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A prediction model for new-onset atrial fibrillation following coronary artery bypass graft surgery: A multicenter retrospective study

Ren-Jian-Zhi Zhang^a, Xin-Yi Yu^a, Jing Wang^b, Jian Lv^c, Yan Zheng^d, Ming-Huan Yu^a, Yi-Rui Zang^a, Jian-Wei Shi^a, Jia-Hui Wang^a, Li Wang^b, Zhi-Gang Liu a^*

^a *Department of Cardiovascular Surgery, TEDA International Cardiovascular Hospital, Chinese Academy of Medical Sciences & Graduate School of Peking Union Medical College, Tianjin, 300457, China*

^b *Department of Cardiovascular Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, 6913114, China*

^c *Department of Cardiovascular Surgery, Nanyang Central Hospital, Nanyang, 473005, China*

^d *First School of Clinical Medicine, Lanzhou University, Lanzhou, 730013, China*

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ABSTRACT

Objective: Developing and assessing a risk prediction model of postoperative atrial fibrillation (POAF) after coronary artery bypass grafting (CABG), and aims to provide a reference for the prediction and prevention. *Design:* A retrospective case-control study. *Setting:* Three major urban teaching and university hospitals and tertiary referral centers. *Participants:* consecutive patients undergoing CABG. *Interventions:* The study was retrospective and no interventions were administered to patients. *Measurements and main results:* In the study, the overall new-onset POAF prevalence was approximately 28%. A prediction model for POAF with nine significant indicators was developed, and identified new predictors of POAF: left ventricular end diastolic diameter (LVEDD), intraoperative defibrillation, and intraoperative temporary pacing lead implantation. The model had good discrimination in both the derivation and validation cohorts, with the area under the receiver operating characteristic curves (AUCs) of 0.621 (95% CI = $0.602-0.640$) and 0.616 (95% $CI = 0.579-0.651$, respectively, and showed good calibration. Compared with CHA_2DS_2 -VASc, HATCH score, and the prediction model of POAF after CABG developed based on a small sample of clinical data from a single center in China, the model in this study had better discrimination. *Conclusion:* We have developed and validated a new prediction model of POAF after CABG using multicenter data that can be used in the clinic for early identification of high-risk patients of POAF, and to help effectively prevent POAF in postoperative patients.

1. Introduction

Atrial fibrillation (AF) is one of the common complications after coronary artery bypass grafting (CABG), with an incidence of about

Corresponding author. *E-mail address:* liuzgtich@126.com (Z.-G. Liu).

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21%–33%, and the onset is usually 2–3 days after surgery [\[1](#page-11-0)–5] . Postoperative AF (POAF) after CABG affects the patient's cardiac function, which in severe cases can lead to risks such as hemodynamic impairment, cerebrovascular accident, acute limb ischemia, renal failure, ventricular arrhythmias [[6,7\]](#page-11-0), which in turn affects the patient's postoperative recovery, resulting in a longer intensive care unit (ICU) stays, longer hospital stays, increased medical costs, intra-aortic balloon pump (IABP) assistance requirements, and even death [\[4,](#page-11-0)8–[10\]](#page-11-0). Therefore, the prediction and prevention of POAF after CABG is particularly important.

In a cost-effectiveness study of intravenous amiodarone for the prevention of POAF in patients undergoing cardiac surgery, Mahoney et al. suggested that the cost-effectiveness of prophylactic intravenous amiodarone varied according to the predicted risk of AF [[11\]](#page-11-0). Therefore, for patients at high risk of POAF, early identification and targeted use of pharmacological or non-pharmacological interventions to prevent POAF are expected to shorten hospital stays, reduce hospital costs, and reduce the incidence of cerebrovascular accidents [\[12](#page-11-0)]. In patients at low risk for POAF, early identification may prevent antiarrhythmic drug abuse and increased hospitalization costs. At present, there is still no effective prediction method for CABG patients with preoperative sinus rhythm in China. Although there are various prediction models for POAF after CABG [\[3,4](#page-11-0),13–[15\]](#page-11-0), the predictive value of POAF in the Chinese CABG population, especially the predictive value of new-onset POAF, remains to be studied.

In summary, this study aimed to establish and validate a reliable and accurate risk prediction model by analyzing clinical data from three medical centers of different sizes in China, and to present the model visualized to improve the practical usability of the prediction model and provide clues for early identification of patients at high risk of POAF after CABG, to provide timely individualized preventive guidance for perioperative clinical management strategies.

2. Methods

2.1. Study population

Derivation cohort data were from consecutive patients undergoing CABG at TEDA International Cardiovascular Hospital from June 2020 to December 2021; Validation cohort data were from consecutive patients undergoing CABG at the First Affiliated Hospital of Zhengzhou University from January 2021 to December 2021, and consecutive patients undergoing CABG at Nanyang Central Hospital from January 2020 to December 2021. All data from national triple A, first-class medical center in China with extensive experience in CABG. And all operations are performed by cardiac surgeons with more than 10 years of experience in CABG.

The inclusion criteria were as follows: (1) patients with no previous history of cardiac surgery who were admitted for the first time and underwent CABG; (2) bypass vascular material was internal mammary artery, radial artery, and/or great saphenous vein; (3) Preoperative admission routine ECG was sinus rhythm and no antiarrhythmic drugs (except β-blockers) were used before undergoing CABG. The exclusion criteria were as follows: (1) patients with preoperative combined aortic coarctation; (2) patients with small incision, thoracoscopic or robotic-assisted CABG; (3) patients with permanent cardiac pacemaker implantation. (4) previous history of atrial fibrillation (5) Perioperative prophylactic use of amiodarone. (i.e., preoperative, intraoperative or postoperative prophylactic use of amiodarone).

2.2. Potential risk factors

Based on the analysis of previous studies and expert consensus, and based on the principle of easy clinical access and refinement, the following potential risk factors were selected for inclusion in this study.

- (1) Preoperative characteristics: gender, age, body mass index (BMI), smoking history, history of diabetes mellitus, history of hypertension (Class 1: systolic blood pressure 140–159 mmHg or diastolic blood pressure 90–99 mmHg; Class 2: systolic blood pressure 160–179 mmHg or diastolic blood pressure 100–109 mmHg; Class 3: systolic blood pressure ≥180 mmHg or diastolic blood pressure ≥110 mmHg), history of percutaneous coronary intervention (PCI) treatment.
- (2) Preoperative medication status: beta-blockers, statins, angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB).
- (3) Preoperative examination and laboratory indicators: last preoperative arterial blood gas (including partial pressure of oxygen, partial pressure of carbon dioxide, pH, lactate); last preoperative routine blood count/blood biochemistry (including white blood cell count, red blood cell count, neutrophil to lymphocyte ratio (NLR), hemoglobin, platelet count, albumin-to-globulin ratio (A/G), low-density lipoprotein to high-density lipoprotein ratio (LDL/HDL), aspartate aminotransferase to alanine aminotransferase ratio (AST/ALT), creatinine, glucose); Coronary angiography and cardiac ultrasound (including left main coronary artery condition of lesion, left ventricular ejection fraction (LVEF), condition of ventricular aneurysm, left ventricular end-diastolic diameter (LVEDD), left atrial diameter (LAD))
- (4) Intraoperative conditions: whether cardiopulmonary bypass (CPB), duration of CPB, intraoperative defibrillation, and temporary pacing lead implantation.
- (5) Postoperative care: The fluid balance in the first 24 h after surgery (the first 24 h after the patient leaves the OR), i.e. the actual net 24-h balance, is the difference between the total 24-h in and total 24-h out volume.

2.3. Definition of new-onset POAF

New-onset AF after CABG was the outcome variable of the prediction model, defined as paroxysmal and permanent AF excluded by

Table 1

Intergroup comparison between the postoperative new-onset AF group and the normal group in the derivation cohort.

Values are mean \pm SD, n (%), or median (interquartile range). BMI^(a): body mass index; PCI^(b): percutaneous coronary intervention; ACEI^(c): angiotensin-converting enzyme inhibitor; ARB^(d): angiotensin receptor blocker; NLR^(e): neutrophil to lymphocyte ratio; A/G^(f): albumin/globulin; $LDL^{(g)}$: low-density lipoprotein; HDL^(h); high-density lipoprotein; AST⁽ⁱ⁾; aspartate aminotransferase; ALT^(j); alanine aminotransferase; LVEF^(k); left ventricular ejection fraction; LVEDD⁽⁰⁾: left ventricular end-diastolic diameter; LAD^(m): left atrial diameter; CPB⁽ⁿ⁾: cardiopulmonary bypass.

both preoperative clinical diagnosis and ECG, and the disappearance of p waves indicated by ECG monitoring or ECG after surgery, replaced by f waves of variable size and the duration of the episode was more than 10 min.

2.4. Ethics and study quality control

The Ethics Review Committee of TEDA International Cardiovascular Hospital approved the study and exempted informed consent. The study followed the TRIPOD guidelines and completed all the items in the guidelines. The study uses Epidata 3.1 for all data entry, and after completing the data entry, a comprehensive systematic review is performed and the original data is carefully checked.

2.5. Statistical methods

Data were analyzed by SPSS (ver 26.0, USA) and R software (ver 4.0.5, USA). Continuous variables that did not conform to a normal distribution were expressed as median and interquartile spacing, and the Mann-Whitney *U* test was used for comparison between groups. Continuous variables that conformed to a normal distribution were expressed as mean \pm standard deviation, and two independent samples *t*-test was used for comparison between groups. The χ^2 test was used for categorical variables, which were statistically described as percentages or frequencies (%). The Box-Tidwell method was used to test the existence of a linear relationship between

Table 2

univariate and multivariate logistic regression analysis.

Variables	Univariate Logistic				Multivariate Logistic				
	$OR^{(a)}$	95%CI of OR		\boldsymbol{P}	β	OR	95%CI of OR		\overline{P}
		Lower	Upper				Lower	Upper	
gender	1.05	0.87	1.27	0.591					
age	1.03	1.02	1.04	0.000	0.034	1.03	1.02	1.05	0.000
$BMI^{(b)}$	1.02	0.99	1.05	0.151	0.033	1.03	1.01	1.06	0.022
smoking history	1.25	1.05	1.49	0.013	0.306	1.36	1.13	1.63	0.001
diabetes	1.13	0.95	1.35	0.173					
hypertension	1.06	0.87	1.30	0.551					
PCI ^(c)	0.87	0.69	1.10	0.237					
β -blockers	1.07	0.87	1.31	0.549					
statins	0.95	0.68	1.34	0.773					
ACEI ^(d) /ARB ^(e)	1.24	1.04	1.49	0.019	0.250	1.29	1.07	1.55	0.008
PaO ₂	1.00	1.00	1.00	0.179					
PaCO ₂	1.02	1.00	1.04	0.134					
PH	0.85	0.04	18.40	0.920					
lactate	1.17	0.96	1.44	0.127					
white blood cell count	0.95	0.90	1.01	0.084					
red blood cell count	0.99	0.90	1.09	0.838					
$NLR^{(f)}$	0.97	0.91	1.03	0.343					
hemoglobin	1.00	1.00	1.01	0.100					
platelet count	1.00	1.00	1.00	0.159					
A/G ^(g)	1.05	0.78	1.41	0.754					
$LDL^{(h)}/HDL^{(i)}$	0.89	0.82	0.98	0.011	-0.102	0.90	0.83	0.99	0.024
AST ^(j) /ALT ^(k)	0.91	0.79	1.04	0.175					
creatinine	1.00	1.00	1.00	0.853					
glucose	0.98	0.94	1.03	0.436					
left main coronary artery lesion	1.15	0.95	1.40	0.159					
$LVEF^{(1)}$	1.01	1.00	1.02	0.005	0.014	1.01	1.00	1.02	0.006
ventricular aneurysm	1.73	1.14	2.62	0.010					
LVEDD ^(m)	1.03	1.02	1.05	0.000	0.024	1.02	1.01	1.04	0.004
LAD ⁽ⁿ⁾	1.01	1.00	1.02	0.211					
CPB ^(o)	0.98	0.81	1.18	0.820					
duration of CPB	1.00	1.00	1.00	0.307					
intraoperative defibrillation	1.20	1.00	1.42	0.051	0.187	1.21	1.01	1.44	0.040
temporary pacing lead implantation	1.61	1.29	2.00	0.000	0.398	1.49	1.18	1.88	0.001
actual 24 h net balance	1.10	0.91	1.32	0.321					

 $β$ is the regression coefficient, and the regression coefficient of "constant" in the multivariate logistic regression analysis is -6.015 . OR(a): odds ratio; BMI^(b): body mass index; PCI^(c): percutaneous coronary intervention; ACEI^(d): angiotensin-converting enzyme inhibitor; ARB^(e): angiotensin receptor blocker; NLR^(f): neutrophil to lymphocyte ratio; A/G^(g): albumin/globulin; LDL^(h): low-density lipoprotein; HDL⁽ⁱ⁾: high-density lipoprotein; AST^(j): aspartate aminotransferase; $ALT^{(k)}$: alanine aminotransferase; $LVEF^{(l)}$: left ventricular ejection fraction; $LVED^{(m)}$: left ventricular end-diastolic diameter; LAD⁽ⁿ⁾: left atrial diameter; CPB^(o): cardiopulmonary bypass.

continuous variables and logit transformed values of dependent variables. Continuous variables that did not conform to a linear relation were transformed into categorical variables according to the Youden index of the receiver operator characteristic curve (ROC) or clinically common cut-off value. Factors relevant to new-onset AF preoperatively, intraoperatively and postoperatively were analyzed by univariate logistic regression, with P *<* 0.2 as the screening criterion, and observed indicators that met the criteria and indicators with clear clinical significance were added to the multivariate logistic regression analysis. Forward stepwise regression analysis based on maximum likelihood estimation was used to select variables and construct a prediction model. The discrimination of the model is evaluated by the ROC curve and calculating the area under the curve (AUC). The calibration of the model was evaluated by the Hosmer-Lemeshow goodness-of-fit test.

3. Results

3.1. Comparison among groups

The study included a total of 3259 patients from three medical centers, including 2531 patients in the derivation cohort and 728 patients in the validation cohort. The incidence of new-onset AF after CABG was 28.45% and 28.98%, respectively ($P = 0.778$). The

Fig 1. a. ROC curve of the prediction model.

b. The calibration curve of the prediction model (the blue line is the calibration curve; the red line is the standard curve, which means that the prediction risk of the model is the same as the actual observed risk. The closer the calibration curve and the standard curve are, the better the calibration capability of the prediction model is).

comparison between the POAF group and the no-POAF group in the derivation cohort is shown in [Table 1.](#page-2-0) Patients in the POAF group had greater age, LVEDD, LAD, and LVEF than those in the no-POAF group (P *<* 0.05), and a higher proportion of patients in the POAF group had intraoperative temporary pacing leads implanted (P *<* 0.05).

3.2. Logistic regression analysis and prediction model development

In this study, 43 items were included in the linearity test, and the significance level should be $\alpha = 0.00116$ corrected by the Bonferroni method ($\frac{0.05}{43}$). According to this level of significance, the p-values of all interaction terms in this study are above 0.00116, so there is a linear relationship between all continuous independent variables and dependent logit transformation values. An univariate logistic regression analysis of potential risk factors for new-onset AF after CABG in the derivation cohort showed that age, BMI, smoking history, history of diabetes mellitus, use of ACEI/ARB, last preoperative arterial partial pressure of oxygen, partial pressure of carbon dioxide, lactate, white blood cell count, hemoglobin, platelet count, LDL/HDL, AST/ALT, presence of left main coronary artery lesion, LVEF, presence of ventricular aneurysm, LVEDD, intraoperative defibrillation, and intraoperative temporary pacing lead implantation may be statistically significant (P *<* 0.2) in association with new-onset AF after CABG ([Table 2\)](#page-3-0).

The above factors were included in a multivariate logistic regression analysis along with gender, and results showed that age, BMI, smoking history, use of ACEI/ARB, LDL/HDL, LVEF, LVEDD, intraoperative defibrillation, and intraoperative temporary pacing lead implantation were independent predictors of POAF ([Table 2\)](#page-3-0). The logistic regression model is as follows: Logit $(P) = -6.015 +$ 0*.*034 × age + 0*.*033 × BMI + 0*.*306(history of smoking) + 0*.*250(use of ACEI */*ARB)− 0*.*102 × LDL*/*HDL + 0*.*014 × LVEF + 0*.*024 × LVEDD + 0*.*187(intraoperative defibrillation) + 0*.*398(intraoperative temporary pacemaker lead implantation). P is the probability of newonset AF after CABG. The model was statistically significant ($\chi^2 = 91.886$, P = 0.000) and its percent correct classification (i.e., agreement rate in diagnostic tests) was 71.8%. ROC curve analysis showed that the area under the curve was 0.621 (95% CI = 0.602–0.640). The sensitivity and specificity at the optimal cut-point (i.e., at POAF probability *>*26.22%) were 73.3% (95% CI = 0.699–0.765) and 46.2% (95% CI = 0.438–0.485), respectively ([Fig. 1](#page-4-0)a). The Hosmer-Lemeshow goodness-of-fit test statistic was 11.448, $p = 0.178 > 0.05$, and the calibration curve is shown in [Fig. 1](#page-4-0)b. The nomogram of the model is shown in Fig. 2.

3.3. External validation

The validation cohort evaluated the model developed in the study in terms of both discrimination and calibration, and the results showed that the area under the ROC curve was 0.616 (95% CI = 0.579 to 0.651). The sensitivity and specificity at the optimal cut-point (i.e., POAF probability *>*24.87%) were 56.9% (95% CI = 0.499–0.637) and 63.3% (95% CI = 0.589–0.674) [\(Fig. 3](#page-6-0)a). The difference between the area under the ROC curve of the derivation cohort and the validation cohort is 0.005. The Z statistic of the Delong test was

Fig. 2. The prediction model is presented as nomogram (BMI: body mass index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; LDL: low-density lipoprotein; HDL: high-density lipoprotein; EF (LVEF): left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter).

0.187, $P = 0.852 > 0.05$, so the difference in AUC between the two cohorts was not statistically significant. The Hosmer-Lemeshow goodness-of-fit test statistic was 5.204, $p = 0.736 > 0.05$, and the calibration curve is shown in Fig. 3b.

3.4. Comparison of different models

The discrimination was assessed in the validation cohort on $CHA₂DS₂-VASC$ [[16\]](#page-11-0), HATCH score [[17\]](#page-11-0), and the prediction model developed based on a small sample of clinical data from a single center in China [\[18](#page-11-0)], and the results are shown in [Fig. 4.](#page-7-0)

3.5. Model visualization

Predictors in the prediction model are classified according to their clinical significance or common cut-off values. Based on logistic regression, appropriate values in each subgroup were selected as reference values to construct the scoring tool [\(Fig. 5](#page-7-0)).

4. Discussion

The majority of patients at TEDA are from northern China, while patients at the other two medical centers are mainly from the mid-China region, covering a large part of China, so the data could better represent the CABG population in China. The study population was derived from 3 medical centers of different sizes (with different annual surgical volumes) in China, and the data were patients consecutively receiving CABG alone in the last 2 years, with an overall incidence of new-onset POAF of about 28%, generally consistent with the results of previous studies [1-[4\]](#page-11-0) As one of the common complications after CABG, POAF is associated with several adverse

Fig 3. a. Discrimination assessment of external validation of prediction model.

b. Calibration assessment for external validation of prediction model (the blue line is the calibration curve; the red line is the standard curve, which means that the prediction risk of the model is the same as the actual observed risk. The closer the calibration curve and the standard curve are, the better the calibration capability of the prediction model is).

Fig. 4. Assessment of the discrimination of the validation group against other models (Model I is the HATCH score, AUC = 0.509, 95%*CI* = 0.472–0.646, *P* = 0.446; Model II is the prediction model developed by Li et al. AUC = 0.541, 95%*CI* = 0.504–0.577, *P* = 0.083; Model III is $CHA₂DS₂-VASC, AUC = 0.521, 95%CI = 0.484-0.558, P = 0.313.$

Fig. 5. Scoring Scale (BMI: body mass index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; LDL: low-density lipoprotein; HDL: high-density lipoprotein; EF (LVEF): left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter).

complications and affects the patient's postoperative recovery, even leading to death [6–[10\]](#page-11-0). Therefore, effective identification of patients at high risk for POAF can guide targeted prevention strategies during the perioperative period. In the study, a prediction model for POAF after CABG was developed by logistic regression based on general demographic characteristics, preoperative biological markers, intraoperative conditions, and postoperative fluid balance in CABG patients, and the model was evaluated and externally

validated in terms of both discrimination and calibration. Multivariate logistic regression analysis showed that age, BMI, smoking history, use of ACEI/ARB, LDL/HDL, LVEF, LVEDD, intraoperative defibrillation, and intraoperative temporary pacing lead implantation were independent predictors of POAF. Among them, age, BMI, smoking history, use of ACEI/ARB, and LDL/HDL were consistent with the results of previous studies [[14,19,20\]](#page-11-0). However, the predictive role of LVEDD, intraoperative defibrillation, and intraoperative temporary pacing lead implantation for new-onset AF after CABG has rarely been reported.

Age is a common risk factor or predictor of POAF after cardiac surgery, and it is generally accepted that the risk of POAF increases with age [\[3,4,13,14,19](#page-11-0)–26]. The results of this study were similar to most previous studies. Multivariate logistic regression analysis revealed that age was a predictor of new-onset POAF after CABG (P *<* 0.05), and the risk of new-onset POAF after CABG increased with age (OR*>*1). A possible explanation may be that age-related atrial fibrosis [\[27](#page-11-0)] and degeneration and loss of atrial myocytes [[28\]](#page-11-0) may increase conduction heterogeneity through discrete regions of slow conduction, thereby promoting and maintaining AF by favoring intra-atrial reentry [\[29](#page-11-0),[30\]](#page-11-0), giving rise to an electrophysiological substrate that predisposes to AF in elderly patients. And the observed negative correlation of increasing age with hypoxic signals (hypoxia-inducible factor-1α, vascular endothelial growth factor, etc.) in atrial tissue may reduce adaptation to hypoxia in old age [[27\]](#page-11-0), and contribute to age-related atrial fibrosis.

In addition to age, overweight and obesity are also considered to be associated with AF $[19,31-33]$ $[19,31-33]$ $[19,31-33]$ $[19,31-33]$. Multivariate logistic regression analysis showed that BMI was a predictor of new-onset POAF after CABG (OR*>*1, P *<* 0.05). The results of Zacharias et al. are the same as our study, which concluded that obesity is an important determinant of new-onset POAF after cardiac surgery and that POAF risk models should incorporate BMI or obesity levels [[34\]](#page-11-0). The results of this study suggest that the risk of POAF after CABG increases with increasing BMI. Possible reasons may be increased BMI or obesity affecting the patient's epicardial adipose volume. Epicardial adipose tissue (EAT) is an adipose depot with specific endocrine functions, producing a large number of adipokines such as adiponectin, leptin, resistin, visfatin, omentin, zinc-alpha 2-glycoprotein, dextran-4, etc [[35](#page-11-0),[36\]](#page-11-0). Since there is no tissue like fascia separating EAT and myocardial tissue, adipokines and/or inflammatory mediators secreted by EAT can act directly on myocardial tissue and interact with surrounding atrial myocytes, extracellular matrix and vascular endothelial cells to induce or participate in the process of AF development [\[37](#page-11-0),[38\]](#page-11-0).

A meta-analysis shows that smoking is associated with an increased risk of AF [[39\]](#page-11-0). The results of this study also confirmed that smoking was associated with an increased risk of new-onset AF after CABG (OR*>*1, P *<* 0.05). Nicotine increases oxidative stress by stimulating sympathetic neurotransmission, thereby altering serum catecholamine concentrations and ion channel status, activating the inflammatory system, and triggering atrial remodeling through pro-fibrotic effects [40–[42\]](#page-11-0). In contrast, carbon monoxide in tobacco induces structural remodeling that may facilitate arrhythmias by causing tissue hypoxia and inducing myocardial fibrosis [[41\]](#page-11-0).

The effect of ACEI on AF is currently controversial. This study found that preoperative use of ACEI increased the risk of POAF after CABG (OR > 1, P < 0.05). Magee et al. found in their prediction model that the use of ACEI was associated with an increased risk of POAF after CABG [[14\]](#page-11-0), contrary to Mathew et al.'s study in the Multicenter Risk Index, in which they stated that pre- and post-operatively initiated ACEI therapy was associated with a reduced risk of AF, while withdrawal from therapy was associated with an increased risk [\[4\]](#page-11-0). ACEI has been shown to reduce the incidence of atrial fibrillation in patients with left ventricular dysfunction after acute myocardial infarction [[43\]](#page-11-0). This may be related to ACEI blocking the myocardial remodeling process associated with the renin-angiotensin system, and atrial remodeling appears to be the central mechanism promoting AF recurrence and maintenance [[44\]](#page-11-0). Therefore, in patients with a high probability of myocardial remodeling, such as heart failure and myocardial infarction, the anti-AF effect of ACEI was demonstrated and reported. However, the effect of ACEI on POAF in patients without preoperative heart failure is unclear and controversial, and further studies are needed.

LDL/HDL has become one of the predictive indicators of atherosclerosis severity [\[45](#page-11-0)], bypass stenosis after CABG [[46,47\]](#page-11-0), and carotid intima-media thickness [[48\]](#page-11-0). And few reports are available on the relationship between LDL/HDL and AF. In the study, multivariate logistic regression analysis showed that LDL/HDL was a protective factor for POAF after CABG (OR*<*1, P *<* 0.05). This result is consistent with previous research suggesting a "cholesterol paradox", in which higher levels of lipids, although an important risk factor for cardiovascular disease, are negatively associated with the risk of AF [\[48](#page-11-0)].

Echocardiographic indices are increasingly being used in the evaluation and prediction of POAF [[49\]](#page-11-0). The previous study results suggested that low LVEF is a predictor of POAF or AF recurrence [[3,49](#page-11-0),[50\]](#page-11-0). In Stefàno et al. [[51\]](#page-12-0), LVEF was found to be independent of AF after cardiac surgery in patients without previous AF. No association between POAF and preoperative LVEF was also found in a study of preoperative sinus rhythm patients who underwent CABG under CPB [\[52](#page-12-0)]. However, high preoperative LVEF is a predictor of POAF after CABG by multivariate logistic regression analysis in our study (OR*>*1, P *<* 0.05). The reasons may be the study population and the definitions of outcomes were different; the population in this study was patients with preoperative sinus rhythm before CABG and the outcome was new-onset AF, whereas the population in previous studies was mostly all cardiac surgery patients and the outcome included new-onset AF and recurrent AF. However, it is not clear why this association was seen, and the relationship between LVEF and new-onset POAF needs further investigation. In addition to LVEF, LVEDD is also considered to be associated with POAF or AF recurrence [[49,](#page-11-0)[53\]](#page-12-0). The same results were observed in our study, i.e., the risk of POAF after CABG increased with preoperative LVEDD (OR*>*1, P *<* 0.05). According to Frank-Starling mechanism, LVEDD reflects left ventricular end-diastolic pressure (LVEDP) to some extent. Animal experiments revealed that in a mouse model of ventricular pressure overload, the extent of atrial remodeling was directly correlated with LVEDP and atrial gene expression related to fibrosis was increased [[54\]](#page-12-0). As mentioned previously, atrial remodeling and atrial fibrosis are involved in the development and progression of AF.

Intraoperative defibrillation and temporary pacing lead implantation were also predictors of POAF after CABG in this study (P *<* 0.05). Patients undergoing intraoperative defibrillation and/or implantation of temporary pacing leads were more likely to develop POAF postoperatively (OR*<*1). Arrigo et al. [[55\]](#page-12-0)demonstrated that in patients with POAF, external electrical cardioversion restored sinus rhythm immediately, but recurrence was common within 24 h. A multicenter study showed the possibility of arrhythmic complications remaining after AF electrical resuscitation [[56\]](#page-12-0). In the CABG population in this study, the potential causes of new-onset POAF in intraoperative defibrillation and temporary pacing of lead implantation may be as follows: (1) Intraoperative electrical cardioversion of the heart surface, although low in energy, where defibrillation electrodes directly interface with the myocardium of the atria and ventricles, may lead to dysfunction of sinus nodes, and thus become a potential risk for POAF. (2) Patients defibrillated intraoperatively for any reason commonly have transient sinus bradycardia and frequently require temporary pacemaker implantation, the common type of implantation is atrial pacing or atrioventricular sequential pacing, regardless of postoperative use or not, the pacemaker electrodes may stimulate the atria and thus produce AF. At present, there are few studies on the mechanism of electrical cardioversion associated with POAF, and the specific causes and potential mechanisms need to be further investigated.

Using the above predictors, the study developed prediction models through logistic regression and presented them visually through nomogram and scoring scale. The model had fair discrimination $(AUC = 0.621)$ and had a high ability to identify patients (sensitivity of 73.3%) but could be misdiagnosed (specificity of 46.2%). The incidence of POAF after CABG predicted by this model was in good consistency with the actual incidence by the Hosmer-Lemeshow goodness-of-fit test.

CHA2DS2-VASc is a clinical scoring tool to assess stroke risk in patients with AF and has also been used in recent years to predict AF or POAF [\[16](#page-11-0)]. The HATCH score is primarily used to assess the progression of persistent AF [\[17](#page-11-0)], but it has also been demonstrated as a predictor of POAF after CABG [\[57,58](#page-12-0)]. Li et al. [[18\]](#page-11-0), on the other hand, developed a prediction model for POAF after non-extracorporeal CABG using a small sample of data from a single center in China. In contrast, this study has a large sample size and the model was externally validated. External validation results showed that the discrimination of the model developed in this study $(AUC = 0.616) >$ Li et al.'s model $(AUC = 0.541) >$ CHA₂DS₂-VASc $(AUC = 0.521) >$ HATCH score (AUC = 0.509).

Nomogram or scoring scale simplifies the cumbersome logistic regression model for clinical use. For example, a 65-year-old male patient with CABG in preoperative sinus rhythm, preoperative BMI of 24 kg/m², no smoking history, without the use of ACEI or ARB, LDL/HDL = 2.08, LVEF = 65%, LVEDD = 50 mm, and no intraoperative defibrillation or temporary pacing lead implantation. The total score obtained by using the nomogram for this patient was approximately $208 = 57 + 16+0 + 0+80 + 30+25 + 0+0$, which corresponds to a risk probability of POAF after CABG *<*35% (Fig. 6). The total score obtained from the scoring scale was 6 = 2.5 + 0.5+0 + 0+0 + 0+2 + 1+0 + 0, which corresponds to a risk probability of POAF after CABG *<*40%.

The study is retrospective and has some limitations: First, some of the preoperative biochemical markers and/or coronary angiography specifics were not included because of severe missing, which may lead to biased study results and also limit the validation and comparison of this study cohort to other more prediction models. Second, the study only recorded AF occurred during the inpatient period, and no long-term follow-up of patients was recorded, which may lead to an underestimation of the incidence of postoperative AF in this study. In future studies, it is highly necessary to conduct prospective multicenter studies, standardize patient follow-up, collect patient survival data, and construct models with COX regression to improve the models.

Fig. 6. Examples of nomogram applications (BMI: body mass index; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; LDL: low-density lipoprotein; HDL: high-density lipoprotein; EF (LVEF): left ventricular ejection fraction; LVEDD: left ventricular enddiastolic diameter).

5. Conclusion

Age, preoperative BMI, smoking history, use of ACEI/ARB, LDL/HDL, LVEF, LVEDD, intraoperative defibrillation, and temporary pacing lead implantation were independent predictors of POAF after CABG. This prediction model can be used for the early identification of patients at high risk of POAF and helps to differentiate patients in the postoperative period. Nomogram and scoring scale visualization models are more convenient for the assessment of POAF and have certain advantages for clinical use. In future studies, it is highly necessary to conduct prospective multicenter studies, standardize patient follow-up, collect patient survival data, and construct models with COX regression to improve the models.

Author contribution statement

Renjianzhi zhang; Xin-Yi Yu; Jing Wang; Jian Lv: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Yan Zheng: Analyzed and interpreted the data.

Ming-Huan Yu; Yi-Rui Zang; Jian-Wei Shi; Jia-Hui Wang: Contributed reagents, materials, analysis tools or data.

Li Wang; Zhi-Gang Liu: Conceived and designed the experiments; Wrote the paper.

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Declaration of interest's statement

The authors declare no conflict of interest.

Abbreviations

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