

# Determinants of Post-Operative Atrial Fibrillation in 1613 Patients Undergoing Coronary Artery Bypass Grafting in the Statin Therapy in Cardiac Surgery (STICS) Trial

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## Introduction

Post-operative atrial fibrillation (POAF) occurs in 20-40% of patients in the first week after cardiac surgery, and is associated with longer hospital stay, higher stroke risk, and worse overall prognosis. The surgery-related inflammatory response has been strongly implicated in POAF pathogenesis; however, lower CRP levels resulting from perioperative rosuvastatin therapy in the Statin Therapy In Cardiac Surgery (STICS) randomized trial were not associated with a reduced incidence of POAF. Furthermore, POAF independently predicts subsequent clinical AF and as such may reflect the presence of a subclinical cardiomyopathic substrate. We tested this hypothesis by investigating determinants of POAF in 1613 patients who underwent isolated coronary artery bypass grafting in China in the STICS trial.

## Methods

Clinical data included age, sex, body mass index, medical history, medications, and type of surgery (on-pump vs off-pump). Blood taken prior to surgery was assayed for troponin I, N-terminal pro-brain natriuretic peptide (NT-proBNP), creatinine, low-density lipoprotein (LDL) cholesterol, and serum CD40 ligand. The biomarkers growth differentiation factor 15, interleukin-6, procalcitonin, and placental growth factor were measured at baseline and at 6 hours after surgery. Echocardiography evaluated left ventricular ejection fraction (LVEF) and left atrial (LA) size. POAF was detected by continuous Holter electrocardiographic monitoring for 5 days after surgery.

## Results

POAF occurred in 314 of 1613 patients (19%). As expected, age was the single strongest predictor of POAF (C-statistic 0.66 [95% CI 0.62-0.70]). After adjustment for age, NT-proBNP, LA size, Troponin, LVEF, sex, calcium-channel blocker use, and prior myocardial infarction were all significantly associated with POAF when assessed individually (all  $P < 0.05$ ). In multivariate analysis, a basic model incorporating only age, NT-proBNP, and LA size had a C-statistic of 0.69 (95% CI 0.66-0.73). This performance was not significantly different to that of models including all available variables, irrespective of whether baseline or post-surgery biomarker results were used (all C-statistics 0.71 [95% CI 0.68-0.75]; **Table 1**). The basic model numerically outperformed more complex risk prediction scores including CHARGE-AF (0.66, 95% CI 0.63-0.70; **Figure 1**), POAF score (0.64, 95% CI 0.61-0.68), CHA<sub>2</sub>DS<sub>2</sub>-VASc (0.60, 95% CI 0.57-0.63), and AF risk index (0.57, 95% CI 0.54-0.60).

## Conclusions

A basic model requiring only age, NT-proBNP, and LA size has good predictive value for POAF in this population, comparing well to more complex risk prediction scores. More broadly, these results suggest that systemic inflammation and perioperative myocardial injury may be less relevant to the pathogenesis of POAF than the effects of aging and cardiac structural and functional changes.

**Table 1: Joint relevance of characteristics to the odds of post-operative atrial fibrillation**

<b>Risk model</b>	<b>DF</b>	<b>Improvement in Fit compared with Null</b>	<b>C statistic (95% CI)</b>
Initial and final selected risk model			
Age and all variables †	33	147.46	0.711 (0.677, 0.745)
Age and all variables ‡	33	153.80	0.714 (0.679, 0.748)
Age and all variables §	33	151.51	0.713 (0.679, 0.747)
Age and all variables significant at the 5% level in age-adjusted models	8	124.27	0.698 (0.663, 0.732)
Incremental relevance of factors in final model			
Age	1	82.52	0.660 (0.624, 0.695)
Age and baseline ln NT-pro BNP	2	107.93	0.683 (0.648, 0.718)
Age, baseline ln NT-pro BNP and baseline left atrial size	3	118.10	0.692 (0.657, 0.726)

Abbreviations: CI, confidence interval; DF, degrees of freedom (i.e., numbers of terms in model);

† Models included growth differentiation factor 15, interleukin-6, procalcitonin, and placental growth factor at baseline.

‡ Models included growth differentiation factor 15, interleukin-6, procalcitonin, and placental growth factor at 6hr.

§ Models included the difference in growth differentiation factor 15, interleukin-6, procalcitonin, and placental growth factor from baseline to 6hr.

**Figure 1: Receiver operating characteristic (ROC) curves for models predicting risk of post-operative atrial fibrillation (AF) using a) a basic model containing age, baseline NT-proBNP and baseline left atrial size, b) the basic model including growth differentiation factor 15, interleukin-6, procalcitonin, and placental growth factor at 6hr, and c) CHARGE-AF score (excluding blood pressure).**