

Left Atrial Size Contribution to the Predictive Capacity of Two Scores for Atrial Fibrillation in the Postoperative Period of Cardiac Surgeries

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Abstract

Background: Postoperative atrial fibrillation (POAF) is a common complication associated with undesirable outcomes; hence, the provision of appropriate tools is important to help identify patients at risk.

Objectives: To evaluate the predictive capacity of the CHADS₂ and CHA₂DS₂-VASc scores, alone and combined with left atrial (LA) size, for the onset of POAF in patients undergoing coronary artery bypass grafting and/or valvular surgery.

Methods: We performed a retrospective cohort study on 144 patients. A decision tree was used to identify the cut-off values of the CHADS₂ and CHA₂DS₂-VASc scores and LA size in order to calculate sensitivity, specificity, predictive-value positive (PVP), and predictive-value negative (PVN), in addition to regression models. The receiver operating characteristic (ROC) curve was used to estimate the accuracy of the models. The level of significance adopted was 5%.

Results: Patients who developed POAF were older ($p = 0.050$), had reduced left ventricular ejection fraction ($p = 0.045$), longer hospital length of stay ($p = 0,018$), but their mean CHADS₂ ($p = 0.077$) and CHA₂DS₂-VASc ($p = 0.109$) scores were similar to those of patients with no arrhythmia. LA size improved the predictive capacity of the CHADS₂ score, in terms of specificity and PVP, and of the CHA₂DS₂-VASc score, in terms of sensitivity and PVN. However, the CHADS₂ (OR = 1.198; CI95% = 0.859-1.156) and CHA₂DS₂-VASc (OR = 1.047; CI95% = 0.784-1.401) scores were not predictors of POAF, either alone or in combination with LA size (OR = 1.163; CI95% = 0.829-1.648 and OR = 1.065; CI95% = 0.795-1.433).

Conclusion: The CHADS₂ and CHA₂DS₂-VASc scores alone or in combination with LA size did not show good predictive capacity for POAF. (Int J Cardiovasc Sci. 2019;32(6):585-593)

Keywords: Atrial Fibrillation; Arrhythmias, Cardiac/ complications; Postoperative Complications; Cardiac Surgical Procedures.

Introduction

Atrial fibrillation (AF) is cardiac arrhythmia resulting from grossly disorganized atrial electrical activity, due to multiple and continuous intra-atrial reentrant circuits, characterized by impaired atrial contraction, followed by absent atrial systole.¹ Certain pathological heart conditions, such as those evolving with structural changes, or surgical manipulation of the organ, may

increase the risk of developing AF.² Arrhythmia occurs in about 30% of patients in the postoperative of coronary artery bypass graft surgery and in up to 60% of postoperative patients submitted to concomitant valvular surgery.^{3,4}

The consequences of AF, especially when it is irreversible, are clearly associated with the risk of thromboembolic phenomena and mortality, affecting 11% of the elderly population, up to 30 days after the

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diagnosis.⁵ In addition, cognitive changes, heart failure and worsened quality of life have been reported.^{6,7}

Having tools for predicting the risk of developing AF in the postoperative period of cardiac surgery (POAF) may contribute to the implementation of measures designed to prevent and improve the monitoring of patients at risk. Different models have been tested to that end,^{4,8,9} such as the CHADS₂ and CHA₂DS₂-VASc scores.⁹⁻¹¹

Although these scores have been originally developed to assess the risk of thromboembolism in patients with AF, their items include risk factors for the onset of arrhythmia itself.^{1,2,12} However, the results of studies that have evaluated the predictive capacity of the CHADS₂ and CHA₂DS₂-VASc scores in relation to POAF are controversial.^{9,10,13}

Recently, a study demonstrated that left atrial (LA) size was the best variable to discriminate between patients with or without POAF.¹⁴ To our knowledge, no study has assessed the contribution of LA size evaluation to the predictive ability of those scores. The objectives of this study were to verify the predictive capacity of the CHADS₂ and CHA₂DS₂-VASc scores for the onset of POAF in patients submitted to coronary artery bypass grafting and/or valvular surgery; and to assess the contribution of LA size to the predictive capacity of these scores.

Methods

This is a retrospective cohort study. Data were collected in the period from June 2017 to October 2017 at the Heart Institute of the Clinics Hospital of the School of Medicine of the University of São Paulo (INCOR-HC-FMUSP).

Population of interest and sample collection

The population of interest for this study included patients submitted to coronary artery bypass grafting and/or valvular surgery, either alone or in combination, during the year 2015.

The sample of the study was determined as 144 patients, considering an incidence of POAF as high as 50%, number of surgical procedures performed in 2015 at the institution, area of data collection and assuming type I error of 5%. We included medical records of patients aged 18 years or more, who had undergone coronary artery bypass grafting and/or valvular surgery. We excluded the medical records of patients diagnosed with pre-

intraoperative AF, from those who had undergone other types of associated surgeries or whose medical records were lacking information needed for the development of this study.

We located medical records for 1,225 individuals in the hospital's electronic records system. Out of these, 234 were excluded (188 belonged to patients with a diagnosis of pre-operative AF and 46, to patients who had undergone other surgical procedures concomitantly). The other medical records (n = 991) were revised and divided into two groups: with POAF (n = 148) and without POAF (n = 843) and, subsequently, they received codes which were used to draw the final sample.

In order to minimize the interference of external factors in this study, six medical records were chosen from the group with POAF and six from the group without POAF every month, for a total of twelve per month. The draw was carried out electronically (sorteador.com). Therefore, each group was composed of 72 patient records.

The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee in Research (approval number 1.957.400). The need for informed consent form was waived because all data were obtained from the patient records.

Variables

The clinical and demographic variables analyzed were: age, sex, skin color, smoking, CHADS₂ and CHA₂DS₂-VASc scores, preoperative echocardiographic data (left atrial size, left ventricle diastolic diameter and left ventricular ejection fraction), use of continuous medication in the preoperative period, intraoperative data (type of cardiac surgery, time of anesthesia, use of extracorporeal circulation (ECC) and the time of ECC); and postoperative data (POAF diagnosis, immediate postoperative laboratory tests, in the immediate postoperative, length of stay and death). Postoperative and POAF data were analyzed during the whole period of hospitalization. The onset of arrhythmia in the postoperative period, registered in electronic medical record system, was considered an episode of POAF.

CHADS₂ and CHA₂DS₂-VASc

The CHADS₂ score was proposed after scientific evidence suggest that certain factors other than AF contributed to the onset of thromboembolic phenomena in these patients.⁵ The identification of the major factors associated with

thromboembolism culminated with the publication in 2001 of this risk score.¹² The main purpose was to identify outpatients at risk who could benefit from treatment with oral anticoagulants. CHADS₂, however, identifies high-risk patients. Nevertheless, due to the inherent risks of arrhythmia itself, as well as to the particular contribution of other risk factors for the onset of thromboembolism, the CHA₂DS₂-VASc score was proposed to identify real low risk patients who did not need anticoagulation.⁵

The CHADS₂ score consists of four items that count for one point each (congestive heart failure, age > 75 years and diabetes mellitus) and one item that counts as 2 points (stroke and transient ischemic attack). The total score ranges from zero to six points. Originally, the higher the score, the higher the risk of thromboembolic phenomena.¹²

The CHA₂DS₂-VASc score includes three additional factors (vascular disease, age 65-74 years and female gender); each additional factor counts as 1 point, while an age > 75 years was upgraded to two points. The total score ranges from zero to nine. Originally, the higher the score, the higher the risk of thromboembolic phenomena.¹⁵

Data analysis

Categorical variables were described by absolute and relative frequencies, and analyzed using Chi-square

test and Fisher's exact test. Quantitative variables were described by using central tendency and dispersion measurements and Student's t-test. The cut-off values of the CHADS₂ and CHA₂DS₂-VASc scores and LA size were determined via decision tree. The predictive capacity of the scores alone and in combination with the LA size was determined by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and logistic regression models. The assumption of normality of the scores was not tested, because they are discrete variables. The adjustment of the models was evaluated by the area under (AUC) the Receiver Operating Characteristic (ROC) curve. All analyses were performed using the statistical software R 3.4.3. The significance level adopted was 5%.

Results

We selected 144 medical records of patients submitted to coronary artery bypass grafting and/or valvular surgery in 2015, half of whom had developed POAF. The demographic and clinical characteristics of interest, registered in the preoperative period, are described in Table 1.

Although table 1 does not show statistically significant difference between patients with and without POAF, in relation to age, it is possible to consider that, clinically,

Table 1 - Demographic and clinical characteristics recorded in the postoperative period of patients with (n = 72) and without (n = 72) postoperative atrial fibrillation

	With POAF	Without POAF	p-value
Age, in years, mean (SD)	65.8 (10.7)	61.8 (13.3)	0.050*
Male gender, n(%)	44 (61.1)	47 (65.3)	0.604†
Skin color, n(%)			
White	61 (84.7)	61 (84.7)	
Other	11 (15.3)	9 (12.5)	0.678†
Not informed		2 (2.8)	
Active smoking, n(%)	9 (12.5)	12 (16.6)	0.478†
Preoperative echocardiographic data			
Left atrial size, in mm, mean (SD)	43.4 (6.6)	41.3 (6.3)	0.059*
LVDd, mm, mean (SD)	53.3 (7.7)	52.1 (7.0)	0.359*
LVEF %, mean (SD)	55.3 (12.4)	59.2 (10.6)	0.045*

POAF: postoperative atrial fibrillation; SD: standard deviation; LVDd: left ventricular diastolic diameter; (*) Student's t-test; (†) Pearson's chi-square test.

the age is associated with the onset of arrhythmia in the postoperative period ($p = 0.050$).

In relation to medication taken on a regular basis at home, the use of different classes was observed, among which, antihypertensives, antiarrhythmics, statins, antiplatelet agents, anticoagulants and diuretics. However, we only found statistically significant difference between patients with or without POAF in relation to the use of digitalis (0%, $n = 0$ vs 6.9%, $n = 5$, respectively; $p = 0.026$).

Laboratory tests results conducted in the preoperative period were not analyzed because they were not available for many patients. Table 2 describes the minimum and maximum values observed in laboratory tests results collected in the first 24 hours after surgery.

The other intra- and postoperative data of interest for this study are described in Table 3.

The CHADS₂ mean scores for patients with and without POAF were, respectively, 1.82+1.05 and 1.49+1.18 ($p = 0.077$). The CHA₂DS₂VASc mean scores, on the other hand, were, 3.38 + 1.53 and 2.96 + 1.56, in this sequence ($p = 0.109$). In order to evaluate the predictive capacity of these scores, alone or combined with LA size, we established the cut-off point of each score to better identify the patients who developed POAF (Chart 1).

Table 4 describes the predictive capacity of these scores, either alone or associated with LA size, to determine the onset of POAF.

Table 2 - Minimum and maximum values observed in the laboratory tests results conducted in the immediate postoperative period of patients with ($n = 72$) and without ($n = 72$) postoperative atrial fibrillation

	Minimum	p-value*	Maximum	p-value*
Magnesium, mEq/L, mean (SD)				
With AF	1.5 (0.4)	0.248	2.1 (0.5)	0.950
Without AF	1.6 (0.4)		2.1 (0.6)	
Potassium, mEq/L, mean (SD)				
With AF	3.8 (0.4)	0.251	4.4 (0.5)	0.780
Without AF	3.9 (0.9)		4.4 (0.9)	
Sodium, mEq/L, mean (SD)				
With AF	135.5 (3.2)	0.194	138.9 (3.7)	0.404
Without FA	136.6 (6.1)		139.6 (5.9)	
Calcium, mEq/L, mean (SD)				
With AF	1.15 (0.06)	0.406	1.25 (0.1)	0.984
Without AF	1.16 (0.06)		1.25 (0.1)	
CRP, mEq/L, mean (SD)				
With AF	8.4 (11.0)	0.019	111.1 (69.7)	0.099
Without AF	16.8 (27.4)		92.6 (64.1)	
Creatinine, mEq/L, mean (SD)				
With AF	1.0 (0.4)	0.277	1.4 (0.6)	0.601
Without AF	1.3 (1.6)		1.6 (1.7)	
Urea, mEq/L, mean (SD)				
With AF	38.1 (16.0)	0.840	48.0 (22.1)	0.210
Without AF	38.7 (18.5)		43.6 (19.8)	

SD: standard deviation; mEq/L: milliequivalents per liter; CRP: C-reactive protein; AF: atrial fibrillation; (*) Student's t-test.

Table 3 - Intra- and postoperative variables of patients with (n = 72) and without (n = 72) postoperative atrial fibrillation

	With POAF (n = 72)	Without POAF (n = 72)	p-value
Type of surgery, n(%)			
Coronary artery bypass grafting	36 (50.0)	35 (48.7)	
Valvular surgery	32 (44.4)	32 (44.4)	1.000*
Both	4 (5.6)	5 (6.9)	
ECC, n (%)	68 (94.4)	65 (90.2)	0.346†
Time of ECC, in hours, mean (SD)	1.4 (0.5)	1.5 (0.8)	0.726‡
Time of anesthesia, in hours, mean (SD)	7.2 (1.3)	7.3 (1.8)	0.640‡
Use of VAD in IPO, n (%)	71 (98.6)	72 (100.0)	1.000*
Total length of stay, in days, mean (SD)	17.8 (13.3)	12.6 (12.4)	0.018‡
Death, n (%)	3 (4.1)	10 (13.8)	0.042†

POAF: postoperative atrial fibrillation; SD: standard deviation; ECC: extracorporeal circulation; IPO: immediate postoperative period; VAD: vasoactive drug; (*) Fisher's exact test; (†) Pearson's chi-squared test; (‡) Student's t-test.

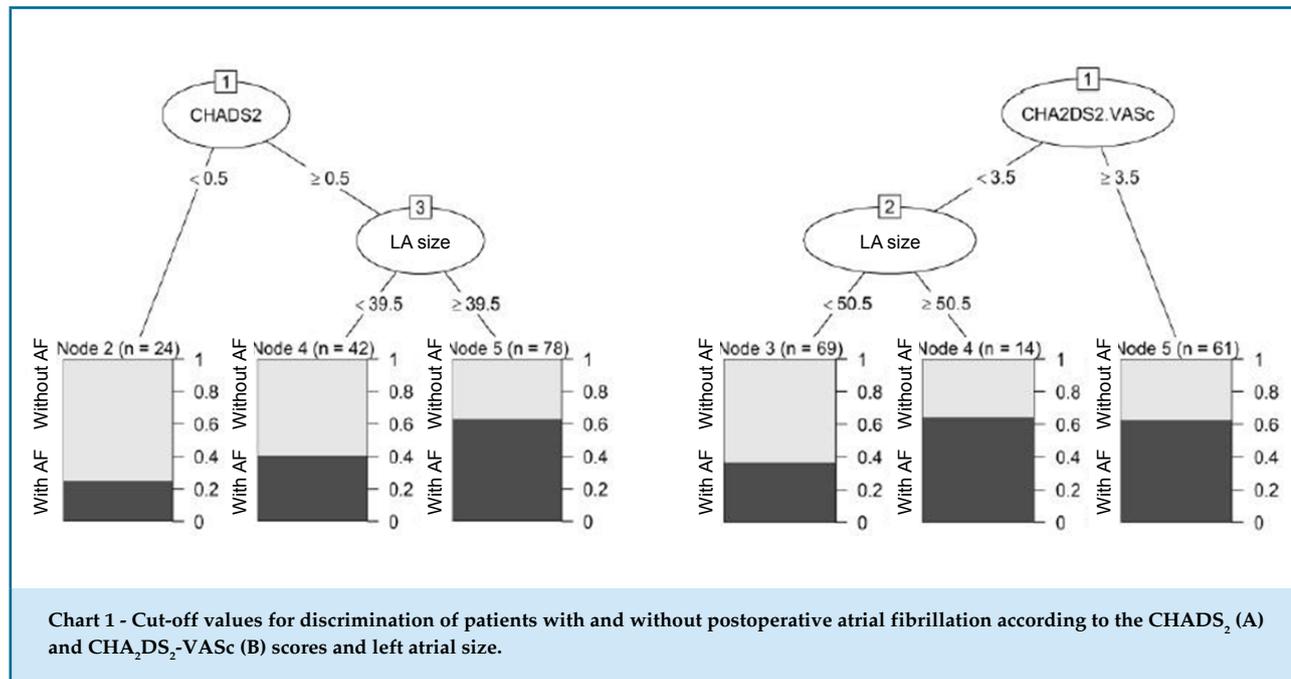


Chart 1 - Cut-off values for discrimination of patients with and without postoperative atrial fibrillation according to the CHADS₂ (A) and CHA₂DS₂-VASc (B) scores and left atrial size.

Tables 5 and 6 show logistic regression models of the CHADS₂ and CHA₂DS₂VASc scores alone and in association with left atrial size.

Chart 2 shows the ROC curve area for the scores alone or in association with LA size.

Discussion

The present study described the prediction capacity of the CHADS₂ and CHA₂DS₂VASc scores, alone or in association with LA size, to determine the onset of POAF

Table 4 - Sensitivity, specificity and positive and negative predictive values of CHADS₂ and CHA₂DS₂VASc scores, alone or in association with LA size, to determine atrial fibrillation following coronary artery bypass grafting and/or valvular surgery

	CHADS ₂ > 0.5	CHA ₂ DS ₂ VASc < 3.5	CHADS ₂ > 0.5 and LA > 39.5 mm	CHA ₂ DS ₂ VASc < 3.5 and LA > 50.5 mm
Sensitivity	91.7	52.8	68.1	65.3
Specificity	25.0	68.1	59.7	61.1
Predictive value positive	55.0	62.3	62.8	62.7
Predictive value negative	75.0	59.0	65.1	63.8

LA: left atrial size.

Table 5 - Logistic regression model of the CHADS₂ score alone (Model 1) and in association with left atrial size (Model 2) for predicting the onset of postoperative atrial fibrillation following coronary artery bypass grafting and/or valvular surgery

		Odds ratio (CI 95%)	p-value	AUC (CI 95%)
Model 1	CHADS ₂	1.198 (0.859-1.156)	0.291	0.611 (0.518-0.714)
Model 2	CHADS ₂	1.163 (0.829-1.648)	0.387	0.643 (0.552-0.733)
	LA size	1.049 (0.995-1.107)	0.078	

AUC: area under the curve; CI: confidence interval.

Table 6 - Logistic regression model of the CHA₂DS₂VASc score alone (Model 3) and in association with left atrial size (Model 4) for predicting the onset of postoperative atrial fibrillation following coronary artery bypass grafting and/or valvular surgery

		Odds ratio (IC 95%)	p-value	AUC (CI 95%)
Model 3	CHA ₂ DS ₂ VASc	1.047 (0.784-1.401)	0.754	0.590 (0.497-0.683)
Model 4	CHA ₂ DS ₂ VASc	1.065 (0.795-1.433)	0.673	0.633 (0.542-0.724)
	LA size	1.052 (0.999-1.110)	0.061	

AUC: area under the curve; CI: confidence interval.

in patients undergoing myocardial revascularization surgery and/or valvular surgery. As far as we know, no other study had added the contribution of left atrial size to the prediction capacity of those scores. Having tools that allows us to predict the risk of POAF in an easy and reliable way is important because it could help identify patients at risk, who would benefit from more careful

monitoring in the postoperative period, as well as, for the institution of prevention measures.

Patients with POAF were older compared to those who did not develop arrhythmia. Advanced age is, admittedly, a major risk factor for AF in patients in general^{16,17} and in those undergoing cardiac surgery.^{18,19} In fact, population aging, especially in emerging countries,

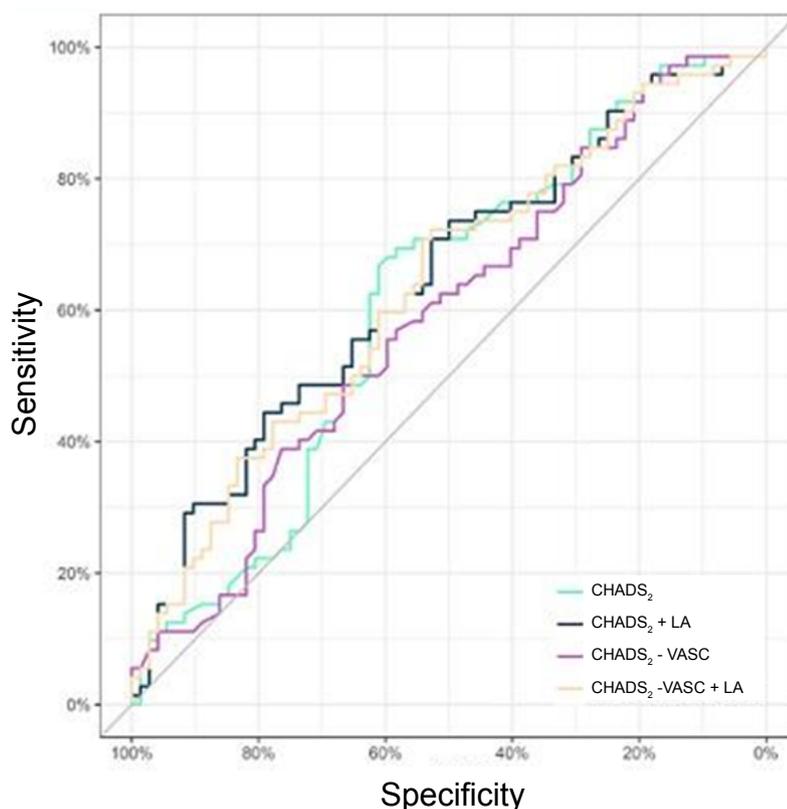


Chart 2 - Predictive ability of models constituted by the scores alone or in association with left atrial size to predict new-onset atrial fibrillation after coronary artery bypass graft surgery and/or valvular surgery.

will play an important role in changing the incidence of this type of arrhythmia in the general population, as well as in patients undergoing cardiac surgery.⁵

The mean ejection fraction in both groups was considered within normal limits, although LA size was slightly increased in both groups.²⁰ When AF is addressed in the context of heart failure, arrhythmia is more frequent in patients with normal ejection fraction, due to volume overload and pressured atrial chambers.²¹ Atrial remodeling, caused by a structural rearrangement of myocardial fibers, is directly linked with the presence of AF.²¹ Other authors have reported that LA size is associated with the occurrence of arrhythmia^{2,4,9,22} and seems to be the best discriminant between postoperative patients who developed POAF and those who did not.¹⁴ Considering the important role played by the LA in the pathophysiology of AF, and the results of previous studies, we decided to test the predictive capacity of the scores alone and combined with this measure, even though no difference was observed between the groups

with and without AF in relation to the size of this heart chamber. This will be further discussed below.

Regarding the use of continuous medication, comparison between the groups with and without AF showed that only the use of digitalis was different. Although this drug was prescribed with the aim of treating heart failure, its action on cell membranes and increased vagal tonus⁵ could contribute to reduce the onset of POAF.

It is known that the risk to develop AF in the postoperative of cardiac surgery may vary depending on the type of surgery. In a multicenter study, the risk of POAF was higher in patients who had undergone coronary artery bypass grafting combined with valvular surgery (OR: 1.8; CI 95%: 1.2 - 2.7) or valve surgery alone (OR: 1.4; CI 95%: 1.1 - 1.9) compared with coronary artery bypass grafting surgery alone.²³ Although studies have associated the use of ECC with increased postoperative complications, among them, the occurrence of atrial fibrillation,²⁴ this study did not find significant differences

between the two groups. In addition, we did not observe any relation with the type of surgical procedure, nor in relation to the other intraoperative variables in the groups with and without POAF.

Several studies have demonstrated the association between arrhythmia and adverse postoperative outcomes.^{23,25} A meta-analysis²³ with over 69 thousand patients showed that the length of stay was significantly higher among patients with and without POAF (11.0 vs 8.9 days, respectively; $p < 0.00001$). In coherence with the literature data, POAF patients, in this study, remained hospitalized for longer periods.

Nevertheless, mortality rates were higher among patients without POAF. These results were surprising, but some hypothesis can help us understand them. Short-term follow-up compared to other studies who had followed the patients after hospital discharge can contribute to decrease the number of new-onset and recurrent cases of POAF, as well as the number of deaths. In a meta-analysis, the recurrence rate of POAF ranged from 61% to 100% within two years.²⁶

With respect to the estimation of the predictive capacity of the scores, the cut-off values of the CHADS₂ and CHA₂DS₂VASc scores that best discriminated patients with and without POAF were > 0.5 and < 3.5 , respectively. In other words, patients would be at risk of developing POAF even if they had relatively few risk factors. In this situation, it is possible that the scores would not be very useful for identifying patients that should receive more intensive monitoring in the postoperative period or other prophylactic measures. Corroborating that perspective, the sensitivity of the CHADS₂ score increased, but specificity was extremely low; and for CHA₂DS₂VASc, they remained far below adequate.

When assessing the effect of LA size on the predictive capacity of these scores, although the sensitivity of the CHADS₂ score has decreased, all the other measures of specificity, PPV and NPV improved, but did not seem to be satisfactory. Similarly, for the CHA₂DS₂VASc score, in spite of a decrease in the specificity value, there was an improvement in all the other measures, which is not enough to ensure its adequacy.

Moreover, the regression models failed to show that the scores, alone or in association with the LA, are predictors of POAF. Therefore, it can be asserted that the models analyzed in this study are not good predictors of POAF. The literature is controversial regarding the

determination of the predictive capacity of the CHADS₂ and CHA₂DS₂VASc scores.^{8,9,10,13}

Some studies have shown that the risk of POAF increased as the CHADS₂ and CHA₂DS₂VASc scores increased, but they did not demonstrate their predictive capacity.^{9,10} Recently, researchers¹³ have analyzed the predictive capacity of different risk scores (Society of Thoracic Surgeons risk of mortality score, Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE)-AF score, POAF score and CHA₂DS₂VASc) and age for the new-onset of AF after coronary artery bypass graft operation. They noted that none of the variables analyzed performed well. The ROC area for CHARGE-AF was 0.6796 (CI 95%: 0.6672-0.6920), whereas for CHA₂DS₂VASc it was 0.5917 (CI 95%: 0.5782-0.6052). Different results were obtained in another study,⁸ which showed good estimations on sensitivity (84.21), specificity (84.54) and negative predictive value (97.23) of the CHA₂DS₂VASc score to predict the risk of AF after coronary artery bypass, with a ROC area of 0.87.

The present study has limitations relating to sample size and to the fact that this is a single-center study. Furthermore, the short follow-up period did not allow for the identification of new-onset and recurring AF after hospital discharge, which might have contributed to poor score performance in predicting arrhythmia, since the items of both scores take into account chronic conditions that can affect myocardial structure and stability in the long term after cardiac surgery.

Conclusion

The CHADS₂ and CHA₂DS₂-VASc scores alone were not good predictors of POAF in patients undergoing coronary artery bypass graft and/or valvular surgery in this study. Although LA size has improved the estimation of sensitivity, specificity, PPV and NPV, it was not enough to improve the predictive capacity of the scores.

Author contributions

Conception and design of the research: Silva NA, Butcher RCGS. Acquisition of data: Silva NA. Analysis and interpretation of the data: Silva NA, Butcher RCGS. Statistical analysis: Silva NA, Butcher RCGS. Writing of the manuscript: Silva NA, Butcher RCGS. Critical revision of the manuscript for intellectual content: Silva NA, Butcher RCGS.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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