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# Establishment and evaluation of a nomogram prediction model for risk of atrial fibrillation recurrence after the cox-maze IV procedure

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**Abstract**

The Cox-Maze IV (CMIV) procedure is the mainstay in surgical treatment of atrial fibrillation (AF), but the rate of AF recurrence after the CMIV procedure in patients with persistent AF is difficult to accurately evaluate. In this study, we aimed to develop and validate a risk prediction model of AF recurrence within 1 year after undergoing the Cox-Maze IV procedure. We retrospectively enrolled 303 consecutive patients who underwent the Cox-Maze IV procedure for persistent AF concomitant with other cardiac procedures at our institute between 2019 and 2021. A nomogram was developed using multivariate logistic regression analysis, and the concordance statistic (C-statistic) was computed. Differentiation, calibration, clinical suitability, and bootstrapping were performed to verify the model. Among the 303 patients, 71 developed recurrent AF within 1 year of CMIV. Factors predictive of postoperative AF recurrence included age, left ventricular hypertrophy (LVH), early atrial tachyarrhythmias (ATAs), and congenital heart disease surgery (namely, ventricular septal defect repair and atrial septal defect repair). Based on the training dataset, the nomogram had a C-statistic of 0.864 (95% CI 0.811–0.918) for predicting AF recurrence. According to the receiver operating characteristic curve, (ROC curve), the cutoff value of the model was 0.293, and the specificity and sensitivity were 0.841 and 0.789, respectively. This model can predict the risk of AF recurrence after the CMIV procedure. Its discrimination, calibration, and clinical applicability are strong, and its clinical application is simple and easy to promote.

**Keywords** Atrial fibrillation, Cox-Maze IV procedure, Risk score model, Prediction, Prognosis

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## Background

Atrial fibrillation (AF) is the most common persistent arrhythmia in adults worldwide. The incidence of AF in adults ranges from 2 to 4% [1]. It can cause stroke and is associated with a high disability rate. Compared with patients with sinus rhythm, Chinese patients with AF have a significantly increased risk of all-cause, cardiovascular, and stroke deaths [2]. Currently, methods for controlling AF can be broadly divided into three categories: drug treatment, catheter radiofrequency ablation, and surgical treatment [3]. In the 1990s, Dr. James Cox first proposed the treatment of AF using the maze procedure [4]. The basic aim of the maze procedure is to make a series of incisions in the atria to form scar tissue and block the abnormal electrical activity that causes arrhythmia. The Cox-Maze IV (CMIV) procedure has improved since it was first proposed, and it is commonly performed. Previous studies have shown that for patients with prior AF, adding the maze procedure during cardiac surgery can increase the conversion rate of postoperative AF, improve quality of life, reduce the long-term risk of stroke, and improve long-term survival without increasing the risk of the entire surgical procedure [5–10]. However, AF recurrence after CMIV is a long-term concern for surgeons. Quantifying the risk of recurrence before surgery can help with screening patients and reducing the rate of recurrence after surgery. Therefore, we aimed to develop a predictive model for the risk of AF recurrence after the CMIV procedure that can be used to assess the risk of AF recurrence more accurately in patients after the CMIV procedure to guide clinical treatment.

## Methods

### Study population

This study included 372 consecutive patients who underwent CMIV concurrently with other cardiac surgeries at the First Affiliated Hospital of the Military Medical University of the Army between January 2019 and December 2021. Seventy-one patients with missing follow-up data, deaths during hospitalization, or automatic discharge were excluded. The clinical data of 303 patients were included in this study. This study was approved by the Ethics Committee of the First Affiliated Hospital of Military Medical University (Chongqing, China; approval number (B)KY2023004). The requirement for informed consent was waived due to the retrospective and observational nature of the study.

AF recurrence [11] was defined as atrial arrhythmia occurring for 30 s at least three months after the CMIV procedure.

### Surgical indications and the maze procedure

Surgical indications: Surgical indications of the cohort were discussed by the institutional heart team in accordance with published guidelines [11]. All patients who underwent the modified maze procedure met the following criteria: (1) symptomatic refractory AF and (2) intolerance to at least one class I or III antiarrhythmic drug. Other open-heart surgeries were performed concurrently. All patients underwent left atrial appendage suture closure, and left atrial folding surgery was performed in patients with a left atrial diameter of 60 mm.

Maze procedure[]: Right atrial ablation path. The entrance to the right atrial appendage was made with a circular ablation line. A longitudinal incision was made on the dorsolateral side of the right atrium, and an ablation line was made from the bottom of the incision to the upward and inferior vena cava inlet and coronary venous sinus. An ablation line was also made from the midpoint of the incision to the blind end of the right atrial appendage and the tricuspid valve annulus at the 2 o'clock, 5 o'clock, and 10 o'clock positions. Last, an ablation line was made from the coronary sinus to the inferior vena cava entrance. Left atrial ablation path: A ring ablation line was made at the left atrial entrance of the left pulmonary vein and at the left atrial entrance of the right pulmonary vein. An annular ablation line was made at the left atrial appendage entrance. Ablation lines were made between the left upper pulmonary vein and left atrial appendage, from the lower end of the atrial septal incision to the midpoint of the posterior mitral annulus, from the right lower pulmonary vein to the left lower pulmonary vein, and from the right upper pulmonary vein to the left upper pulmonary vein. Box lines were burned using a bipolar radiofrequency ablation system.

### Postoperative medication and follow-up strategy

All patients included in the study were taking vitamin K antagonists (e.g. warfarin sodium) and antiarrhythmic drugs for at least three months after surgery. When the patient's ECG findings were normal or the above drugs could not be tolerated, anticoagulant and antiarrhythmic therapies were discontinued. Standard 12-lead ECG was performed 3, 6, and 12 months after surgery, during which patients with arrhythmias underwent a 24-hour ambulatory ECG.

### Study design and statistical analysis

This report was prepared in compliance with the STROBE checklist for observational studies [12] and the TRIPOD statement to develop and validate the prediction model [13].

The 303 patients were divided into a recurrent AF group ($n=71$) and a non-recurrent AF group ($n=232$) according to whether they developed recurrence within 3–12 months after surgery. Variables with significant differences between the two groups were analyzed using univariate analysis. A multivariate logistic regression model was constructed by combining these variables with relevant variables reported in previous studies. The rms package in R was used to visualize the model and draw nomograms. The sensitivity and specificity of the model were evaluated using receiver operating characteristic (ROC) curves. To assess the ability of the nomogram model to discriminate patients who would develop AF recurrence, a concordance statistic (C-statistic; equal to the area under the receiver operating curve [AUC]) and 95% confidence intervals (CIs) were calculated, and the calibration degree of the model was evaluated using a calibration curve. The clinical applicability of the model was analyzed using decision curve analysis (DCA). Internal validation of the model was performed by repeating bootstrap extraction 1000 times.

Categorical data were reported as counts and percentages. Continuous data were reported as means ± standard deviations for normally distributed data and as medians (interquartile ranges) for non-normally distributed data. Comparisons were performed using the chi-square test or Fisher's exact test for categorical variables and the Student's t-test or the Mann–Whitney Wilcoxon test, as appropriate, for continuous variables.

Statistical significance was set at P : 0 to < 0.001. All data were analyzed using the SPSS software (version 26.0; SPSS Inc., Chicago, IL, USA) or R software (version 4.2.1; R Project for Statistical Computing, Vienna, Austria).

## Results

### Univariate analysis of patient data between the recurrent AF group and non-recurrent AF group

At 12 months postoperative follow-up, 71 patients (23.4%) had recurrent AF and 232 (76.6%) had no recurrent AF. The baseline data of the two patient groups are shown in Table 1. There were significant differences between the two groups in the levels of coronary heart disease ($P = 0.009$), concurrent congenital heart disease operations ($P = 0.028$), rapid atrial arrhythmias before discharge (P : 0 to < 0.001), left ventricular hypertrophies (LVH) ($P = 0.046$), mitral valve lesions ($P = 0.035$), moderate or more severe regurgitation insufficiency ($P = 0.021$), age (P : 0 to < 0.001), and the ratio of left atrial diameter to body surface area ($P = 0.020$).

### Multivariate logistic regression analysis of patient data between the recurrent AF group and non-recurrent AF group

Based on the results of the univariate analysis, we included age, coronary heart disease, congenital heart disease operation, early atrial tachyarrhythmias (ATAs), LVH, mitral valve disease, and left atrial diameter index (i.e., the ratio of left atrial diameter to body surface area) in the multivariate logistic regression analysis. The results showed that age, congenital heart disease, ATAs, and LVH were independent predictors of AF recurrence after the CMIV procedure (Table 2).

### Development of the model

Points were assigned to each risk factor according to the OR(odds ratio), enabling the development of a model to predict the rate of AF recurrence. The rate of AF recurrence: $P = 1/(1 + e^{-Z})$ $Z = 2.826 \times \text{ATAs} + 1.493 \times \text{congenital heart surgery} + 0.05 \times \text{age} + 1.004 \times \text{LVH} — 5.348$. One point was assigned if the risk factor was present, and 0 points were assigned if the risk factor was not present. The assignments are as follows: concomitant congenital heart disease operation, tachyarrhythmias before discharge, and LVH present before surgery. For the age variable, patients were assigned the number of points that corresponded to their age in years. Based on the final multivariate model, a nomogram was generated by assigning a weighted score to each factor associated with AF recurrence (Fig. 1).

### Evaluation and validation of the model

The ROC curve shows that the truncation value of the model is 0.293, the specificity and sensitivity are 0.841 and 0.789, respectively, and the AUC of the model is 0.864 (95% CI 0.811–0.918) (Fig. 2). The AUC of the model was 0.864 after 1000 repeated samples in the training set through bootstrapping, and the gradient of the model calibration curve was 0.944 (Fig. 3). The Hosmer-Lemeshow goodness-of-fit test showed that the $X^2$ of the model was 3.945 and the P value was 0.862. The decision curve analysis (DCA) showed that the model had high clinical utility (Fig. 4).

## Discussion

The maze procedure is currently the gold standard for the surgical treatment of AF; however, there is a risk of AF recurrence after the maze procedure. The probability of AF recurrence varies depending on the AF type. The 1-and 3-year rates of freedom are 94.6% and 87.5%, respectively, for recurrent paroxysmal AF, 82.1% and 81.9% for persistent AF, and 84.1% and 78.1% for long-term persistent AF [14]. The probability of recurrence of postoperative AF also differs depending on the concomitant cardiac surgery, and the freedom rate 1 year after simple maze surgery is > 90% [15]. When other cardiac surgeries are performed concurrently, the 1-year postoperative freedom rate is approximately 75% [16, 17]. In cases of AF associated with rheumatic valvular disease, the rate of freedom of the maze procedure is 46–95% [18–22]. In this study, the freedom rate of patients one year after the CMIV procedure was 76.6%, which may be related to the CMIV procedure being performed in conjunction with other cardiac surgeries and the presence of AF associated with rheumatic valvular disease.

We developed this model to quantify the risk probability of AF recurrence after the CMIV procedure, assist doctors in making clinical decisions, help patients better understand the risks of surgery, and guide perioperative and postoperative individualized treatment. We aimed to identify the factors that predict the recurrence of postoperative atrial fibrillation. In addition, a nomogram and calculation formula that can predict the risk of atrial fibrillation recurrence after CMIV were developed and verified. In this study, we identified several independent predictors of AF recurrence: ATAs, age, concurrent congenital heart disease surgery, and LVH.

**Table 1** Baseline characteristics of patients in the overall population

| Variables | non-recurrent AF group($n=232$) | recurrent AF group($n=71$) | t/$X^2$/Z | *P* |
|---|---|---|---|---|
| **Demographics** | | | | |
| Age | 53(48, 58) | 56(53, 65) | -3.756 | 0 to < 0.001 |
| Male sex | 73(31.5) | 23(32.3) | 0.022 | 0.885 |
| BMI (kg/$m^2$) | 24.14(21.87, 26.57) | 23.24(21.1, 25.71) | -1.758 | 0.079 |
| LADI (mm/$m^2$) | 31.52(28.18, 34.6) | 33.38(29.08, 37.32) | -2.321 | 0.02 |
| **Medical history** | | | | |
| Hypertension | 29(12.5) | 9(12.7) | 0.002 | 1 |
| Diabetes | 6(2.6) | 2(2.8) | 0.011 | 1 |
| Apoplexy | 5(2.2) | 2(2.8) | 0.000 | 1 |
| Chronic kidney disease | 1(0.4) | 2(2.8) | 0.000 | 0.138 |
| Smoking | 59(25.4) | 19(26.8) | 0.050 | 0.823 |
| Long-term drinking | 53(22.8) | 24(33.8) | 3.753 | 0.053 |
| Coronary heart disease | 5(2.15) | 7(9.85) | 8.483 | 0.009 |
| Dyslipidemia | 68(29.3) | 21(29.6) | 0.002 | 0.966 |
| Hyperthyroidism | 8(3.4) | 3(4.2) | 0.000 | 0.723 |
| Clinical characteristics | | | | |
| NYHA functional class III or IV | 187(80.6) | 60(84.5) | 0.550 | 0.458 |
| CHA2DS2-VASc score | 2(2, 3) | 2(2, 3) | -1.512 | 0.131 |
| early ATAs | 31(13.36) | 48(67.61) | 82.987 | 0 to < 0.001 |
| LVH | 35(15.1) | 18(25.4) | 3.970 | 0.046 |
| Aortic valve disease | 92(39.7) | 31(43.7) | 0.362 | 0.547 |
| Mitral valve disease | 228(98.3) | 66(93.0) | 0.000 | 0.035 |
| Tricuspid regurgitation | 197(84.9) | 60(84.5) | 0.007 | 0.933 |
| RAD(mm) | 43(38, 49) | 44(39, 51) | -1.405 | 0.16 |
| LAD(mm) | 53(47, 58) | 54(50, 60) | -1.236 | 0.216 |
| MVLA(m/s) | 4.3(3.5, 5) | 4(3, 5) | -1.648 | 0.099 |
| MVLA(m/s) | 2.1(1.6, 2.4) | 1.9(0, 2.2) | -1.637 | 0.102 |
| MVA($cm^2$) | 0.9(0.5, 1.3) | 0.83(0, 1.2) | -1.390 | 0.164 |
| LVEF | 56(50, 61) | 56(51, 60) | -0.331 | 0.741 |
| LVFS | 29(26, 33) | 29(26, 32) | -0.632 | 0.527 |
| EDV(mL) | 114(92, 147) | 114(86, 144) | -0.660 | 0.509 |
| Cardiac mural thrombus | 35(15.1) | 16(22.5) | 2.155 | 0.142 |
| **Operation** | | | | |
| CMIV+AVO | 1(0.4) | 0(0) | 0.000 | 1 |
| CMIV+MVO | 17(7.3) | 2(2.8) | 0.000 | 0.262 |
| CMIV+TVO | 4(1.7) | 3(4.2) | 0.000 | 0.361 |
| CMIV+MVO + TVO | 133(57.3) | 41(57.7) | 0.004 | 0.950 |
| CMIV+AVO + MVO | 9(3.9) | 1(1.4) | 0.000 | 0.462 |
| CMIV+AVO + MVO + TVO | 68(29.3) | 22(31.0) | 0.073 | 0.787 |
| CMIV+CHDO | 14(6.0) | 10(14.1) | 4.830 | 0.028 |
| CMIV+Other operations | 26(11.2) | 10(14.1) | 0.430 | 0.512 |
| CPB time(min) | 144(126, 176) | 148(122, 178) | -0.173 | 0.862 |
| ACC time(min) | 101(81, 130) | 99(79, 126) | -0.416 | 0.677 |
| **Laboratory** | | | | |
| RBC($10^{12}$/L) | 4.41(4.05, 4.85) | 4.27(3.93, 4.73) | -1.598 | 0.11 |
| WBC($10^9$/L) | 5.93(4.97, 7.42) | 5.88(4.83, 7.37) | -0.617 | 0.537 |
| MWBC($10^9$/L) | 18.8(14.68, 22.53) | 18.53(15.89, 21.9) | -0.190 | 0.85 |
| Hemoglobin(g/L) | 132(120, 145) | 129(121, 140) | -1.397 | 0.163 |

**Table 1** (continued)

| Variables | non-recurrent AF group($n=232$) | recurrent AF group($n=71$) | t/$X^2$/Z | *P* |
|---|---|---|---|---|
| PLT($10^9$/L) | 176(143, 222) | 165(122, 209) | -1.673 | 0.094 |
| BNP(Pg/ml) | 1591(880, 2818) | 1253(708.3, 2022) | -1.587 | 0.113 |

Categorical data are reported as counts and percentages. Continuous data are reported as means ± standard deviations for normally distributed data, and as medians (interquartile ranges, IQRs)for non-normally distributed data, number (%);BMI: body mass index; LADI: left atrial diameter index (=the ratio of left atrial diameter to body surface area); ATAs: atrial

tachyarrhythmias; LVH: left ventricular hypertrophy; RAD: right atrium dimension; LAD: left atrium diameter; MVLA: maximum velocity of left atrial side turbulence of mitral valve during systole ; MVLA: maximum velocity of left ventricular side turbulence of mitral valve in diastole ; MVA: mitral valve opening area; LVEF: left ventricle ejection fraction; LVFS: left ventricular fractional shortening; EDV: end-diastolic volume; CMIV: Cox-Maze IV procedure; AVO: aortic valve operation; MVO: mitral valve operation; TVO: tricuspid valve operation; CHDO: congenital heart disease operation; CPB time: cardiopulmonary bypass time; ACC time: aortic cross clamping time; RBC: red blood cell count; WBC: white blood cell count; PLT: platelet; BNP: B-type natriuretic peptide; MWBC: maximum number of white blood cells after operation.

**Table 2** Predictive factors for atrial fibrillation recurrence by a logistic regression model

| Multivariate analysis | Odds | 95% Confidence | *P*-value |
|---|---|---|---|
| | ratio | interval | |
| Coronary heart disease | 3.716 | 0.814, 16.955 | 0.090 |
| Congenital heart disease operation | 4.451 | 1.348, 14.694 | 0.014 |
| Early ATAs | 16.878 | 8.129, 35.043 | <0.001 |
| LVH | 2.73 | 1.177, 6.333 | 0.019 |
| Mitral valve disease | 0.226 | 0.032, 1.579 | 0.134 |
| Mitral Regurgitation | 0.545 | 0.222, 1.342 | 0.187 |
| Age | 1.051 | 1.009, 1.096 | 0.018 |
| LADI | 1.055 | 0.996, 1.116 | 0.067 |

ATAs: atrial tachyarrhythmias; LVH: left ventricular hypertrophy; LADI: left atrial diameter index (=the ratio of left atrial diameter to body surface area)

Niv et al. showed that cardiac rhythm at discharge predicted sinus rhythm 24 months after CMIV surgery, with significantly higher freedom rates in patients discharged with sinus rhythm [23]. Ralph et al. suggested that early postoperative ATAs are an independent predictor of AF recurrence 1 year postoperatively [24]. Our study found that early AF recurrence may be a marker of a more advanced pathology of the atrial substrate, which would logically make these patients more prone to late recurrence [25]. However, the underlying mechanisms require further investigation.

We found that older patients are at greater risk of postoperative AF recurrence, and these results are similar to those of Jules et al. [25]. However, in our study, we treated age differently. Jules et al. grouped the ages into 5-year increments, which increased the likelihood of finding differences between age groups. Additionally, in their study, the average age of participants was approximately 69 years. In our study, we treated age as a continuous variable, and the mean age of the participants was approximately 55 years. This may indicate that maze surgery works differently across different age groups. Interestingly, in other studies age was not an independent predictor of AF recurrence after the maze procedure [26–28]. This may be related to the different treatments of the age variable or age range of the participants.

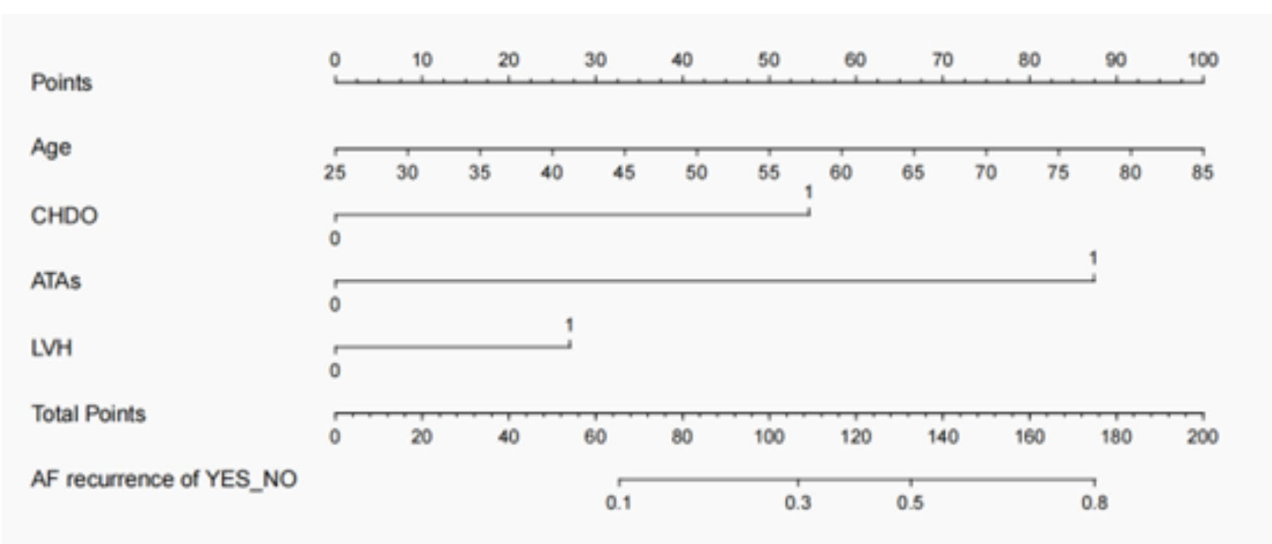


**Fig. 1** Characteristics in the nomogram to predict probability of AF recurrence in patients. The nomogram for assessing AF recurrence risk. The method for calculating the risk of AF recurrence was as follows. First, points for each variable are assigned by corresponding values from the "Points" axis. Second, the "Total points" is obtained by summing up points of all predictors. Third, a vertical line should be drawn down the total points to get the risk of AF recurrence. CHDO: congenital heart disease operation; ATAs: atrial tachyarrhythmias; LVH: left ventricular hypertrophy

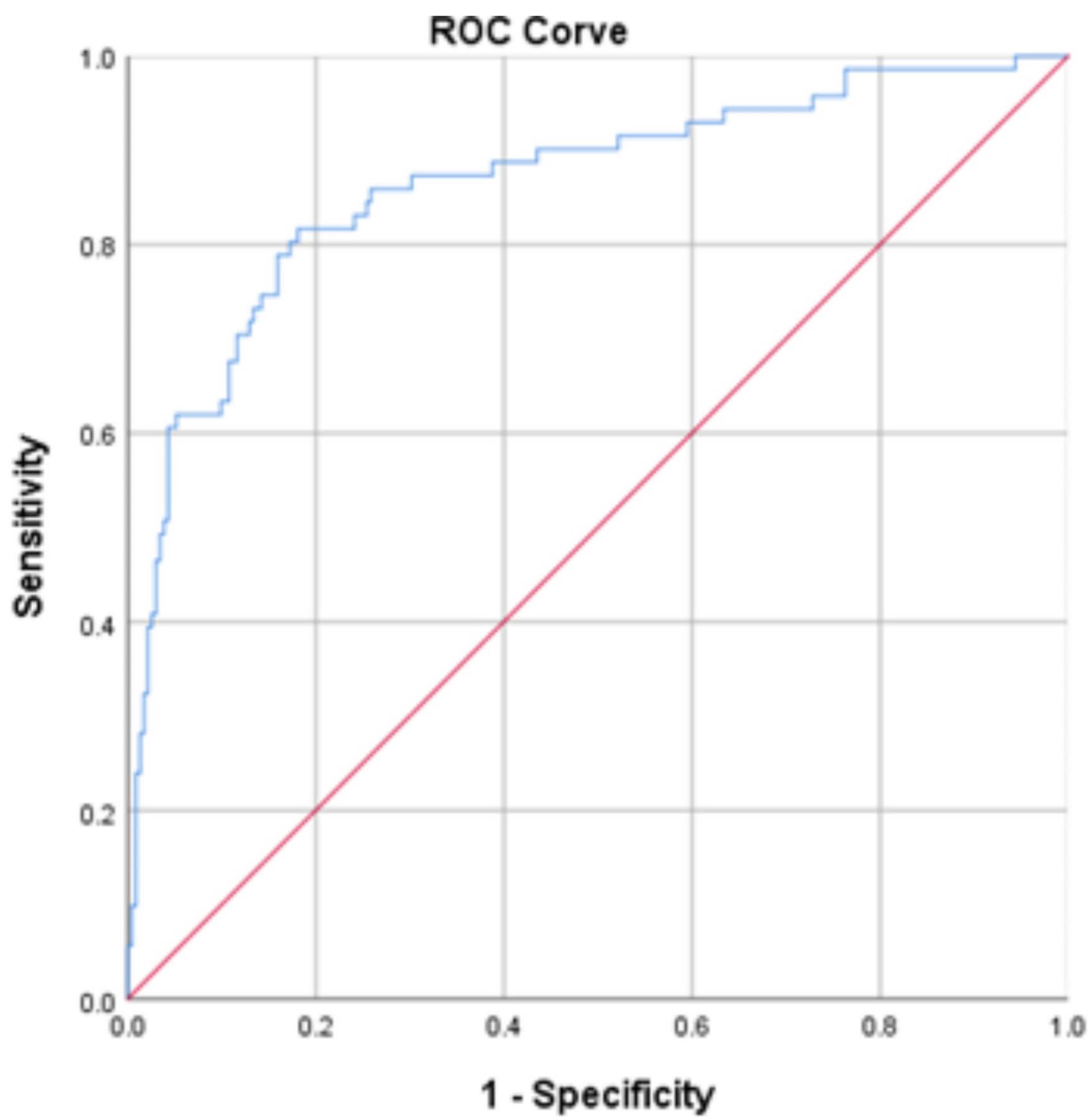


**Fig. 2** Receiver operating characteristic curves of the model for identifying recurrent AF and non-recurrent AF

Studies have shown that the CMIV procedure is effective in the treatment of AF in patients with congenital heart disease or valvular disease [5, 6, 29, 30]. However, in patients with valvular disease combined with congenital heart disease, the effect of the CMIV procedure in the treatment of AF has rarely been reported. Our findings suggest that congenital heart surgery in patients undergoing CMIV combined with valve surgery reduces the success rate of the CMIV procedure within one year. This may be because atrial myocyte remodeling occurs more frequently in patients with AF and valvular and congenital heart diseases.

A recent meta-analysis [31] found that LVH is a prognostic predictor of all-cause mortality in patients with severe LVH [32] and low CHA2DS2-VASc scores, and that LVH is an independent predictor of AF recurrence after the maze procedure. In our study, LVH was also an independent predictor of AF recurrence within one year of the CMIV procedure. Previous studies have shown that left atrial fibrosis predicts AF recurrence [33], and patients with atrial fibrillation and LVH have significant left atrial fibrosis [34]. This may explain why LVH predicts the recurrence of atrial fibrillation.

Many studies have found that left atrial volume is an important factor in predicting the effect of the maze procedure. However, in these studies, the absolute value of left atrial volume is used as a predictor of AF recurrence after modified maze surgery, which does not account for the differences between patients with the same left atrial diameter and different body surface areas [35–39]. Therefore, we introduced the concept of the left atrial diameter index (i.e., the ratio of left atrial diameter to body surface

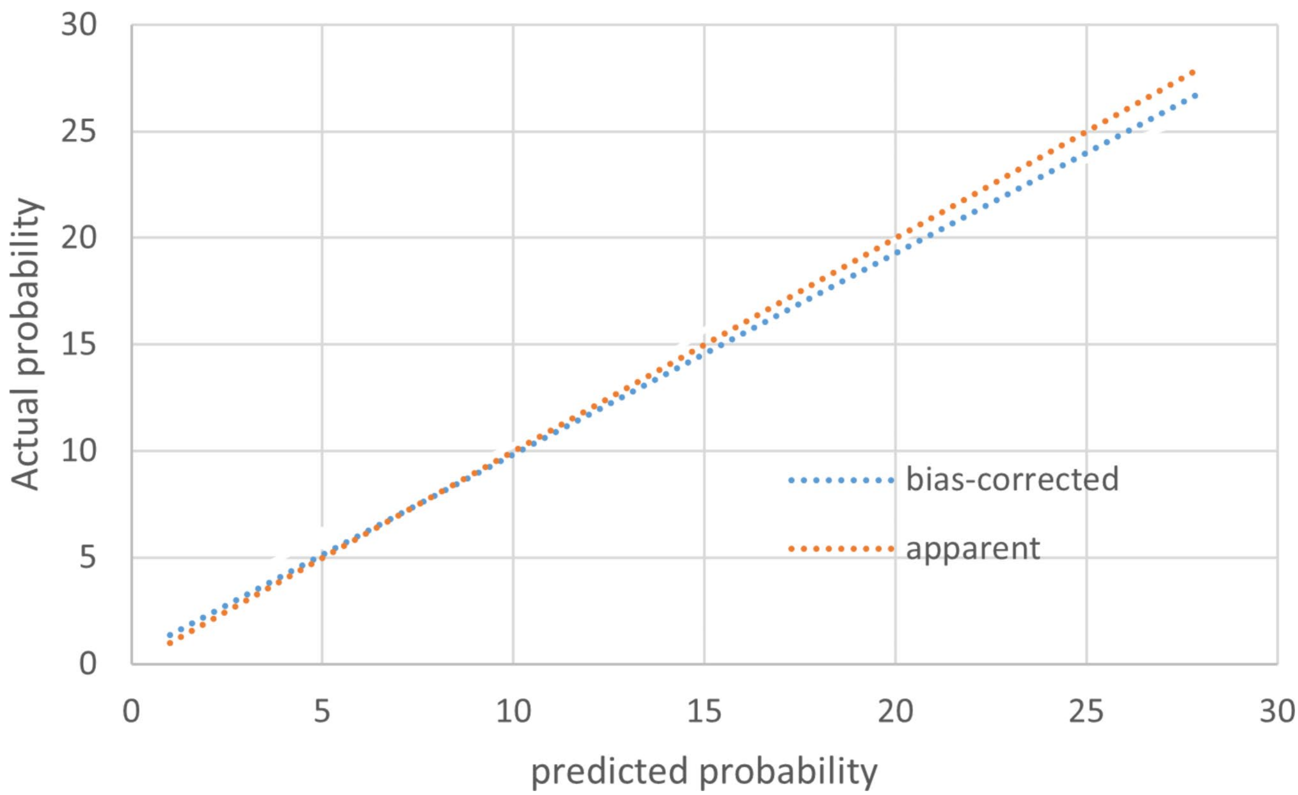


**Fig. 3** The calibration curve for the nomogram

area) in this study. By including this variable, we aimed to better understand the differences between patients with different body surface areas but the same left atrial diameter. In this study, we did not find a significant difference in the left atrial diameter between the two groups on univariate analysis ($P = 0.216$); however, the difference in the left atrial diameter index was significant ($P = 0.004$). The larger the left atrial diameter index, the greater the risk of postoperative atrial fibrillation recurrence. Left atrial enlargement can cause myocardial interstitial fibrosis, endocardial remodeling, and myocardial cell hypertrophy, resulting in electrophysiological changes in ion channels, which in turn alter myocardial excitability and autonomia and induce atrial fibrillation [40]. Unfortunately, when we included the left atrial diameter index in our multivariate logistic regression analysis, we did not find that the left atrial diameter index was a predictor of atrial fibrillation recurrence within 1 year after modified maze surgery. This may be related to the small sample size of the present study.

In previous predictive models, the duration of AF was an important predictor [36, 41, 42]. However, whether AF duration is an independent risk factor for AF recurrence after CMIV is controversial [25, 28]. Under the current medical conditions in China, it is difficult to accurately determine the duration of AF in patients; therefore, our predictive model does not include the variable of AF duration, which may help increase the scope of application of this model.

This study had some limitations. First, the data collection was retrospective. Some of the data of interest were not fully recorded during the patient's hospital stay. Second, some patients showed poor adherence to antiarrhythmic drugs after discharge, which may have affected the test results. Finally, we only used single-center data and bootstrap to repeat sampling 1000 times in the training cohort to validate the model internally and not externally. In future studies, external validation from multiple centers and larger sample sizes are required.

## Conclusions

Our nomogram and calculation formula are simple and can be used to calculate the probability of AF recurrence in all eligible patients, which can inform the next management strategy for doctors and patients. Simultaneously, the data required for the model can be easily obtained clinically, which may be conducive to the promotion of the model.

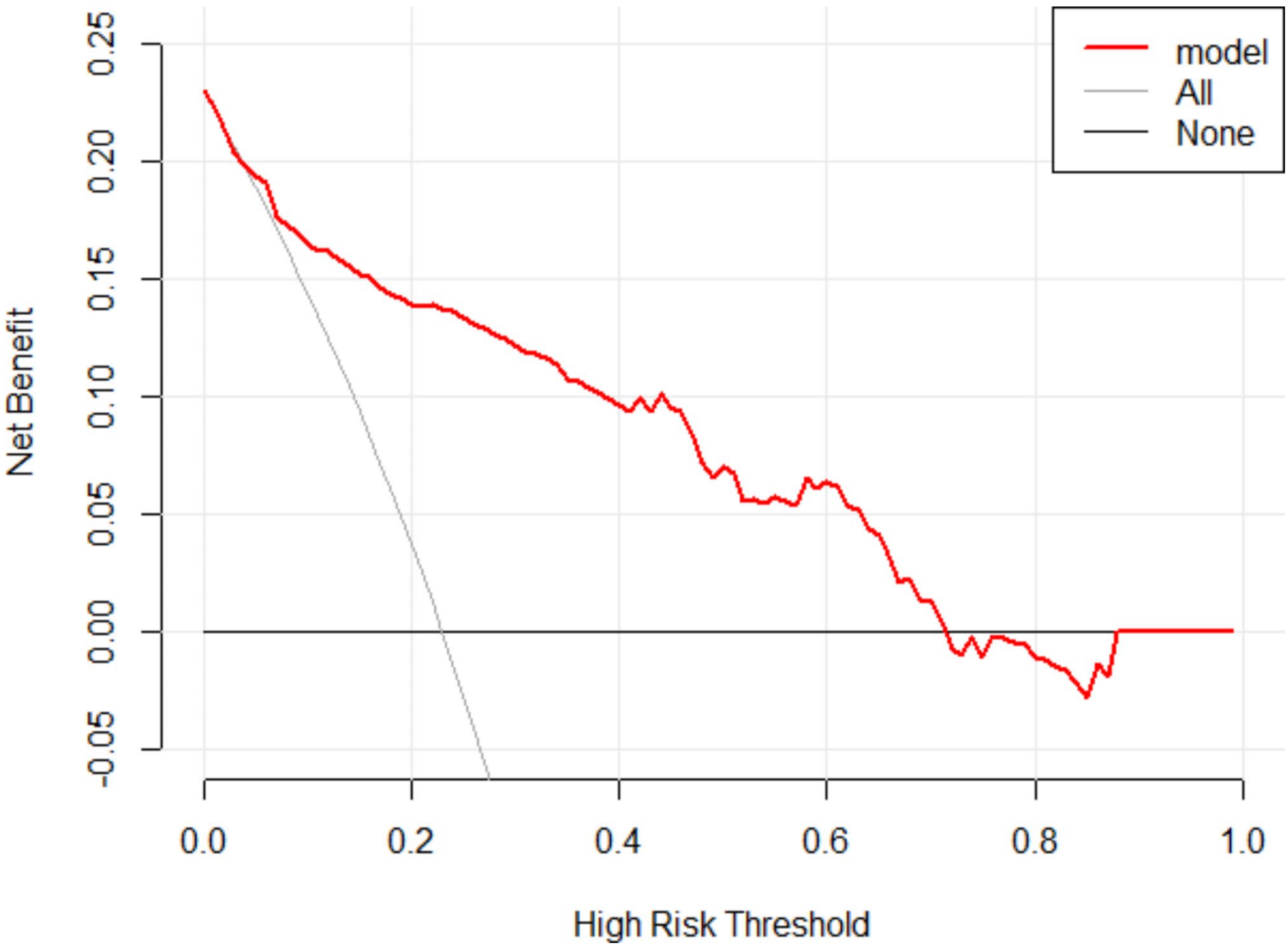


**Fig. 4** Decision curve analysis (DCA) of the nomogram. The y-axis shows the net benefit. The x-axis shows the corresponding high risk threshold. The grey line represents the assumption that all patients were AF recurrence. The black line represents the assumption that all patients were AF non-recurrent


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**Author contributions**
PH and WC were responsible for the study concept and design. CY, YNW, HJZ, SJY, YBC, CJY, and JL were responsible for the acquisition and analysis of data. All authors contributed to the interpretation of the data. CY and YNW drafted the manuscript. The corresponding author attests that all listed authors meet authorship criteria. All authors read and approved the final manuscript.


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**Data availability**
The data that support the findings of this study are available from the corresponding authors upon reasonable request.

## Declarations

**Ethical approval and consent to participate**
This study was approved by the Institutional Review Board of Southwest Hospital of Third Military Medical University (Army Medical University) and conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board of Southwest Hospital of Third Military Medical University (Army Medical University) waived the need for informed consent.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare that they have no competing interests.


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