Left Atrial Volume Predicts the Risk of Atrial Fibrillation After Cardiac Surgery

A Prospective Study

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OBJECTIVES
This study sought to identify preoperative predictors of postoperative atrial fibrillation (POAF) among patients undergoing cardiac surgery.

BACKGROUND
Postoperative atrial fibrillation is frequent after cardiac surgery and is associated with increased morbidity, mortality, prolonged hospital stay, and increased costs. Left atrial volume (LAV), a marker of chronically elevated left ventricular filling pressure, is a predictor of atrial fibrillation (AF) in the nonsurgical setting.

METHODS
A total of 205 patients (mean age 62 ± 16 years; 35% women) undergoing cardiac surgery were prospectively enrolled. Clinical risk factors were obtained by detailed medical record review and patient interview. Preoperative transthoracic echocardiograms were performed for assessment of LAV, left ventricular ejection fraction, and diastolic function. Follow-up was complete. Detection of POAF was based on documentation of AF episodes by continuous telemetry throughout hospitalization.

RESULTS
Postoperative atrial fibrillation occurred in 84 patients (41.4%) at a median of 1.8 days after cardiac surgery. The LAV was significantly larger in patients in whom AF developed (49 ± 14 ml/m² vs. 39 ± 16 ml/m², p = 0.0001). Patients with LAV >32 ml/m² had an almost five-fold increased risk of POAF, independently of age and clinical risk factors (adjusted hazard ratio 4.84, 95% confidence interval 1.93 to 12.17, p = 0.001). Age and LAV were the only independent predictors of POAF. The area under the receiver-operator characteristics curve to predict POAF was 0.729 for LAV and 0.768 for the combination of LAV and age (both p < 0.0001).

CONCLUSIONS
The LAV is a strong and independent predictor of POAF. Risk stratification using LAV and age enables clinicians to identify high-risk patients before cardiac surgery. (J Am Coll Cardiol 2006;48:779–86) © 2006 by the American College of Cardiology Foundation

Postoperative atrial fibrillation (POAF) is common after cardiac surgery and is associated with increased morbidity, mortality, and prolonged hospital stay (1–4). The impact of POAF on hospital resources is substantial, with annual estimated expenditures exceeding $1 billion in the U.S. (3). The risk for perioperative stroke is almost three-fold higher for patients with POAF (1,3). Recently, a retrospective study of patients undergoing mitral valve surgery showed that POAF was independently associated with stroke, congestive heart failure, and AF at 10-year follow-up (5). The incidence of POAF varies depending on definition, patient characteristics, type of operation, and method of arrhythmia monitoring (1–4). In a large series, Creswell et al. (1) found the incidence of POAF detected by continuous electrocardiographic telemetry monitoring to be 32% after coronary artery bypass grafting (CABG), 42% after mitral valve surgery, 49% after aortic valve surgery, and 62% after combined CABG and valve surgery.

Several risk indices provided adequate discriminative power to identify patients with POAF. However, they included mainly intraoperative and postoperative variables (2,6), and are therefore not clinically helpful for risk stratifying patients before surgery who may benefit from preoperative preventive antiarrhythmic therapy.

Left atrial volume (LAV) can be measured easily before surgery, and increased LAV has been shown to predict the development of AF in nonsurgical populations (7), but its utility in the prediction of POAF is unknown. The increase in LAV is hemodynamically closely related to the chronic burden of elevated ventricular filling pressure (8,9) and diastolic dysfunction (10).

In the current study, we hypothesized that LAV, as a surrogate measure of preoperative chronically increased filling pressure, is an independent predictor of POAF and represents a clinically useful test for risk stratification.

MATERIALS AND METHODS

Patient selection. After approval of the study protocol by the institutional review board, consecutive patients sched-
uled to undergo open heart surgery at the Mayo Clinic, Rochester, Minnesota, were prospectively enrolled on the day before surgery. Participants had to be in sinus rhythm as documented by 12-lead electrocardiogram. Patients undergoing CABG surgery and surgery involving the aortic valve, ascending aorta, tricuspid valve, pericardium, cardiac masses, and myectomy were eligible. We excluded patients with AF, past or planned Cox’s maze procedure, more than moderate mitral valve stenosis or regurgitation, mitral valve prosthesis, congenital cardiac abnormalities, emergency surgery, or inability to provide informed consent. By excluding mitral valve disease or prosthesis, hemodynamic changes purely related to mitral valve pathology that could potentially affect LAV or impede diastolic function assessment were avoided.

Clinical variables. Demographic and baseline clinical data were obtained through Mayo Clinic Registration, review of medical records, and a structured interview at enrollment. Baseline clinical variables included New York Heart Association functional class, Canadian Cardiovascular Society angina class, history of AF, myocardial infarction, stroke, history of systemic hypertension (>140/90 mm Hg, or treated), diabetes mellitus, dyslipidemia (hypercholesterolemia, hypertriglyceridemia, reduced high-density lipoprotein cholesterol, or any combination), congestive heart failure requiring hospitalization, thyroid disorder, chronic obstructive pulmonary disease, renal insufficiency, and smoking (current or past). Use of medications was documented. In particular, the preoperative use of beta-blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers, as well as their postoperative withdrawal or resumption, was assessed. Any antiarrhythmic medication that was given to prevent POAF was also noted. Clinically indicated preoperative angiograms were evaluated. The degree of stenosis in the individual coronary arteries was noted. The number of vessels with significant (>75%) stenosis was counted.

Echocardiography. All preoperative echocardiograms were reviewed in a blinded fashion. Offline measurements of study variables were performed according to established methods (11–13). The LAV was obtained by the biplanar area-length method and indexed to body surface area as previously described (12,13). This validated method has been shown to correlate better than LA diameter or monoplanar methods with the actual volume of the atrial chamber because it relies on fewer geometric assumptions (14–16). For the biplanar area-length method, the maximal LA area is planimetered at end-ventricular systole just before opening of the mitral valve in the four- and two-chamber views. The recesses of the pulmonary veins and the LA appendage are excluded. The length of LA is that of the perpendicular line measured from the middle of the plane of the mitral annulus to the superior aspect of the LA. The LAV is calculated as: 0.85 × four-chamber area × two-chamber area ÷ shorter of the two lengths. An LAV above 32 ml/m² representing the upper 95th percentile of normal subjects (18) was used as a cutoff to define LA enlargement, a cutoff previously validated by our group for risk prediction (7,18,19). A random sample of 20 (10%) studies was re-assessed by a co-investigator for quality assurance purposes. The linear correlation (r = 0.87, p < 0.0001) was good, and the mean difference of −1.03 ml/m² was not different from zero (p = 0.47). From the same views, left ventricular ejection fraction (EF) was calculated using the biplanar Simpson method.

Doppler interrogation of cardiac hemodynamics included mitral inflow peak early (E) and late (atrial, A) velocities, deceleration time, pulmonary venous systolic and diastolic forward flow velocities, and pulmonary vein atrial reversal velocity. Tissue Doppler imaging of septal annulus motion velocity (E’) was obtained. Resting left ventricular filling pressures were estimated by the ratio of mitral E velocity and septal mitral annulus motion velocity (E/E’) (20).

Five diastolic function grades (DFG) were determined (11,21,22):

- Normal: mitral E/A ratio of 0.75 to 1.5, mitral deceleration time 150 to 240 ms, E/E’ <8, pulmonary venous systolic forward flow velocity > diastolic, pulmonary venous atrial reversal <0.30 m/s.
- Grade I: relaxation abnormality; mitral E/A ratio of <0.75, mitral deceleration time >240 ms, pulmonary venous systolic forward flow velocity > diastolic.
- Grade Ia: patients with a mitral inflow pattern consistent with grade I but E/E’ >10.
- Grade II: pseudonormal filling; mitral E/A 0.75 to 1.5 (with decrease of >0.5 on Valsalva maneuver), mitral deceleration time 150 to 240 ms, E/E’ >10, pulmonary venous systolic forward flow velocity < diastolic.
- Grade III: restrictive filling; mitral E/A >1.5, mitral deceleration time <150 ms, E/E’ >15, pulmonary venous systolic forward flow velocity < diastolic.

Patients with limited Doppler signal quality or discrepancy among Doppler measurements were not assigned a DFG to avoid any misclassification.

Left ventricular mass was calculated and indexed to body surface area. Pulmonary artery pressure was estimated with the simplified Bernoulli equation [(4 × tricuspid regurgitation velocity) + estimated right atrial pressure]. Mitral regurgitation was qualitatively described.

Outcome ascertainment. Continuous telemetry recordings from surgery until hospital discharge were complete in
all patients and were reviewed for POAF. Episodes of more than 30 s were considered clinically relevant AF. A pre-
dismissal 12-lead electrocardiogram was performed on each 
patient. Ventilation time, intensive care unit time and 
clinical postoperative complications, reoperation, bleeding, 
shock, stroke, infection, death, arrhythmias other than AF, 
renal failure, pulmonary complications, and length of stay 
were determined based on hospital notes and by contacting 
the treating physician.

**Statistical analysis.** Data are presented as proportions (%) 
for categorical variables and as mean ± SD for continuous 
variables. For skewed variables, the median (first to third 
quartile) is reported. Characteristics were compared across 
groups using chi-square tests for categorical variables and 
Student’s t test for continuous variables. The Mann-Whitney 
U test was used for variables with skewed distributions.

To account for varying lengths of hospital stay, the main 
outcome (POAF) was modeled using survival analyses: the 
Kaplan-Meier product limit method and Cox proportional 
hazards models. Variables with a skewed distribution were 
transformed using natural logarithm. In Cox models, for 
each variable, the hazard ratio (HR), 95% confidence 
interval (CI), and p value are provided. Differences between 
groups were tested using the log rank statistic, and inde-
dendent predictors were identified in multivariable analyses.

Predictors identified in univariable analyses were used to 
build separate multivariable models for clinical, surgical, and 
echocardiographic variables. All of these models were ad-
justed for age, which has been consistently found to be 
related to POAF. From these models, the significant 
variables that can be obtained before surgery in all patients, 
complemented by variables of clinical interest, were used to 
build a final model with at least 10 outcome events per 
variable to ensure model stability. A p value of 0.05 was 
selected for the threshold of statistical significance. All 
analyses were performed using SPSS version 11.5 (SPSS 

**RESULTS**

A total of 205 consecutive patients undergoing cardiac 
surgery were prospectively enrolled. The mean age was 
62.0 ± 16.3 years, and 34.6% were women. Two patients 
died intraoperatively, and two patients died during their 
hospital stay. Patients in whom POAF developed were 
older, had higher systolic blood pressures and pulse pres-
ures, had a greater degree of left main coronary artery 
stenosis, and were more likely to have chronic obstructive 
pulmonary disease (Table 1). Combined aortic valve and 
CABG surgery and the number of bypass grafts were 
predictive of POAF. Intraoperatively, increased pulmonary 
artery pressure was associated with POAF, whereas other 
inooperative variables and treatment were not (Table 2).

**Occurrence of POAF.** Of 203 patients surviving the 
surgery (99.0%), 84 patients (41.4%) experienced POAF 
after a median (first to third quartile) of 1.8 days (1.2 to 2.9 
days) at a mean heart rate of 116 ± 26 min⁻¹ and a mean 
SBP of 118 ± 18 mm Hg. Thirty-three patients had a 
single episode, 14 had multiple episodes, and 37 had 
persistent AF lasting longer than 24 h. The median total

**Table 1.** Baseline Characteristics

<table>
<thead>
<tr>
<th>No AF (n = 119)</th>
<th>AF (n = 84)</th>
<th>HR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>56.9 ± 17.6</td>
<td>69 ± 11.2</td>
<td>1.04</td>
</tr>
<tr>
<td>History of CHF</td>
<td>46 (38.6%)</td>
<td>42 (50.0%)</td>
<td>1.25</td>
</tr>
<tr>
<td>History of AF</td>
<td>11 (9.2%)</td>
<td>12 (14.1%)</td>
<td>1.39</td>
</tr>
<tr>
<td>History of MI</td>
<td>15 (12.6%)</td>
<td>12 (14.3%)</td>
<td>1.14</td>
</tr>
<tr>
<td>Hypertension</td>
<td>65 (54.6%)</td>
<td>43 (51.2%)</td>
<td>0.84</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9 (7.6%)</td>
<td>12 (14.3%)</td>
<td>1.51</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>60 (50.4%)</td>
<td>50 (59.5%)</td>
<td>1.31</td>
</tr>
<tr>
<td>Smoking</td>
<td>45 (37.8%)</td>
<td>43 (51.2%)</td>
<td>1.47</td>
</tr>
<tr>
<td>Thyroid disorder</td>
<td>12 (10.1%)</td>
<td>11 (13.3%)</td>
<td>1.30</td>
</tr>
<tr>
<td>COPD</td>
<td>3 (2.5%)</td>
<td>6 (7.1%)</td>
<td>2.40</td>
</tr>
<tr>
<td>Chronic renal insufficiency</td>
<td>4 (3.4%)</td>
<td>6 (7.2%)</td>
<td>1.99</td>
</tr>
<tr>
<td>No. of diseased vessels (n = 157)</td>
<td>0.9 ± 1.2</td>
<td>1.2 ± 1.2</td>
<td>1.19</td>
</tr>
<tr>
<td>LM stenosis (%) (n = 157)</td>
<td>10.5 ± 18.7</td>
<td>19.6 ± 21.3</td>
<td>1.01</td>
</tr>
<tr>
<td>RCA stenosis (%) (n = 157)</td>
<td>35.4 ± 39.4</td>
<td>45.6 ± 39.9</td>
<td>1.01</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>72 (60.5%)</td>
<td>53 (63.3%)</td>
<td>1.05</td>
</tr>
<tr>
<td>Diuretic</td>
<td>29 (24.4%)</td>
<td>29 (34.5%)</td>
<td>1.44</td>
</tr>
<tr>
<td>Thyroxin</td>
<td>12 (10.1%)</td>
<td>11 (13.3%)</td>
<td>1.26</td>
</tr>
<tr>
<td>Antiarrhythmic therapy</td>
<td>6 (5.0%)</td>
<td>4 (4.8%)</td>
<td>0.91</td>
</tr>
<tr>
<td>Statin</td>
<td>42 (35.3%)</td>
<td>40 (47.6%)</td>
<td>1.40</td>
</tr>
</tbody>
</table>

AF = atrial fibrillation; CHF = congestive heart failure; CI = confidence interval; COPD = chronic obstructive pulmonary disease; HR = hazard ratio; LM = left main coronary artery; NYHA = New York Heart Association; PP = pulse pressure; RCA = right coronary artery; SBP = systolic blood pressure.
duration of POAF was 12 h, and the median single longest episode was 9 h. Seventy-one patients with POAF (84.5%) did not experience symptoms at the onset of AF. Among the 84 patients who experienced POAF, 13 (15.5%) did not receive any specific treatment, 2 (2.4%) underwent electrical cardioversion, 67 (79.8%) were given drug treatment, and 2 (2.4%) received both. Drugs used were class III antiarrhythmicics in 57 patients, beta-blockers in 12 patients, and digitalis in 12 patients. Overall, more than one treatment modality, including multiple antiarrhythmic drugs, was needed in 13 patients. Seven (8.3%) patients were discharged from the hospital with AF.

Postoperative complications other than AF occurred in 42 patients (20.7%) and were not significantly associated with the incidence of POAF apart from a trend for renal failure (Table 3). All but 1 patient stayed at least 4 days in the hospital and, according to telemetry recordings of the complete hospital stay, 76 (90.0%) of the 84 patients with POAF experienced the event before the end of the fourth postoperative day. The median length of hospital stay was significantly longer in patients with POAF compared with those without POAF (7 vs. 5 days, p < 0.00001). Echocardiographic predictors of POAF. Among all echocardiographic parameters, only DFG and LAV were predictive of POAF. The DFG was successfully determined in 181 (88.3%) patients and was moderately correlated with LAV (Fig. 1). Ventricular relaxation estimated by E’ in 162 patients was close to being statistically significant. The DFG had the strongest predictive value when considered as normal versus abnormal with a HR of 3.36 (95% CI 1.35 to 8.35).

At univariable analysis, LAV was the most powerful predictor of POAF with a 26% increase in the risk of AF for every 10 ml/m² increase in LAV (HR = 1.26, 95% CI 1.13 to 1.40, p = 0.0001) and an HR of 6.55 (95% CI 2.65 to 16.18, p < 0.0001) for patients with an abnormal LAV >32 ml/m² (Table 4). The proportion of patients who experienced any type of POAF increased with each quartile of LAV, as did the subgroup of persistent AF (Fig. 2A). Survival free from POAF progressively worsened with increasing quartiles of LAV (p < 0.00001) (Fig. 2B). In a multivariable analysis of echocardiographic variables, only LAV remained a significant predictor of POAF (p < 0.0001). The LAV tended to be larger in patients requiring multiple treatment modalities to convert to sinus rhythm (54.7 ± 18.5 ml/m² vs. 47.6 ± 12.8 ml/m², p = 0.09) and in those with symptoms at the onset of POAF (55.1 ± 18.5 ml/m² vs. 47.5 ± 12.8 ml/m², p = 0.07). An LAV >32 ml/m² was a significant predictor of POAF in patients with (p = 0.007) and without beta-blockers (p = 0.004).

Figure 1. Box plots of left atrial volume (LAV) according to diastolic function grade (DFG). Using linear regression, the correlation coefficient r was 0.56 (p < 0.0001).

![Figure 1](image-url)
Table 4. Univariable Echocardiographic Predictors of POAF

<table>
<thead>
<tr>
<th></th>
<th>No AF (n = 119)</th>
<th>AF (n = 84)</th>
<th>HR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAV &gt;32 ml/m²</td>
<td>74 (62.2%)</td>
<td>79 (94.0%)</td>
<td>6.55</td>
<td>0.0001</td>
</tr>
<tr>
<td>LAV (ml/m²)</td>
<td>39.2 ± 16.3</td>
<td>48.7 ± 13.9</td>
<td>3.02</td>
<td>0.21</td>
</tr>
<tr>
<td>Abnormal DFG (n = 179)</td>
<td>80 (74.8%)</td>
<td>67 (93.1%)</td>
<td>3.36</td>
<td>0.009</td>
</tr>
<tr>
<td>DFG (5 grades) (n = 179)</td>
<td>1.7 ± 1.4</td>
<td>2.3 ± 1.1</td>
<td>1.26</td>
<td>0.015</td>
</tr>
<tr>
<td>E’ (cm/s⁻¹) (n = 163)</td>
<td>7.1 ± 3.1</td>
<td>6.1 ± 2.5</td>
<td>0.92</td>
<td>0.07</td>
</tr>
<tr>
<td>E/E’ (n = 162)</td>
<td>13.7 ± 6.7</td>
<td>15.0 ± 6.6</td>
<td>1.01</td>
<td>0.38</td>
</tr>
<tr>
<td>PVARV (cm/s⁻¹) (n = 145)</td>
<td>0.30 ± 0.1</td>
<td>0.32 ± 0.2</td>
<td>3.11</td>
<td>0.14</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>59.9 ± 12.4</td>
<td>57.9 ± 12.1</td>
<td>0.99</td>
<td>0.40</td>
</tr>
<tr>
<td>Mitral regurgitation (&gt;trivial)</td>
<td>54 (45.4%)</td>
<td>49 (58.3%)</td>
<td>1.44</td>
<td>0.09</td>
</tr>
<tr>
<td>LV mass indexed (g/m²) (n = 148)</td>
<td>125.3 ± 40.5</td>
<td>122.5 ± 39.4</td>
<td>0.99</td>
<td>0.53</td>
</tr>
<tr>
<td>PA pressure (mm Hg) (n = 157)</td>
<td>34.6 ± 10.7</td>
<td>36.8 ± 10.2</td>
<td>1.01</td>
<td>0.25</td>
</tr>
</tbody>
</table>

DFG = diastolic function grade; E = peak early mitral inflow velocity; E’ = early myocardial relaxation; LAV = left atrial volume; LV = left ventricular; PA = pulmonary artery; PVARV = pulmonary vein atrial reversal velocity; other abbreviations as in Tables 1 and 2.

Final model for the prediction of POAF. Apart from age, LAV indexed to body surface area was the only independent predictor of POAF, with a 32% increase in the risk of AF for every 10 ml/m² increase in LAV (adjusted HR = 1.32, 95% CI 1.15 to 1.52, p = 0.0001) (Table 5). Compared with patients with a normal LAV, those with an abnormal LAV (>32 ml/m²) had an almost five-fold increased risk of POAF, independent of other risk factors (adjusted HR = 4.84, 95% CI 1.93 to 12.17, p = 0.001). When considering only persistent POAF, results were similar, with only LAV (adjusted HR = 1.03, 95% CI 1.01 to 1.05, p = 0.004) and age (adjusted HR = 1.05, 95% CI 1.01 to 1.08, p = 0.005) emerging as significant predictors.

Survival free of POAF, stratified by established cutoffs for age and LAV, was significantly different among the four groups (p < 0.00001) and is shown in Figure 3. No patient under the age of 65 years with a normal LAV experienced POAF, and only 5 patients older than 65 years with a normal LAV had POAF. Conversely, the majority of events (n = 64) occurred in older patients with enlarged atria.

To assess the predictive accuracy of this risk stratification, we ranked the 4 possible combinations of normal/abnormal LAV and young/old according to the risk for AF that we observed in the Kaplan–Meier analysis shown in Figure 3, and assigned numeric values ranging from 0 to 3. In a receiver-operator characteristics analysis, the area under the curve for this algorithm was 0.768, compared with 0.729 when LAV was used as a continuous variable (both p < 0.0001).

An LAV >32 ml/m² and age >65 years identified patients with POAF with 76.2% sensitivity and 71.4% specificity, for a positive predictive value of 65.5%. The negative predictive value of LAV ≤32 ml/m² or age <65 years was 81.0%.

DISCUSSION

We found that LAV >32 ml/m² was the strongest predictor of POAF, with an almost five-fold increased risk of POAF independent of age and other clinical and surgical parameters. There was a progressive increase in risk of POAF with increasing quartiles of LAV, suggesting causality in terms of a dose response. The preoperative grade of diastolic function, although univariately associated with POAF and LAV, was superseded by LAV in multivariable analyses.

Other investigators have suggested various risk scoring systems for the prediction of POAF (2,6). Although some achieved moderate degrees of accuracy, they are limited by a cumbersome point scoring system incorporating up to eight variables (2). Importantly, apart from age, the vari-

Figure 2. (A) Incidence of different types of postoperative atrial fibrillation (AF) (single episode, multiple episodes, persistent more than 24 h) according to quartiles of left atrial volume (LAV). (B) Survival free from postoperative AF stratified by quartiles of LAV.
ables that were found to be the strongest predictors were mainly intraoperative or postoperative, such as postoperative impaired atrial function (23), postoperative low cardiac output (6), postoperative beta-blocker or angiotensin-converting enzyme inhibitor administration (2), or the postoperative use of adrenergic drugs (24). Furthermore, the generalizability of many studies is limited to specific types of surgery (5,23) or by the exclusion of patients with a history of atrial fibrillation (5,6,23,25), previous cardiac surgery (5,6), or antiarrhythmic therapy (25). Although the observations made in these studies are of interest and give insight into POAF, they are of limited clinical use and are unlikely to be widely applied in practice. Conversely, we sought to identify a reproducible marker of the risk for POAF that can be obtained before surgery and is consistent with a pathophysiological model derived from experimental research and validated in epidemiologic studies of nonsurgical AF.

**Cardiac filling pressures and AF.** The pathophysiological causes of elevated filling pressure have been attributed to endothelial dysfunction, vascular stiffening, up-regulation of the renin-angiotensin-aldosterone system (26–28), delayed myocyte relaxation, cell death, and fibrosis (29). The thinned areas of atrial myocardium are vulnerable to stretch caused by increased filling pressures (30). Myocyte stretch increases the atrial effective refractory period dispersion through mechano-electrical feedback and, amplified by collagen deposition, lowers the arrhythmogenic threshold (31,32). These observations have been confirmed in community-based cohorts using diastolic dysfunction as a surrogate for elevated filling pressures to predict nonsurgery-related AF (33).

In the present study, resting DFG was defined according to established criteria (11), and proved to be a strong univariate predictor of POAF. Early diastolic myocardial relaxation velocity, which has been shown to correlate with left ventricular filling pressure (20), did show a trend toward significance. Other investigators found that plasma B-type natriuretic peptide levels, another marker of elevated ventricular filling pressure (34), moderately predicted POAF (25). However, all of these measures are merely reflections of a momentary state that is heavily dependent on loading conditions. The latter are especially variable during the course of major surgery. Thus, the preoperative assessment of diastolic function or B-type natriuretic peptide levels may give an indication of the average pathophysiological state of a group of patients before surgery, but is not a permanent feature of individual patients that determines risk throughout varying conditions.

**LAV as a predictor of POAF.** Our group and others have shown that the measurable increase in LAV precedes the onset of non–surgery-related AF (7,33). Enlarged atria are best correlated with increased wall tension because of intermittent yet chronic elevation of ventricular filling pressures (8–10). The relationship between LAV and diastolic dysfunction has been compared with the association between glycosylated hemoglobin and serum glucose, i.e., as a marker of the duration and severity of disease (10,33). Chronic myocyte stretch increases the intercellular matrix, collagen production, and fibrosis, mediated through the renin-angiotensin-aldosterone system (35). Enlarged atria reflect the remodeling process, and represent a quantifiable surrogate of the arrhythmogenic substrate. The volume of remodeled atria is relatively insensitive to varying loading conditions (36). Increased LAV seems to be a reliably measurable indicator of the burden of cardiovascular disease (10), and the remodeled cardiovascular system can be expected to be more susceptible to increased adrenergic stress and dynamic volume changes associated with surgery.

In accordance with these pathophysiological mechanisms, in a retrospective analysis of patients undergoing mitral valve surgery, Kernis et al. (5) found anteroposterior LA dimension to be related to POAF, which in turn was associated with a higher incidence of late stroke or congestive heart failure. The LA diameter, however, is known to systematically underestimate LAV (14–16). Consequently, we prospectively assessed LAV from digitally recorded echocardiographic images in a broader surgical population and monitored the postoperative course using continuous electronic telemetry recordings. The LAV clearly emerged to be the strongest predictor of POAF, and we were able to identify a clinically useful cutoff that is consistent with previous population-based literature on LAV and risk prediction (18,37). The only other risk factor of similar

**Table 5. Multivariable Cox Model Predicting POAF**

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>1.04 (1.02–1.06)</td>
<td>0.0002</td>
</tr>
<tr>
<td>LAV (ml/m²)</td>
<td>1.03 (1.01–1.04)</td>
<td>0.0001</td>
</tr>
<tr>
<td>History of CHF</td>
<td>1.21 (0.77–1.92)</td>
<td>0.41</td>
</tr>
<tr>
<td>History of AF</td>
<td>1.38 (0.73–2.61)</td>
<td>0.32</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.50 (0.95–2.36)</td>
<td>0.08</td>
</tr>
<tr>
<td>CAGB + AV</td>
<td>1.54 (0.88–2.70)</td>
<td>0.14</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>1.01 (0.99–1.02)</td>
<td>0.42</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>1.00 (0.99–1.02)</td>
<td>0.65</td>
</tr>
</tbody>
</table>

n = 203; chi-square = 49.94.

AV + CABG = aortic valve and coronary artery bypass graft surgery; CHF = congestive heart failure; LAV = left atrial volume; SBP = systolic blood pressure; other abbreviations as in Table 2.
strength was age, which is in accordance with virtually all studies on POAF (2,5,6,23). Risk prediction based on two strictly preoperative parameters, age, and LAV, resulted in an area under the receiver-operator characteristics curve of 0.77. A comparable level of discriminative power had so far only been obtained in a multicenter study by Mathew et al. (2) using a complex scoring system of mostly postoperative variables. The results in the current study were identical when considering only the clinically more relevant persistent POAF (>24 h) or when stratifying the patients by preoperative beta-blocker use. The proportion of patients with persistent POAF increased across LAV quartiles (Fig. 1), consistent with a dose-response association suggesting causality.

Clinical implications. Despite a higher rate of beta-blocker administration before and after CABG surgery in our study population (88%) compared with a nationwide multicentric study (60%) (38), overall, beta-blockers were used in less than two-thirds of patients across all types of cardiac surgery, which included aortic valve replacement. A large clinical trial (39) (PAPABEAR [Prophylactic Oral Amiodarone for the Prevention of Arrhythmias That Begin Early After Revascularization, Valve Replacement, or Repair]) found amiodarone to be effective in reducing the incidence of POAF. However, there were no differences in serious postoperative complications, in-hospital mortality, readmission to the hospital within 6 months of discharge, or 1-year mortality. In our observational study, preoperative therapy with amiodarone to prevent POAF was infrequently used and was almost exclusively limited to patients with a history of AF, attenuating the increased risk of POAF in this group. The need for several days of preoperative treatment, drug-related adverse events observed with amiodarone (39), and costs of the drug most likely contribute to this clinical practice. It is evident that: 1) not all patients may require preventive treatment, and 2) current treatment is not adequately targeting the patients at risk for POAF.

As part of the standard evaluation before cardiac surgery, echocardiography is useful for preoperative risk stratification. The cutoff value of LAV >32 ml/m² defining an abnormally large left atrium is consistent with the literature (18,37) and provides clinicians with a practical, noninvasive tool for identifying those patients who benefit most from preventative treatment.

Study strengths and limitations. The strengths of this study include the prospective design, which allowed for accurate assessment of the patient’s baseline clinical status and outcome. Uninterrupted telemetry recordings until hospital discharge ensured that no asymptomatic episodes of POAF were missed and enabled a quantification of POAF. The proposed risk stratification scheme is simple and relies on strictly preoperative parameters (LAV and age), making it useful in clinical practice.

We included most types of cardiac surgery and patients with a history of paroxysmal AF to increase the generalizability of our results. When excluding patients with a history of AF in a separate analysis, the results were unchanged. We did not include patients with mitral valve surgery or congenital heart disease, and therefore our findings cannot be directly extrapolated to these groups. In the current study, the number of postoperative complications other than AF was too low to detect a risk association, as reported elsewhere (1–3). The absence of an association between preoperative medications and POAF in the total population or in subgroups such as different types of surgery is related to the nonrandomized nature of our study. Patients on beta-blockers tended to be at higher risk compared with patients not on beta-blockers (history of myocardial infarction p = 0.025, previous percutaneous coronary intervention p = 0.002, history of hypertension p = 0.0003, history of renal failure p = 0.04, greater number of coronary arteries diseased p = 0.03). Our observations are limited to the period of hospitalization; we cannot draw conclusions regarding long-term outcomes. Further studies investigating the predictive value of LAV for long-term outcome and clinical trials to assess the efficacy of targeted preventive therapy are needed.

Conclusions. Postoperative atrial fibrillation is a frequent complication after cardiac surgery and is associated with a prolonged hospital stay. The LAV, as a marker of chronically increased filling pressures, is strongly related to the occurrence of POAF, even after adjusting for other risk factors. Both LAV and age are useful for preoperative risk stratification in clinical practice.

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