

Article

# Application of Machine Learning Algorithms to Predict New-Onset Postoperative Atrial Fibrillation and Identify Risk Factors Following Isolated Valve Surgery

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## Abstract

**Background:** New-onset postoperative atrial fibrillation (POAF) is the most common complication after valvular surgery, but its etiology and risk factors are incompletely understood. This study investigates the benefits of machine learning methods in risk prediction and in identifying relative perioperative variables for POAF after valve surgery. **Methods:** This retrospective study involved 847 patients, who underwent isolated valve surgery from January 2018 to September 2021 in our institution. We used machine learning algorithms to predict new-onset postoperative atrial fibrillation and to select relatively important variables from a set of 123 preoperative characteristics and intraoperative information. **Results:** The support vector machine (SVM) model demonstrated the best area under the receiver operating characteristic (AUC) value of 0.786, followed by logistic regression (AUC = 0.745) and the Complement Naive Bayes (CNB) model (AUC = 0.672). Left atrium diameter, age, estimated glomerular filtration rate (eGFR), duration of cardiopulmonary bypass, New York Heart Association (NYHA) class III–IV, and preoperative hemoglobin were high-ranked variables. **Conclusions:** Risk models based on machine learning algorithms may be superior to traditional models, which were primarily based on logistic algorithms to predict the occurrence of POAF after valve surgery. Further prospective multicenter studies are needed to confirm the performance of SVM in predicting POAF.

## Keywords

heart valve surgery; atrial fibrillation; machine learning; prediction

## Introduction

New-onset postoperative atrial fibrillation (POAF) is the most common complication after valve surgery, with a reported incidence rate of 30%–60% [1]. Ninety percent

of POAF cases are detected in the first several days after surgery, and the peak incidence is on the second postoperative day [1,2]. Despite advances in surgical concepts, perioperative care, and prophylactic medicine, POAF incidence following valve surgery has not decreased over the past few decades [3].

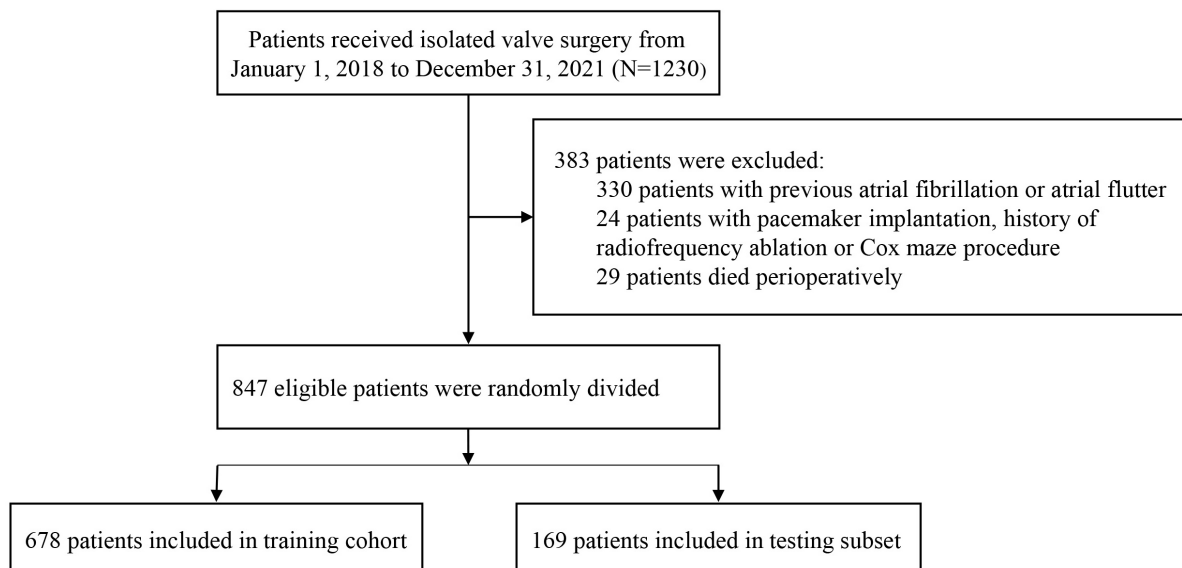
Though a reasonable number of studies have focused on related risk factors of POAF—some of which developed models for risk stratification, such as the POAF Score and CHA2DS2-VASc Score—none of them concentrated on valvular surgery, which carries different risks of POAF compared with other types of cardiac surgery [4,5]. Unfortunately, the observed performances of these models in valve surgery were not very optimistic, with the most commonly reported area under the receiver operating characteristic (AUC) ranging from 0.593 to 0.651 [6]. Furthermore, in the process of developing these predictive tools, some variables, such as data of echocardiography, electrocardiogram, medical history, and laboratory tests, were not involved; this may explain why their performances were not entirely satisfactory.

Machine learning (ML), which refers to computer algorithms that learn from data, has been gaining importance in the medical area. Though it remains controversial, some studies have demonstrated that the ML method may better analyze complex data because it requires no assumptions, regarding the data's structure [7]. Our study aimed to compare different machine learning algorithms to predict individual risk of POAF after valve surgery and to identify the most influence preoperative and intraoperative variables.

## Materials and Methods

### Study Population

The study protocol is illustrated in Fig. 1. We first identified 1230 adult patients (age  $\geq 18$  years) who underwent isolated valve surgery at the First Medical Center of Chinese PLA General Hospital (Beijing, China) from January 2018 to December 2021. The exclusion criteria of this study were patients with incomplete or nonavailabil-



**Fig. 1. Flow chart showing patient selection and exclusion.**

ity of medical records, non-sinus electrocardiogram before surgery, medical history of atrial fibrillation or atrial flutter, implantation of a pacemaker, history of radiofrequency ablation or Cox maze procedure for arrhythmia, and operative mortality (defined as the patients who died within 30 days after surgery). A total of 383 patients were excluded because of the above reasons; thus, the final sample consisted of 847 patients. The study was approved by the institutional review board of the Chinese PLA General Hospital (approval number S2022-360-01). Given the observational nature of the study, informed consent was waived. All identifiable information about the patients was hidden, and their identities could not be determined based on the context. This study was conducted following the ethical principles of the Declaration of Helsinki and its later amendments.

### Study Endpoint

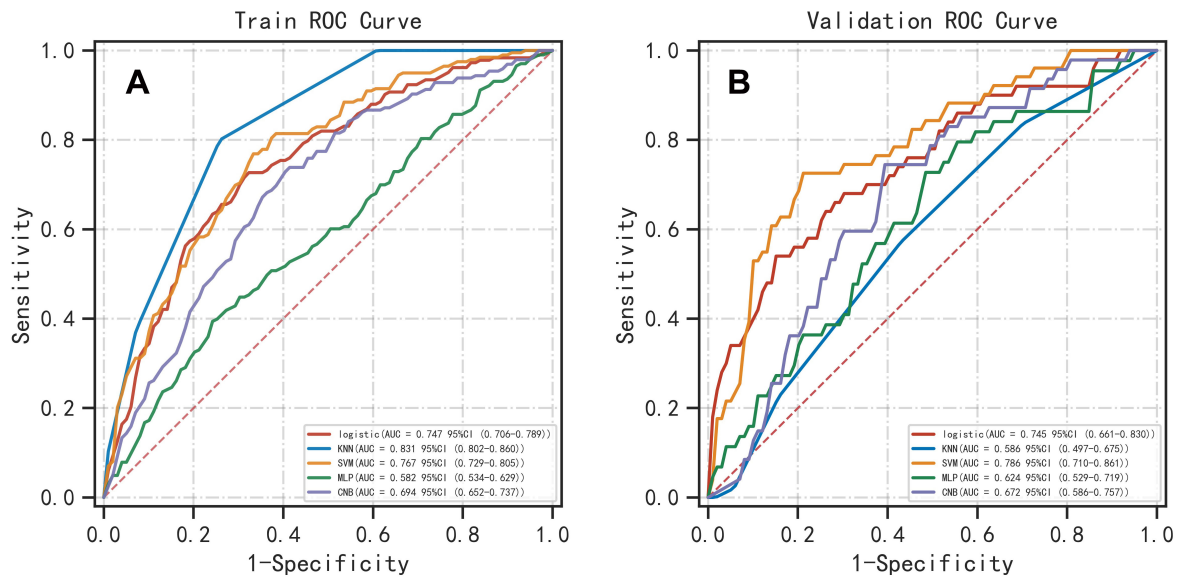
The primary outcome was POAF, defined as any episode of atrial fibrillation (AF) (occurrence of irregular heart rhythm, without detectable P waves) lasting more than 60 s in cardiac telemetry or requiring treatment (including antiarrhythmic drugs, such as amiodarone, or electrical cardioversion) during hospitalization. This standard was consistent with most previous studies [8]. All patients were on continuous electrocardiogram (ECG) monitoring at ICU for at least 48 h postoperatively. After the telemetry was removed, a standard 12-lead ECG was routinely recorded on the first and third day after leaving the ICU. Even without telemetry, episodes of AF were detected by a change in clinical status, which led to an immediate bedside electrocardiogram. The ECG and telemetry were double-checked by a cardiac surgeon and an electrophysiologist. If there was a disagreement, a third cardiologist was required to judge the ECGs.

### Surgical Classification

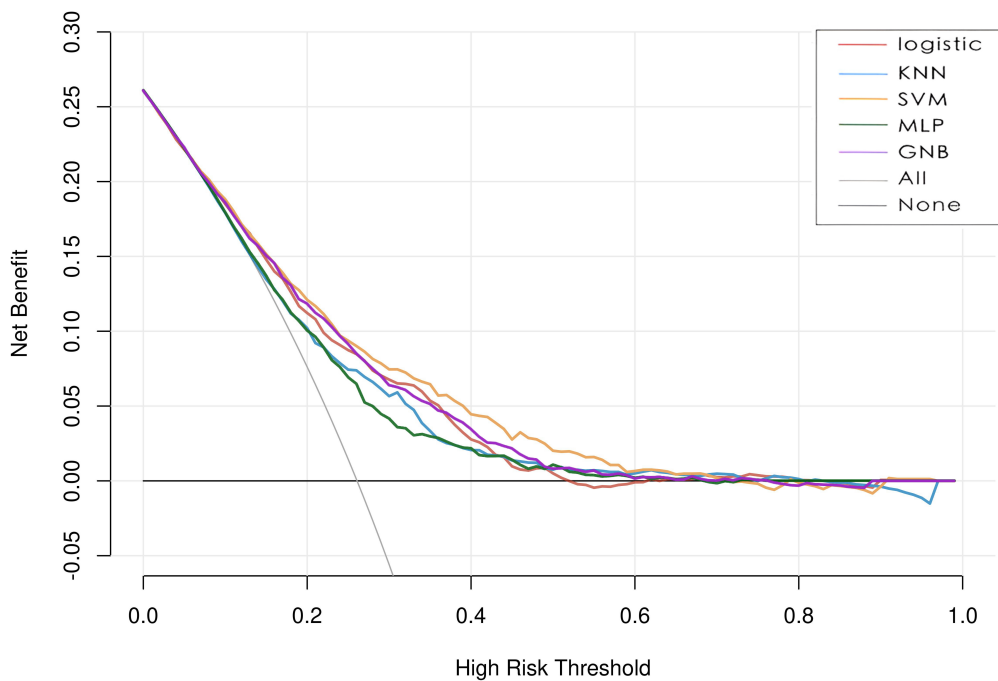
The surgery types comprised aortic valve replacement (AVR), aortic valvuloplasty (AVP), mitral valve replacement (MVR), mitral valvuloplasty (MVP), and combined aortic and mitral procedures. Concomitant tricuspid repair was not separately listed. Elective, urgent, and emergency procedures all were included. The full sternotomy surgery was performed by three surgeons, one of whom used only this approach, whereas the other two performed minimally invasive surgery (MIS) as well. MIS techniques in this study included partial median sternotomy, right anterolateral thoracotomy, surgery with thoracoscope assistance, a totally thoracoscopic approach, and the robotic-assisted approach. Cardiopulmonary bypass (CPB) was established with ascending aortic and bicaval venous cannulation in surgery performed with sternotomy. In MIS surgery, femoral arterial and venous cannulations were used to establish CPB.

### Statistical Analysis and Models Development

Before analysis, all the collected data from our hospital's electronic health records had been preprocessed and cleaned; no extreme or missing values were found. The normality of continuous variables in baseline characteristics was judged by the Shapiro–Wilks test. The Student's *t*-test was used for continuous variables, and the Mann–Whitney U test for non-normally distributed variables. Normally distributed continuous data were expressed as mean and standard deviation (SD), and non-normally distributed variables were presented as median (IRQ, interquartile range). Categorical variables were depicted as percentages and compared using the Pearson chi-squared test. Univariate analysis was used to select variables for multivariable logis-



**Fig. 2.** Area under the ROC curve showing the performance of different models in derivation (A) and validation (B) cohorts.



**Fig. 3.** Decision curve analysis for the different models in validation cohorts.

tic regression analysis with backward stepwise selection. Multivariate analysis was performed using stepwise logistic regression with a backward selection, where two-sided  $p$ -values  $< 0.05$  were considered an indication of statistical significance.

The whole patients' data randomly were split into a model training cohort and testing cohort, which accounted for 80% and 20% of patients, respectively. This process was repeated until the data in these two cohorts were equally distributed. Five types of ML algorithms were developed: logistic regression (Logistic), K-nearest neighbors (KNN), support vector machine (SVM), multiple-layer perceptron

(MLP), and Complement Naive Bayes (CNB). In the model training process, the training cohort was further randomly divided into five sub-groups called folds. Hyperparameters of each ML model were obtained for a set of four-folds, then a risk model was developed with these hyperparameters and evaluated with the withheld fold. This process is called fivefold cross-validation. Because there were five folds in the training cohort, five different combinations could be generated, and cross-validation could be performed five times to obtain five probabilities. The final risk model of each ML algorithm was the average of these five probabilities and was then applied to the testing cohort. The pre-

**Table 1. Demographic and clinical features of all patients grouped by POAF.**

Characteristics	Total (N = 847)	POAF (N = 243)	No POAF (N = 604)	<i>p</i> -value
Gender				0.686
Male, n (%)	511 (60.3)	144 (59.3)	367 (60.8)	
Female, n (%)	336 (39.7)	99 (40.7)	237 (39.2)	
Age, years, median (IQR)	55 (43–64)	62 (54–68)	53 (38–61)	<0.001
Smoking, n (%)	263 (31.1)	76 (31.3)	187 (31)	0.928
Body-mass index, kg/m <sup>2</sup> , median (IQR)	24.2 (21.8–26.6)	24.3 (21.4–26.8)	24.2 (22.0–26.6)	0.688
NYHA class III–IV, n (%)	312 (36.8)	111 (45.7)	201 (33.3)	<0.001
Chronic kidney disease, n (%)	36 (4.3)	17 (7)	19 (3.1)	0.012
Hypertension, n (%)	280 (33.1)	97 (40)	183 (30.3)	0.007
Ejection fraction <50%, n (%)	94 (11.1)	46 (19)	48 (7.9)	<0.001
Valve involved				0.179
Aortic, n (%)	280 (33.1)	83 (34.2)	197 (35.1)	
Mitral, n (%)	458 (52.3)	121 (49.8)	337 (53.3)	
Aortic + Mitral	109 (12.9)	39 (16)	70 (11.6)	
Redo-surgery, n (%)	95 (11.2)	41 (16.9)	54 (8.9)	<0.001
Minimal invasive surgery, n (%)	276 (32.6)	57 (23.5)	219 (36.3)	<0.001

Abbreviations: POAF, postoperative atrial fibrillation; NYHA, New York Heart Association.

dictive ability of each model was compared using the AUC value and the corresponding sensitivity and specificity. All statistical analyses were performed using Python (version 3.6, Free Software Foundation, Boston, MA, USA).

## Results

### Demographics Features

A total of 1232 adult patients underwent isolated valve surgery between January 1, 2018, and December 31, 2021, of whom 847 were enrolled in the study. Table 1 summarizes the basic demographic and surgical characteristics of all patients. The median age of the enrolled 847 eligible patients was 55 years (IQR 43–64). The ratio of male to female patients was 3:2. Mitral valve surgery composed 52.3% of the total cases, aortic surgery comprised 33.1%, and the fewest patients underwent double valve surgery.

### Univariate and Multivariate Analyses of POAF

In univariable analysis, age, NYHA class III–IV, four kinds of preoperative complications, two kinds of preoperative medicines, four kinds of preoperative laboratory tests, a few valves of echocardiogram and electrocardiogram, and some surgery-related factors were significantly associated with the occurrence of POAF ( $p < 0.05$ ), whereas most did not depict a significant correlation in multivariable logistic regression. Then, parameters with a  $p$ -value less than 0.1 in univariable analysis underwent multivariable analyses. The result shows that only old age (OR 1.05, 95% CI: 1.036–1.066), left atrium diameter (OR 1.055, 95% CI: 1.034–1.077), left ventricle ejection fraction (EF) less than 50%

(OR 1.532, 95% CI: 0.946–2.457), and volume of platelet transfusion during operation (OR 1.542, 95% CI: 1.109–2.142) were predictors of POAF (Table 2).

### Performance of Machine Learning Algorithms

Fig. 2A displays the training receiver operating characteristic (ROC) curves of the five ML algorithms for predicting POAF, and Fig. 2B presents the testing result. Among all models tested, SVM and Logistic displayed favorable discrimination ( $AUC \geq 0.7$ ) in both the training and testing subsets. In the training cohort, KNN revealed the highest AUC value with 0.831 (95% CI: 0.802–0.860), followed by SVM (0.767, 95% CI: 0.729–0.805), Logistic (0.747, 95% CI: 0.706–0.789). In the testing cohort, SVM demonstrated the highest AUC (0.786, 95% CI: 0.710–0.861), and KNN suffered a great decline in AUC (0.585, 95% CI: 0.497–0.675). We observed that SVM and MLP depicted a slight improvement in testing compared with training, whereas the others demonstrated opposite trends. Considering performances in both cohorts, SVM demonstrated the best predictive ability, with a sensitivity of 0.768, specificity of 0.695, and accuracy of 0.612 in the testing cohort (Table 3). Decision curve analysis was used to facilitate the comparison between different prediction models in the testing cohort. In Fig. 3, the x-axis represents a continuum of potential thresholds for POAF risk. The y-axis measures the net benefit that was calculated by subtracting the proportion of all patients who are false positive from the proportion who are true positive. The black line represents the assumption that no patients would suffer POAF after surgery, the thin grey line represents the assumption that all patients would suffer POAF after surgery. In this analysis, the SVM model also provided a larger net benefit

**Table 2. Univariate and multivariate logistic regression analysis of variables in predicting POAF in whole cohort.**

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Age	1.065 (1.053–1.081)	<0.001	1.05 (1.036–1.066)	<0.001
NYHA class III–IV	2.123 (1.389–3.244)	0.001	1.268 (0.917–2.108)	0.859
Preoperative complications				
Hypertension	1.528 (1.121–2.084)	0.007	1.024 (0.659–1.587)	0.914
Diabetes	2.034 (1.290–3.209)	0.002	1.699 (1.229–2.982)	0.511
Chronic kidney disease	2.316 (1.183–4.536)	0.014	1.762 (0.81–3.823)	0.150
Infective endocarditis	0.350 (0.177–0.692)	0.003	0.555 (0.248–1.138)	0.127
Preoperative medicines				
β-blockers	1.821 (1.338–2.478)	<0.001	1.003 (0.65–1.538)	0.990
Insulins	2.118 (1.288–3.483)	0.003	2.225 (0.769–6.769)	0.145
laboratory tests				
White blood cell	0.929 (0.864–0.998)	0.045	0.945 (0.841–1.054)	0.320
Platelet	0.994 (0.992–0.997)	0.036	0.995 (0.992–0.999)	0.096
Serum creatinine	1.002 (1.000–1.004)	0.020	1.001 (0.997–1.004)	0.820
Estimated glomerular filtration rate	0.983 (0.977–0.988)	0.001	1.005 (0.995–1.015)	0.332
Echocardiogram				
Left atrium diameter	1.071 (1.051–1.091)	<0.001	1.055 (1.034–1.077)	<0.001
Interventricular septum	2.418 (1.485–3.937)	0.001	1.246 (0.599–2.592)	0.555
Ejection fraction <50%	2.705 (1.749–4.182)	<0.001	1.532 (0.946–2.457)	0.042
Electrocardiogram abnormal T wave	2.141 (1.574–2.912)	0.001	1.487 (1.055–2.102)	0.024
Surgery related factors				
Emergency	2.225 (0.858–5.903)	0.099	1.3 (0.302–6.022)	0.726
Redo surgery	2.067 (1.336–3.200)	0.001	1.557 (0.93–2.595)	0.090
Minimal invasive surgery	0.739 (0.583–0.957)	0.001	0.092 (0.894–1.231)	0.394
Cardiopulmonary bypass time	1.003 (1.001–1.005)	0.007	1.004 (0.997–1.009)	0.017
Anesthesia time	1.171 (1.069–1.283)	0.001	1.046 (0.811–1.354)	0.699
Red blood cell transfusion	1.117 (1.063–1.173)	<0.001	1.053 (0.974–1.14)	0.197
Platelet transfusion	2.152 (1.611–2.847)	<0.001	1.542 (1.109–2.142)	0.010

Abbreviation: CI, confidence interval.

**Table 3. Predictive performance comparison of machine learning algorithms in the testing cohort.**

Methods	AUROC	Sensitivity	Specificity	Accuracy
Logistic	0.745	0.699	0.654	0.676
KNN	0.586	0.621	0.520	0.612
SVM	0.786	0.768	0.695	0.743
MLP	0.624	0.572	0.543	0.557
CNB	0.672	0.718	0.573	0.645

Abbreviations: Logistic, Logistic regression; KNN, K-nearest neighbors; SVM, Support vector machine; MLP, Multiple-layers perceptron, CNB, Complement Naive Bayes.

across the range of POAF risk compared with both the other scores (Fig. 3).

**Relative Important Variables in Machine Learning Algorithms**

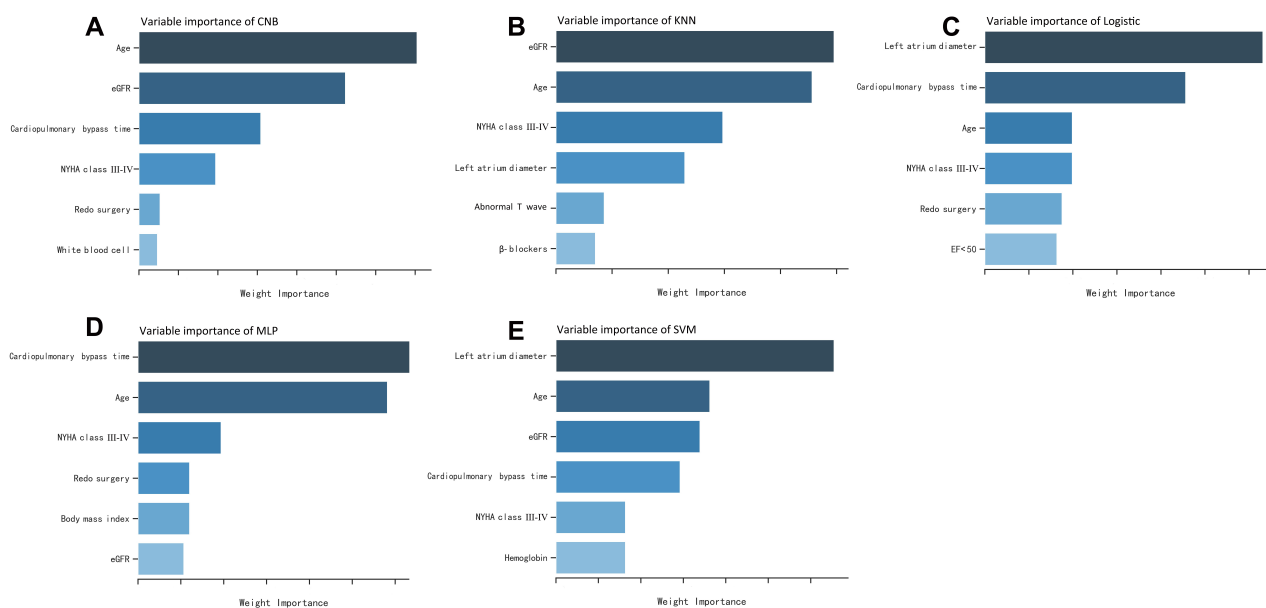
Fig. 4 depicts the relative importance of variables in each POAF-predicting ML algorithm. The descending order top variables in the SVM model are left atrium diameter, age, estimated glomerular filtration rate (eGFR), du-

ration of cardiopulmonary bypass (CPB), NYHA class III–IV, and preoperative hemoglobin. In addition to the above factors, the following variables were identified as important among other models: redo surgery, body mass index (BMI), EF <50%, abnormal T wave on preoperative ECG, and count of preoperative WBC.

**Discussion**

Postoperative atrial fibrillation (POAF) is the most common complication after adult valve surgery, with an incidence of approximately 40%–60%. Our study demonstrated an overall POAF rate of 28.7%, slightly lower than most previous studies. The younger age and lower comorbidity of our study population, as well as the exclusion of the combined valve and CABG procedure, which has a higher incidence of POAF, might account for this difference.

Although POAF is believed to be self-limiting and more than 90% patients with POAF converted to normal sinus rhythm (SR) before hospital discharge, most previous studies revealed that patients who developed POAF had in-



**Fig. 4. Relative importance ranking of each input variable for prediction of POAF.** (A) Complement Naive Bayes. (B) K-nearest neighbors. (C) Logistic regression. (D) Multiple-layers perceptron. (E) Support vector machine. Abbreviations: eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association.

creased risk of 30-days and 6-months mortality and were more likely to suffer from postoperative stroke, respiratory infections, and gastrointestinal dysfunction [9]. To recognize these high-risk patients preoperatively could enable prophylaxis against POAF and avoid exposing all the surgical patients to drug side effects, such as hypotension, bradycardia, or heart block. To achieve this goal, some preoperative risk models have been developed, most of which were designed to predict POAF after CABG. Only two widely used models can be applied to CABG and valve surgery: the POAF score and CHA2DS2-VASc score. The CHA2DS2-VASc score originally was developed to guide antithrombotic treatment in patients with AF and subsequently was found helpful in predicting POAF after cardiac surgery [5]. When applying these two models to valve patients, most studies found their effectiveness unsatisfactory, with most reporting an AUC ranging from 0.593 to 0.651 [4,6]. Partly due to some influencing factors, such as parameters of preoperative echocardiography, intraoperative variables were not collected in the model formulation process [4,10].

Machine learning (ML) is a branch of artificial intelligence that relates to computers' ability to learn from data, build recognition patterns, make predictions, and support decision-making [11]. The ML process can be based on a simple decision-making tree, such as if-then, to draw a conclusion, or deep learning algorithms that imitate the human brain by processing several types of data and making decisions. In this study, we sought to develop a prediction model for POAF after valve surgery based on preoperative and intraoperative information. Several ML algorithms that are commonly utilized in dealing with binary problems were applied to build the models; the SVM model

showed the strongest performance, with higher discriminative accuracy. Variables that the ML algorithms identified as the important contributing predictors of POAF have left atrium diameter (LAd), age, estimated glomerular filtration rate (eGFR), duration of cardiopulmonary bypass (CPB), NYHA class III–IV, preoperative hemoglobin, redo surgery, body mass index (BMI), EF <50%, and abnormal T wave on preoperative ECG.

Through multivariable logistic regression, we found that minimally invasive surgery was not significantly associated with POAF. However, we discovered that video-assisted thoracoscopic surgery (VATS) may reduce the incidence of POAF more than directly visualized surgery approaches, such as median/partial sternotomy, parasternal approach, and anterolateral thoracotomy. After conducting 1:1 propensity score matching, we found that VATS, including both robotic and thoracoscopic approaches, was associated with a lower incidence of POAF than directly visualized approaches (Table 4). The reduction in POAF incidence in VATS may be attributed to two potential factors. First, the video-assisted approach provides an improved and magnified surgical visual field, facilitating the suturing procedure and reducing blood oozing on the atrium and pericardium incisions. Second, in VATS, we employed an interrupted suture technique when closing the pericardial incision, which facilitates drainage of effusions. In contrast, the continuous suture technique was utilized in directly visualized approaches. These techniques could reduce fluid or thrombi in the pericardium after surgery, leading to fewer patients in the VATS group suffering from pericardial effusions postoperatively (5 versus 18,  $p < 0.01$ ). Previous studies have demonstrated that even a moderate amount of

**Table 4. Clinical data of propensity-matched patients.**

Variables	VATS (N = 70)	DVS (N = 70)	p-value
Age, years, median (IQR)	59 (51–65)	59 (51–66)	0.697
Body-mass index, kg/m <sup>2</sup> , median (IQR)	25.3 (22.9–27.2)	25.6 (23.6–28.0)	0.186
NYHA class III–IV, n (%)	23 (32.9)	25 (35.7)	0.706
Left atrium diameter, mm, median (IQR)	42 (37–48)	40 (35–46)	0.063
Ejection fraction <50%, n (%)	3 (4.3)	5 (7.1)	0.473
Redo-surgery, n (%)	8 (11.4)	13 (15.6)	0.062
Valve involved			0.074
Aortic	15 (21.4)	26 (31.7)	
Mitral	55 (78.6)	44 (62.9)	
Cardiopulmonary bypass time, min, median (IQR)	116 (84–179)	102 (72–151)	0.053
POAF, n (%)	13 (18.6)	22 (31.4)	0.008

Abbreviations: NYHA, New York Heart Association; VATS, video-assisted thoracoscopic surgery; DVS, directly visualized surgery.

fluid in the pericardium can trigger POAF [12,13]. This may help explain the lower incidence of POAF observed in the VATS group in our study.

While the definitive mechanism has remained elusive, most studies presume that POAF usually requires triggers and an atrium substrate change. Remodeling resulting from myocardial fibrosis and collagen deposition can lead to electrical conduction disturbances and makes the atrium vulnerable to ectopic firing and re-entry. Risk factors for atrium remodeling, such as age, LAd dilation, and left ventricular systolic dysfunction (EF <50%), are strongly associated with POAF, as reported by many existing studies [14]. Aging may also increase susceptibility to ischemia/reperfusion injury and oxidative stress. Yamashita *et al.*'s [15] meta-analysis demonstrated that POAF patients had a higher mean age by 5.45 years (95% CI: 4.29–6.61), a larger mean LAd of 2.01 mm (95% CI: 1.03–2.99), and a lower mean in EF by 3.01% (95% CI: 1.43–4.58), compared with patients without POAF.

Inflammation has been proposed as another main pathogenesis for POAF, resulting in apoptosis of cardiomyocytes and change in electrical activity, which can cause POAF. Inflammation-related risk factors include duration of CPB and white blood cell (WBC) count. A few studies have found that preoperative WBC counts were higher in POAF patients [16]. WBC was relevant with plasma levels of IL-2 and IL-6, which are important cytokines in mediating inflammatory responses. The use of CPB also can lead to ischemia-reperfusion injury, which enhances the risk of POAF. Some researchers found that an increase in sympathetic tone can lead to an increased heart rate and atrial ectopic activity, which are associated with the occurrence of POAF [17]. This finding demonstrates that using  $\beta$ -blockers to regulate the sympathetic system can influence the incidence of POAF [3].

Compared with previous studies that attempted to predict POAF after cardiac surgery, there were several advantages of our work. First, we focused on only valve surgery,

whereas most prior research involved CABG and other kinds of cardiac procedures. Several studies demonstrated that each kind of cardiac surgery had a different probability of POAF. Second, most types of surgical approaches were included in this research, such as sternotomy, partial sternotomy, right anterolateral thoracotomy, surgery with thoracoscope assistance, totally thoracoscopic approach, and the robotic-assisted approach. Furthermore, to the best of our knowledge, this is the very first study to develop a prediction model using ML algorithms for POAF, and our model demonstrated better performance than previous linear predictive models adopted by prior researchers. Finally, unlike previous predictive models that were mainly based on relatively few factors, a total of 123 potentially influential variables were enrolled in our studies, such as preoperative ECGs, intraoperative drugs, and volume of blood product transfusion. This shows the advantage of ML in processing a huge number of factors.

Unlike the studies that concentrated on different types of cardiac surgery, our predictive model was derived exclusively from valvular patients. The heterogeneity of pathophysiology, preoperative medications, co-morbidities, and certain intraoperative variables (with or without CPB, usage of inotropic drug, etc.) of different kind of cardiac surgery affects which parameters are relatively important for predicting POAF, which may explain why we found our models did not perform well in CABG, concomitant valve and CABG, or congenital heart surgery. The limitations of our study were: First, the inherent limitations of a retrospective study resulted in selection bias. Second, the sample size of the training cohort may not be sufficient for ML algorithms, which tend to yield better performance with more numerous cases. Third, though we demonstrated that the SVM algorithm had relatively better performance in predicting POAF, it would be beneficial for clinicians to visualize the working process of the model or make the model into a calculator with a specific forecast value using data. Finally, as all the patients were from a single medical in-

stitution, our results may not be generalizable. Therefore, future prospective validation based on a larger multicenter sample is still required.

## Conclusions

Machine learning algorithms may predict the occurrence of POAF after valve surgery, with better performances than traditional methods. Integrating both preoperative variables and intraoperative information is likely to improve the accuracy of the prediction. Large multicenter prospective trials are needed to validate this ML-based approach.

## Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

## Author Contributions

SZ designed the study, collected the data, and wrote the initial draft. HC analyzed the data and contributed to data presentation and visualization. YF, SJ made equal contributions to data collection. SJ revised the initial draft of the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

## Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the institutional review board of the Chinese PLA General Hospital (approval number S2022-360-01). Informed consent was waived by the ethics committee due to the observational nature.

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## Conflict of Interest

The authors declare no conflict of interest.

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