Perioperative heart-type fatty acid binding protein levels in atrial fibrillation after cardiac surgery

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BACKGROUND Postoperative atrial fibrillation (POAF) is common and associated with poor outcomes. Perioperative ischemia can alter arrhythmic substrate.

OBJECTIVE To demonstrate an association between perioperative measurements of heart-type fatty acid binding protein (HT-FABP), a sensitive marker of ischemic myocardial injury.

METHODS Blood samples from 63 inpatients undergoing coronary artery bypass surgery, valve surgery, or both were obtained before and up to 4 days after surgery. Continuous telemetry monitoring was used to detect POAF. Fifty-nine patients had at least 3 HT-FABP measurements. The relationship of enzyme-linked immunosorbent assay-measured HT-FABP with POAF was assessed by using joint logistic regression adjusted for age and surgery type.

RESULTS Thirty-five patients (55%) developed POAF; these were, on average, older (69.3 ± 10 years vs 60 ± 11 years; $P = .0019$), with a higher prevalence of heart failure (43% vs 17%; $P = .034$), chronic obstructive lung disease (26% vs 4%; $P = .017$), preoperative calcium channel blocker use (29% vs 7%; $P = .031$), and more likely to undergo combined surgery (21% vs 11%, $P = .049$). The joint age- and coronary artery bypass surgery-adjusted model revealed that postoperative but not preoperative HT-FABP levels predicted POAF (coefficient 1.9 ± 0.87; $P = .03$). Longer bypass time, prior infarction, and worse renal function were all associated with higher postoperative HT-FABP.

CONCLUSIONS A greater rise of HT-FABP is associated with atrial fibrillation after cardiac surgery, suggesting that ischemic myocardial damage is a contributing underlying mechanism. Interventions that decrease perioperative ischemic injury may also decrease the occurrence of POAF.

KEYWORDS Atrial fibrillation; Postoperative; Biomarker; Ischemia; CABG; Valve surgery

ABBREVIATIONS **AF** = atrial fibrillation; **CABG** = coronary artery bypass grafting; **HT-FABP** = heart-type fatty acid binding protein; **PAC** = premature atrial complex; **POAF** = postoperative atrial fibrillation; **TnT** = troponin T

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Atrial fibrillation (AF) occurs in up to 60% of the patients undergoing coronary artery bypass grafting (CABG) or valve surgery[1,2] and is associated with poor outcomes and increased costs.[3] The mechanisms underlying postoperative atrial fibrillation (POAF) are poorly understood, and current prophylactic medications are empiric and lack reliable efficacy.[4] Paired with undesirable adverse effects from such medications,[5–8] routine application is currently not employed. Perioperative ventricular and atrial ischemia changes arrhythmic substrate directly on a cellular level and indirectly via inflammation and myocardial strain. To better elucidate the pathophysiology of POAF, we hypothesized that a greater rise of heart-type fatty acid binding protein (HT-FABP), a sensitive biomarker of ischemic myocardial damage,[9,10] would be associated with POAF in patients undergoing cardiac surgery.

Patients and methods

Patients

From November 2009 through June 2010, 71 inpatients were prospectively enrolled in our study. Three patients died

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before they went to surgery; 1 patient refused participation after signing the consent form; and 4 patients were treated with percutaneous coronary intervention instead of CABG after enrollment into the study, leaving 63 patients in sinus rhythm at the time of surgery and without antiarrhythmic drug therapy, who were prospectively followed until hospital discharge. Only 1 patient had a history of AF. Because we enrolled hospitalized patients only, there was a relatively high prevalence of cardiac and noncardiac comorbidities, many of which are known risk factors for POAF (Table 1). Patients were predominantly white (94%), males (63%), and underwent isolated CABG (n = 33). However, isolated valve surgery (n = 14) and combined CABG plus valve surgery (n = 16) were represented as well. Among those, 21 patients underwent aortic valve replacement, 5 mitral valve replacement, and 6 mitral valve repair.

Patient data

Epidemiologic, cardiac, and noncardiac clinical and procedural characteristics were prospectively collected. The Cleveland Clinic Institutional Review Board approved the study, and informed consent was obtained from all participants.

Definition and ascertainment of POAF

POAF was prospectively defined as any episode of AF or atrial flutter (there was none) after surgery and before discharge, lasting for at least 5 minutes. AF was detected by continuous telemetry monitoring throughout the hospital stay, and the presence of AF was confirmed by a cardiologist.

Blood sample processing and laboratory testing methods

Venous blood samples were obtained at prespecified equal intervals in ethylenediaminetetraacetate plasma tubes and serum tubes prior to surgery (mean interval to surgery 1.9 days, 95% confidence interval 0.99–2.75 days) and on first (0.99 ± 0.18 days), second (2.01 ± 0.14 days), third (3.02 ± 0.16 days), and fourth (4.01 ± 0.16 days) day after surgery. Plasma tubes were kept on ice immediately after blood draw and, together with serum tubes, centrifuged at 4°C and 3000 rpm for 20 minutes. Plasma and serum aliquots were obtained immediately after and stored at −80°C. HT-FABP levels were measured by using enzyme-linked immunosorbent assay (Cell Sciences, Canton, MA). Troponin T (TnT) was measured as part of routine care only on postoperative day 1 in our core laboratory by using an electrochemiluminescence immunoassay performed on a Roche E170 modular analytics immunoassay analyzer.

Statistical analysis

Because distribution of HT-FABP levels was highly skewed, a logarithmic transformation was used, resulting in a near-normal distribution. To account for a variable number of measured data points between patients, we compared biomarker levels of patients with and without AF in 4 groups (E-Table 1 in the Appendix). After exclusion of patients with only 2 data points (n = 4; group A in E-Table 1), we created 3 logistic regression models with common regression parameters and different intercepts for each model (a joint shared

Table 1

Variable	n (%) or mean ± SD			
	All patients (n = 63)	POAF (n = 35)	POAF (n = 28)	*P*
Demographic				
Age (y)	65 ± 12	69 ± 11	60 ± 11	.0019
Sex: Female	23 (37)	14 (40)	9 (32)	.52
Caucasian race	59 (94)	34 (97)	25 (89)	.2
Cardiac morbidity				
Heart failure	20 (32)	15 (43)	5 (18)	.034
Aortic valve stenosis	16 (25)	12 (34)	4 (14)	.07
Left ventricular ejection fraction (%)	46 ± 13	46 ± 14	47 ± 11	.89
Left atrial volume (mL)	41 ± 25	41 ± 23	47 ± 28	.3
Noncardiac comorbidity				
COPD	10 (16)	9 (26)	1 (1.6)	.017
Diabetes mellitus	21 (33)	10 (29)	11 (39)	.37
Hypertension	51 (81)	30 (86)	21 (75)	.28
Preoperative creatinine	1.1 ± 0.42	1.16 ± 0.41	1.08 ± 0.43	.19
Medication use				
ACE inhibitors	32 (51)	20 (57)	12 (43)	.26
Angiotensin receptor blocker	11 (17)	7 (20)	4 (14)	.55
Beta-blockers	51 (81)	29 (83)	22 (79)	.94
Calcium channel blockers	12 (19)	10 (29)	2 (7.1)	.031
Statins	54 (86)	30 (86)	24 (86)	1
Procedure				
Isolated CABG	33 (52)	14 (40)	19 (68)	.028
Isolated valve surgery	16 (25)	10 (29)	6 (21)	.52
CABG and valve surgery	14 (22)	11 (31)	3 (11)	.049

ACE = angiotensin-converting enzyme; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; POAF = postoperative atrial fibrillation; SD = standard deviation.