomes of the multivariate analysis, and all had a pathophysiological rationale related to the occurrence of POAF.

Specifically, age comprises all four risk scores mentioned (Table 4), and represents the single most important predictor[22]. Regarding the LA, several studies failed to demonstrate a correlation between the enlargement of this cardiac chamber and the occurrence of POAF. Nevertheless, the sole score that indirectly involved the LA was that described by the pioneering study conducted in 2000, in which an increased duration of the P wave (>155 ms) was associated with a higher occurrence of POAF[19].

Table 4. Risk scores specifically created to predict POAF

Study	PAUL et al. 2000	MATTHEW et al. 2004	MARISCALCO et al. 2014	SILVA et al. 2010	THE AUTHORS. 2022
Participants	N=326	N=4657	N=17.262	N=452	N=989
POAF incidence	28.2%	32.3%	26.4%	22.1%	23%
Surgery types	CABG	CABG	CABG and/or valve surgery	CABG and/or valve surgery	All except heart transplantation and VAD implant
	Age > 70 years	Advanced age	Advanced age	Age > 70 years	Age ≥ 60 years
	Male gender	AF or COPD history	COPD	Mitral valve disease	Echocardiographic LA enlargement
Preoperative variables	Increased p-wave duration		GFR < 15ml/min/m² or dialysis		
			IABP use in the preoperative period		
Intra- and postoperative variables		Valve surgery	Valve surgery	Water balance above 1500ml	Inotropic use in the first 24 hours
		Beta blocker or ACE inhibitor withdrawal	Emergency surgery	Non-use or discontinuation of beta-blocker	Early reoperation
Study Location	United Kingdom	17 countries (4 continents)	United Kingdom and Italy	Brazil	Brazil
AUC	-	0.77	0.62	0.76	0.63

POAF: Postoperative atrial fibrillation. CABG: Coronary artery bypass graft. VAD: Ventricular assist device. AF: Atrial fibrillation. COPD: Chronic obstructive pulmonary disease. LA: Left atrium. GFR: Glomerular filtration rate. IABP: Intraaortic ballon pump. ACE: Angiotensin Converting Enzy. Source: Elaborated by the authors using data from PAUL (2000), MATTHEW (2004), MARISCALCO (2014) and SILVA (2010).

In the present study, two novel variables were introduced as components of a risk score for predicting POAF. First, the use of inotropes within 24 hours of surgery triggers an exacerbated sympathetic activity, which is known to be a predisposing factor for the outcome[6]. The need for reoperation results in endocrine, metabolic, and inflammatory responses to the new surgical procedure; therefore, the importance of this predictor variable was justified.

The score proposed during this study demonstrated satisfactory prediction accuracy, with a correlation coefficient of 0.77. However, the discrimination, as expressed by the ROC curve, was mediocre, similar to that of other scores[22,23]. This mediocrity can be explained by the multifactorial nature of the disease. For example, the main score used for patients with AF (CHA2DS2VASc) has an area under the ROC curve of 0.61[25], thereby highlighting that this parameter is not the most important predictive score.

In conclusion, the proposed score is composed by easily understandable components, providing adequate representation of the pathophysiology of the disease. Besides, it is strongly recommended that patients with score higher than 3 should receive prophylactic treatment (amiodarone or beta-blocker) as soon as possible after surgery. If using inotropic drugs, amiodarone should be administered.

With regard the outcomes related to POAF, it should be noted that the study was not designed to provide a definitive assessment of the incidence of stroke (CI: 0.98-7.23). This may be explained by the low incidence of this adverse event (1.6%) observed in the present study. Besides, it is often the case that strokes are misdiagnosed due to the reliance on computed tomography scans of the brain, with magnetic resonance imaging of the brain being overlooked.

The main limitation of this study is its retrospective nature, which limited the data collection process (such as missing medical records and incomplete data). Another significant limitation was that sampling was performed for convenience, which may have caused sample selection bias; however, this was mitigated by the large size of the sample.

CONCLUSION

This study developed a score for predicting POAF, which involved age ≥60 years, echocardiographic LA enlargement, inotrope use within 24 hours after surgery, and the need for early reoperation. Furthermore, the score proposed during this study has been demonstrated to have good accuracy and reliably reflects the pathophysiology of POAF.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: Araujo Neto JL, Rocha EA; **Methodology:** Araujo Neto JL, Rocha EA; **Investigation:** Araujo Neto JL; **Writing – Original Draft:** Araujo Neto JL; **Writing – Review and Editing:** Rocha EA; **Resources:** Araujo Neto JL, Rocha EA; **Supervision:** Rocha EA; **Final approval:** Rocha EA.

DATA AVAILABILITY STATEMENT

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

FUNDING

Not applicable.

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