Increased late mortality after coronary artery bypass surgery complicated by isolated new-onset atrial fibrillation: A comprehensive propensity-matched analysis

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Objectives: The association of new-onset postoperative atrial fibrillation (POAF) and late death after coronary artery bypass grafting (CABG) has been confounded by the frequent concomitant serious complications that co-occur with POAF. We aimed to define the magnitude and time dependence of the effect of isolated POAF on late survival after uncomplicated CABG to comprehensively account for comorbidity and perioperative confounding factors.

Methods: Nonsalvage CABG patients with no history of AF, no concomitant aortic or valvular surgery, and no perioperative complications other than POAF were studied (n = 6305). Patients were divided into AF (n = 1211, 68 years old, 72% male) and no-AF (n = 5094, 63 years old, 70% male) groups. Propensity matching was done using 55 patient variables, including coronary grafts, completeness of revascularization, and transfusion data. The AF effect was quantified using time-segmented hazard ratios by Cox regression analysis.

Results: Single (1-to-1), double (1-to-2), and triple (1-to-3) propensity matching of the AF and no-AF was achieved for 1196, 993, and 719 cases, respectively. The AF group showed significantly worse, yet time-varying, 0- to 18-year survival: 0 to 1 year, HR, 1.18 (95% confidence interval, 0.77-1.81); 1 to 6 years, HR, 1.37 (95% confidence interval, 1.12 to 1.67); and 6 to 17 years, HR, 1.25 (95% confidence interval, 1.05 to 1.49).

Conclusions: Isolated POAF was associated with a time-varying increase in mortality after CABG. Given these findings and the high incidence of POAF, efforts to reduce POAF should be pursued to potentially improve resource usage, morbidity, and mortality. (J Thorac Cardiovasc Surg 2014;148:1860-8)

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Supplemental material is available online.

New-onset postoperative atrial fibrillation (POAF) is a frequent complication of cardiac surgery (10%-65%)[1-6] and has been associated with increased morbidity, in-hospital mortality, and greater resource usage.[1-10] Imbalance of the autonomic nervous system, enhanced inflammation, ischemia, and a predisposing anatomic substrate has been implicated in PAOF; however, the exact pathophysiology of POAF is poorly understood. The incidence of POAF after coronary artery bypass grafting (CABG; 15%-40%) has reportedly been predicted by patient demographics, including older age, lower ejection fraction, hypertension, heart failure, prolonged cardiopulmonary bypass, enlarged left atrium, perioperative medications, and enhanced inflammatory and oxidative stress.[7-10]

A number of recent studies have extended the adverse effects of POAF after CABG to include significantly worse late mortality.[2,9,11-16] If true, this finding is of substantial clinical importance, given the high incidence of POAF; however, the specific mechanism by which an ostensibly limited perioperative arrhythmia, such as POAF, affects long-term survival is unclear. The available evidence on this POAF–late mortality association has been limited by the nonuniformity of the analyses and findings and/or incomplete accounting for known determinants of late mortality after CABG. No studies, thus far, account for (1) extent of arterial grafting and (2) completeness of coronary revascularization.[17-22] Furthermore, homologous blood product transfusion, which has been notably more frequent in patients with a greater likelihood of POAF and has been identified as a predictor of late mortality has also been largely ignored in studies of the effects of

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Abbreviations and Acronyms

AF	= atrial fibrillation
AF group	= isolated POAF without other complications
AF/C group	= POAF and other complications
no-AF group	= no POAF or any other postoperative complication
no-AF/C group	= no POAF but other complications
CABG	= coronary artery bypass grafting
CI	= confidence interval
HR	= hazard ratio
HR_t	= time-segmented HR
POAF	= postoperative atrial fibrillation

POAF.[23-25] In addition, POAF has frequently been associated with other serious postoperative complications. Consequently, the interplay between these nonarrhythmic complications and POAF might have confounded the independent effects of these conditions on operative and, possibly, late death.[2,8,9,11] Separating the late effects of POAF and concurrent complications is difficult, and studies, thus far, have either ignored this[13,26] or have relied on multivariate Cox regression modeling to account for some, but not all, such complications.[2,9,11,14,27] Finally, the potentially time-varying POAF effect on late mortality, its duration, and the period of greatest risk has not been described.

Within this construct, we reasoned that if POAF independently leads to increased late CABG mortality, it should do so even (1) in the absence of other nonarrhythmic postoperative complications, and (2) after more comprehensive adjustment for other known pre-, intra-, and postoperative predictors of late survival. Accordingly, we investigated the POAF–late CABG survival association in a manner that avoids these limitations by more comprehensive accounting of patient variables, operative and grafting details, transfusion status, and, most importantly, by excluding patients with other complications.

METHODS

The present investigation was a retrospective analysis of a prospectively collected data from the Society of Thoracic Surgeons Adult Cardiac Surgery National Database. The Mercy Saint Vincent Medical Center (Toledo, Ohio; 1994-2007) institutional review board approved our study. Data collection was performed in compliance with the Society of Thoracic Surgeons Database definitions and criteria and did not involve an additional review of the hospital records or interviewing the patients; thus, the informed consent requirement was waived.

Patients

Patients undergoing isolated CABG from 1994 to 2007 were included in the present analysis. CABG patients with concurrent coronary or carotid reconstruction were also included. Patients were excluded in the case of concomitant valvular, congenital cardiac or aortic surgery, a documented history of preoperative atrial fibrillation (AF) or atrial flutter, or emergency salvage status. A total of 7610 patients qualified for inclusion, and these patients were subsequently grouped as follows: (1) 5094 patients, who had not developed POAF or any other postoperative complication (no-AF; control group); (2) 1211 patients with isolated POAF without other complications (AF; study group); (3) 832 patients without POAF but who had developed other complications (no-AF/C); and (4) 473 patients, who had developed POAF and other complications (AF/C). To mitigate any potential confounding effects of concurrent non–rhythm-related perioperative complications on long-term survival, the subcohort of patients without any other perioperative complications, aside from POAF, was selected as the principal focus of the present investigation. Time 0 was defined as the time of discharge. In-hospital deaths were considered the same as patients with complications and were therefore excluded from the AF and no-AF groups. POAF was defined, as per the Society of Thoracic Surgeons Database, as the occurrence of POAF or atrial flutter requiring treatment (ie, β-blockers, calcium channel blockers, amiodarone, anticoagulation, or cardioversion) throughout hospitalization or at readmission within 30 days postoperatively. Telemetry was used in 100% of the patients during hospitalization.

Surgery

Our surgical techniques have been previously reported.[17,19] Cardiopulmonary bypass (96%) and aortocoronary grafting (97%) were used in a large majority of patients. Evidence-based critical pathways were used and periodically updated, in compliance with emerging data documented to optimize outcomes, improve care, or decrease resource usage. Treatment of POAF, if it occurred, is described in the Online Data Supplement. All efforts were made to discharge patients in a normal sinus rhythm. Patients discharged in rate-controlled AF were routinely discharged with warfarin, unless contraindicated. The database is not granular enough to derive the subset of patients with POAF discharged in a non–sinus rhythm.

Perioperative Medications

Aspirin and β-blocker use was consistent throughout the 1994 to 2007 study period. In all patients, β-blockers were routinely administered orally until the morning of surgery and, in stable patients, were reinstituted on postoperative day 1. Accordingly, the point of β-blocker withdrawal (if any) was minimized in the present series of patients. An angiotensin-converting enzyme inhibitor was used routinely in patients with normal renal function, including those who had been taking 1 preoperatively, who had a history of congestive heart failure, or who had a low ejection fraction (<35%), if hemodynamically tolerated (systolic blood pressure >100 mm Hg) in the early phases of the study period and routinely in the later phase of the study period in compliance with the practice guidelines. Aspirin (325 mg by way of a nasogastric tube) was always given to patients on arrival at the cardiovascular intensive care unit and was decreased to 162 mg orally daily on postoperative day 1. Amiodarone (intravenous or orally), once approved for clinical use, was routinely used after the onset of AF, including intraoperatively. Starting in July 1999, prophylactic amiodarone was used routinely in all patients (200 mg daily by mouth started on postoperative day 1). Before the availability of amiodarone, quinidine and/or procainamide, in conjunction with calcium channel antagonists, were used to treat POAF.

Follow-up

All-cause mortality was secured from the cardiothoracic surgery follow-up data and verified from scheduled searches of the US Social Security Death Index database (available at: http://ssdi.genealogy.rootsweb.com), last performed in November 2011. The follow-up period was 56 (minimum) to 214 (maximum) months.