Duration of Postoperative Atrial Fibrillation After Cardiac Surgery Is Associated With Worsened Long-Term Survival

Martin I. Sigurdsson, MD, PhD, Nicholas T. Longford, PhD, Mahyar Heydarpour, PhD, Louis Saddic, MD, PhD, Tzuu-Wang Chang, PhD, Amanda A. Fox, MD, MPH, Charles D. Collard, MD, Sary Aranki, MD, Prem Shekar, MD, Stanton K. Shernan, MD, Jochen D. Muehlschlegel, MD, MMSc, and Simon C. Body, MBChB, MPH

Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; Division of Medicine, Imperial College, London, United Kingdom; Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center, Dallas, and Division of Cardiovascular Anesthesia, Texas Heart Institute, Baylor St. Luke's Medical Center, Houston, Texas; and Division of Cardiac Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts

Background. **Studies of the effects of postoperative atrial fibrillation (poAF) on long-term survival are conflicting, likely because of comorbidities that occur with poAF and the patient populations studied. Furthermore, the effects of poAF duration on long-term survival are poorly understood.**

Methods. **We utilized a prospectively collected database on outcomes of cardiac surgery at a large tertiary care institution between August 2001 and December 2010 with survival follow-up through June 2015 to analyze long-term survival of patients with poAF. In addition, we identified patient- and procedure-related variables associated with poAF, and estimated overall comorbidity burden using the Elixhauser comorbidity index. Survival was compared between patients with poAF (n = 513) and a propensity score matched control cohort, both for all patients and separately for subgroups of patients with poAF lasting less than 2 days (n = 218) and patients with prolonged poAF (n = 265).**

Results. **Patients with poAF were older and had a higher burden of comorbidities. Survival was significantly worse for patients with poAF than for the matched control group (hazard ratio 1.43, 95% confidence interval: 1.11 to 1.86). That was driven by decreased survival among patients with prolonged poAF (hazard ratio 1.97, 95% confidence interval: 1.37 to 2.80), whereas survival of patients with poAF for less than 2 days was not significantly different from that of matched controls (hazard ratio 0.91, 95% confidence interval: 0.60 to 1.39).**

Conclusions. **After close matching based on comorbidity burden, prolonged poAF is still associated with decreased survival. Therefore, vigilance is warranted in monitoring and treating patients with prolonged poAF after cardiac surgery.**

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Postoperative atrial fibrillation (poAF) is observed in 26% to 32% of patients after isolated coronary artery bypass graft (CABG) surgery, and 30% to 50% of patients after isolated valve or combined valve and CABG surgery [1]. Several clinical risk factors for poAF have been identified, including older age [2, 3], male sex [2], and obesity [4]. Comorbidities such as history of prior atrial fibrillation (AF) [5], hypertension [3], congestive heart failure [5], chronic obstructive lung disease [5], and chronic kidney disease [6] have also been associated with poAF. Furthermore, valve repair or replacement and an increased aortic cross-clamp time also contribute to an increased risk of poAF [2, 5]. More recently, several genetic variants associated with ambulatory AF have also been associated with the risk of poAF, indicating a genetic predisposition to poAF [7, 8]. Therefore, poAF remains a complex disorder associated with risk factors of numerous etiologies.

An association between the occurrence of poAF and higher long-term mortality for patients with poAF has been reported [2, 9, 10], but not consistently [11], and seems to vary depending on type of surgery [12]. Many of these studies, however, are retrospectively designed and have a relatively short observation time. Furthermore,

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Address correspondence to Dr Body, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115; email: scbody@partners.org.

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practices controlling for confounding variables associated with both poAF and long-term mortality vary widely. The majority of these studies only control for variables related directly to the cardiac surgical procedure and omit quantification of important aspects of the overall health of the patient, including cancer and neurologic comorbidities that can also be associated with both poAF and mortality. This overall comorbidity burden can be quantified using indices that have high correlation with both short-term and long-term outcomes over a wide range of populations and conditions [13–16].

We investigated the long-term survival of patients having poAF after cardiac surgery with adjustments for the validated Elixhauser index for overall quantification of preoperative comorbidity burden and also with adjustments for clinical variables associated with poAF or worse overall survival. Propensity score matching was also performed to minimize confounder effects. We hypothesized that both the occurrence of poAF after heart surgery and its duration were associated with worse long-term survival, even after adjustment for patient characteristics, overall patient comorbidity burden, and procedure-specific variables associated with both poAF and worse long-term mortality.

Material and Methods

Patients and Clinical Variables

We analyzed a prospective cohort of 1,712 cardiac surgical patients from the Identification of Genomic Predictors of Adverse Events After Cardiac Surgery (CABGGenomics)/Perigren study (http://clinicaltrials.gov/show/NCT00281164), enrolled between August 2001 and December 2010 at Brigham and Women's Hospital, Boston, Massachusetts. We included study variables for occurrence of AF, hospital diagnoses, and mortality. Patients with a baseline hematocrit less than 25% and patients who had undergone bone marrow transplant were excluded from enrollment in the primary cohort. The study protocol was approved by the Institutional Review Board, and all patients provided written informed consent.

Included patients were not in AF on the day of surgery but inclusion of patients with a prior self-reported history of AF was permitted. We defined poAF as any episode of AF of any duration diagnosed by treating clinicians using electrocardiography or telemetry, occurring postoperatively during the primary surgical hospitalization. Patients were monitored for the onset of poAF until postoperative day 7 or until hospital discharge if hospital discharge occurred before postoperative day 7 [8]. For patients in whom poAF developed, the first day and the last day that poAF occurred (continuous or intermittent poAF during the 7 days) was registered, and the interval between these times was reported as poAF duration. After studying the distribution of poAF duration and before survival analysis, patients were further classified into two equal-sized subgroups: (1) duration of poAF less than 2 days; or (2) duration of poAF 2 days or longer, or poAF present at

Table 1. Patient Characteristics

Characteristics	No PoAF (n = 1,196)	PoAF (n = 513)	*p* Value
Age, years			
<50	111 (9)	16 (3)	…
50–59	335 (28)	69 (13)	…
60–69	390 (33)	161 (31)	…
70–79	297 (25)	194 (38)	…
>85	63 (5)	73 (14)	<0.001
Female	273 (23)	106 (21)	0.36
Body mass index, kg/m^2	29.4 ± 5.5	29.1 ± 5.6	0.45
Medical history			
Prior atrial fibrillation	83 (7)	64 (12)	<0.001
Hypertension[a]	855 (72)	413 (81)	<0.001
Diabetes mellitus	403 (34)	162 (32)	0.42
Myocardial infarction	463 (39)	216 (42)	0.21
COPD	55 (5)	25 (5)	0.89
ECI score			
0–3	464 (39)	142 (28)	…
4–5	519 (43)	229 (45)	…
6–12	213 (18)	142 (28)	<0.001
Preoperative assessment			
Creatinine >1.5 mg/dL	75 (6)	38 (7)	0.45
LVEF < 40%[a]	144 (13)	66 (14)	0.85
Preoperative medications			
ACE/AR inhibitors[a]	550 (46)	249 (48)	0.38
Aspirin	945 (79)	390 (76)	0.19
Beta-blocker	929 (78)	411 (80)	0.29
Calcium-channel inhibitor[a]	159 (13)	82 (16)	0.17
Diuretic	281 (23)	146 (28)	0.03
Statin	915 (77)	375 (73)	0.15
Operative characteristics			
CPB duration, minutes	110 ± 46	123 ± 60	<0.001
CABG only	1,055 (88)	415 (81)	…
Any valve surgery	141 (12)	98 (19)	<0.001
Aortic valve surgery	81 (7)	59 (12)	0.002
Replacement	66 (6)	48 (9)	0.005
Other	15 (1)	11 (2)	0.25
Mitral valve surgery	65 (5)	42 (8)	0.04
Repair	27 (2)	22 (4)	0.03
Replacement	22 (2)	11 (2)	0.82
Other	16 (1)	9 (2)	0.66
Tricuspid valve surgery	14 (1)	4 (2)	0.61
Replacement	4 (0.3)	1 (0.2)	1.00
Repair	4 (0.3)	1 (0.2)	1.00
Other	6 (0.5)	2 (0.4)	1.00
Pulmonary valve			
Reconstruction	1 (0.1)	0 (0.0)	1.00
Ablation/maze	27 (2)	8 (2)	0.45

[a] Variable contains 1 or more patients with missing data.

Values are n (%) or mean ± SD.

ACE = angiotensin-converting enzyme; AR = angiotensin receptor; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; CPB = cardiopulmonary bypass; ECI = Elixhauser comorbidity index; LVEF = left ventricular ejection fraction; PoAF = postoperative atrial fibrillation; SD = standard deviation.