

## Usefulness of CHA2DS2-VASc scoring system in predicting atrial fibrillation after coronary artery bypass grafting

*Koroner arter baypas greftleme sonrası atriyal fibrilasyonun öngörülmesinde CHA2DS2-VASc skorlama sisteminin kullanışlılığı*

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### ABSTRACT

**Background:** This study aims to assess whether CHADS2 and CHA2DS2-VASc scoring systems are useful in predicting atrial fibrillation after coronary artery bypass grafting.

**Methods:** Between January 2010 and July 2013, a total of 478 patients (305 males, 173 females; mean age 62.1 years; range 40 to 83 years) who underwent coronary artery bypass grafting in our clinic were enrolled in the study. Data were obtained from the medical files of the patients and hospital records. All patients were monitored in the intensive care unit after surgery. Atrial fibrillation lasting more than 30 seconds in irregular rhythm without P waves on telemetry was classified as postoperative atrial fibrillation. All patients were evaluated using CHADS2 and CHA2DS2-VASc scoring systems.

**Results:** Of 478 patients, 102 had postoperative atrial fibrillation. CHADS2 and CHA2DS2-VASc scores were statistically significantly higher in patients with postoperative atrial fibrillation than others (2.1±0.8 vs 1.1±0.8, p<0.001 and 4.3±1.1 vs 2.2±1.1, p<0.001). Age, left atrial diameter, left ventricular ejection fraction, and CHA2DS2-VASc scores were independently associated with postoperative atrial fibrillation. A CHA2DS2-VASc score of ≥2 predicted postoperative AF with %96.3 sensitivity and %74.6 specificity (AUC=0.906, 95% CI=0.875-0.938, p<0.001).

**Conclusion:** The CHA2DS2-VASc score is a strong predictor of atrial fibrillation development after isolated coronary artery bypass grafting surgery. Therefore, the CHA2DS2-VASc scoring system can be used as a stratification tool to estimate atrial fibrillation after coronary artery bypass grafting.

**Keywords:** CHA2DS2-VASc scoring system; coronary artery bypass grafting; postoperative atrial fibrillation.

### ÖZ

**Amaç:** Bu çalışmada CHADS2 ve CHA2DS2-VASc skorlama sistemlerinin koroner arter baypas greftleme sonrası atriyal fibrilasyonu öngörmeye kullanışlı olup olmadıkları değerlendirildi.

**Çalışma planı:** Ocak 2010 - Temmuz 2013 tarihleri arasında kliniğimizde koroner arter baypas greftleme yapılan toplam 478 hasta (305 erkek, 173 kadın; ort yaş 62.1 yıl; dağılım 40-83 yıl) çalışmaya alındı. Veriler, hastaların tıbbi dosyalarından ve hastane kayıtlarından elde edildi. Hastaların tümü ameliyat sonrası yoğun bakım ünitesinde monitörize edildi. Telemetride P dalgası olmaksızın düzensiz ritim ile 30 saniyeden uzun süren atriyal fibrilasyon, ameliyat sonrası atriyal fibrilasyonu olarak tanımlandı. Tüm hastalar CHADS2 ve CHA2DS2-VASc skorlama sistemleri ile değerlendirildi.

**Bulgular:** Dört yüz yetmiş sekiz hastanın 102'sinde ameliyat sonrası atriyal fibrilasyon gelişti. CHADS2 ve CHA2DS2-VASc skorları, ameliyat sonrası atriyal fibrilasyonu gelişen hastalarda, diğerlerine kıyasla, istatistiksel olarak anlamlı düzeyde daha yüksekti (2.1±0.8'e karşın 1.1±0.8, p<0.001 ve 4.3±1.1'e karşın 2.2±1.1, p<0.001). Yaş, sol atriyum çapı, sol ventrikül ejeksiyon fraksiyonu ve CHA2DS2-VASc skoru ameliyat sonrası atriyal fibrilasyonu ile bağımsız olarak ilişkiliydi. CHA2DS2-VASc skorunun ≥2 olması, ameliyat sonrası atriyal fibrilasyonu gelişimini %96.3 duyarlılık ve %74.6 özgüllük ile öngördü (AUC=0.906, 95% GA=0.875-0.938, p<0.001).

**Sonuç:** CHA2DS2-VASc skoru, izole koroner arter baypas greftleme ameliyatı sonrası atriyal fibrilasyonu gelişiminin güçlü bir öngördürücüsüdür. Bu nedenle, CHA2DS2-VASc skorlama sistemi, koroner arter baypas greftleme sonrası atriyal fibrilasyonu öngörmeye sınıflandırma aracı olarak kullanılabilir.

**Anahtar sözcükler:** CHA2DS2-VASc skorlama sistemi; koroner arter baypas greftleme; ameliyat sonrası atriyal fibrilasyon.



Available online at  
www.tgkdc.dergisi.org  
doi: 10.5606/tgkdc.dergisi.2016.11751  
QR (Quick Response) Code

Received: March 20, 2015 Accepted: July 03, 2015

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Postoperative atrial fibrillation (AF) is the most common cardiac arrhythmia, which accounts for about 20 to 40% of patients after coronary artery bypass grafting (CABG).<sup>[1,2]</sup> Although earlier studies demonstrated that postoperative AF was harmless, temporary, and self-limited without any clinical significance, recent studies has shown an association with several adverse outcomes including increased duration of hospitalization [hospital and in intensive care unit (ICU)], risk of stroke, and more importantly in-hospital and long-term mortality.<sup>[3-5]</sup> Several studies were performed to identify demographic characteristics of the patients and related risk factors for postoperative AF after CABG. However, the results of these studies were found to be inconsistent except the increasing age.<sup>[4,6]</sup>

The CHADS2 and CHA2DS2-VASc scores are used for an embolic risk stratification and guidance for the treatment of AF.<sup>[7]</sup> The acronym of CHADS2 score refers to congestive heart failure, hypertension, age  $\geq 75$  years, diabetes and stroke.<sup>[7]</sup> The CHADS2 and CHA2DS2-VASc scores of most components are also risk factors for atherosclerosis.<sup>[8-12]</sup> Moreover, these factors are closely associated with postoperative AF. However, the predictive value of each component of the CHADS2 and CHA2DS2-VASc scoring systems is limited for the development of postoperative AF. As a result, we hypothesized that clustering of these factors might have a more predictive value for the development of AF after CABG.

There are only two studies investigating the relationship between CHADS2 and CHA2DS2-VASc scores and the development of AF after CABG.<sup>[13,14]</sup> In this study, therefore, we aimed to assess whether CHADS2 and CHA2DS2-VASc scoring systems are useful in predicting AF after CABG.

## PATIENTS AND METHODS

This retrospective and two-center study included a total of 478 patients (305 males, 173 females; mean age 62.1 years; range 40 to 83 years) who underwent elective isolated CABG in the cardiovascular surgery clinic January 2010 and July 2013. Data were obtained from the medical files of the patients and hospital records. The study protocol was approved by the local ethics committee.

All patients underwent standard CABG requiring cardiopulmonary bypass (CPB) except simultaneous valvular surgery. Before surgery, we performed standard 12-lead electrocardiography (ECG) recorded on chart paper at a speed of 25 mm/sec. The study population consisted of the patients who were in sinus

rhythm and underwent isolated CABG. The exclusion criteria were as follows: emergency surgery, repeated CABG, acute coronary syndrome, significant valvular heart disease, pacemaker implantation, atrial flutter or fibrillation, pulmonary disease, pericarditis, congenital heart disease, overt hypothyroidism or hyperthyroidism, renal or hepatic disease, and cardiac failure during postoperative period. A total of 35 patients were excluded the study.

Surgery was performed through median sternotomy, aortic cannulation, a single right atrial cannula with membrane oxygenator (Avant D903, Dideco, Mirandola, Modena, Italy), a single cross-clamp, initially antegrade via the aorta than retrograde blood cardioplegia every 15 minutes via coronary sinus, a roller pump and mild systemic hypothermia (32-34 °C). After CPB, heparin sodium was antagonized at the rate of 1 mg heparin/1 mg protamine sulfate.

All patients were monitored constantly during their ICU stay. The patients receiving preoperative beta-blockers continued their treatment after surgery to avoid withdrawal. In case of electrolyte imbalance, the patient was immediately treated. After ICU discharge, the patients were monitored continuously by five-lead telemetry and also by 12-lead electrocardiograms every morning. According to the definition of the Society of Thoracic Surgeons, new-onset postoperative AF was defined as AF occurred during hospitalization after CABG in patients without a history of AF. Accordingly, the patients without preoperative AF who experienced AF lasting more than 30 seconds in irregular rhythm without P waves on telemetry any time during the hospitalization after surgery were described with new-onset postoperative AF (irrespective of whether the patient responded to the medical treatment or converted into sinus rhythm spontaneously). Additional ECGs were also obtained from the clinical records and the medical files of the patients, if required or in case of palpitation reported by the patient.

As aforementioned, the CHADS2 score refers to congestive heart failure, hypertension, age  $\geq 75$  years, diabetes, and stroke.<sup>[7]</sup> In addition, the CHA2DS2-VASc score additionally includes vascular disease, age 65-74 years, and female sex. In our study, the CHADS2 score was calculated as the sum of points assigned to each of the following items; one point for congestive heart failure (CHF), hypertension, age  $\geq 75$  years, and diabetes mellitus; two points for a history of a prior stroke or transient ischemic attack. The CHA2DS2-VASc score was calculated as the sum of

points assigned to each of the followings: one point for a history of CHF, hypertension, age 65-74 years, diabetes mellitus, female sex, and vascular diseases; two points for a history of a prior stroke or transient ischemic attack, and for age  $\geq 75$  years.

The CHADS2 and CHA2DS2-VASc scores were analyzed for all patients by a computer system in our hospital. Each risk factor relevant to the risk scores was noted. Congestive heart failure was defined as a left ventricular ejection fraction (EF) of  $\leq 40\%$ , as assessed by echocardiography or invasive testing and/or if clinical signs of heart failure were present at the given time point. Hypertension was defined as a history of hypertension and/or currently treated hypertension preoperatively. Diabetes was defined as a history of diabetes and/or current treatment with an oral hypoglycemic medication and/or insulin. Stroke was defined as neurological deficit lasting for 24 hours (TIA) or longer (stroke) caused by ischemia; however, hemorrhage-related ischemia was excluded. Vascular disease was defined as a prior myocardial infarction, a history of percutaneous

coronary intervention and/or CABG, and a history of peripheral artery disease and/or aortic plaque. 0 indicates low risk, 1 or 2 indicates moderate risk, and  $\geq 3$  indicates high risk.

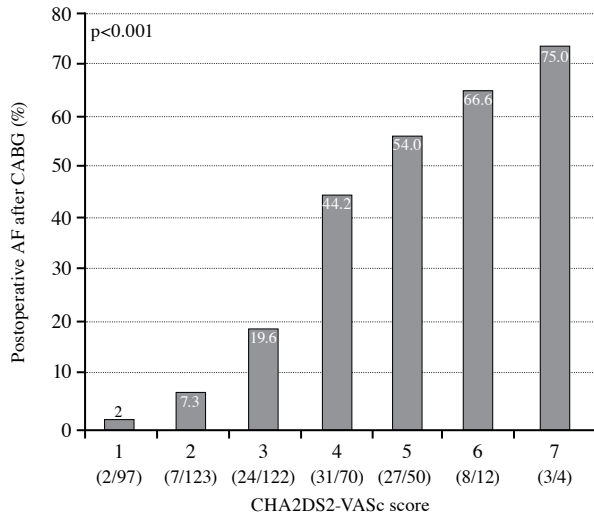
### Statistical analysis

Statistical analysis was performed using PASW version 17.0 software (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to analyze the normality of the variables. Parametric variables were expressed in mean  $\pm$  standard deviation (SD), while non-parametric variables were expressed in percentage. Abnormally distributed variables were expressed in medians. The chi-square test or Fisher's exact test, where applicable, were used to compare the patients characteristics. A *p* value of  $<0.1$  in the univariate analysis was used for the multivariate regression analysis. The multivariate logistic regression analysis was performed to analyze independent predictors of postoperative AF. The receiver operating characteristic (ROC) curve was done to determine whether the sensitivity and specificity of

**Table 1. Demographic and laboratory characteristics of the patients and related surgical data**

Variables	Without postoperative AF (n=376)			With postoperative AF (n=102)			<i>p</i>
	n	%	Mean $\pm$ SD	n	%	Mean $\pm$ SD	
Age (years)			59.0 $\pm$ 9.8			67.8 $\pm$ 9.9	<0.001
Gender							
Male	305	81.3		63	61.7		0.001
Hypertension	186	49.4		72	70.5		0.001
Diabetes mellitus	113	30.1		46	45.0		0.002
Smoking	207	55.1		59	58.0		0.550
Beta-blocker use	188	50.0		45	40.1		0.001
Statin use	178	47.3		48	46.6		0.412
Stroke/transient ischemic attack	4	1.06		7	6.8		0.048
ACEI or angiotensin receptor blocker	188	50.0		50	49.0		0.569
Heart rate, bpm			73.1 $\pm$ 16			74.1 $\pm$ 17	0.252
Left ventricle ejection fraction			55.6 $\pm$ 9.0			49.6 $\pm$ 12.1	0.001
Left atrium diameter (mm)			35.9 $\pm$ 3.1			38.1 $\pm$ 3.5	0.001
Glucose (mg/dL)			95.7 $\pm$ 18.4			99.2 $\pm$ 21.8	0.186
Creatinine (mg/dL)			0.81 $\pm$ 0.18			0.83 $\pm$ 0.17	0.212
Total C (mg/dL)			181 $\pm$ 62			180 $\pm$ 56	0.815
C-high-density lipoprotein cholesterol (mg/dL)			36 $\pm$ 9			35 $\pm$ 8	0.811
Low-density lipoprotein cholesterol (mg/dL)			113 $\pm$ 35			117 $\pm$ 41	0.141
Cardiopulmonary bypass time (min)			95 $\pm$ 31			94 $\pm$ 38	0.654
Cross-clamp time (min)			61 $\pm$ 22			62 $\pm$ 23	0.666
No. of anastomosis			3.0 $\pm$ 1.5			3.1 $\pm$ 1.4	0.639
Need for inotropic support	56	15.4		17	16.4		0.234
CHADS2 score			1.1 $\pm$ 0.8			2.1 $\pm$ 0.8	<0.001
CHA2DS2-VASc score			2.2 $\pm$ 1.1			4.3 $\pm$ 1.1	<0.001

POAF: Postoperative atrial fibrillation; SD: Standard deviation; ACEI: Angiotensin-converting enzyme inhibitor; Independent sample t-test; Mann-Whitney U test and Chi-square tests.



**Figure 1.** Postoperative atrial fibrillation rates continuously increased, as the CHA2DS2-VASc scores increased.

CHA2DS2-VASc scores were useful tools in predicting new-onset postoperative AF. A  $p$  value of  $\leq 0.05$  was considered statistically significant.

## RESULTS

Postoperative AF was observed in 102 including 63 males and 39 females with a mean age of  $67.8 \pm 9.9$  years. Demographic and laboratory characteristics of the patients and related surgical data are shown in Table 1.

Age, left atrial diameter, and CHADS2 and CHA2DS2-VASc scores were significantly higher in patients with postoperative AF than those without postoperative AF (Table 1). The left ventricular ejection fraction (LVEF) was significantly lower in patients with postoperative AF than those without postoperative AF ( $49.6 \pm 12.1$  vs  $55.6 \pm 9.0$ ,  $p=0.001$ ). Male gender was lower in patients with postoperative AF than those without postoperative AF (61.7% vs 81.3%). The ratio of the patients with hypertension and diabetes mellitus was significantly higher in postoperative AF group (70.5% vs 49.4%,  $p=0.001$  and 45.0% vs 30.1%,  $p=0.002$ ), whereas beta-blocker use was significantly lower in the same group (40.1% vs 50.0%,  $p=0.001$ ). However, there were no significant differences in smoking, preoperative creatinine and glucose levels, heart rate, history of myocardial infarction (MI), the number of anastomosis, need for inotropic support, statin therapies, and the use of angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) between the groups (Table 1).

There was a significant and negative correlation between LVEF and postoperative AF ( $r = -0.256$ ,  $p=0.001$ ). In addition, age and CHADS2 and CHA2DS2-VASc scores were positively and significantly correlated with postoperative AF ( $r=0.71$ ,  $p<0.001$ ,  $r=0.473$ ,  $p<0.001$  and  $r=0.615$ ,  $p<0.001$ ). Additionally, postoperative AF rates continuously increased, as the CHA2DS2-VASc scores increased (Figure 1).

The univariate logistic regression analysis revealed that age, left atrial diameter, LVEF, male gender, beta-blocker use, hypertension, diabetes mellitus, and CHADS2 and CHA2DS2-VASc scores were associated with postoperative AF (Table 2). However, the multivariate logistic regression analysis demonstrated that age, left atrial diameter, LVEF, and CHA2DS2-VASc scores were independently associated with postoperative AF (OR=1.051, 95% CI=0.999-1.111,  $p=0.049$ ; OR=1.414, 95% CI=1.169-1.719,  $p=0.012$ ; OR=1.060, 95% CI=1.005-1.118,  $p=0.032$  and OR=14.983, 95% CI=4.815-46.627,  $p<0.001$ ) (Table 2).

As analyzed by the ROC curve, a CHA2DS2-VASc score of  $\geq 2$  predicted postoperative AF with 96.3% sensitivity and 74.6% specificity (AUC=0.906, 95% CI=0.875-0.938,  $p<0.001$ ) (Figure 2).

## DISCUSSION

The results of the present study showed that age, male gender, hypertension, diabetes mellitus, beta-blocker use, left atrial diameter, LVEF, and CHADS2 and CHA2DS2-VASc scores were significantly associated with AF after isolated CABG. However, only age, left atrial diameter, LVEF, and CHA2DS2-VASc scores were the significant independent predictors of AF after isolated CABG. Moreover, the CHA2DS2-VASc scores were found to be the most important independent predictors for postoperative AF. Therefore, we can conclude that the CHADS2 scores are not strong enough in predicting postoperative AF; however, CHA2DS2-VASc scores are apparently useful in predicting AF after CABG.

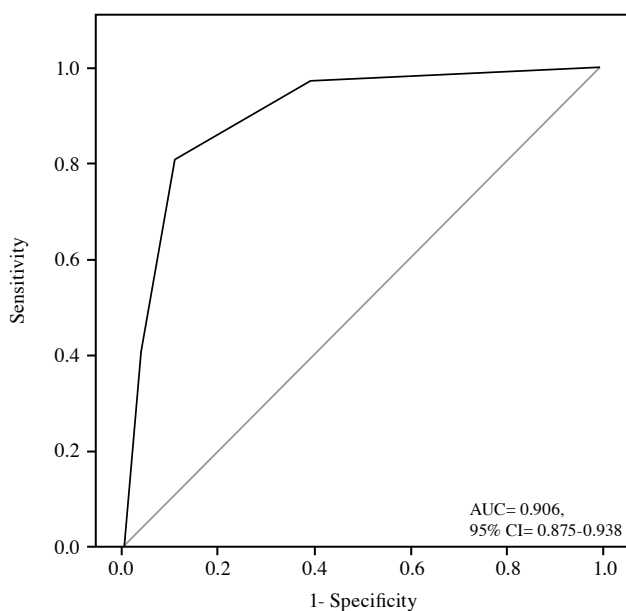
Previously, several risk factors were reported independently in predicting postoperative AF such as advanced age, sex, diabetes mellitus, prior myocardial infarction, heart failure,<sup>[15]</sup> systemic hypertension, peripheral vascular disease,<sup>[16]</sup> and left atrial enlargement.<sup>[17]</sup> Ozlu et al.<sup>[18]</sup> demonstrated that patients with postoperative AF were older age and had lower EF values compared to those without postoperative AF. In another study, Helgadottir et al.<sup>[19]</sup> showed that patients with postoperative AF were significantly older, were more often females, and had lower EF values with chronic heart failure. Similarly,

**Table 2. Univariate and multivariate logistic regression analyses of independent variables for postoperative atrial fibrillation**

Variables	Univariate			Multivariate		
	Odds ratio	95% CI	<i>p</i>	Odds ratio	95% CI	<i>p</i>
Age	1.133	1.098-1.171	<0.001	1.051	0.999-1.111	0.049
Beta-blocker use	0.737	0.509-0.994	0.011	1.337	0.403-4.439	0.536
Left artium diameter (mm)	1.324	1.228-1.427	0.001	1.414	1.169-1.719	0.012
Ejection fraction	0.944	0.930-0.969	0.001	1.060	1.005-1.118	0.032
Gender						
Male	0.770	0.529-0.995	0.012	1.589	0.407-6.209	0.351
Hypertension	2.452	1.530-3.928	<0.001	0.883	0.178-4.337	0.127
Diabetes mellitus	2.012	1.284-3.153	<0.001	1.099	0.337-3.580	0.461
CHADS2	2.219	1.662-2.961	0.001	1.092	0.334-3.568	0.884
CHA2DS2-VASc	4.353	3.265-5.803	<0.001	14.983	4.815-46.627	<0.001
Stroke/transient ischemic attack	1.014	0.991-1.025	0.239			
Smoking	1.193	0.670-2.114	0.548			
Total-cholesterol	0.997	0.991-1.004	0.478			
LDL-cholesterol	1.005	0.991-1.012	0.451			
HDL-cholesterol	0.999	0.963-1.058	0.552			
Triglycerides	1.009	0.996-1.021	0.239			
ACEI/ARB	0.878	0.563-1.371	0.545			
Statin use	1.251	0.803-1.987	0.340			

CI: Confidence interval; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker.

in our study, we revealed that age, LVEF, sex, diabetes mellitus, systemic hypertension, beta-blocker use, left atrial diameter, and CHADS2 and CHA2DS2-VASc



**Figure 2.** Receiver operating characteristic curve analysis of CHA2DS2-VASc scores in predicting postoperative atrial fibrillation in coronary artery bypass surgery (AUC=0.906, 95% CI=0.875-0.938,  $p<0.001$ ).

scores were significantly associated with AF after CABG. On the other hand, in the univariate logistic regression analysis, we found that although these risk factors are critical determinants of postoperative AF, the CHA2DS2-VASc scoring system was the optimal and accessible variable in predicting AF after CABG, as assessed by multivariate logistic regression analysis.

Recently, two studies used the CHADS2 and CHA2DS2-VASc scores in predicting the risk of postoperative AF.<sup>[13,14]</sup> Chua et al.<sup>[13]</sup> demonstrated that the CHADS2 and CHA2DS2-VASc scores were predictive of AF after cardiac surgery, as confirmed by several multivariate regression analyses. The Kaplan-Meier analysis revealed a higher incidence of postoperative AF according to the CHADS2 and CHA2DS2-VASc scores of  $\geq 2$  compared to the scores  $< 2$  (both log rank,  $p<0.001$ ). Similarly, we found that the CHADS2 and CHA2DS2-VASc scores were associated with postoperative AF (OR=2.219,  $p<0.001$  and OR=4.353,  $p<0.001$ ). Although multivariate logistic regression analysis showed no association between the CHADS2 scores and postoperative AF, the CHA2DS2-VASc scores were independently associated with postoperative AF (OR=14.983,  $p<0.001$ ). Moreover, our study included 478 patients; however, aforementioned study consisted of only 277 patients. In another study, Borde et al.<sup>[14]</sup> used only CHA2DS2-VASc

scores in predicting postoperative AF and reported that the incidence of postoperative AF increased with increasing CHA2DS2-VASc scores after cardiac surgery. This study consisted of 729 patients; however, postoperative AF occurred in only 13% patients with a cut-off value of CHA2DS2-VASc 3. On the other hand, the incidence of postoperative AF was found to be 21.3% in our study. Also, in our study, the cut-off value for CHA2DS2-VASc scores was 2; indicating a sensitivity of 96.3% and specificity of 74.6%.

Furthermore, Açıl et al.<sup>[20]</sup> showed that the left atrial diameter was a significant predictor for postoperative AF in patients undergoing CABG. In the present study, inconsistent with the aforementioned study findings, we observed that the left atrial diameter were significantly higher in patients with postoperative AF than those without postoperative AF. However, we were unable to identify that the left atrial diameter was independently associated with postoperative AF in the multivariate logistic regression analysis.

In another study, Halkos et al.<sup>[21]</sup> reported that preoperative neurological events or peripheral vascular disease were risk factors for postoperative neurological events including postoperative AF, stroke, in-hospital mortality, and renal failure. Similarly, we demonstrated that postoperative AF was more often in patients with preoperative stroke. However, in our study, we had a few patients with a history of stroke. Therefore, we concluded that preoperative stroke was not an independent risk factor for postoperative AF.

Zuo et al.<sup>[22]</sup> reported that the CHADS2 and CHA2DS2-VASc scores might be used to identify high-risk individuals for the development of AF. As shown in our study, the components of the CHA2DS2-VASc scoring system are useful and reliable in predicting postoperative AF risk in patients undergoing CABG, however, it is not adequate to predict AF after CABG. On the other hand, CHA2DS2-VASc scores are the most significant variables in predicting AF after CABG.

While postoperative AF can be transient and without implications, it may cause serious complications, such as increased mortality and morbidity, hemodynamic instability, and prolonged hospital stay, cardiac failure, and increased disability.<sup>[1,23,24]</sup> Also, the presence of AF after CABG is associated with higher incidence of heart failure and stroke, which can be attributed to higher surgery costs, prolonged hospital stay, and increased morbidity and mortality.<sup>[25]</sup> Therefore, the occurrence of postoperative AF is of utmost importance for patients undergoing cardiac surgery.

All components of the CHA2DS2-VASc scoring system has a limited ability in predicting AF after CABG. Increasing CHADS2-VASc scor has been validated to correlate with an increased occurrence of AF after CABG. Also, it can predict postoperative AF with 96.3% sensitivity and 74.6% specificity after isolated CABG.

On the other hand, there are some limitations to this study. The major limitation is its retrospective design. Second, our study findings are limited to new onset in-hospital postoperative AF and do not address episodes of AF occurring after discharge. Another limitation of our study is that the study population includes only those undergoing isolated CABG. Therefore, the results may not be extrapolated to patients undergoing simultaneous cardiac or extra-cardiac procedures.

In conclusion, identifying high-risk patients for postoperative atrial fibrillation may prevent adverse cardiovascular events. Based on our study findings, the CHA2DS2-VASc score is a strong predictor of atrial fibrillation development after isolated coronary artery bypass grafting surgery. Therefore, the CHA2DS2-VASc scoring system can be used as a stratification tool to estimate atrial fibrillation after coronary artery bypass grafting. We believe that our study may inspire further studies using the CHA2DS2-VASc scoring system to provide prophylactic atrial fibrillation therapies to the high-risk patients preoperatively.

#### **Declaration of conflicting interests**

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

#### **Funding**

The authors received no financial support for the research and/or authorship of this article.

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