



Predicting Postoperative Atrial Fibrillation using CHA2DS2-VASC Score: A Retrospective Observational Study

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ABSTRACT

Objective: Postoperative atrial fibrillation (POAF) is an arrhythmia most commonly seen after cardiac surgery. Its association with increased mortality, cost and adverse events has made it crucial to identify those at risk and to prevent POAF through preoperative therapy. In order to do that, we have studied the utilization and predictive power of the CHA2DS2-VASc score, and the relationship between other factors such as preoperative medications and patient clinical characteristics. **Methods:** A retrospective observational study was conducted by reviewing medical charts for patients who underwent coronary arteries bypass grafting (CABG) with or without aortic valve replacement or mitral valve/tricuspid valve repair and aged >18 years. Patients with a preoperative history of atrial fibrillation (AF) or flutter, patients with a pacemaker, patients with prior antiarrhythmic drugs use within the last 6 months, patients who underwent MAZE procedures, or patients with mechanical mitral valve were excluded. **Results:** At a cut-off score of ≥ 2 the CHA2DS2-VASc showed a 96.8% sensitivity and 23.1% specificity for predicting POAF. It also showed an increased risk at higher scores, a score of at least 3 significantly predicted the occurrence of events ($p < 0.000$). Age, male gender, high BMI were significant predictors of POAF ($p < 0.001$, $p < 0.05$, $p < 0.001$). Patients who received statins preoperatively were at significant lower risk ($p < 0.001$). **Conclusion:** The CHA2DS2-VASc score is a strong predictor of adverse events postoperatively.

Keywords: Cardiac surgery, Post-operative atrial fibrillation, POAF, Arrhythmia

INTRODUCTION

Postoperative atrial fibrillation (POAF) is a type of arrhythmia most commonly seen after cardiac surgery [1,2]. This arrhythmia occurs more frequently within the first 5 days of operation, and infrequently after the first week [3,4]. POAF occurs in approximately 30% of patients undergoing coronary artery bypass grafting (CABG) [5,6]. In Arab populations, it has been documented in 19% of patients; its incidence was 22% in patients undergoing CABG with cardiopulmonary bypass, and 12% in patients undergoing off-pump coronary artery bypass grafting (OPCAB) [7].

POAF has been associated with increased mortality, cost, and adverse events [8,9]. Mechanisms that might be involved in the development of POAF include sympathetic activation, oxidative stress, and inflammatory response [10]. Current strategies for POAF prevention depend mainly on the pre-operative use of medications such as beta-blocking agents, sotalol, amiodarone, and magnesium [10]. However, in patients undergoing CABG, the use of these medications is not cost-effective and may be associated with adverse effects [11].

To prevent the development of POAF through targeted pre-operative therapy, it would be helpful to be able to identify

patients who are at risk of developing POAF. Commonly identified pre-operative risk factors for POAF include age, gender, obesity, valvular heart disease, history of atrial fibrillation (AF), chronic obstructive pulmonary disease (COPD), hypertension, and diabetes [12]. No pre-operative scoring system is currently available for predicting those patients who are at high risk of developing POAF. CHA2DS2-VASc (congestive heart failure, hypertension, age >75 years [doubled], diabetes, stroke [doubled], vascular disease, age 65-74, and sex category [female]) score is routinely used to guide antithrombotic therapy in patients with AF [13]. Many components of this algorithm are also known to be associated with an increased incidence of POAF [14-18]. The purpose of this study, therefore, was to test the hypothesis that the CHA2DS2-VASc score is useful for predicting *de novo* POAF in patients undergoing cardiac surgery.

MATERIALS AND METHODS

In this study, medical charts were reviewed for all the adult patients admitted to the Abdulaziz Cardiac Center (KACC), which has approximately 32 beds in across ward numbers 29 and 30, and the Adult Cardiac Intensive Care Unit. KACC is one of the largest cardiac centers in the Gulf region and performs an average of 500 adult cardiac surgeries per year. KACC uses a state-of-the-art computer-based electronic health records system (Apollo, Inc.). This retrospective observational study was approved by King Abdullah International Medical Research Center.

Study Design

A retrospective observational study was conducted by reviewing the medical charts of patients aged ≥ 18 years and admitted to KACC between January 2010 and December 2014 for a coronary artery bypass grafting (CABG) or off-pump coronary artery bypass grafting (OPCAB) procedure, with or without valvular surgery. Patients excluded from the study were those with a preoperative history of AF or flutter, a pacemaker, use of anti-arrhythmia drugs within the last 6 months, previous maze procedures, or those with a mechanical mitral valve.

Data Sources and Collection

The medical records of patients who met the inclusion criteria and had cardiac surgery between January 2010 and December 2014 were retrospectively reviewed. Patients were selected by convenience sampling. Patient records were retrieved from institutional databases (Quadra Med, KFHI, and Apollo electronic documentation systems). Data were collected from patient charts and computerized databases were demographic characteristics; medical history; pre-operative medications; pre-operative ejection fraction (%); date of surgery; type of surgery; CHA2DS2-VASc score; indicator for POAF (yes/no), and if yes, date of POAF development; and time (in days) between cardiac surgery and development of POAF. All variables were collected and analyzed using SPSS version 21.0 (release 21.0.0.0).

Definition and Main End Point

The aim of this study was to test the ability of CHA2DS2-VASc score to predict *de novo* POAF. CHA2DS2-VASc is an established scoring system to predict the risk of developing stroke in patients with AF. It has the following elements:

- C: Congestive heart failure (or left ventricular systolic dysfunction)
- H: Hypertension (blood pressure consistently above 140/90 mmHg, or treated hypertension on medication)
- A2: Age 75 years (doubled)
- D: Diabetes mellitus
- S2: Prior stroke, transient ischemic attack or thromboembolism (doubled)
- V: Vascular disease (previous myocardial infarction, peripheral arterial disease or aortic plaque)
- A: Age 65-74 years
- Sc: Sex category (female gender)

De novo POAF is defined by the STS Adult Cardiac Surgery Database as AF requiring treatment, lasting at least 30

seconds, and recorded by continuous telemetry or by electrocardiography within 30 days of the original surgery, or before discharge from hospital. A standard 12-lead electrocardiogram was recorded for each patient with a suspected arrhythmic event.

Data Analysis

Descriptive statistical analyses were performed on data collected from the study sample. Continuous variables were summarized as means \pm SD, and medians (interquartile range, IQR). Proportions were used for categorical variables. The unadjusted analysis was performed to examine the relationship between POAF and CHA2DS2-VASc score, as well as other demographic and clinical factors. Categorical data were analyzed using the Chi-square test. The distribution of all continuous data was examined. A t-test was used to analyze continuous variables with approximately normal distributions. A Cox proportional hazards regression model was used to examine the effect of CHA2DS2-VASc score on POAF risk. The model was adjusted for several patient demographic and clinical characteristics. Adjusted Kaplan Meier curves were used to evaluate and compare the rate of POAF by CHA2DS2-VASc score group at various follow-up times after cardiac surgery. Statistical significance was considered at $p < 0.05$. All statistical analyses were performed using SPSS version 21.0 (release 21.0.0.0, IBM, USA).

RESULTS

The mean age of our cohort (1254 patients) was 60.68 ± 10.21 years old, and 84.6% were male. Patients' average weight was 67.56 ± 14.59 kg, and an average body mass index (BMI) was 28.5 ± 5.8 kg/m². In terms of medical history, 87.8% of patients in the cohort had triple vessel coronary heart disease, 70% were diabetic, 67.1% had hypertension, and 9.5% had congestive heart failure. Most patients reviewed had no carotid artery disease (91.8%), cerebrovascular accident (95.5%), or peripheral disease (93.7%). Patients' clinical characteristics are summarized in Table 1.

Table 1 Patients' clinical characteristics

Variables	%	
Gender	Female	15.4%
	Male	84.6%
Coronary heart disease	No	0.1%
	Single vessel	1.4%
	Double vessel	10.7%
	Triple vessel	87.8%
Congestive heart failure	No	90.5%
	Yes	9.5%
Diabetes	No	29.6%
	Yes	70.4%
Hypertension	No	32.9%
	Yes	67.1%
Carotid artery disease	Bruit-Doppler stenosis <75%	3.6%
	Bruit-Doppler stenosis=75%	0.1%
	Bruit-Doppler stenosis >75%	0.7%
	Endarterectomy	0.2%
	No	91.8%
	No Bruit-Doppler stenosis >75%	2.2%
Cerebrovascular accident	Missing	1.5%
	No	93.7%
Peripheral vascular disease	Yes	6.3%
	No	95.5%
Type of operation	Yes	4.5%
	CABG	98.1%
	CABG off-pump	1.8%

The distribution of CHA2DS2-VASc scores is presented in Table 2. Total 68 patients had an intermediate risk of stroke, and 1186 (94.57%) patients had a CHA2DS2-VASc score ≥ 1 , identifying them as being in the high-risk category.

Table 2 Distribution of CHA2DS2-VASc score

CHA2DS2-VASc score	Frequency	%
1	68	5.4%
2	227	18.1%
3	378	30.1%
4	344	27.4%
5	162	12.9%
6	53	4.2%
7	15	1.2%
8	5	0.4%
9	2	0.2%

CHA2DS2-VASc Score for Predicting Postoperative Atrial Fibrillation (POAF)

Patients were categorized by CHA2DS2-VASc score as ≤ 1 or ≥ 2 . The number of patients with a moderate to low risk of developing stroke (CHA2DS2-VASc score ≤ 1), and who had POAF, was 9 (13.2%), while 59 (86.8%) patients with CHA2DS2-VASc score ≤ 1 did not have POAF. This suggests that, at this low cut-off point, CHA2DS2-VASc score has low specificity (6.1%), and thus it is a poor indicator of POAF. On the other hand, at a CHA2DS2-VASc score ≥ 2 , indicating a high risk of developing stroke, 23% of patients had POAF, thus demonstrating high sensitivity of the CHA2DS2-VASc score (96.8%) and a high ability of CHA2DS2-VASc score to correctly detect the percentage of patients who will develop POAF (Table 3). At a CHA2DS2-VASc score cut-off of ≥ 2 , its accuracy in predicting POAF was 26.5%. However, as the cut-off point increased, i.e. to ≥ 3 , the sensitivity decreased (76.5% versus 96.8%), specificity increased (25.6% versus 6.1%), and accuracy was 38.7%.

Table 3 CHA2DS2-VASc score and risk of postoperative atrial fibrillation (POAF)

Score categorized		POAF	
		No	Yes
Moderate to low risk CHA2DS2-VASc score ≤ 1	Count	59	9
	% within score categorized	86.8	13.2
	% within POST AF/atrial flutter	6.1*	3.2
High Risk CHA2DS2-VASc score ≥ 2	Count	912	274
	% within score categorized	76.9	23.1
	% within POST AF/atrial flutter	93.9	96.8**
Total	Count	971	283
	% within score categorized	77.4	22.6
	% within POST AF/atrial flutter	100	100

*Specificity; **Sensitivity

Relationship between CHA2DS2-VASc Scores and the Risk of Postoperative Atrial Fibrillation (POAF)

Post-cardiac surgery POAF rates increased with increasing CHA2DS2-VASc scores. At the cut-off point of 2, Kaplan-Meier survival analysis revealed that patients with CHADS2 scores ≥ 2 had a marginally higher POAF rate than patients with CHADS2 scores < 2 ($p=0.075$). At the cut-off point of 3, a CHA2DS2-VASc score of at least 3 significantly predicted the occurrence of events ($p=0.000$) (Figure 1).

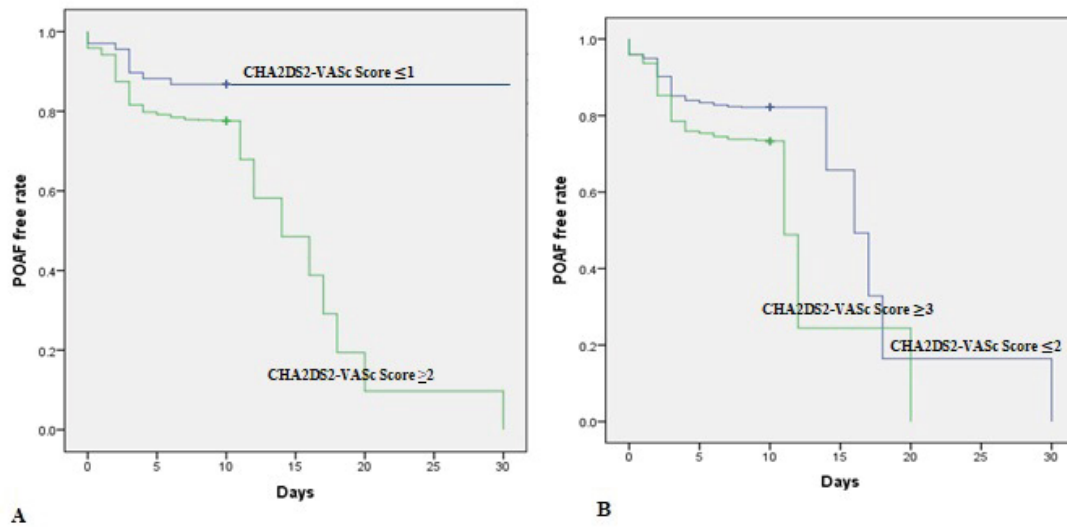


Figure 1 Postoperative atrial fibrillation (POAF)-free rate curves for patients and CHA2DS2-VASc scores. Kaplan-Meier survival analysis showed that patients with CHADS2-VASc scores of at least 2 had a marginally higher event rate than did patients with CHADS2 scores lower than 2 (log-rank, p=0.075; A). In addition, a CHA2DS2-VASc score of at least 3 significantly predicted occurrences of POAF (log-rank, p=0.000; B)

CHA2DS2-VASc score and incidence of new onset postoperative atrial fibrillation (POAF)

Almost 79% of patients developed POAF within the first 3 days of surgery; 96% had a CHA2DS2-VASc score ≥ 2 (Table 4). The mean ± SD time to develop AF after cardiac surgery was 2.84 ± 3.194.

Table 4 CHA2DS2-VASc score and onset of postoperative atrial fibrillation (POAF)

Variables		Number (%) of patients with score categorized		Total
		Moderate to low-risk CHA2DS2-VASc score ≤ 1	High risk CHA2DS2-VASc score ≥ 2	
Onset	Within 3 days	7 (2.9%)	182 (75.8%)	189 (78.7%)
	Within 1 week	1 (0.4%)	39 (16.25%)	40 (16.6%)
	After 1 st week but within 1 month	0 (0.0%)	11 (4.58%)	11 (4.58%)
Total		8 (3.3%)	232 (96.6%)	240 (100%)

Predictors of Postoperative Atrial Fibrillation (POAF)

Male and female patients were at similar risk of developing POAF (p=0.934). However, patients aged 75 years or older were at higher risk of developing POAF compared to others (21.4% versus 35.8%, p=0.001). Comparing the type of cardiac surgery with risk of developing AF, patients who underwent OPCABG were at marginally higher risk of developing POAF than CABG patients (34% versus 22.4%, p=0.371). Diabetic patients were at similar risk to non-diabetic patients (22.5% versus 23.5%, p=0.628), as well as peripheral to non-peripheral vascular disease patients (22.1% versus 22.6%, p=0.779). POAF risk was similar between heart failure and non-heart failure patients (22.4% versus 24.4%, p=0.767), and between patients with carotid artery disease compared to others (29.4% and 22%, p=0.119). Hypertensive patients had a significantly higher risk of developing POAF compared to non-hypertensive patients (25.1% versus 17.5%, p=0.003). There was no statistical difference between patients with a history of stroke and others in developing POAF (29.1% vs 22.1%, p=0.15) as well as those with a history of triple vessel surgery (23%) versus others (18.9%). Significant predictors of POAF, according to Cox regression analysis, are shown in Table 5.

Table 5 Cox regression model for postoperative atrial fibrillation (POAF)

Variables	Hazard ratio	95.0% CI		p-value
		Lower	Upper	
Age	1.037	1.025	1.050	<0.001
Male	1.39	0.994	1.945	0.050
BMI	1.038	1.025	1.051	<0.001
Creatinine	1.001	1.000	1.002	0.004
Double vessel coronary artery disease	0.736	0.483	1.122	0.150
Hypertension	1.237	0.955	1.605	0.100
CHA2DS2-VASc score ≥ 3	1.725	1.360	2.186	<0.001
Angiotensin receptor blockers (ARBs)	1.188	0.890	1.585	0.240
Lipid-lowering agents (statins)	2.33	1.199	4.536	0.013

Pre-Operative Medication Intake and Postoperative Atrial Fibrillation (POAF)

Patients who received lipid-lowering agents (statins) were at significantly lower risk of developing POAF than others ($p=0.001$) (Table 4). According to Cox regression analysis, patients who received statins before their cardiac operation were at a 1.4-fold lower risk than patients who did not receive statins (Table 5). There was a non-statistically significant difference in POAF risk between patients who received beta-adrenoceptor blockers (beta-blockers; $p=0.508$); angiotensin-converting enzyme inhibitors (ACE inhibitors; $p=0.216$) or angiotensin receptor blockers (ARBs; $p=0.108$) before cardiac surgery, and those who did not receive these drugs (Table 6).

Table 6 Pre-operative medication intake and risk of POAF

Pre-operative Medication	POAF			p-value
	No	Yes	Total	
Lipid-lowering agents (statins)	No	85 (90.4%)	9 (9.5%)	0.002
	Yes	886 (76.4)	273 (23.6%)	
Beta-adrenoceptor blockers (beta-blockers)	No	129 (77.7%)	37 (22.3%)	0.927
	Yes	842 (77.4%)	246 (22.6%)	
Angiotensin-converting-enzyme inhibitors (ACE inhibitors)	No	347 (76.1%)	109 (23.9)	0.184
	Yes	624 (78.2%)	174 (21.8%)	
Angiotensin receptor blockers (ARBs)	No	799 (77.4%)	233 (22.5%)	0.392
	Yes	172 (74.7%)	60 (24.3%)	

When patients were categorized according to their CHA2DS2-VASc score, those scoring ≥ 2 were most likely to have benefited from statins ($p=0.002$) or ARBs ($p=0.147$) (Table 7).

Table 7 Pre-operative medication intake and risk of postoperative atrial fibrillation (POAF) based on CHA2DS2p-VASc score

CHA2DS2-VASc score	Pre-operative medications	POAF			p-value
		No	Yes	Total	
≤ 1	Lipid-lowering agents (statins)	Not received	7 (87.5%)	1 (12.5%)	0.948
		Received	52 (86.6%)	8 (13.3%)	
≥ 2	Lipid-lowering agents (statins)	Not received	78 (90.6%)	8 (9.3%)	0.002
		Received	834 (75.9%)	265 (24.1)	
≤ 1	Angiotensin-converting-enzyme inhibitor (ACE inhibitor)	Not received	22 (81.4%)	5 (22.7%)	0.297
		Received	37 (90.2%)	4 (9.7%)	
≥ 2	Angiotensin-converting-enzyme inhibitor (ACE inhibitor)	Not received	327 (76.2%)	104 (24.4%)	0.483
		Received	587 (77.4%)	170 (22.6%)	
≤ 1	Angiotensin receptor blockers (ARBs)	Not received	48 (85.7%)	8 (14.3)	0.581
		Received	11 (91.7%)	1 (8.3%)	
≥ 2	Angiotensin receptor blockers (ARBs)	Not received	751 (82.4%)	215 (23.6)	0.147
		Received	161 (73.2%)	59 (26.8%)	

≤ 1	Beta-blocker	Not received	10 (76.9%)	3 (23.1%)	13	0.244
		Received	49 (89.0%)	6 (10.9%)	55	
≥ 2		Not received	119 (77.7%)	34 (22.2%)	153	0.782
		Received	793 (76.7%)	240 (23.2%)	1033	

DISCUSSION AND CONCLUSION

The increases in patient mortality and morbidity, and hospital costs, associated with POAF, have prompted researchers to identify the risk factors underlying its incidence. There is a need for a stratification system because it is unfeasible to start anti-arrhythmic prophylaxis for all cardiac surgery patients. The CHADS2 and CHA2DS2-VASc scoring systems have traditionally guided the use of oral anticoagulants for AF, while also calculating patients' risk of stroke. In this study, we attempted to use the same scoring system to predict patients' risk of developing POAF after cardiac surgery. We also sought to find a relationship between factors independent of the CHA2DS2 score, and the role of pre-operative medications.

In a study of 518 cardiac valve surgeries (valvuloplasty and valve repairs), in which 45% of the cohort developed POAF, Yin, et al., showed a significant predictive association between high pre-operative CHA2DS2-VASc scores and an increased incidence of POAF. The incidence increased with increasing scores [19]. However, this study only included valve surgery, thus limiting its use to coronary bypass surgery.

In a study of a bigger cohort of 729 patients undergoing OPCABG, Borde, et al., found that 13% of the cohort developed POAF; a lower incidence rate than previous reports [20]. Borde, et al., also used a CHA2DS2-VASc score cut-off of 3, which predicted POAF incidence with a sensitivity of 84.21%, specificity of 84.54%, a positive predictive value of 43.96% (95% CI, 36.3-52.5) and a negative predictive value of 97.23% (95% CI, 95.5-98.4) [21].

In a study of 277 consecutive cardiac surgeries, Chua, et al., reported that 30% of patients developed POAF within an average of 2 days. A significant rise in POAF incidence was also seen with increasing CHA2DS2-VASc score in this study. Chua, et al., also showed that patients with a score of ≥ 2 had worse left ventricular diastolic function than those with scores lower than 2, justifying the use of 2 as a cut-off point for prediction and intervention. They further classified patients with CHADS2 scores of 0 or 1 into 2 groups using CHA2DS2-VASc with different POAF risks [22].

In our study, 22.6% of the 1254 patients in our cohort developed POAF. Similar to results found in the literature, we noted a significant increase in POAF incidence with higher CHA2DS2-VASc score. Kaplan-Meier survival analysis revealed that patients with scores of 2 or greater had a marginally higher POAF rate than patients with scores less than 2 ($p=0.075$), justifying the use of a cut-off point of 2, contrary to Borde, et al. Defining a score of 2 or more as being high risk for POAF, we were able to detect POAF at 96.8% sensitivity and an accuracy of 26.5%. Increasing the cut-off point to a value of 3 demonstrates higher specificity (25.6% versus 6.1%), but at the expense of sensitivity (76.5% versus 96.8%).

In our study, we also sought to determine isolated pre-operative predictors of POAF, and the strength of association of risk factors calculated in the CHA2DS2-VASc score. In terms of demographic data, we found that older age (75 years and older) contributed a significantly high risk for developing POAF (HR, 1.037; CI, 1.025-1.050; $p<0.001$). In a cohort of 18,517 patients undergoing coronary revascularization, El-Chami, et al., showed that advanced age significantly predicted the incidence of POAF (OR, 1.059/year; 95% CI, 1.055-1.063) [23]. In a smaller but more recent study by Folla, et al., 19% of among 105 patients who underwent CABG developed POAF, with an age older than 64.5 years proving to be significantly related [24]. Nisanoglu, et al., studied the risks of developing POAF in a cohort of 426 CABG patients, all of whom were aged 65 years and older. They showed that being aged 75 years or older increased the risk of postoperatively developing AF [25].

In our study, height and weight calculated as BMI was another patient characteristic associated with a risk of developing AF (HR, 1.038; CI, 1.025-1.051; $p<0.001$). Previously, Zacharias, et al., showed a strong link between obesity and the risk of developing POAF [26].

Concurrent with the literature, male gender was a strong predictor of POAF in our study [27]. Our study also showed

hypertension to be a significant risk factor: hypertensive patients had a much higher incidence of POAF than those without hypertension (HR, 1.237; CI: 0.955-1.605; p=0.1).

We also found that high creatinine, an indicator of renal insufficiency, was another predictor for increased risk of POAF. In a study by Perrier, et al., of 1481 patients, 21% developed POAF. Furthermore, it was noted that severe obesity, renal insufficiency, and high creatinine levels were at considerable risks [28].

In our study, we evaluated the effects of taking pre-operative medications on the incidence of POAF. Cox regression analysis showed that patients receiving statins were 1.4-fold less likely to develop POAF. However, evidence of the efficacy of the prophylactic use of statins in decreasing POAF risk is conflicting [29]. In a review of 15 randomized controlled trials, Chopra, et al., showed that peri-operative use of statins decreases the risk of AF, and is even beneficial for decreasing the risk of postoperative MI, and decreasing length of hospital stay [30].

Traditionally, beta-blockers have been used as part of the pre-operative and postoperative prophylaxis regimen to decrease the risk of POAF. However, contradicting the early literature, we found beta-blockers to have no significant protective value [31,32].

In our study, we found that the use of ACE inhibitors or ARBs made no significant difference in POAF incidence. Indeed, the available results provide either conflicting evidence or non-statistically significant conclusions [33,34]. That said, when we categorized patients by CHA2DS2-VASc score, those with a score ≥ 2 benefited the most from pre-operative statin (p=0.002) and ARB use (p=0.147). It would be necessary to evaluate a bigger cohort of patients to better determine the effect of ARB use on the incidence of POAF.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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