Electrophysiology

Implications of new-onset atrial fibrillation after cardiac surgery on long-term prognosis: A community-based study

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Background Postoperative atrial fibrillation (POAF) is a common complication after cardiac surgery. Data are lacking on the long-term prognostic implications of POAF. We hypothesized that POAF, which reflects underlying cardiovascular pathophysiologic substrate, is a predictive marker of late AF and long-term mortality.

Methods We identified 603 Olmsted County, Minnesota, residents without prior documented history of AF who underwent coronary artery bypass graft and/or valve surgery from 2000 to 2005. Patients were monitored for first documentation of late AF or death at >30 days postoperatively. Multivariate Cox regression models were used to assess the independent association of POAF with late AF and long-term mortality.

Results After a mean follow-up of 8.3 ± 4.2 years, freedom from late AF was less with POAF than no POAF (57.4% vs 88.9%, $P < .001$). The risk of late AF was highest within the first year at 18%. Univariate analysis demonstrated that POAF was associated with significantly increased risk of late AF [hazard ratio (HR), 5.09; 95% CI, 3.65-7.22] and long-term mortality (HR, 1.79; 95% CI, 1.38-2.22). After adjustment for age, sex, and clinical and surgical risk factors, POAF remained independently associated with development of late AF (HR, 3.52; 95% CI, 2.42-5.13) but not long-term mortality (HR, 1.16; 95% CI, 0.87-1.55). Conversely, late AF was independently predictive of long-term mortality (HR, 3.25; 95% CI, 2.42-4.35). Diastolic dysfunction independently influenced the risk of late AF and long-term mortality.

Conclusions Postoperative atrial fibrillation was an independent predictive marker of late AF, whereas late AF, but not POAF, was independently associated with long-term mortality. Patients who develop new-onset POAF should be considered for continuous anticoagulation at least during the first year following cardiac surgery. (Am Heart J 2015;170:659-68.)

Atrial fibrillation (AF) is a major public health problem. It is the most prevalent clinically important arrhythmia and portends a substantial risk of thromboembolism.[1,2] Because cardiovascular disease is the leading cause of death in the world, particularly in middle- and high-income countries,[3,4] the aging population has led to an increasing number of persons who will require a cardiac operation. A major complication of these operations is postoperative AF (POAF), which occurs in approximately 30% to 40% of patients.[5–7] Although this arrhythmia is generally considered to be an incidental and transient event,[8] previous clinical and experimental investigations have shown that AF is a progressive disorder.[9–11] It has been estimated that paroxysmal AF eventually progresses to permanent AF in 25% of patients over 5 to 10 years, with the majority of the patients having underlying heart disease.[10,12,13] Similar to paroxysmal AF, POAF is an associated disorder with an increased burden of cardiovascular comorbidities.[14,15] Likewise, POAF may logically be a risk marker of future AF. There are limited data on the predictive factors and pathophysiology of AF recurrence and long-term mortality of patients following cardiac surgery with cardiopulmonary bypass. Previous studies have yielded inconsistent results.[15–20] We hypothesized that POAF, which reflects the existence of underlying pathophysiologic factors,[14,21] is a predictive marker for development of late AF and long-term mortality.

The objective of this study was to systematically assess whether new-onset POAF after cardiac surgery was independently associated with late AF and long-term mortality in a large, community-based cohort.

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Material and methods

Basic study design

This study was approved by the Mayo Clinic Institutional Review Board. The study was conducted in Olmsted County,

Minnesota, which has an estimated 2014 population of 150,287; 86.2% of these residents are white. Population–based research is possible because medical care is mainly self-contained within the community. Data from all Olmsted County patients undergoing cardiac surgery, prospectively maintained in a clinical database, were retrospectively reviewed to investigate the relation between new-onset POAF after cardiac surgery and the risk of late AF and long-term mortality.

Patient population

This population-based cohort study involved the 752 patients in Olmsted County who had cardiac surgery during the index period of January 1, 2000, through December 31, 2005. For this investigation, inclusion criteria were residents of all ages with preoperative sinus rhythm (SR) who underwent isolated coronary artery bypass graft (CABG) or valvular repair or replacement (or some combination thereof) and survived for 30 days following the index operation. Patients with a preoperative history of AF, a Cox Maze or radiofrequency ablation procedure for atrial arrhythmia, ≥moderate mitral stenosis, and congenital heart disease were excluded. The final study cohort was 603 patients.

Echocardiography

Comprehensive echocardiography was performed before surgery according to a previously described protocol[14] in 363 patients (12 died within 30 days of surgery and were excluded). The following classification of diastolic function on echocardiography was defined:

Grade 0: normal left ventricular (LV) filling
Grade 1: impaired relaxation or mild diastolic dysfunction
Grade 2: pseudonormal or moderate diastolic dysfunction
Grade 3: restrictive LV filling or severe diastolic dysfunction

Definitions of exposure and outcome ascertainment

New-onset POAF was defined as AF occurring within 30 days of cardiac surgery based on documentation of AF episodes (≥30 seconds in duration) by continuous telemetry throughout hospitalization, electrocardiograms (ECGs), or Holter monitoring. All patients were monitored up to their last clinical visit, repeat cardiac surgery, or death. *Late AF* was defined as AF occurring after 30 days postoperatively from regular follow-up visits with ECGs or Holter monitoring. was defined as patients who died at >30 days following their index cardiac surgery and was determined through review of medical records and by querying the Social Security Death Index. Patients who died within 30 days after surgery were excluded (n = 16).

Statistical analysis

Categorical variables were expressed as numbers and percentages and continuous variables as mean ± SD and median (interquartile range [IQR]) as appropriate and compared with Pearson χ^2 or Fisher exact test. Continuous variables were compared with the Student *t* test for independent samples or the Wilcoxon rank sum test in the case of non-normally distributed data. Cox proportional hazards models were used to evaluate the association between POAF and late AF and, likewise, for long-term mortality after adjusting for potential confounding variables. The covariates included in the multivariable models were based on a priori knowledge and statistical evidence of a univariate association with late AF and, separately, long-term mortality. For each variable, hazard ratio (HR), 95% CI, and *P* value were provided. To account for missing diastolic function data and include all these subjects in the analysis, a dummy variable for "missing diastolic function" was included in all models, making it possible to impute a value for the missing diastolic function variable without any effect on the analysis. Assumptions for proportional hazards models were tested by including main effects and product terms of covariates and logarithmic-transformed time factor, and it was found that the null hypothesis that the assumptions were not violated was accepted. Ties were handled using the Efron method. Kaplan-Meier analyses and log-rank tests were used to compare event-free survival among those with versus those without POAF. Age-adjusted effect of POAF and diastolic function grade on late AF and long-term survival was assessed with an age-stratified, weighted Kaplan-Meier and log-rank procedure, with weights reflecting the age stratum proportions in the overall sample.[22] All *P* values were based on 2-sided tests, and values of .05 or less were considered statistically significant. All statistical analyses were performed using SAS software version 9.3 (SAS Institute Inc, Cary, NC).

Results

Baseline characteristics

The baseline characteristics of the study population are summarized in Table I. Follow-up was complete for all patients. The patients were observed for a maximum duration of 14.7 years (mean, 8.3 ± 4.2 years). The mean age of the overall study population was 65.6 ± 13.2 years, and 70.4% of study patients were male. At the time of the operation, all patients were in SR and had no documented history of prior AF. New-onset POAF developed in 226 patients (37.5%) and lasted a median (IQR) of 2 (1-3) days. Among the patients who had POAF, 95% (n = 215) were detected during the index hospitalization and 5% (n = 11) within 30 days after hospital discharge. In general, POAF either spontaneously converted to SR without (33.2% [n = 75]) or with (50.0% [n = 112]) antiarrhythmic drug therapy (95.5% [n = 107] received amiodarone) or was cardioverted electrically (16.8% [n = 38] to SR). Only 1 (0.4%) patient was discharged in AF and stayed in persistent AF on follow-up.

Actuarial analysis

Late AF. During the follow-up period, late AF developed in 49.3% (n = 108) of patients with POAF versus 13.6%