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Cardiac Surgery

Diastolic Dysfunction in Patients Undergoing Cardiac Surgery

A Pathophysiological Mechanism Underlying the Initiation of New-Onset Post-Operative Atrial Fibrillation

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Objectives Our goal was to investigate whether left ventricular (LV) diastolic dysfunction was an important pathophysiological mechanism underlying the initiation of new-onset post-operative atrial fibrillation (POAF).

Background Atrial fibrillation is a common complication after cardiac surgery. However, the precise mechanism underlying its development remains poorly understood. Pre-existing alterations of myocardial diastolic function may predispose patients to the development of POAF.

Methods Patients were residents of Olmsted County, Minnesota, who underwent complete LV diastolic function assessment before coronary artery bypass grafting and/or valve surgery between January 1, 2000, and December 31, 2005. All were in sinus rhythm and had no history of atrial fibrillation, a pacemaker, mitral stenosis, or congenital heart disease. POAF was defined as any episode of atrial fibrillation within 30 days after surgery.

Results POAF occurred in 135 of 351 patients (38.5%). Patients with POAF were older (mean age 72.5 ± 10.3 years vs. 63.1 ± 14.1 years; $p < 0.001$) and more likely to have abnormal diastolic function. The rate of POAF increased exponentially with diastolic function grade (DFG) severity ($p < 0.001$). By multivariate analysis, after adjusting for clinical and surgical risk factors, independent predictors of POAF were older age (odds ratio [OR]: 1.05; $p < 0.001$), higher body mass index (OR: 1.06; $p = 0.03$), and abnormal LV DFG (DFG 1, OR: 5.12 [$p = 0.006$]; DFG 2, OR: 9.87 [$p < 0.001$]; and DFG 3, OR: 28.52 [$p < 0.001$]).

Conclusions LV diastolic dysfunction is a powerful, independent predisposing substrate for the initiation of POAF. Evaluation may be useful during risk stratification of patients undergoing cardiac surgery. (J Am Coll Cardiol 2011;58: 953–61) © 2011 by the American College of Cardiology Foundation

Atrial fibrillation (AF) occurs in a substantial subset of patients after cardiac surgery. It has been ascribed to various clinical risk factors closely linked to alterations of myocardial diastolic properties, including advanced age, hypertension, left ventricular (LV) hypertrophy, obesity, metabolic syndrome, LV dysfunction, and left atrial enlargement (1–5). New-onset post-operative atrial fibrillation (POAF) is a major cause of morbidity and mortality. It is associated with increased risk of stroke and death and constitutes a substantial use of healthcare resources, including increased duration of hospitalization and hospital costs (1,4,6–8).

Despite the documented clinical impact of POAF, there are no uniformly accepted treatments for its prevention, in part due to a lack of mechanistic understanding. Previous studies have focused on the determinants of POAF, but most factors are not modifiable, nor have researchers provided a clear physiological basis for pre-operative risk stratification or potential prophylactic treatment (1,4,9). Age, which is often associated with abnormal myocardial relaxation due to alterations in ventricular compliance (10–12), is the only risk factor most consistently identified as a major independent predictor for the development of POAF (1,3,9). The pathophysiological mechanisms of POAF therefore may be linked to pre-existing, age-related, and

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Abbreviations and Acronyms

AF = atrial fibrillation
CABG = coronary artery bypass graft
CI = confidence interval
DFG = diastolic function grade
LV = left ventricular
OR = odds ratio
POAF = post-operative atrial fibrillation

degenerative structural and functional changes in the atrial and ventricular myocardium; these changes may contribute to the development of a proarrhythmic substrate that subsequently promotes the development of POAF. In this study, we sought to assess the hypothesis that impaired LV compliance is a principal culprit for the changing hemodynamic properties of the left atrium, predisposing patients to atrial arrhythmogenesis after cardiac surgery.

Methods

Study patients. The study was approved by the Mayo Clinic Institutional Review Board, and all patients gave written informed consent for participation in the study. It was conducted in Olmsted County, Minnesota, where comprehensive healthcare records with high-quality information have been maintained. Records covered all healthcare encounters and included clinical reports, echocardiographic reports, laboratory test results, pathology reports, and autopsy results. Complete medical records from consecutive Olmsted County patients were prospectively entered into a clinical database and retrospectively reviewed to investigate the relationship between diastolic dysfunction severity and the risk of developing new-onset POAF.

For the present investigation, eligible patients were residents of Olmsted County and could be of any age. The age of the study population was 66.7 ± 13.6 years, and 236 patients (67.2%) were men. All had pre-operative sinus rhythm and underwent isolated coronary artery bypass graft (CABG) and/or valvular repair or replacement (or some combination thereof), and survived the operation (n = 752). Our cohort did not include patients with congenital heart disease. We excluded patients with a pre-operative history of AF (n = 71), pacemaker (n = 37), Cox's maze or radiofrequency ablation procedure for atrial arrhythmias (n = 8), moderate or severe mitral stenosis (n = 16), and incomplete diastolic function assessment (n = 269). Standard care for these patients involved coordinated treatment between cardiologists and cardiac surgeons. All patients included in the study (n = 351) were Olmsted County residents, which facilitated prospective follow-up.

Echocardiographic data. All patients underwent a pre-operative, comprehensive transthoracic, 2-dimensional and Doppler echocardiographic evaluation with state-of-the-art technology within 3 months before surgery (median 6 days; interquartile range [IQR]: 1 to 25 days). All pre-operative echocardiograms were independently reviewed by 2 experienced echocardiographers in a blinded fashion. Disagreements about the diastolic function grade between the 2 independent physician reviews were resolved either by consensus or by arbitration by a third reviewer. Measurements of study variables were performed according to established methods (13–15). Diastolic parameters were integrated to form a global diastolic function score (grades 0–3) (13–17).

- Grade 0: Normal LV filling pressure; mitral E/A ratio of 0.75 to 1.5, mitral deceleration time 160 to 240 ms, e' ≥8, E/e' <8, pulmonary venous systolic forward flow velocity > diastolic, pulmonary venous atrial reversal duration shorter than mitral A flow duration, and left atrial volume index <34 ml/m^2.
- Grade 1: Normal to mildly elevated LV filling pressure or impaired LV relaxation; mitral E/A ratio of <0.75, mitral deceleration time >240 ms, e' <8, E/e' ≤8, pulmonary venous systolic forward flow velocity ≥diastolic, pulmonary venous atrial reversal duration shorter than mitral A flow duration, and left atrial volume index ≥34 ml/m^2.
- Grade 2: Moderately elevated LV filling pressure or pseudonormal LV diastolic filling; mitral E/A 0.75 to 1.5 with a decrease of ≥0.5 with Valsalva maneuver, mitral deceleration time 160 to 240 ms, e' <8, E/e' 9 to 12, pulmonary venous systolic forward flow velocity < diastolic, pulmonary venous atrial reversal duration longer than mitral A flow duration (by ≥30 ms), and left atrial volume index ≥34 ml/m^2.
- Grade 3: Severely increased LV filling pressure or restrictive LV diastolic filling; mitral E/A >1.5 with a decrease of ≥0.5 (reversible) or <0.5 (fixed) with Valsalva maneuver, mitral deceleration time <160 ms, e' <8, E/e' ≥13, pulmonary venous systolic forward flow velocity < diastolic, pulmonary venous atrial reversal duration longer than mitral A flow duration (by ≥30 ms), and left atrial volume index ≥34 ml/m^2.

Electrocardiography. All patients were monitored for the occurrence of POAF with continuous electrocardiographic telemetry until the day of hospital dismissal. A standard, 12-lead electrocardiogram was recorded on the day of dismissal for each patient. POAF was based on documentation of AF episodes by continuous telemetry throughout hospitalization or electrocardiogram during follow-up within 30 days after cardiac surgery.

Angiography. Coronary angiography results were obtained from clinical reports composed by experienced angiographers at the time of cardiac catheterization. The degree of coronary artery stenosis was visually estimated as a percentage of the normal segment preceding the stenosis. Clinically significant coronary stenoses were defined as ≥70% narrowing of the luminal diameter of ≥1 major epicardial arteries or a ≥50% left main artery stenosis. Patients with left main coronary artery stenosis were considered to have 2-vessel disease if there was right coronary dominance and 3-vessel disease if there was left dominance.

Clinical predictors. On the basis of previous reports (1–5,8,9,18), the covariates analyzed included pre-operative