New Combined Risk Score to Predict Atrial Fibrillation after Cardiac Surgery: COM-AF

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ABSTRACT

Background and Aims: Atrial fibrillation frequently occurs in the postoperative period of cardiac surgery, associated with an increase in morbidity and mortality. The scores POAF, CHA2DS2-VASc and HATCH demonstrated a validated ability to predict atrial fibrillation after cardiac surgery (AFCS). The objective is to develop and validate a risk score to predict AFCS from the combination of the variables with highest predictive value of POAF, CHA2DS2-VASc and HATCH models.

Methods: We conducted a single-center cohort study, performing a retrospective analysis of prospectively collected data. The study included consecutive patients undergoing cardiac surgery in 2010-2016. The primary outcome was the development of new-onset AFCS. The variables of the POAF, CHA2DS2-VASc and HATCH scores were evaluated in a multivariate regression model to determine the predictive impact. Those variables that were independently associated with AFCS were included in the final model.

Results: A total of 3113 patients underwent cardiac surgery, of which 21% presented AFCS. The variables included in the new score COM-AF were: age (75: 2 points, 65-74: 1 point), heart failure (2 points), female sex (1 point), hypertension (1 point), diabetes (1 point), previous stroke (2 points). For the prediction of AFCS, COM-AF presented an AUC of 0.78 (95% CI 0.76-0.80), the rest of the scores presented lower discrimination ability ($P < 0.001$): CHA2DS2-VASc AUC 0.76 (95% CI 0.74-0.78), POAF 0.71 (95% CI 0.69-0.73) and HATCH 0.70 (95% CI: 0, 67-0.72). Multivariable analysis demonstrated that COM-AF score was an independent predictor of AFCS: OR 1,91 (IC 95% 1,63-2,23).

Conclusion: From the combination of variables with higher predictive value included in the POAF, CHA2DS2-VASc, and HATCH scores, a new risk model system called COM-AF was created to predict AFCS, presenting a greater predictive ability than the original ones. Being necessary future prospective validations.

Keywords: Atrial fibrillation, cardiac arrhythmia, cardiac surgical procedures, thoracic surgery

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INTRODUCTION

Atrial fibrillation (AF) is the most common sustained arrhythmia and one of the most frequent complications after cardiac surgery.[1,2] The incidence varies with the type of cardiac surgery: it is common after coronary artery bypass graft surgery (CABG) (16-40%) and more frequent after combined CABG/valvar surgery (36-63%).[3]

While atrial fibrillation after cardiac surgery (AFCS) may have been considered a transient and predominantly benign complication once, its associations with increased morbidity

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such as postoperative stroke, sternal and respiratory tract infections, and gastrointestinal and renal dysfunction, as well as an increased short- and long-term mortality are now well established.[3-6] It has also been associated with an increased length of hospital stay which leads to greater economic costs.[7]

In order to avoid these outcomes, several prophylactic methods have been studied with the aim of preventing AFCS, but some of them failed to prove net clinical benefit because of the potential complications when used routinely.[8] Therefore, the constant effort to find a suitable method to predict AFCS lies in the need of limiting prophylaxis to high-risk patients, so as to minimize the global burden of complications associated with these therapies.[9] A method that could accurately identify patients at high risk would enable targeted preventive/therapeutic interventions without exposing the overall population to the risk of antiarrhythmic toxicity or the added drug costs.[10]

Currently, there is no widely accepted risk model for predicting AFCS. Several models were created and validated to predict new-onset AF after cardiac surgery,[11-16] such as the POAF[17] and HATCH score.[18] Moreover, the CHA2DS2-VASC score,[19] originally created to predict the risk of thromboembolism in patients with AF, was both prospectively and retrospectively validated for the prediction of AFCS.[20-22] We have previously compared these three models in a cohort study of postoperative cardiac patients, demonstrating that the three scoring systems have good discrimination and calibration to predict AFCS.[23]

We aimed to develop and validate a risk score for the prediction of new-onset atrial fibrillation after cardiac surgery, from the combination of the variables with highest predictive value of POAF, CHA2DS2-VASc and HATCH risk scores.

METHODS

A single-center cohort study was conducted. We performed a retrospective analysis of prospectively collected data. The study included consecutive patients undergoing cardiac surgery between 2010 and 2016. We excluded patients with previous AF or other atrial arrhythmias.

As a primary outcome, we analyzed the development of new onset postoperative AF during the index hospitalization.

We defined AFCS as it was defined in previous studies: documented AF episode lasting >30 seconds recorded either by continuous telemetry throughout hospitalization or on a twelve-lead electrocardiogram performed daily and when the patient referred symptoms. All patients had continuous telemetry monitoring at least during the first 48 hours by an off-site central monitor unit, and once identified, every arrhythmic event was confirmed by a cardiologist.

The variables of the POAF, CHA2DS2-VASc and HATCH scores were evaluated in a multivariate regression model to determine the predictive impact. Those variables that were independently associated with AFCS were included in the final model. The new combined model was called COM-AF.

Risk scoring systems

We calculated the scores retrospectively:

- CHA2DS2-VASc score: history of heart failure (HF): 1 point; hypertension (HT): 1 point, age ≥75: 2 points, 65-74 years: 1 point; diabetes: 1 point; female sex: 1 point; stroke/transient ischemic attack (TIA): 2 points; peripheral vascular disease: 1 point[19,20]
- POAF score: chronic obstructive pulmonary disease (COPD): 1 point; preoperative intra-aortic balloon pump (IABP): 1 point; age: 60-69 years: 1 point; 70-79 years: 2, ≥80 years: 3; emergency surgery: 1 point; glomerular filtration rate <15 ml/min/1.73 m2 o dialysis: 1 point; left ventricular ejection fraction (LVEF) <30%: 1 point; any heart valve surgery: 1 point[17]
- HATCH score: stroke or TIA: 2 points; hypertension 1 point; heart failure: 2 points; age ≥75 years: 1 point; COPD: 1 point.[18]

Statistical analysis

Quantitative data were expressed as mean ± SD and compared with 2-sample t tests for independent samples, whereas dichotomous variables were reported as absolute values and proportions. Differences in proportion were compared using a x2 test or Fisher's exact test, as appropriate. Ordinal data and continuous variables inconsistent with normal distribution were expressed as median and interquartile range (IQR), and were compared with the U Mann-Whitney test. Variables significantly associated with AFCS after univariate analysis (A *P* value of <0.05) were entered in a multivariable logistic regression model with backward elimination to identify the independent predictors of AFCS, and each variable score was inserted in different time. The final model variables were presented as odds ratios (ORs) along with the 95% confidence intervals (CIs).

The Youden index[24] was used to establish the best cut-off point for the new score. We compared ROC curves with the method of DeLong *et al.*[25]

Calibration was assessed using the Hosmer-Lemeshow (HL) goodness-of-fit test, which evaluates the difference between the real rate observed and the rate predicted by the model in different risk groups, a P value >0.05 indicates that the model is best fit for the data thus predicting the probability of developing AFCS. We calculated the area under the curve ROC (AUC-ROC) curve to assess the predictive value the scores. A power analysis was performed using the dichotomous outcome variable of AFCS. For group comparisons, $\alpha = 0.05$, a prevalence of 0.20, and a sample size of 3113, the statistical power is 100%.

Ethical considerations

Committee on Ethics and Research approval was obtained with waiver of consent for retrospective review of previously collected de-identified data.

RESULTS

In the analyzed period, 3113 patients were included. The baseline characteristics of the population are described in Table 1. The surgeries performed were: 45% coronary artery bypass grafts (CABG), 24% valve replacements, 15% combined procedures (revascularization-valve surgery) and 16% other cardiovascular procedures. Cardiopulmonary bypass (CPB) was used in 52.9% of the procedures and in 2,2% of the CABG surgeries.

Twenty-one percent (n = 654) presented AFCS. Patients with atrial fibrillation were more comorbid and significantly older (71,5 ± 8,7 vs. 64,7 ± 12,4 years), with higher additive EuroSCORE 7 vs. 4 (P < 0.001). The presence of comorbidities such as hypertension, COPD, stroke/AIT, diabetes left ventricular dysfunction and heart failure was also more frequent in the AFCS group. We did not find differences in the preoperative use of beta blockers (P = 0,063).

Postoperative evolution was more torpid in the group with AF, with longer hospital stay (median 10 days vs. 6 days, P < 0.001), most frequent use of inotropic drugs (10.6% vs. 5.5%, P < 0.001) and higher in-hospital mortality (9% vs. 3.7%, P < 0.001) in the patients with AFCS.

The variables that presented an independent association with the occurrence of new onset AFCS were included in the new risk score COM-AF: age (≥75: 2 points, 65-74: 1 point), heart failure (2 points), female sex (1 point), hypertension (1 point), diabetes (1 point), previous stroke (2 points) [Table 2]. The HATCH score variables: COPD, CHA2DS2-VASc score variables: history of vascular disease, and the POAF score: COPD, chronic kidney disease, emergency surgery, use of preoperative intra-aortic balloon pump, valve surgery, and LVEF <30% did not

Table 1: Baseline characteristics of study participants with and without atrial fibrillation after cardiac surgery

	With AFCS (n=654)	Without AFCS (n=2459)	P
Age[1] (mean±SD)	71.5 (± 8.7)	64.7 (± 12.4)	<0.001
Male sex (%)	449 (68%)	1892 (77%)	<0.001
BMI (median. IQR 25-75)	27 (24-30)	27 (25-30)	0.1
Aditive EuroSCORE (median. IQR 25-75)	7 (5-8)	4 (2-6)	<0.001
Current smoker and former smoker (%)	322 (49%)	1356 (55%)	0.007
Diabetes (%)	201 (30.7%)	507 (20.6%)	0.001
HT (%)	492 (75.2%)	1742 (70.8%)	0.02
CKF (CRCL<15) (%)	10 (1.5%)	23 (0.9%)	0.1
Stroke/TIA (%)	50 (7.6%)	83 (3.4%)	0.001
Peripheral vascular disease	220 (33%)	819 (33%)	0.8
COPD (%)	58 (9%)	128 (5.2%)	<0.001
LVEF<30 (%)	44 (6.7%)	72 (2.9%)	<0.001
HF (%)	99 (15.1%)	174 (7.1%)	<0.001
Pre-operative IABP (%)	15 (2.3%)	36 (1.5%)	0.1
Urgent surgery (%)	210 (32%)	715 (29%)	0.1
Type of surgery			<0.001
CABG (%)	205 (31.3%)	1204 (49%)	
Valve surgery (%)	224 (30.1%)	519 (21.1%)	
CABG + valve surgery (%)	137 (20.9%)	340 (13.8%)	
Other (%)	88 (13.5%)	396 (15.9%)	
Inotropic agents (%)	69 (10.6%)	133 (5.5%)	<0.001
CPB (%)	427 (65%)	1221 (49%)	<0.001
CPB time[2] (median. IQR 25-75)	94 (71-123)	97 (67-129)	0.4
Hospital stay[3] (median. IQR 25-75)	10 (6-16)	6 (5-10)	<0.001

BMI: Body mass index. HT: Hypertension. PVD: Peripheral vascular disease. CKF: Chronic kidney failure. COPD: Chronic obstructive pulmonary disease. LVEF: Left ventricular ejection fraction. HF: Heart failure IABP: Intraaortic balloon pump. CPB: Cardiopulmonary bypass. 1: Years. 2: Minutes. 3: Days present an independent association when other variables were taken into account in the multivariate model.

The AUC-ROC for the new combined risk model COM-AF was 0.78 (95% CI 0.76-0.80) [Figure 1], the rest of the scores presented lower discrimination ability: CHA2DS2-VASc AUC 0.76 (95% CI 0.74-0.78), $P = 0{,}0019$; POAF 0.71 (95% CI 0.69-0.73), $P < 0{,}0001$ and HATCH 0.70 (95% CI: 0, 67-0.72), $P < 0{,}0001$ [Table 3].

The best cut-off point to predict postoperative AF with the new score was >2, with a sensitivity of 82% (CI 95% 78-85%) and a specificity of 65.9% (64-68%), presenting a high negative predictive value: 92.9% (CI% 91-94%). The test showed good calibration (HL test $P = 0.21$) [Table 4 and Figure 2].

In the univariate analysis, the variables summarized in Table 1 presented a significant association with the occurrence of the primary outcome. Those variables were: age, female sex, use of CPB, diabetes, stroke/AIT, COPD, smoking habit, hypertension, left ventricular dysfunction, type of surgery and use of inotropic drugs. At the multivariable analysis, the new combined model, CHA2DS2-VASc, POAF and HATCH scoring systems proved to be independent predictors of POAF ($P < 0.05$), but the highest OR was achieved by the new combination score: 1.91 as the score was one point higher (95% CI, 1.63-2.23, $P < 0.001$) [Table 5].

DISCUSSION

This large cohort study demonstrates the ability of a new clinical model created from variables with highest predictive value of the CHA2DS2-VASc, HATCH and POAF scoring systems to predict the development of AF after cardiac surgery, proving good performance in terms of discrimination and calibration, with a high negative predictive value.

The benefit of this scoring system lies on the inclusion of simple preoperative variables that would predict AFCS appropriately from the moment the patient is admitted to the hospital in order to take preventive measures such as drug therapy or atrial pacing according to the risk.[6]

Our final predictive model includes four simple variables from CHA2DS2-VASc score: age, female sex, hypertension, and stroke/AIT, and heart failure, a variable taken from HATCH which sums an additional point. The variables like vascular disease from CHA2DS2-VASc score, COPD from HATCH score, glomerular filtration rate <15 ml/min/1.73 m2 or dialysis requirement, emergency surgery, preoperative intra-aortic balloon pump, left ventricular ejection fraction <30% and any heart valve surgery from

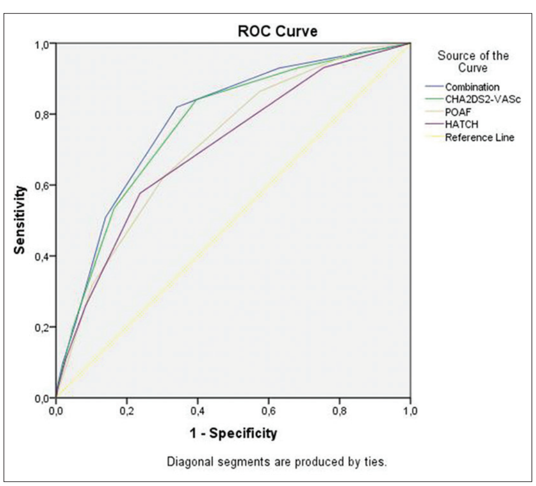

Figure 1: Area under the ROC curve for COM-AF. CHA2DS2-VASc. POAF and HATCH scores

Table 2: New combined risk model - COM-AF

Variable	OR (CI 95%)	*P*
Age		
65-74 years	3.14 (2.29-4.31)	<0.001
≥75 years	8.68 (6.32-11.93)	<0.001
Female sex	3.36 (2.68-4.22)	<0.001
Heart failure	2.45 (1.82-3.31)	<0.001
Stroke/TIA	2.33 (1.45-3.76)	<0.001
Arterial hypertension	1.68 (1.28-2.2)	<0.001
Diabetes	1.72 (1.31-2.25)	<0.001

TIA: Transient ischemic attack

Table 3: Area under the ROC curve and its 95% confidence interval for the COM-AF. CHA2DS2-VASc. POAF and HATCH scores

Risk moder	AUC ROC	Std. error	95% confidence interval	
			Lower bound	Upper bound
COM-AF	0.78	0.010	0.761	0.800
CHA2DS2-VASc	0.76	0.010	0.747	0.787
POAF	0.71	0.011	0.694	0.736
HATCH	0.70	0.012	0.680	0.726

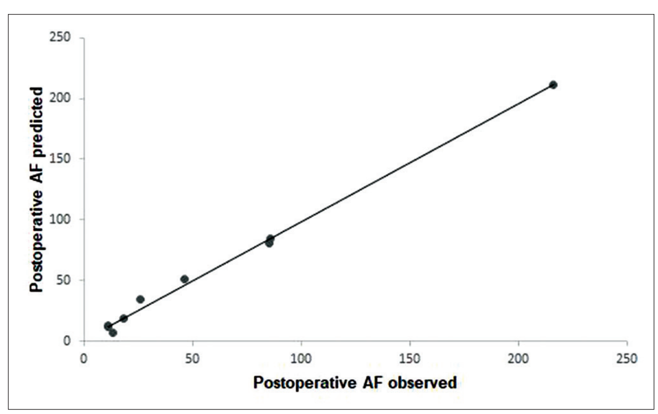

Figure 2: Calibration plot for COM-AF score

Table 4: Contingency table for Hosmer Lemeshow test for COM-AF score

Deciles	Atrial fibrillation after cardiac surgery			
	No		Yes	
	Observed	Expected	Observed	Expected
1	238	244.1	13	6.8
2	273	271.1	11	12.8
3	228	227.3	18	18.6
4	118	117.4	11	11.6
5	241	232.4	26	34.5
6	236	231.1	46	50.8
7	227	228.2	86	84.7
8	138	141.9	85	81
9	154	159	216	210.9
Total	1853	1853	512	512

Table 5: Multivariable analysis to predict AFCS for each score

	Multivariable analysis		
	OR	95% CI	*P*
COM-AF score	1.91	1.63-2.23	<0.001
CHA2DS2-VASc score	1.87	1.64-2.13	<0.001
POAF score	1.18	1.018-1.36	0.04
HATCH score	1.62	1.37-1.92	<0.001

1 By one score point

POAF score were excluded as they were not independent predictors of AFCS at the multivariable analysis.

The POAF score was the only scoring system that was created and validated to predict postoperative AF in patients undergoing CABG or valve surgery using 7 variables identified in a multivariable analysis The discriminative ability of the score was moderate, with an AUC-ROC of 0.66 in the original cohort and of 0.65 in the validation cohort.[17]

The HATCH score was developed by De Vos *et al.*[18] to predict atrial fibrillation progression from paroxysmal to persistent, and includes simple clinical parameters that can be easily calculated. Each variable of the HATCH score is associated with long-term left atrial enlargement, which could be important for the development of postoperative AF. Emren *et al.*[26] evaluated the discriminative ability of the HATCH score in patients undergoing CABG surgery compared with the CHA2DS2-VASc score to predict AFCS. Unlike our findings, the HATCH score presented a higher predictive ability with an AUC-ROC of 0.77 versus 0.71 for the CHA2DS2 -VASc score. However, a more recent study aimed to investigate the association between HATCH score and AFCS after isolated CABG, showing that the HATCH score was an independent predictor of AF after CABG surgery (OR 1.334; 95% CI 1.022 to 1.741, $P = 0.034$), but with a poor discriminative ability to predict AFCS with an AUC-ROC of 0.57.[27]

Several retrospective studies have demonstrated the independent association between the CHA2DS2-VASc score and the incidence of postoperative AF, proving a different discriminative ability. In a prospective study, Chua *et al.*[20] analyzed 277 patients undergoing CABG or valve surgery, and proved an AUC-ROC of 0.87, higher than the one in our study. Kashani *et al.*[21] conducted a retrospective evaluation of 2385 patients who underwent CABG or valve surgery. The multiple regression analysis showed that high-risk patients (score ≥2) had a greater probability of developing postoperative AF as compared with the low-risk group (OR 5.21; $P < 0.0001$), with an AUC-ROC of 0,65. Finally, Yin L *et al.*[22] evaluated this score system only in cardiac valve surgery, demonstrating that CHA2DS2-VASc score was a significant predictor of AFCS and showed a similar a AUC-ROC that the one in our study (0.765, 95%CI, 0.723-0.807).

A prospective study compared the predictive ability of the POAF score, the CHA2DS2-VASc and the Atrial Fibrillation Risk Index in patients undergoing elective CABG surgery or valve surgery. The incidence of AFCS was remarkably higher (34%), with a limited discrimination for the 3 scoring systems, with AUC-ROC of 0.651 (95% confidence interval [CI], 0.621-0.681) for the POAF score, 0.593 (95% CI, 0.557-0.629) for the CHA2DS2-VASc score.[15] Recently, Waldron *et al.* also compared the predictive ability of perioperative atrial fibrillation risk scores in cardiac surgery patients, finding limited ability to predict AFCS as well, with AUCROC of 0.58 and 0.66 for CHA2DS2-Vasc and POAF scores, respectively.[14]

This study has some limitations. First of all its retrospective and observational design entails its own biases. To remediate this, data was collected prospectively. Second, as it was conducted in a single high-complexity cardiovascular center, the sample may not be representative of the reality of other centers. Third, the fashioned prediction model was not externally validated, thus lacking generalizability. Fourth, not all patients had the same amount of time of continuous telemetry. Therefore, asymptomatic or transient episodes of atrial fibrillation could have been underdiagnosed after the first 48 h after surgery.

Future prospective research is necessary to determine the generalizability of our risk model in larger populations and should not only focus on developing better predictive models, but also on identifying effective strategies for AFCS prophylaxis.

CONCLUSION

From the combination of variables with higher predictive value included in the POAF, CHA2DS2-VASc, and

HATCH scores, a new risk system called COM-AF was created in a large cohort to predict atrial fibrillation after cardiac surgery, presenting a greater predictive ability than the original ones. Future prospective validations are necessary to broaden its use.

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Conflicts of interest

There are no conflicts of interest.

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