

Predicting Postoperative Atrial Fibrillation Using HARMS₂-AF Score

ABSTRACT

Background: Postoperative atrial fibrillation (POAF) remains a common complication after cardiac surgery. The ability to accurately identify patients at risk through previous risk scores is limited. This study aimed to evaluate the new HARMS₂-AF risk score to predict POAF after coronary artery bypass grafting (CABG) surgery.

Methods: In this retrospective cohort study, we included 265 patients undergoing CABG surgery from 2022-2023. Data were obtained from the medical files of the patients and hospital records. Each patient was assigned a HARMS₂-AF risk score. A univariate and multivariate regression analyses were done to analyze independent predictors of POAF.

Results: Of 265 patients, 49 had postoperative atrial fibrillation. HARMS₂-AF score was significantly higher in patients with POAF. Age, sleep apnea, left atrial diameter (LAd), and HARMS₂-AF score were independently associated with POAF. A HARMS₂-AF score \geq 4.5 predicted POAF with 91% sensitivity and 64% specificity (AUC = 0.787, 95% CI = 0.731-0.842, $P < .001$).

Conclusion: The HARMS₂-AF score is a strong predictor of atrial fibrillation (AF) development after isolated CABG surgery. It can be used as a novel stratification tool to estimate AF after cardiac surgery.

Keywords: HARMS₂-AF score, coronary artery bypass grafting, atrial fibrillation

INTRODUCTION

Postoperative atrial fibrillation (POAF) is an important complication after coronary artery bypass graft (CABG) surgery, which occurs in nearly 30% of cases.¹ It is associated with increased mortality and morbidity, including a higher risk of ischemic stroke.²

It has been demonstrated that patients with hypertension, diabetes mellitus, obesity, increased age, degenerative or rheumatic valvular heart disease, left atrial remodeling, and enlargement were under risk for development of POAF.³ Several studies have focused on identifying the demographic and clinical characteristics of POAF patients and related risk factors. Altered sympathetic activity with increased oxidative stress, as well as exaggerated inflammatory status during the postoperative period, is thought to be the underlying pathophysiological mechanisms.⁴

A simple, reproducible, and cost-effective scoring system needs to be developed to predict the probability of POAF because routine prophylactic antiarrhythmic treatment is associated with adverse clinical events and impaired surgical improvement. The HARMS₂-AF score is a new risk score that evaluates established and emerging lifestyle factors on incident AF risk.⁵

In the present study, we aimed to evaluate the utility of the HARMS₂-AF score in predicting the risk of developing POAF in CABG surgery patients to provide earlier prophylactic interventions to high-risk patients in the preoperative period.

METHODS

This retrospective study evaluated a total of 310 patients who underwent isolated CABG surgery from September 2021-January 2024 at a university hospital. Data

ORIGINAL INVESTIGATION

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were obtained from the medical records of the patients. Patients with previous atrial fibrillation/flutter, acute coronary syndrome, renal failure, significant valvular heart disease, thyroid dysfunction, or heart failure (45 patients) were excluded from the study. The Local Ethics Committee approved the study protocol.

HARMS₂-AF score refers to hypertension (4 points), age (60-64 years: 1 point; ≥65 years: 2 points), increased body mass index (BMI) (≥ 30 kg/m²: 1 point), gender (male sex: 2 points), sleep apnea (2 points), smoking (1 point), alcohol (7-14 standard drinks/week: 1 point; ≥15 standard drinks/week: 2 points) (Table 1). The total HARMS₂-AF score was analyzed for all patients. Patients were divided into 2 groups: those who developed postoperative atrial fibrillation (POAF group) and those who did not (NPOAF group).

Surgical Technique

The patients underwent on-pump CABG surgery using a conventional technique. To summarize, after a median sternotomy, the ascending aorta was cannulated for the arterial line, and a single-stage venous cannula was inserted via the right atrial auricle. Aortic root venting and cold crystalloid cardioplegia were administered via the antegrade route. Cardiopulmonary bypass (CPB) with moderate systemic hypothermia (30-32°C) and hemodilution (Hct > 0.22) was the technique used. Antegrade cold crystalloid cardioplegia was administered sporadically to each subject. Peripheral and central anastomoses were created as a result of a single aortic blockage. The bypass conduits were either the saphenous veins, the internal mammary artery, or both.

Postoperative Follow-ups

We monitored the patients while they were in the hospital, keeping in mind that the risk of atrial fibrillation after surgery rises about 48 hours after the procedure. We analyzed ECG readings, in-hospital progress notes, nursing charts, discharge notes, and replies for cardiologist consultation, in addition to using postoperative diagnosis based on the International Classification of Diseases-10 categories. We also noted patients with postoperative atrial fibrillation who needed electrical cardioversion for rhythm or rate control, or who needed intravenous antiarrhythmic medication such as amiodarone, beta-blockers, propafenone, diltiazem, or verapamil.

HIGHLIGHTS

- Postoperative atrial fibrillation (POAF) is associated with an increased mortality and morbidity, including a higher risk of ischemic stroke after coronary artery bypass surgery.
- HARMS₂-AF score is a new risk score that evaluates established and emerging lifestyle factors on incident AF risk.
- HARMS₂-AF score could be used to identify patients at the highest risk of developing POAF, thus avoiding non-selective arrhythmia prophylaxis as well as triggering aggressive risk factor management.

Table 1. HARMS₂-AF Scoring Criteria

Hypertension	4 points
Age	
60-64 age	1 point
≥65 age	2 points
Body mass index ≥ 30 kg/m ²	1 point
Male gender	1 point
Sleep apnea	1 point
Smoking	1 point
Alcohol use	
7-14 standard drinks/ week	1 point
≥15 standard drinks/ week	2 points

Statistical Analysis

The normal distribution was evaluated using the Kolmogorov-Smirnov test. Categorical variables were identified using numbers and percentages, whereas continuous variables were expressed using mean ± SD. Continuous variables were compared using either a 1-way analysis of variance (ANOVA) or the Student's t-test. The chi-square technique was employed to assess the differences in distributions of categorical variables. In this inquiry, the Bonferroni multiple comparison test was employed to effectively manage type I error for all possible multiple comparisons.

The forward elimination strategy using default values was used to identify prognostic factors. In the context of the Bonferroni multiple comparison test, statistical significance was determined by a *P*-value below .025. The application of the forward stepwise selection in multiple logistic regression analysis allowed for the identification of the most influential factors in determining the development of postoperative atrial fibrillation in patients. All variables that had a *P*-value less than .25 in the univariable test were considered as potential candidates for the multiple models, along with other variables of acknowledged clinical importance. The multiple logistic regression analysis was performed to analyze significant factors of POAF. In addition, we calculated 95% confidence intervals (CIs) and adjusted odds ratios. The receiver operating characteristic (ROC) curve method was used to determine whether the sensitivity and specificity of the HARMS₂-AF score were useful in predicting new-onset of postoperative atrial fibrillation. The results were considered significant if the *P*-value was less than .05. The investigation was carried out utilizing the Statistical Package for the Social Sciences 24 (SPSS). The sample power was measured using the Power and Sample Size Calculations program version 3.1.2, and it was 0.86.

RESULTS

Of the 310 patients who underwent CABG surgery during the study protocol, 265 patients were included in the analysis. The enrolled patients were classified into 2 groups according to the occurrence of postoperative AF or maintained sinus rhythm after coronary artery bypass surgery (POAF group vs. NPOAF group). Postoperative new-onset AF occurred in 49 (18.4%) patients. It was studied with a margin of error of 0.04 within a

Table 2. Baseline Demographic, Clinical and Operative Characteristics

Demographic	AF; n (%) 49 (18.4%)	NPOAF; n (%) 216 (81.5%)	P
Diabetes mellitus n (%)	13 (26)	50 (23)	.998
Dyslipidemia n (%)	25 (51)	124 (57)	.416
HARMS ₂ -AF score	6.02 ± 1.76	3.48 ± 2.54	<.001
HARMS ₂ -AF Characteristics			
Hypertension n (%)	19 (39)	86 (40)	.893
Age (mean ± SD, years)	66.34 ± 7.09	63.08 ± 6.62	.001
Body mass index (kg/m ²)	28.2 ± 2.02	28.10 ± 2.13	.827
Male gender n (%)	34 (69)	131 (60)	.255
Sleep apnea n (%)	6 (12)	4 (1.5)	.001
Smoking history n (%)	19 (38,7)	92 (42.5)	.74
Alcohol Use, n (%)			.001
7-14 per week	18 (36.7)	17 (7.8)	
≥15 per week	4 (8.1)	6 (2.7)	
Laboratory			
Hemoglobin (g/dL)	11.7 ± 0.82	12.2 ± 0.68	.098
White blood cell (×10 ³ µg)	9.40 ± 0.77	8.82 ± 0.77	.382
Creatinine (mg/dL)	1.03 ± 0.07	0.95 ± 0.14	.16
Sodium (mEq/L)	137.2 ± 1.41	138.53 ± 1.68	.122
LDL cholesterol (mg/dL)	140 ± 17	138 ± 23	.321
Echocardiography			
Left atrium diameter (mm)	38.36 ± 2.6	34.66 ± 2.66	<.001
LVDD (mm)	45.57 ± 2.05	45.41 ± 2.03	.689
LVSD (mm)	28.32 ± 2.4	26.74 ± 1.4	.103
Preoperative LVEF (%)	62.87 ± 2.29	62.24 ± 2.03	.056
Medications			
ACEI/ARB use (%)	10 (20)	35 (16)	.479
Beta-Blocker use (%)	13 (26.5)	70 (32.4)	.423
Statin use (%)	18 (36.7)	78 (36.1)	.935
Inotrope use (%)	10 (20.4)	28 (12.7)	.179
Operative Characteristics			
Pump time (minutes)	96.87 ± 4.25	90.10 ± 5.25	.092
Aortic cross-clamp time (minutes)	55.81 ± 3.18	48.25 ± 5.47	.001
Number of grafts used			.163
LIMA	5 (10)	35 (16)	
2 vessel	9 (18)	21 (9.7)	
≥ 3 vessel	35 (71)	160 (74)	

ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; LDL, low-density lipoprotein; LIMA, left internal mammary artery; LVDD, left ventricular end-diastolic diameter, LVEF, left ventricular ejection fraction; LVSD, left ventricular end-systolic diameter, NPOAF, postoperative atrial fibrillation.

96% confidence interval. The baseline demographic and clinical characteristics of the study subjects are shown in Table 2.

When the demographic, clinical, and echocardiographic data of the groups are evaluated, the number of patients with hypertension ($P = .893$), male sex ($P = .255$), and the BMI ($P = .827$), preoperative left ventricular ejection fraction

($P = .056$) values were observed to be the same between 2 groups. Also, no difference was observed in terms of the ACE-i/ARB, beta-blocker, and statin use between the patients in which sinus rhythm was maintained, and in which the POAF developed ($P = .479$, $P = .423$, $P = .935$, respectively). In the group where AF was observed to develop, the HARMS₂-AF score was higher than those where normal sinus rhythm was maintained (6.02 ± 1.76 vs 3.48 ± 2.54 , $P < .001$).

The univariate logistic regression analysis showed that pre-operative left ventricular ejection fraction (LVEF), left atrium diameter (LAd), aortic cross-clamp time, and HARMS₂-AF scores were associated with postoperative AF. In the multivariate logistic regression analysis carried out after the formation of the model based on the parameters related to AF development, the relationship with HARMS₂-AF score, LAd, and aortic cross-clamp time were observed to be prevalent (OR = 1.261, 95% CI = 1.174-1.554 $P < .001$; OR = 3.703, 95% CI = 2.865-7.104 $P = .003$; OR = 7.070, 95% CI = 5.688-9.466 $P = .021$) (Table 3).

As analyzed by the ROC curve, a HARMS₂-AF score ≥ 4.5 predicted postoperative AF with 91% sensitivity and 64% specificity (AUC = 0.787, 95% CI = 0.731-0.842, $P < .001$) (Figure 1).

DISCUSSION

The results of the present study showed that a higher HARMS₂-AF score was significantly associated with an increased risk of developing postoperative atrial fibrillation. Previously, several risk factors, including advanced age, sex, diabetes mellitus, heart failure, and left atrial enlargement, were demonstrated independently in predicting POAF.^{6,7} Postoperative atrial fibrillation has been thought to be temporary and self-limited without any clinical significance, but previous studies have reported an association with several adverse outcomes, including increased duration of hospitalization, risk of stroke, in-hospital and long-term mortality.^{8,9}

HARMS₂-AF risk score is the first atrial fibrillation (AF) risk score which takes the relative contribution of lifestyle factors to AF development into consideration. The primary purpose of this AF score is to help physicians determine at-risk patients and potentially establish management of AF symptom burden, disease progression, as well as complications. This score includes 4 categorical (hypertension, male sex, sleep apnea, smoking) and 3 continuous (age, body mass index, alcohol consumption).¹⁰ Lu et al¹¹ showed that regular smoking was associated with an increased risk of AF independent of the age at initiation or the number of cigarettes smoked per day. They also showed that heavy alcohol intake was linked to an increased risk of AF. Wang et al¹² demonstrated that the prevalence of AF was significantly common in older patients with obstructive sleep apnea (OSA). The prevalence of AF was 9.5% and tended to further increase with OSA severity. In fact, multiple risk factors are common to OSA and AF. Obesity, advanced age, male gender, alcohol use, and smoking are important etiological components of OSA.¹³ In addition, a strong link between obesity and the risk of developing POAF has been demonstrated previously.¹⁴ Also concurrent with the literature, men develop postoperative atrial fibrillation at higher rates than do women.¹⁵

Table 3. Univariate and Multivariate Logistic Regression Analyses of Independent Variables for Postoperative Atrial Fibrillation

Variables	Univariate			Multivariate		
	Odds Ratio	95% CI	P	Odds Ratio	95% CI	P
HARMS ₂ -AF score	1.086	1.043-1.322	<.001	1.261	1.174-1.557	<.001
Preoperative EF	0.896	0.823-1.021	.043	0.695	0.494-1.313	.16
LAd	1.073	0.985-1.337	.001	3.703	2.865-7.104	.003
Aortic cross-clamp time	1.218	1.132-1.673	.001	7.070	5.688-9.466	.021

CI, confidence interval; LAd, left atrium diameter; EF, ejection fraction.

As POAF is associated with poor clinical outcomes, risk models are needed to guide POAF risk stratification in cardiac surgery patients. Existing clinical risk scores, such as EUROSCOREII, Society of Thoracic Surgeons, EUROSCORE, CHADS₂, POAF score, HATCH, CHADS₂VASC, and SYNTAX scores, offer at best moderate prediction for AF after cardiac surgery.¹⁶⁻²⁰

HARMS₂-AF risk score could be a better model for risk stratification as it includes individual lifestyle risk factors to AF development that have previously been shown to be important. In our study, we revealed that age, left atrium diameter, sleep apnea, and HARMS₂-AF score 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 POAF, HARMS₂-AF score was the optimal and accessible variable in predicting AF after CABG, as assessed by multivariate logistic regression analysis. Also in our study, the cutoff value for HARMS₂-AF score was ≥ 4.5 , indicating a sensitivity of 91% and specificity of 64%.

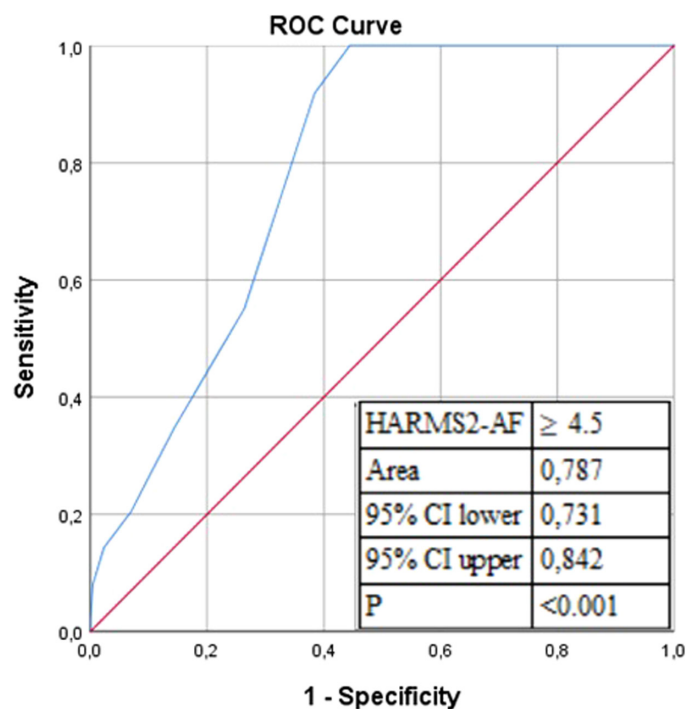


Figure 1. Receiver operating characteristic curve analysis of HARMS₂-AF score in predicting postoperative atrial fibrillation in coronary artery bypass surgery.

Several organizations have produced guidelines for prophylaxis against POAF.²¹⁻²³ However, routine prophylaxis may expose up to 70% of cardiac surgery patients to antiarrhythmic drugs and their subsequent side effects.^{24,25} In a recent study, authors reported that HARMS₂-AF score ≥ 5 was associated with a more than ninefold increased AF risk and should trigger aggressive risk factor management.⁵ HARMS₂-AF score could be used to identify patients at the highest risk of developing POAF, thus avoiding nonselective prophylaxis.

Our study has several limitations. The major limitation is its retrospective design. Second, our study findings are limited to *de-novo* postoperative atrial fibrillation 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. Also, we do not compare the HARMS₂-AF score with other risk scores.

CONCLUSION

In conclusion, identifying high-risk patients for POAF may prevent adverse cardiovascular events. Based on our study findings, the HARMS₂-AF score is a strong predictor of atrial fibrillation development after isolated CABG. We believe that our study may inspire further studies using the HARMS₂-AF scoring system to provide prophylactic atrial fibrillation therapies to high-risk patients preoperatively.

Ethics Committee Approval: Alaaddin Keykubat University Ethics Committee decision number and decision date: 10354421-2023/16-02.

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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