LEFT ATRIAL APPENDAGE FUNCTION AS A PREDICTOR OF THE RISK OF ATRIAL FIBRILLATION AFTER CORONARY ARTERY BYPASS GRAFT SURGERY

Thesis for Partial Fulfillment of Master's Degree in Cardiology Submitted by

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Abstract

Out of 60 patients included in our study, 9 patients had post operative atrial fibrillation . According to our results, Left Atrial Volume was the most significant factor associated to post operative atrial fibrillation, but this volume showed no significant association to post operative atrial fibrillation when indexed to body surface area.

Left atrial volume (LAV) can be measured easily before surgery, other studies agree with our study that, increased LAV has been shown to predict the development of AF [14], but its utility in the prediction of post operative atrial fibrillation is unknown.

The increase in LAV is hemodynamically closely related to the chronic burden of elevated ventricular filling pressure and diastolic dysfunction [197].

Key Words: ***LEFT ATRIAL APPENDAGE FUNCTION AS A PREDICTOR OF THE RISK ATRIAL FIBRILLATION AFTER CORONARY ARTERY BYPASS GRAFT SURGERY***

List of Abbreviations

AF = atrial fibrillation

POAF = post operative atrial fibrillation

LA = left atrium

LAV = left atrial volume

LAA = left atrial appendage

CABG = coronary artery bypass graft

SEC = spontaneous echo contrast

TEE = transesophageal echocardiography

TDI = tissue Doppler imaging

MDI = myocardial Doppler imaging

SR = sinus rhythm

IABP = intra aortic balloon pump

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Aims and Objectives

Despite the prevalence of atrial fibrillation (AF) occurring after cardiac surgery, its pathophysiology is incompletely understood.

Specifically, whether left atrial (LA) structural remodeling occurs, contributing to a decrement in atrial function and AF has not been previously determined.

This study sought to determine the relationship between left atrial (LA) and left atrial appendage (LAA) function in association to post-operative AF.

Preoperative, intraoperative and postoperative predictors of postoperative atrial fibrillation (POAF) have been studied as well.

Impairment of left atrial function as a predictor of post-operative atrial fibrillation after coronary artery bypass graft surgery

Atrial fibrillation (AF) occurs in 10–50% of patients after cardiothoracic surgery,[1–4] with accompanying longer and more costly hospitalisations.[2,5] Despite its prevalence, it is commonly believed that post-operative AF is short-lived and possibly benign and may be mechanistically different from chronic AF that occurs in the older population. The etiology of post-operative AF remains incompletely understood despite some recent evidence from several small clinical studies suggesting the role of a variety of heterogeneous factors including oxidative stress,[6] inflammation,[7] atrial fibrosis,[8] and altered connexin expression leading to a proarrhythmic substrate.[9]

Previous epidemiological studies have suggested a strong relationship between aging and AF in both the non-surgical and surgical population. Age-related changes in the atria may include atrial dilatation, hypertrophy and patchy fibrosis with destruction of the SA node. Therefore, measurements of both the geometry and function of the atria are crucial in understanding how age-related changes may impact on the development of AF.

To date, several demographic and preoperative factors such as age, sex, history of previous AF, hypertension, chronic obstructive pulmonary disease, diseased right coronary artery, and use or withdrawal of medication have been shown to be risk factors for postoperative AF.

Unfortunately, none of these factors is powerful enough to predict postoperative AF after coronary artery bypass graft(CABG) surgery to any clinically meaningful extent.[10] On the other hand, several echocardiographic

approaches to post operative AF have been previously reported,[11-14] but one must not lose sight of the fact that conventional echocardiographic parameters have their own limitations.

The LA volume has an independent predictive value for determining the risk of AF. Nevertheless, several studies have reported that the LA dimensions in patients with paroxysmal AF are not necessarily larger than those in control subjects.[15,16] Furthermore, the relationship between the LA chamber size estimated by echocardiography and lone paroxysmal AF is controversial.

Echocardiographic LA chamber size usually is measured as a short-axis dimension in the parasternal and apical views, but this method possibly is insensitive in the detection of LA enlargement.[17]

Transmitral flow velocity during early diastolic filling (E), atrial contraction (A), and E/A ratio are affected in paroxysmal AF.[18] Decreased A velocity is correlated with reduced atrial contraction.[19] Decreased E/A ratio is related mainly to left ventricular diastolic dysfunction and not directly to atrial impairment.[20] Both parameters are less sensitive and less specific because they are influenced by such cardiac conditions as heart rate, preload, and afterload.[21]

Left Atrial Size and Postoperative Atrial Fibrillation

Left atrial (LA) size serves as a marker of cardiovascular risk factors, an indicator of existing cardiac disease, and a predictor of cardiovascular outcomes [22-25] , as well as the source of disease itself. Both LA dilation and geometric distortion may be primary or may be secondary to left ventricular diastolic dysfunction.

Therefore, it is a common final pathway for such diverse disease entities as hypertension, valvular heart disease, and atrial fibrillation (AF). Controlled animal studies have shown that AF is difficult to induce in very small animals and requires sufficient atrial tissue [26]. Data from the population-based Framingham and Strong Heart studies show that increased LA size is an independent risk factor for AF [23-25].

Interest in LA size and structure as a marker of cardiac disease has increased steadily since Feigenbaum et al.[27] first reported that the unidimensional M-mode LA diameter correlates with angiographic LA size.

Since then, ultrasound technology has advanced, adding 2-dimensional (2D) and, more recently, real-time 3-dimensional (RT3D) capabilities to its diagnostic value. Reflecting these advances, a recent position statement from the American Society of Echocardiography

supported a transition to more volumetric approaches to cardiac chamber quantification [28].

In its normal, nondilated state, the LA is a spherical structure, and thus its volume may be well approximated by $4/3\pi r^3$, where r is a single measure of radius. However, even with minor LA distortion, the LA may enlarge asymmetrically because of the constraints of the surrounding structures, such as aorta and chest wall, as well as the eccentrically directed mitral regurgitation jets, making a unidimensional assessment inadequate [29]. The assumption regarding the spherical nature of an enlarged LA may be partially tempered by using three separate radius measurements, or by the application of a biplanar area method [30].

To further minimize geometric assumptions regarding the shape of the LA, true volumetric techniques can be used. These include cardiovascular magnetic resonance, cardiac computed tomography, and RT3D echocardiography. Cardiovascular magnetic resonance can accurately quantify LA dimensions, volume, and function, and can be performed with or without contrast agents [31,32]. Cardiac computed tomography is occasionally used for anatomic imaging of LA around the time of pulmonary vein isolation [33], but exposes the patient to ionizing radiation and nephrotoxic contrast. Three-dimensional reconstruction of 2D images is a reliable estimate of LA volume, and RT3D echocardiography has proven promising in measuring LA volume directly [34].

Although RT3D is now becoming more widely available, 2D echocardiographic methods are still easier to implement, and thus remain the

mainstay of diagnosis in most laboratories. Therefore, current practice of LA volume estimation by echocardiography relies on its approximation from biplanar 2D measurements [35,36] with LA enlargement identified above a gender-neutral, body mass index-corrected volume of 32 ml/m^2 [37].

Atrial arrhythmias, including AF, are encountered frequently after CABG surgery. These arrhythmic complications are associated with an increased incidence of systemic thromboembolism and stroke, hemodynamic instability, and prolonged hospital stay and increased resource use [38]. Clinical risk factors for postoperative atrial fibrillation include advanced age, obesity, mitral valve disease, and prior history of AF or congestive heart failure [38,39].

The feasibility and effectiveness of prophylaxis for AF among patients undergoing cardiac surgery has been previously shown. A Cochrane review of data from 58 trials, together enrolling over 8,500 patients, identified that beta-adrenergic blockers, sotalol, and amiodarone, as well as atrial overdrive pacing, all reduce the incidence of postoperative AF [40].

In a recent PAPABEAR (Prophylactic Oral Amiodarone for the Prevention of Arrhythmias That Begin Early After Revascularization, Valve Replacement, or Repair) trial, perioperative amiodarone therapy reduced the postoperative risk of atrial tachyarrhythmias by approximately 50% overall, with a similar benefit in patients older and younger than 65 years [41]. However, almost a week of pretreatment was prespecified in that study, which limits its applicability in the clinical setting. In addition, the strategy of routine preoperative administration of amiodarone exposes a large

population of patients at variable risk for AF to potentially serious adverse effects of this therapy. Therefore, objective preoperative stratification or patients with respect to their risk of developing postoperative AF is desirable.

In a prospective study of LA volume and incidence of postoperative AF. The LA volume was determined by 2D echocardiography using the biplanar area-length method [37,43], although using a slightly different formula from their recent publication on LA volume and cardiovascular outcomes, in which they used the mean of the 4-chamber and 2-chamber lengths rather than the shortest length [22].

In a cohort of 205 patients undergoing cardiac surgery at the Mayo Clinic, the investigators show that preoperative LA volume index was an independent predictor of postoperative AF, with an LA volume index >32 ml/m^2 conferring an almost 5-fold increased risk of postoperative AF (compared with the LA volume index ≤32 ml/m^2). Surprisingly, amiodarone or beta-blockade were not protective against development of postoperative AF [42]. Data are also not provided for us to determine whether LA volume measures were superior to LA dimension or area measures in predicting AF incidence after cardiac surgery.

Echocardiographic LA volume estimated by the biplanar method has been used previously as a risk predictor of AF in older outpatients [14], as a marker of long-term adverse events in those with lone AF [44], and as a predictor of cardiovascular events [22]. The current study by Osranek et al. [42] builds on these previous investigations and provides simple means for

preoperative risk stratification of a large and common population of cardiac surgical patients.

Although the investigators have chosen to correct LA volume for body size, they have not used gender-specific thresholds. An argument against any normalization is animal data supporting the theory of re-entry and AF that show that a minimum amount of atrial tissue is required (equal to the distance traveled by the cardiac impulse in one refractory period) and is critical to determination of the likelihood of re-entry [45] . These data suggest that raw/non-normalized indexes may be more appropriate predictors.

None of the studied patients younger than 65 years of age and with an LA volume <32 ml/m^2 did postoperative AF develop, identifying a "low-risk" group in whom the risks of preoperative prophylaxis may in principle outweigh its benefits [42]. The clinical implications of actually withholding prophylactic beta-blockers in younger patients with normal-sized atria before cardiac surgery will have to be assessed in formal clinical studies.

Old habits are often difficult to break. Parasternal LA dimension measurements have been a cornerstone of clinical echocardiography for almost 40 years. Advances in technology facilitated area measurement more than 2 decades ago. This study have now given us another good reason to think about the heart volumetrically, as echocardiography advances to the RT3D world.

Left atrial appendage:

structure, function, and role in thromboembolism and atrial fibrillation