# Predicting New-Onset Postoperative Atrial Fibrillation in Cardiac Surgery Patients

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***Objective:*** **To derive a simple clinical prediction rule identifying patients at high risk of developing new-onset postoperative atrial fibrillation (POAF) after cardiac surgery.**

***Design:*** **Retrospective analysis on prospectively collected observational data.**

***Setting:*** **A university-affiliated cardiac hospital.**

***Participants:*** **Adult patients undergoing coronary artery bypass grafting and/or valve surgery.**

***Interventions:*** **Observation for the occurrence of new-onset postoperative atrial fibrillation.**

***Measurements and Main Results:*** **Details on 28 preoperative variables from 999 patients were collected and significant predictors ($p < 0.2$) were inserted into multivariable logistic regression and reconfirmed with recursive partitioning. A total of 305 (30.5%) patients developed new-onset POAF. Eleven variables were associated significantly with atrial fibrillation. A multivariable logistic regression model included left atrial dilatation, mitral valve disease, and age. Coefficients from the model were converted into a simple 7-point predictive score. The risk of POAF per score is: 15.0%, if 0; 20%, if 1; 27%, if 2; 35%, if 3; 44%, if 4; 53%, if 5; 62%, if 6; and 70%, if 7. A score of 4 has a sensitivity of 44% and a specificity of 82% for POAF. A score of 6 has a sensitivity of 11% and a specificity of 97%. Bootstrapping with 5,000 samples confirmed the final model provided consistent predictions.**

***Conclusions:*** **This study proposed a simple predictive score incorporating three risk variables to identify cardiac surgical patients at high risk of developing new-onset POAF. Preventive treatment should target patients $\geq$ 65 years with left atrial dilatation and mitral valve disease.**



***KEY WORDS: postoperative complication, cardiac surgery, atrial fibrillation, prediction rule***

THE POSTOPERATIVE PERIOD AFTER cardiac surgery is associated with a high incidence of new-onset atrial fibrillation, ranging from 23% after coronary artery bypass grafting (CABG) to 40% after combined valve and CABG procedures.[1] The peak incidence for the development of postoperative atrial fibrillation (POAF) is between the second and fourth postoperative days, with few initial POAF events occurring after a week.[2] POAF is associated with increased morbidity in the immediate postoperative period such as stroke, intra-aortic balloon pump use, infections, respiratory failure, renal failure, and prolonged length of hospital stay.[3,4] Long-term survival analyses have demonstrated an increased mortality in CABG[5,6] and aortic valve replacement[7] patients who developed POAF.[8] In a study involving 16,169 CABG patients registered in the Society of Thoracic Surgeons Adult Cardiac Surgery Database, a 25% mortality increase was found in patients who had POAF versus those who did not, after a mean follow-up period of 6 years.[9]

Many interventions have been proposed to prevent POAF, often resulting in decreased hospital cost and length of stay.[10–12] Most preventive measures involve medications to control heart rate or rhythm: Beta-blockers,[13–15] amiodarone,[16–19] diltiazem,[20,21] digoxin,[22] propafenone,[23,24] and sotalol.[25,26] Other therapies target anti-inflammatory mechanisms: HMG-CoA reductase inhibitors,[27–29] corticosteroids,[30] angiotensin-converting enzyme inhibitors,[31] angiotensin-receptor blockers,[32] n-3 fatty acids,[33–35] and naproxen.[36] Intraoperative interventions also have been proposed. Those include rate control by means of atrial pacing,[37,38] attenuation of the inflammatory response by performing off-bypass surgery,[39,40] leukofiltration,[41] adjusting cardioplegia delivery,[42] adding pulmonary vents,[43] and incising the pericardium to prevent pericardial effusions.[44]

Despite the evidence supporting the efficacy of prophylactic treatment for POAF, prevention protocols are not implemented routinely in many cardiac surgery centers.[45,46] Cited reasons for nonuse include the lack of convincing evidence, the complexity of some drug regimens, and the potential risks associated with the proposed drug regimens. The concern with complications and side effects associated with those prophylactic treatments could be alleviated by targeting only high-risk patients, thus achieving the

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best possible risk: benefit ratio of preventive therapy. Because most effective preventive therapies of POAF must be started before or during cardiac surgery, it is important to identify patients at moderate-to-high risk before surgery.[47]

Many models to identify high-risk patients for POAF have been proposed.[48–52] Most previous models used variables obtained intraoperatively[53] or postoperatively.[48,51,54–56] Not only are those models complex to use in clinical practice, but they are inappropriate for preoperative identification of patients at risk of POAF, as interventions need to be administered either preoperatively or intraoperatively to effectively prevent POAF. Other models included patients with pre-existing atrial fibrillation,[49,57] a subpopulation that probably should be given prophylaxis without need for a prediction model.

This study was, therefore, designed to develop simple clinical prediction rules to identify cardiac surgical patients at higher risk of developing new-onset POAF and to whom prophylactic treatment could be administered before surgery.

## MATERIALS AND METHODS

This observational study was approved by the Human Research Ethics board and conducted in a single tertiary center dedicated to cardiovascular disease. Data were extracted from a prospectively collected institutional perioperative database supplemented by extensive chart reviews. Chart reviews were performed by 8 individuals and 5% of the charts were audited by a second reviewer.

All patients undergoing nonemergent CABG and/or valve surgery from January 1, 2010 until December 31, 2010 were screened for inclusion in the study. Patients were excluded if they were $<18$ years of age, had any history of preoperative atrial fibrillation, or underwent ineligible procedures, including: Atrial fibrillation ablation, heart transplantation, pulmonary thromboendarterectomy, isolated thoracic aorta procedures, ventricular assist device insertion, extracorporeal membrane oxygenator insertion, and percutaneous valve replacements. Left atrial dilatation was defined as a left atrial size of $>41$ mm on the most recent echocardiogram or described as mild dilatation or greater. Age categorization was chosen based on clinical cut-offs. Mitral valve disease was described as either mitral stenosis or insufficiency, whichever condition was more severe. Mitral stenosis was graded as per published guidelines.[58] Regurgitant mitral valves were coded mild if described as 1-2+ and moderate-severe if 3-4+.[59]

The primary outcome was new-onset POAF defined as the onset of an irregularly irregular heart rhythm (as recorded on electrocardiogram or telemetry) requiring treatment from the completion of surgery until hospital discharge. Treatment could entail either pharmacologic (such as amiodarone) or electrical cardioversion. A list of preoperative risk factors for POAF obtained from literature review was shortened to 28, a priori, by an expert panel (2 cardiac anesthesiologists, 2 intensive care physicians, and a cardiac surgeon) as candidates for insertion into model derivation.

### Statistical Analysis

Statistical Analysis Software (SAS) 9.2 was used for all analyses except for recursive partitioning, which was done using KnowledgeSEEKER 7.6 (Angoss Toronto Canada 2012). All multilevel categoric variables were dichotomized when possible, if not they were simplified to clinically important levels. Continuous variables were reported with the range as well as mean and standard deviations. Categoric variables were presented in proportions and assessed for outliers by frequency tables and manual checks. Univariate analysis was performed using Pearson chi-square test or Fisher's exact test when applicable to test the association between the predictor and the primary outcome. A cut-off p value $< 0.2$ from the univariate analysis was chosen for inclusion into the multivariable logistic and recursive partitioning modelling.

The logistic regression model was derived by step-wise forward selection with a p value entry of 0.2 and removed if $p > 0.05$. A small portion of data was missing because of lack of echocardiogram reporting: Left ventricular systolic function (0.5%), right ventricular systolic function (3%), and left atrial size (4.9%). Sensitivity analyses were performed assuming the missing data were either all normal or all abnormal and compared to the model with complete data only. Discrimination of the models was assessed using the area under the curve of the receiver operating characteristic, the c-statistic with 95% confidence intervals. Assessment of model fit was tested using the Hosmer-Lemeshow goodness-of-fit. The odds ratio with 95% confidence limits and the beta coefficients for all variables in the final model were reported. A risk score was derived by dividing all the beta coefficients of the variables in the final model by the smallest beta coefficient.[60] The values were rounded to the nearest whole number and a total risk score was calculated for each patient in the study. This risk score was inserted into a logistic regression model with the original dataset to produce the probabilities of developing new-onset postoperative atrial fibrillation for each score. Internal validation of the final models was performed using bootstrapping. Five thousand bootstrap samples of equal size to the study population were selected with replacement. The mean and standard deviations for the average estimates of the beta coefficients were reported.

In addition to logistic regression, a different approach to modelling was explored to assess the consistency of the variables. Classification and regression trees methods were used to perform recursive partitioning, isolating predictors that would produce a prediction rule with the desired sensitivity and highest possible specificity. Chi-squared analysis was performed between the variables and the outcome, to divide individuals into groups of high and low risk for developing the outcome. The decision rules produced by this method then were eliminated if their sensitivity did not meet the lower limit cut-off of 80% for the 95% confidence interval. Considerations then were given to the variables within the rules, preferring those that were more clinically practical. The remaining candidate rules then had their specificities compared and the model with the highest specificity was favored. The chosen decision rule was applied to the entire cohort and a comparison between the predicted status of each patient with their actual status, with regard to postoperative atrial fibrillation, was made. This produced an estimate of the specificity and sensitivity of the prediction rule with 95% confidence intervals.

The sample size was calculated on the basis of previous studies, estimating the incidence of new-onset postoperative