





Echocardiography is useful to predict postoperative atrial fibrillation in patients undergoing isolated coronary bypass surgery: A prospective study European Heart Journal: Acute Cardiovascular Care 2019, Vol. 8(2) 104–113 © The European Society of Cardiology 2017 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/2048872616688419 journals.sagepub.com/home/acc

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Abstract

Objective: Postoperative atrial fibrillation is a major complication following coronary artery bypass graft. We hypothesized that, beyond clinical and electrocardiogram (ECG) data, transthoracic echocardiography could improve the prediction of postoperative atrial fibrillation.

Methods: We prospectively studied 169 patients in sinus rhythm who underwent isolated coronary artery bypass graft in our institution. Clinical, biological, ECG and transthoracic echocardiography data were collected within 24 h before surgery. The patients were continuously monitored during the first five days, and then had daily 12-lead ECG afterwards until discharge. Postoperative atrial fibrillation was defined by any episode >10 min.

Results: Postoperative atrial fibrillation was found in 65 patients (38%). Compared with those without, patients with postoperative atrial fibrillation were significantly older (p=0.008), had more frequently a history of hypertension (p=0.009), history of atrial fibrillation (p<0.001) and New York Heart Association class \geq III (p=0.004). They also had longer PR interval (p=0.005), higher preoperative NT-pro brain natriuretic peptide level (p=0.006), left ventricle end-diastolic volume (p=0.002), indexed left ventricle mass (p<0.0001), indexed maximal left atrial volume (p<0.001) and lower left ventricle ejection fraction (p=0.04). In multivariate analysis, history of atrial fibrillation (odds ratio =6.1, 95% confidence interval: 1.4–26.0, p=0.02) and indexed maximal left atrial volume (odds ratio =1.13, 95% confidence interval: 1.1–1.2, p=0.001) were the only two independent predictive factors of postoperative atrial fibrillation. The addition of echocardiographic parameters improved the predictive value (χ^2) of the model, from 34 to 57.

Conclusion: A history of atrial fibrillation and indexed left atrial maximal volume are the best predictors of the occurrence of postoperative atrial fibrillation following coronary artery bypass graft. The identification of high risk population of postoperative atrial fibrillation using these two factors could lead to the development of targeted strategies to limit this frequent complication in these patients.

Keywords

Coronary artery bypass graft, atrial fibrillation, echocardiography, left atrial volume

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Introduction

Following cardiac surgery, the incidence of postoperative atrial fibrillation (POAF) is elevated, around 30% after coronary artery bypass graft (CABG) and up to 50% in the case of valvular intervention.¹ The underlying pathophysiologic mechanisms are multiple and influenced by clinical and biological preoperative factors, as well as operative and postoperative factors.² POAF is associated with markedly increased postoperative morbidity and mortality, including higher risk of stroke, thromboembolic events and ventricular arrhythmias.^{1,3} Additionally, the use of anticoagulant and anti-arrhythmic drugs to manage POAF episodes is not totally safe and may expose patients to serious side effects. Furthermore, POAF is also associated with prolonged hospital stay with significant cost.⁴ Consequently, it remains crucial to identify adequately patients at risk of POAF for appropriate preventive management. In this regard, the most recent guidelines of the European Society of Cardiology recommend, as class I indication (level of evidence A), the introduction of β-blockers before surgery.⁵ They also suggest the use of amiodarone as prophylactic treatment in patients with high risk of POAF. However, the accurate definition and the clinical tools available to identify 'high risk' patients are not specified in these guidelines. In these respects, the role of preoperative echocardiography to stratify the risk of POAF is unclear. Overall, left atrial parameters, as assessed using echocardiography, are well-recognized as powerful predictors of new onset of atrial fibrillation in various clinical conditions such as heart failure or valvular heart disease.^{6,7} It could thus be speculated that these parameters may also be good predictors of POAF.

The objective of this study was to assess the interest of preoperative echocardiographic parameters to predict the risk of POAF following isolated CABG. We hypothesized that echocardiography could provide incremental predictive information for risk stratification of POAF, beyond clinical and biological parameters.

Methods

From January 2013 to June 2014, 169 consecutive patients on sinus rhythm receiving isolated CABG at our institution were enrolled in the present study. Patients with preoperative supra-ventricular arrhythmia or those scheduled for CABG combined with valvular intervention were excluded. At baseline, a comprehensive clinical examination was performed and risk factors, comorbidities, treatments, demographic and clinical data were prospectively collected and recorded in a computerized database. A 12-lead electrocardiogram (ECG) was also performed the day prior to surgery. In addition, N-terminal pro-brain natriuretic peptide (NT-proBNP), C-reactive protein and thyreostimulin hormone levels were measured preoperatively.

Echocardiography

All patients underwent a comprehensive transthoracic echocardiography (TTE) including conventional M-mode, Doppler and 2D assessment. All echocardiographic studies were performed on the Artida, Toshiba Medical Systems, Tustin, CA, USA. Doppler and 2D echocardiographic data were collected following the American Society of Echocardiography and the European Association of Cardiovascular Imaging recommendation.⁸ These include: (1) left ventricle (LV) end-diastolic and -systolic diameters, end-diastolic thickness of the interventricular septum and posterior wall and LV mass in the parasternal long axis view; (2) LV ejection fraction using the Simpson biplan method: (3) diastolic LV function using the transmitral E/A ratio and E/e' ratio at the lateral mitral annulus; (4) lateral mitral S-wave velocity; (5) left atrial size using the endsystolic and end-diastolic volume in the four- and twochamber views, and left atrial empting fraction was calculated as the difference between end-systolic and enddiastolic left atrial volume divided by the end-systolic volume; (6) tricuspid annular plane systolic excursion; (7) lateral tricuspid S-wave velocity; (8) systolic pulmonary arterial pressure derived from the tricuspid regurgitation velocity + estimation of right atrial pressure using inferior vena cava diameter and degree of collapse.

Peri-operative data

During the surgical procedure, the following parameters were collected: number of grafted vessels, the use of onpump surgery and subsequent cardiopulmonary bypass time and aortic cross clamp time.

Detection of POAF

The end-point of the study was the occurrence of atrial fibrillation during the early postoperative period (i.e. the time between surgery and discharge, without exceeding 10 days after surgery) defined as any sustained (i.e. >10 min) recorded episodes.⁹ During the hospital stay period, all patients were continuously ECG-monitored during five days after surgery, and then ECGs were performed daily, until discharge or the 10th postoperative day.

Statistical analysis

Patients were separated into two groups according to the occurrence of POAF. Continuous data were expressed as mean \pm SD and were compared using Student's *t*-test. Categorical data were given as numbers and percentages and were compared using the χ^2 test or Fisher exact test, as appropriate.

The independent determinants of the occurrence of POAF were identified using logistic regression and backward

stepwise approach. Variables with a univariate p-value <0.15 were considered for the multivariate analysis. A first multivariate model was built using clinical variables; a second model included only significant clinical variables identified in the first model plus ECG and biologic variables; and the third model used only significant variables from the second model plus echocardiographic data. The results of the multivariate models reported are only those from the last step of the backward logistic regression. Of note, age and gender were systematically added in the three models, regardless of their level of significance. In order to avoid collinearity and to save statistical power, echocardiographic variables were carefully selected and, from a category of variables (e.g. left atrial size and function) only those with the best association with POAF, as assessed by receiver operative characteristics (ROC) curves analysis and area under the curve (AUC), were entered into multivariate model. The odds ratio (OR) and 95% confidence intervals (95% CIs) were reported.

The ROC curves analysis was also performed to identify the best cut-off value of echocardiographic parameters independently associated with POAF, using the Youden J index. All statistical analyses were performed with a commercially available software package, SPSS V23, SPSS Inc., Chicago, IL, USA.

Results

General data and occurrence of POAF

The study population characteristics are presented in Table 1.

During the early postoperative period, POAF occurred in 65 (38%) patients, mostly (63%) within the first 72 h after surgery, >80% in four days. The distribution of the occurrence of the first episode of POAF is presented in Figure 1.

As compared with patients without, those with POAF (Table 1) were significantly older, had more frequently a history of hypertension, previous atrial fibrillation, chronic heart failure and had a higher rate of New York Heart Association (NYHA) functional class \geq III. There was also a trend for higher rates of chronic lung disease in patients with POAF. Regarding ECG and biological data (Table 2), patients with POAF were found with significantly longer PR interval and higher NT-pro BNP level (*p*=0.006) than those without. Of note, the rates of preoperative β -blockers were high but not statistically different in patients with and without POAF.

The operative data and hospitalization lengths are reported in Table 2. The cardiopulmonary bypass time was significantly higher in patients with POAF and there was a trend for higher aortic cross clamp time and greater number of grafts. Finally, their intensive care stay was longer (6±2 vs. 4±2 days in POAF-free patients, p<0.001).

Echocardiographic data

Table 2 reports all baseline preoperative data. Patients with POAF had significantly higher LV volumes and mass, mitral

e'-wave velocity and E/e' ratio, left atrial size and function parameters, systolic pulmonary arterial pressure and right atrial surface, as compared with those without POAF. They also had significantly lower LV ejection fraction and mitral S-wave velocity. Among the whole population, none/trace, mild and moderate preoperative mitral regurgitation (MR) were found in 94 (55%), 66 (39%) and nine (5%) patients, respectively. There was no significant difference between patients with POAF and no POAF with regard to preoperative MR frequency and severity (p=0.55).

Among left atrial and LV parameters (Figure 2), the best predictors of POAF occurrence were indexed maximal left atrial volume (AUC=0.84) and indexed LV mass (AUC=0.73).

The best cut-off value identified for indexed left atrial volume was 32 ml/m² (sensitivity=77%, specificity=78%), while the optimal threshold for indexed LV volume was 110 g/m² (sensitivity=68%, specificity=65%). The related positive and negative predictive values were respectively at 70% and 83% for indexed left atrial volume and 55% and 74% for indexed LV mass. Of note, diastolic and Doppler parameters showed weaker AUCs (all <0.60).

Patients with elevated indexed left atrial maximal volume (i.e. >32 ml/m²) presented more often POAF (70%) as compared with those with normal volume (70% *vs.* 17%, p<0.0001), and 76% of patients with POAF had an indexed left atrial volume >32 ml/m². According to tertiles of indexed left atrial volume, the occurrence of POAF was 11%, 34% and 75% in tertiles 1, 2 and 3, respectively (p<0.0001).

High (>110g/m²) preoperative indexed LV mass was also associated with higher rate of POAF (57% vs. 30%, p<0.0001).

Multivariate determinants of POAF

Among baseline clinical variables, only male gender, advanced NYHA functional class and preoperative history of atrial fibrillation remained independently associated with POAF in multivariate analysis (Table 3, model#1). When adding biological and ECG variables to this previous model, independent determinants of POAF were previous history of atrial fibrillation, and the NT-pro BNP levels (Table 3, model#2). In the final model, indexed LV mass and indexed maximal left atrial volume were selected and added (Table 3, model #3). Only previous atrial fibrillation (OR=6.07, 95% CI: 1.46-26, p=0.015) and indexed left atrial volume (OR=1.12, 95% CI: 1.05-1.2, p=0.001) remained independently associated with POAF occurrence. Of note, the addition of TTE data improved significantly the overall information provided by the multivariate models (Figure 3).

When indexed LV mass and indexed maximal left atrial volume were added to the model#3 as categorical variables, according to the pre-identified cut-off values, only elevated indexed maximal left atrial volume (>32 ml/m², *n*=67) was

Table 1. Demographic data, risk factors and comorbidities.

| | Whole cohort | No POAF | POAF | Þ |
|--|--------------|----------------|-------------|--------------|
| | n=169 | n=104, 62% | n=65, 38% | |
| Demographic data | | | | |
| Age, years | 66 ± 10 | 64 ± 11 | 69 ± 9 | 0.008 |
| Male gender, n (%) | 149 (88) | 89 (86) | 60 (92) | 0.140 |
| Risk factors | | | | |
| Obesity, n (%) | 40 (23.5) | 25 (24) | 15 (23) | 0.886 |
| Dyslipidaemia, n (%) | 121 (72) | 71 (68) | 50 (77) | 0.225 |
| Hypertension, <i>n</i> (%) | 118 (70) | 65 (63) | 53 (82) | 0.009 |
| Smoking, n (%) | 33 (20) | 24 (23) | 9 (14) | 0.334 |
| Diabetes, n (%) | 54 (32) | 33 (31.7) | 21 (32.3) | 0.194 |
| Comorbidities | | | | |
| Previous PCI, n (%) | 29 (17) | 20 (19) | 9 (14) | 0.366 |
| Previous CABG, n (%) | L (I) | 1(1) | 0 (0) | N/A |
| Previous atrial fibrillation, n (%) | 22 (13) | 5 (5) | 17 (26) | 0.001 |
| Peripheral artery disease, n (%) | 32 (19) | 19 (18) | 13 (20) | 0.780 |
| Stroke, n (%) | 15 (9) | 8 (8) | 7 (11) | 0.494 |
| Chronic lung disease, n (%) | 61 (36) | 32 (31) | 29 (45) | 0.068 |
| Chronic heart failure, n (%) | 62 (37) | 32 (31) | 30 (48) | 0.04 |
| ECG data | | | | |
| Heart rate, beats/min | 65 ± 11 | 65 ± 11 | 65 ± 10 | 0.85 |
| PR interval, ms | 174 ± 31 | 169 ± 31 | 183 ± 30 | 0.005 |
| Symptoms | | | | |
| Asymptomatic, n (%) | 57 (34) | 34 (34) | 23 (35) | 0.72 |
| Stable angina, n (%) | 70 (41) | 46 (44) | 24 (37) | 0.35 |
| Unstable angina, n (%) | 22 (13) | 13 (12) | 9 (14) | 0.80 |
| NSTEMI, n (%) | 18 (11) | 9 (9) | 9 (14) | 0.29 |
| STEMI, n (%) | 2 (1) | 2 (2) | 0 (0) | 0.26 |
| NYHA functional class \geq III, <i>n</i> (%) | 17 (10) | 5 (5) | 12 (18) | 0.004 |
| Angiographic data | 17 (10) | 5 (5) | 12 (10) | 0.001 |
| Three vessels disease, n (%) | 120 (71) | 71 (68) | 49 (75) | 0.51 |
| Left main artery disease, n (%) | 55 (32) | 33 (32) | 22 (34) | 0.78 |
| Baseline treatment | 55 (52) | 55 (52) | 22 (34) | 0.78 |
| β -blockers, <i>n</i> (%) | 126 (75) | 78 (75) | 48 (74) | 0.87 |
| Amiodarone, n (%) | . , | | | |
| Calcium channel blockers, n (%) | 4 (2) | () 7 (4) | 3 (5) | 0.13 0.55 |
| | 30 (18) | 17 (16) | 13 (20) | 0.33 |
| Statins, n (%) | 142 (84) | 85 (82) | 57 (88) | |
| Diuretics, n (%) | 50 (30) | 26 (25) | 24 (37) | 0.10 |
| ACE inhibitors, <i>n</i> (%) | 110 (65) | 65 (62) | 45 (69) | 0.37 |
| ARBs, n (%) | 37 (22) | 21 (20) | 16 (25) | 0.50 |
| Biological data | 404 + 700 | | 700 : 007 | 0.007 |
| NT-proBNP, ng/l | 486 ± 708 | 348 ± 516 | 700 ± 897 | 0.006 |
| CRP, UI/I | 5 ± 11 | 6 ± 14 | 4 ± 6 | 0.19 |
| TSH, UI/I | 1.93 ± 1.17 | 1.89 ± 1.11 | 1.95 ± 1.22 | 0.73 |
| Operative data | | 00 (0 1 10) | | |
| On-pump surgery, n (%) | 136 (80.5%) | 88 (84.6%) | 48 (73.8%) | 0.09 |
| Aortic cross clamp time, min | 71 ± 29 | 67 ± 27 | 78 ± 31 | 0.06 |
| Cardiopulmonary bypass time, min | 105 ± 42 | 98 ± 39 | 115 ± 42 | 0.02 |
| Surgery length, min | 228 ± 69 | 228 ± 69 | 228 ± 68 | 0.96 |
| Number of grafted vessels \geq 3, <i>n</i> (%) | 124 (73.3%) | 71 (68.3%) | 53 (81.5%) | 0.06 |

POAF: postoperative atrial fibrillation; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; ECG: electrocardiogram; NSTEMI: non-ST elevation myocardial infarction; STEMI: ST elevation myocardial infarction; NYHA: New York Heart Association; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; NT-proBNP: N-terminal pro-brain natriuretic peptide; CRP: C-reactive protein; TSH: thyreostimulin hormone. significantly and strongly associated with higher risk of POAF (OR=6.6, 95% CI: 2.7–16.1, *p*<0.0001).

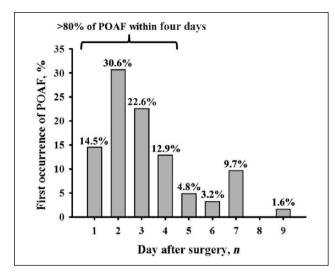


Figure 1. Timing of occurrence of the first episode of postoperative atrial fibrillation. POAF: postoperative atrial fibrillation.

Determinant of POAF in patients free from prior atrial fibrillation

In a sub-analysis excluding patients with preoperative history of atrial fibrillation (n=22), the occurrence of POAF was 11%, 34% and 75% in tertiles 1, 2 and 3 of indexed left atrial volume, respectively (p<0.0001).

In this sub-analysis, only indexed maximal left atrial volume (OR=9.7, 95% CI: 3.8–24.8, p<0.0001) and indexed LV mass (OR=3.2, 95% CI: 1.2–8.1, p=0.016) were independently associated with POAF. As in the whole cohort, the use of TTE data in this sub-analysis markedly improved the overall predictive value of POAF of the multivariate models (+134% from model#2 to model#3, p<0.0001) (Figure 3).

Discussion

The present study shows that in patients nowadays undergoing CABG, POAF remains frequent and its main clinical and biological determinants are previous history of atrial fibrillation and NT-pro BNP. Nevertheless, the addition of echocardiographic data to other preoperative variables

| | Whole cohort | No POAF | POAF | Þ |
|--|--------------|-------------|-------------|--------|
| | N=169 | n=104, 62% | n=65, 38% | |
| LV size | | | | |
| LVED volume, ml | 100 ± 34 | 94 ± 32 | 110 ± 35 | 0.002 |
| LVES volume, ml | 41 ± 25 | 37 ± 21 | 49 ± 29 | 0.005 |
| LV mass, g | 216 ± 70 | 197 ± 56 | 245 ± 79 | 0.0001 |
| Indexed LV mass, g/m ² | 113 ± 33 | 104 ± 27 | 126 ± 37 | 0.0001 |
| LV function | | | | |
| LV ejection fraction, % | 6 ± | 62 ± 9 | 58 ± 13 | 0.04 |
| E-wave velocity, m/s | 68 ± 18 | 69 ± 17 | 68 ± 19 | 0.71 |
| E/A ratio | 0.91 ± 0.33 | 0.90 ± 0.27 | 0.94 ± 0.41 | 0.51 |
| Lateral e'-wave velocity, cm/s | 9.4 ± 2.6 | 9.8 ± 2.6 | 8.8 ± 2.5 | 0.01 |
| E/e' ratio | 8.1 ± 2.7 | 7.7 ± 2.4 | 8.7 ± 3.1 | 0.02 |
| S-wave velocity, cm/s | 10.6 ± 2.5 | 11 ± 2.3 | 10 ± 2.6 | 0.02 |
| LA size and function | | | | |
| LA diameter, mm | 41 ± 7 | 38 ± 6 | 44 ± 6 | 0.0001 |
| LA surface, cm² | 20 ± 5 | 18 ± 4 | 23 ± 5 | 0.0001 |
| Maximal LA volume, ml | 61 ± 21 | 52 ± 13 | 75 ± 24 | 0.0001 |
| Indexed maximal LA volume, ml/m ² | 32 ± 10 | 28 ± 6 | 38 ± 11 | 0.0001 |
| Minimal LA volume, ml | 31 ± 14 | 25 ± 9 | 40 ± 16 | 0.0001 |
| LA emptying volume, ml | 31 ± 11 | 28 ± 9 | 35 ± 12 | 0.001 |
| LA emptying fraction, % | 52 ± 12 | 55 ± 12 | 47 ± 9 | 0.0001 |
| RV function | | | | |
| TAPSE, mm | 22 ± 4 | 22 ± 4 | 22 ± 4 | 0.91 |
| S-wave velocity, cm/s | 14.2 ± 2.8 | 14.3 ± 2.8 | 14.2 ± 2.8 | 0.95 |
| Fractional area changes, % | 42 ± 7 | 42 ± 7 | 41 ± 7 | 0.49 |
| Systolic PAP, mmHg | 31 ± 7 | 29 ± 7 | 33 ± 8 | 0.003 |
| Right atrial surface, cm ² | 16.4 ± 3.9 | 15.1 ± 3.1 | 18.1 ± 4.4 | 0.0001 |

POAF: postoperative atrial fibrillation; LV: left ventricular; ED: end-diastolic; ES: end-systolic; LA: left atrial; RV: right ventricular; TAPSE: tricuspid annular plane systolic excursion; PAP: pulmonary arterial pressure.

improved considerably the prediction of occurrence of POAF. We found preoperative indexed maximal left atrial volume to be the most powerful independent determinant of POAF. In addition, in patients without previous history of atrial fibrillation, indexed left atrial maximal volume and indexed LV mass improved markedly the prediction of POAF.

Comparison with previous studies

Several studies assessed the clinical predictors of POAF in patients with isolated CABG. Among them, age was frequently identified in previous studies. Indeed, older patients seem more prone to have enlarged left atrial with higher rate of myocardial fibrosis, which may be involved in the pathogenesis of POAF. Although patients with POAF were

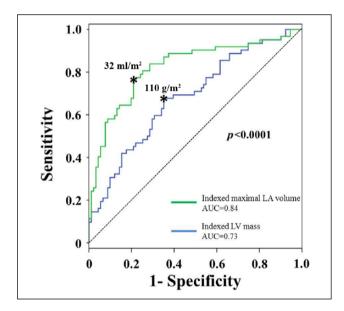


Figure 2. Receiver operative characteristic curves for the prediction of the occurrence of postoperative atrial fibrillation. LA: left atrial; LV: left ventricular; AUC: area under the curve.

statistically older in our cohort, age was not ultimately found to be a significant predictor of POAF after adjustments to other confounders (Table 3). Furthermore, male gender was previously reported as a risk factor for POAF, in part confirmed by our data.

In our study, the most powerful clinical parameter associated with POAF was previous atrial fibrillation, which concurs with several studies (Table 4). Patients with anterior episodes of atrial fibrillation are at higher risk to develop atrial fibrillation in the early postoperative course, mainly due to atrial ischaemia, atrial cannulation, autonomous nervous system activation, electrolytic disorders (e.g. hyperkalaemia, or hypomagnesaemia) and inflammation activation.^{1,10} Amongst biological variables (Table 3, model#2), we found the NT-proBNP to be an independent predictor of POAF prior to the addition of echocardiographic data, which overwhelmed this biological parameter when added to the model. Gibson et al.¹¹ reported this biomarker as a predictor of postoperative atrial fibrillation. They also identified a strong interaction between NT-pro BNP and age and concluded that this biomarker stratifies better the POAF risk in younger patients (i.e. <65 years old). These results were confirmed by Wazni et al.,12 who reported a graded relationship between increased risk of POAF and increased BNP level. NT-proBNP is an accurate marker of myocardial wall stress and its levels rise in patients with heart failure or cardiomyopathy. Furthermore, diastolic parameters are the main determinants of NT-proBNP levels with good correlations reported between the E/e' ratio or left atrial dimension and NT-proBNP in various cardiac diseases. The close relationship between left atrial size and function and NT-proBNP levels, as reported by current literature,¹¹ may explain, at least in part, the good independent value of NT-proBNP to predict POAF, as compared with other clinical and ECG markers.

Compared with patients without POAF, those with POAF had significantly higher LV volumes and mass and lower LV ejection fraction. The best predictive LV parameter found was indexed mass, which was associated only

Table 3. Logistic regression to identify predictors of postoperative atrial fibrillation in the whole study population.

| Variables | Mode | l# I | | Mode | l#2 | | Mode | l#3 | |
|--|------|-----------|-------|------|-----------|-------|--------------|------------------------|------------------|
| | OR | 95% CI | Þ | OR | 95% CI | Þ | OR | 95% CI | Þ |
| Age, per year | 1.03 | 0.99–1.07 | 0.14 | 1.01 | 0.97-1.06 | 0.57 | 1.01 | 0.96-1.05 | 0.816 |
| Male gender | 4.05 | 1.04-15.9 | 0.04 | 3.32 | 0.83-13.3 | 0.09 | 3.13 | 0.49–0.05 | 0.229 |
| NYHA functional class ≥ III | 5.12 | 1.4–18.8 | 0.01 | 2.77 | 0.8–9.57 | 0.108 | 1.42 | 0.32-6.3 | 0.639 |
| Previous AF | 6.16 | 1.9–20.1 | 0.003 | 6.84 | 2.07–22.6 | 0.002 | 6.07 | 1.42–26 | 0.015 |
| PR interval, per 10 ms | | | | 1.12 | 0.98-1.27 | 0.09 | 1.01 | 0.99-1.02 | 0.457 |
| NT-proBNPª | | | | 1.51 | 1.05-2.17 | 0.03 | 1.17 | 0.77-1.80 | 0.463 |
| Indexed LV mass >110 g/m² Indexed maximal LA volume >32 ml/m² | | | | | | | 1.96 7.75 | 0.84-4.55 3.22-18.6 | 0.117 <0.0001 |

^aThe NT-proBNP was natural-log transformed.

OR: odds ratio; CI: confidence interval; NYHA: New York Heart Association; AF: atrial fibrillation; NT-proBNP: N-terminal pro-brain natriuretic peptide; LV: left ventricular; LA: left atrial.

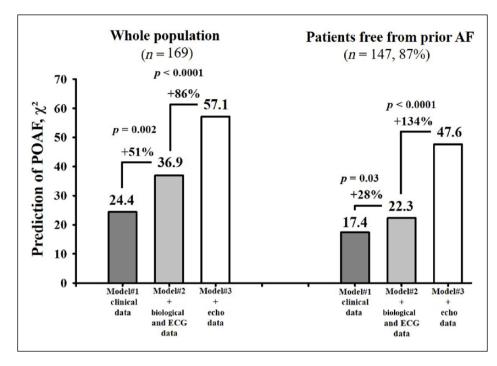


Figure 3. Incremental value of biological, ECG and echocardiographic variables over clinical data in the prediction of occurrence of postoperative atrial fibrillation.

AF: atrial fibrillation; POAF: postoperative atrial fibrillation; ECG: electrocardiogram.

with modest sensitivity and specificity. In addition, in the multivariate analysis, indexed LV mass was not significantly associated with POAF, although a higher number of patients may enable us to confirm this association. However, indexed LV mass was an independent predictor of POAF in the subset of patients without preoperative history of atrial fibrillation. By contrast, indexed left atrial maximal volume was found as a strong independent predictor of POAF, even after adjustments for clinical, biological and ECG parameters. Prior to our report, Osranek et al.13 identified that enlarged left atrial volume was associated with five-fold increase in risk of POAF, using the same cut-off of 32 ml/ m². In contrast, Gibson et al. found no statistical difference between the two groups (i.e. POAF vs. no POAF) in terms of indexed left atrial volume. This may be explained, at least in part, by the exclusion of patients with prior atrial fibrillation in this later study.

Thanks to all these previous studies, we have been able to test and validate the hypothesis of the incremental predictive value of echocardiographic parameters over clinical, demographic and biological variables (Figure 3). In this regard, the present study is original and reports new findings.

Clinical implications

Trials demonstrated a reduction of 50% of POAF when patients were preoperatively treated with amiodarone, and this strategy also decreased the risk of postoperative stroke,

ventricular arrhythmias and length of hospital stay. The benefit of amiodarone in preventing POAF is also reported in patients with β-blocker. However, the use of amiodarone is associated with increased risk of postoperative bradycardia and hypotension, limiting its wide use in every patient with cardiac surgery indication. As a matter of fact, current guidelines only recommend amiodarone treatment in 'high risk' patients of POAF. The present study identifies patients with enlarged indexed left atrial volume (i.e. >32 ml/m²) as at high risk of POAF, independent of other reported clinical and biological predictors of POAF. Similarly, elevated indexed LV mass was also independently associated with POAF occurrence, in the subset of patients without any preoperative history of atrial fibrillation. Hence, an improved risk stratification using these variables could focus the prophylactic use of amiodarone in patients at high risk of POAF (i.e. those with a history of atrial fibrillation and/or an indexed left atrial volume >32 ml/m² or indexed LV mass >110g/m²). However, the appropriate timing to preoperatively start this treatment is still a source of debate.^{14–16} Whereas previous study seemed to promote initiating the treatment seven days before CABG, others reported good tolerance, safety and efficacy with accelerated loading regimen one or two days before surgery. Such prophylactic strategy, as well as the best timing to start treatment and the optimal length for this treatment, requires further evaluation. Furthermore, the indexed left atrial volume is an easy parameter, widely available and measurable in daily practice and with good reproducibility.

| Author, year, reference | <i>n/</i> mean age in years/% male | POAF definition | Length of monitoring | Type of monitoring | POAF prevalence, % | Average POAF occurrence time, days | Determinant of POAF |
|--|---------------------------------------|--------------------|-------------------------|--|--------------------------|--|---|
| Nakai et al. 2002 ⁹ | 93/63/79.5 | >10 min | Up to discharge | Telemonitoring | 30 | I | Age, BSA, LA surface |
| Amar et al. 2004' ⁷ | 1553/64/67 | >5 min | Up to discharge | Telemonitoring | 33 | I | Age, preoperative P-wave>110ms, postoperative low cardiac output |
| Acil et al. 2007' ¹⁸ | 102/61/78 | Unknown | Unknown | Scopic monitoring in ICCU and then daily ECG | 18 | I | Age, prior AF, LA diameter |
| Benedetto et al. 2007 ¹⁹ | 96/67/61 | Unknown | Unknown | Telemonitoring | 25 | 3 ± 2 | Age, preoperative β-blocker, LA diameter, LA surface |
| Gibson et al. 2009 ¹¹ | 275/65/84 | >30 s | Up to day 7 | Scopic monitoring during three days and then daily ECG | 39 | 3 ± 2 | Age, Euroscore, BNP; NT-proBNP, E/A ratio, septal and averaged e'-wave velocity |
| Parsaee et al. 2014 ²⁰ | I 50/60/75 | >5 min | Up to day 5 | Scopic monitoring in ICCU and then daily ECG | 12.7 | 4 ± 2 | Age, BMI, PR interval, LVES volume, LA surface, indexed LA volume, LA empting fraction. E/A ratio. CPB time |
| Present study | l 69/66/88 | >10 min | Up to day 10 | Scopic monitoring in ICCU, telemonitoring during five days and, when required, daily ECG | 38 | 3 ± 2 | Prior AF, indexed maximal LA volume |
| POAF: postoper: | ative atrial fibrillation | ; BSA: body surf | ace area; LA: left atr | ial; ICCU: intensive coronary care unit; E | ECG: electrocardi | ogram; AF: atrial fibrill | POAF: postoperative atrial fibrillation; BSA: body surface area; LA: left atrial; ICCU: intensive coronary care unit; ECG: electrocardiogram; AF: atrial fibrillation; NT-proBNP: N-terminal pro-brain natri- |

Table 4. Atrial fibrillation after isolated CABG in series after 2000. Literature review and comparison with our series.

uretic peptide; BMI: body mass index; LVES: left ventricular end-systolic; CPB: cardiopulmonary bypass.

Limitations

Advanced echocardiographic parameters, such as twodimensional speckle tracking-derived LV or left atrial strain, were not measured in the present study. Although promising, the reproducibility of these parameters (e.g. peak left atrial strain) may be poorer than left atrial volume in centres with less experience. We aimed to identify echocardiographic parameters used in daily clinical practice, which could be easily assessed within days prior to surgery.

Our definition of POAF considered only sustained episodes of atrial fibrillation for more than 10 min, whereas some previous studies have used a more permissive definition with 30 s of atrial fibrillation. Such definition also allows identifying occurrence of POAF even in the late hospitalization phase, when the monitoring is stopped and only daily or symptom-motivated ECGs are performed. In addition, asymptomatic episodes of atrial fibrillation may have been missed once monitoring had been removed after day 5. The literature suggests that the vast majority of episodes of POAF occur within the first 3–4 days and are generally sustained for more than 1 hour. Consequently, the risk of undetected episodes appears particularly low.

Conclusion

In patients undergoing isolated CABG, the rate of POAF currently remains high, despite the frequent use of preoperative β -blockers. A history of previous atrial fibrillation and the indexed maximal left atrial volume are the best predictors for the occurrence of POAF. Furthermore, in the absence of any preoperative history of atrial fibrillation, both indexed maximal left atrial volume and LV mass are powerful predictors of POAF, underlining the key role of preoperative echocardiography. The identification of high risk population of POAF using these two factors could lead to the development of targeted therapeutic strategies (e.g. prophylactic use of anti-arrhythmic agents) to limit this frequent complication. Nevertheless, such selective preoperative preventive strategy aiming to reduce the burden of POAF requires further evaluation.

Conflict of interest

The authors declare that there is no conflict of interest.

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