

# Left Atrial Dysfunction and New-Onset Atrial Fibrillation After Cardiac Surgery

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**Introduction and objectives.** Postoperative atrial fibrillation is a common complication of carrying out cardiac surgery with extracorporeal circulation (ECC). The aim of this study was to determine whether preoperative left atrial contractile dysfunction, as assessed by tissue Doppler echocardiography, is associated with the development of postoperative new-onset atrial fibrillation (PAF).

**Methods.** Transthoracic Doppler echocardiography was performed preoperatively in patients undergoing elective cardiac surgery. Left atrial contractile function was evaluated by tissue Doppler imaging (TDI) of the mitral annulus.

**Results.** The study included 92 patients in sinus rhythm preoperatively who underwent elective cardiac surgery with ECC: 73 (79%) were male and 19 (21%) were female, and their mean age was 67 (10) years. Of these, 19 (20.6%) developed PAF 34 (12) h postoperatively. Bivariate analysis showed that PAF was associated with older age (71 [7] years vs 66 [10] years;  $P=.034$ ), a large left atrial diameter (LAD), and a low peak atrial systolic mitral annular velocity (A velocity) and a high mitral E/A ratio on TDI. Logistic regression analysis showed that PAF was independently associated with a large LAD (odds ratio [OR] = 2.23; 95% confidence interval [CI], 1.05-4.76;  $P=.033$ ) and a low A velocity (OR=0.70; 95% CI, 0.55-0.99;  $P=.034$ ).

**Conclusions.** Preoperative left atrial dysfunction, as assessed by TDI, was associated with an increased risk of PAF.

**Key words:** Echocardiography. Atrial fibrillation. Atrium. Cardiopulmonary bypass.

## Disfunción auricular izquierda y fibrilación auricular de reciente comienzo en cirugía cardíaca

**Introducción y objetivos.** La fibrilación auricular postoperatoria es una complicación frecuente de la cirugía cardíaca con circulación extracorpórea (CEC). Hemos estudiado si la función contráctil auricular izquierda preoperatoria evaluada mediante ecocardiografía Doppler tisular se asocia a la aparición de fibrilación auricular postoperatoria (FAP) de reciente comienzo.

**Métodos.** Realizamos una ecocardiografía transtorácica preoperatoria a pacientes intervenidos de cirugía cardíaca electiva. La función contráctil auricular izquierda se evaluó mediante el análisis por Doppler tisular del anillo mitral (DTm).

**Resultados.** Estudiamos a 92 pacientes en ritmo sinusal previo intervenidos de cirugía coronaria electiva con CEC, 73 (79%) varones y 19 (21%) mujeres, con una media de edad de  $67 \pm 10$  años; 19 (20,6%) pacientes presentaron FAP en torno a las  $34 \pm 12$  h postoperatorias. En el análisis bivariable, una edad mayor ( $71 \pm 7$  frente a  $66 \pm 10$ ;  $p = 0,034$ ), un mayor tamaño de la aurícula izquierda (TAI), una menor velocidad del pico sistólico auricular del anillo mitral (a) y una mayor relación e/a (DTm) se asociaron con la FAP. En el análisis de regresión logística, el TAI (odds ratio [OR] = 2,23; intervalo de confianza [IC] del 95%, 1,05-4,76;  $p = 0,033$ ) y una menor (a) (OR = 0,70; IC del 95%, 0,55-0,99;  $p = 0,034$ ) se asociaron de forma independiente con la FAP.

**Conclusiones.** Una disfunción auricular izquierda preoperatoria evaluada mediante DTm se asoció con un mayor riesgo de FAP.

**Palabras clave:** Ecocardiografía. Fibrilación auricular. Aurícula. Circulación extracorpórea.

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## INTRODUCTION

Atrial fibrillation is one of the most common postoperative complications of heart surgery, with an incidence of up to 50%.<sup>1</sup> It is associated with considerable morbidity and high healthcare

## ABBREVIATIONS

LA: left atrium.

PAF: new-onset postoperative atrial fibrillation.

TDI: tissue Doppler imaging.

expenditure.<sup>2</sup> Recent guidelines for the prevention of postoperative atrial fibrillation have been published,<sup>3</sup> as well as studies investigating its pathophysiology<sup>4,5</sup> and the factors predicting<sup>6,7</sup> its development.

Assessment of possible left atrial dysfunction in patients with coronary disease, which<sup>8</sup> is usually done by tissue Doppler echocardiographic imaging (TDI) of the mitral annulus,<sup>9</sup> may be of use to identify patients with new-onset postoperative atrial fibrillation (PAF).

The aim of this study is to determine the role of preoperative left atrial dysfunction assessed by TDI of the mitral annulus, together with parameters of left ventricular diastolic dysfunction, as factors related to PAF in on-pump coronary surgery.

## METHODS

### Patients

From January 1 to October 31 2007, transthoracic echocardiography with TDI of the mitral annulus was used to examine 92 consecutive patients from the cardiology or cardiac surgery hospital wards about to undergo elective on-pump surgery for myocardial revascularization. All patients were in sinus rhythm before the procedure. The exclusion criteria were off-pump surgery, prior atrial fibrillation, known thyroid disease, and poor quality of the echocardiographic image. The study protocol was approved by the hospital ethics committee.

### Perioperative Protocol

No specific protocol was applied for prophylaxis of PAF. The patients' usual medication with beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, or statins was maintained before the procedure. The same anesthesia method was used in all patients. Anesthesia was induced and maintained with propofol, midazolam, fentanyl, and cisatracurium. All procedures were performed by the same surgical team. The extracorporeal system was

composed of a membrane oxygenator (Optima XP, Cobe Cardiovascular Inc, Denver, Colorado, United States), an extracorporeal circuit (Tygon, Dideco, Mirandola, Italy), and a centrifugal pump (Biopump, Medtronic, Minneapolis, Minnesota, United States). With hypothermia at 30°C, pump flow was adjusted to maintain a mean arterial pressure of >45 mm Hg and a flow index of 2.2 L/min/m<sup>2</sup>. St. Thomas 4:1 sanguineous cardioplegic solution at 12°C was used.

### Echocardiographic Recordings

All echocardiographic recordings were performed by the same 2 examiners, 2 to 4 days before the surgical procedure. Images were obtained in accordance with the guidelines of the American Society of Echocardiography<sup>10,11</sup> using a GE Vivid echocardiograph (GE Ultrasound Europe, Solingen, Germany),<sup>3</sup> then stored on the hard drive of the unit and analyzed by the same operators. Left atrial size was measured in M mode (long parasternal view), as well as in the apical 4-chamber view; the long axis of the left atrium was recorded from its inferior margin (midpoint of mitral annulus plane) to its superior-posterior margin (midpoint of the posterior wall). The mean of 5 consecutive beats was recorded to optimize the measurement.<sup>12</sup> Left ventricular ejection fraction was obtained with the biplane Simpson method from the 2-chamber and 4-chamber apical views.

Interobserver variability in our laboratory is less than 7% for this measure.<sup>13</sup> Diastolic function was evaluated by recording the diastolic filling velocities (E and A waves, E/A ratio, deceleration time) and the left ventricular isovolumetric relaxation time by pulsed Doppler study of the mitral and aortic transvalvular flow. The pulmonary vein velocities were also recorded. Left atrial function by TDI of the mitral annulus was assessed following the recommendations established by the American Society of Echocardiography.<sup>11</sup> The sample size (3 mm for the septal annulus and 5 mm for the lateral annulus) and Doppler angle in the 4-chamber apical view were adjusted so that the cursor would be parallel to the plane of the mitral annulus. Determinations were performed with the patient in maintained expiration. The mean of 5 consecutive heart cycles was calculated.

### Variables Analyzed

The following data were recorded: demographic variables, comorbid conditions, pharmacological treatments prior to the procedure, surgery-related variables, and postoperative clinical progress in the intensive care unit.

## Arrhythmia Recording

All patients hospitalized for elective surgery in the cardiac surgery and cardiology wards underwent daily electrocardiography before surgery. In addition, the presence of sinus rhythm was noted at the preoperative echocardiographic study. In the immediate postoperative period in the intensive care unit, patients were continuously monitored until they were discharged to a hospital ward. Moreover, 12-lead electrocardiography was performed at the time of transferal to the intensive care unit and daily thereafter until transfer to the cardiac surgery ward. Later, at least 1 additional 12-lead electrocardiographic study was carried out before hospital discharge.

Episodes of atrial fibrillation that were not self-limited and lasted more than 30 seconds were considered valid for the purposes of the study<sup>14</sup>; in all cases therapeutic measures were required for reversion.

## Statistical Analysis

Quantitative variables are expressed as the mean (SD), and categorical variables as frequency and percentage. After confirming normal distribution of each variable with the Levene test and Kolmogorov-Smirnov goodness-of-fit test, the Student *t* and Mann-Whitney *U* tests (as appropriate) were used to compare quantitative variables. Qualitative variables were compared with the  $\chi^2$  test. Variables with a *P*-value <.10 were selected for inclusion in a logistic regression analysis. To estimate the relationship between the statistical value and the clinical value of the variables, a simple analysis was performed according to the maximum likelihood method for each of the variables selected. Simple regression analyses were performed, in which the independent variables were age, left atrial (LA) size, mitral annulus A wave size (a-wave), and the E/A ratio of the mitral annulus (e/a), and the dependent variable was development of atrial fibrillation. In addition, the association between the independent variables, age, peak atrial systolic mitral annular velocity (a), e/a ratio, and LA size was confirmed with the Spearman rho correlation coefficient. We found that the shared variance between (a) and e/a was significant; hence, e/a was not included in the final analysis because it was a variable derived from (a). Lastly, a multiple logistic regression model with asymptotic analysis and Monte Carlo methods, including age, LA size, and (a), was used to obtain probability values. All *P* values <.05 were considered statistically significant. The SPSS software, version 15 (Chicago, Illinois, United States) and LogXact (Cytel Co, Massachusetts, United States) were used for the analyses.

## RESULTS

A total of 92 patients, previously in sinus rhythm, underwent on-pump coronary surgery; 73 (79%) were men and 19 (21%) women, with a mean age of 67 (10) years, ischemia time of 43 (20) minutes, and on-pump time of 84 (25) minutes. Nineteen of them (21%) experienced PAF, which presented at around 34 (12) hours postoperatively.

In the bivariate analysis, older patients showed a significantly greater incidence of PAF; there were no other differences in the demographic variables or the characteristics of the surgical procedures between the 2 groups (Table 1). Regarding the echocardiographic variables, significant differences were only found for LA size, (a) velocity, and the e/a ratio (Table 2).

The results of simple logistic regression analysis of the variables described above are shown in Table 3. After confirming that the a-wave and e/a ratio presented  $\rho = -0.57$  ( $P < .001$ ), the e/a ratio was excluded because it is a factor derived from the a-wave. LA size did not correlate significantly with (a) ( $\rho = -0.21$ ;  $P = .10$ ). Hence, the a-wave was added to age and LA size in the model. LA size and a-wave remained in the final adjusted model, which yielded a rate of correctly classified cases of 79% (Table 3).

Observed mortality was 4 (4.3%) patients (Table 1). The remaining patients recovered sinus rhythm before being transferred to the hospital ward.

## DISCUSSION

The incidence of PAF in the present study was 21%, a rate in keeping with reported values in the recent literature.<sup>1-3,7</sup> Among the echocardiographic parameters analyzed, an enlarged left atrium and lower peak atrial systolic mitral annular velocity were associated with the development of PAF.

New-onset postoperative atrial fibrillation is one of the most common complications occurring after coronary surgery. The condition is associated with considerable morbidity, and the factors contributing to its cause have not been completely defined.<sup>1</sup> With regard to the risk factors favoring its development, advanced age is one of the most commonly encountered.<sup>15</sup> In our series, this factor was displaced by atrial dysfunction, although this finding should be interpreted with caution, in view of the sample size.

Recent studies have focused on obesity and metabolic syndrome,<sup>16</sup> concentrations of type 1 plasminogen activator inhibitor (PAI-1),<sup>17</sup> and oxidative<sup>5</sup> stress, among other factors. Nonetheless, these studies do not generally report whether preoperative prophylaxis was given for atrial fibrillation,<sup>3</sup> and the patients included are not

**TABLE 1. Characteristics of the Population**

Variable	PAF (n=19)	No PAF (n=73)	P*
Age, years	71 (7)	66 (10)	.03
Men, n (%)	13 (68)	60 (82)	.19
BMI	28.1 (3.4)	28.5 (3.7)	.71
Hypertension, n (%)	8 (42)	42 (58)	.42
Diabetes mellitus, n (%)	11 (58)	37 (50)	.37
Dyslipidemia, n (%)	10 (53)	36 (49)	.48
COPD, n (%)	1 (5)	8 (11)	.66
Renal failure, n (%)	1 (5)	3 (4)	.91
LVEF (%)	63 (10)	66 (10)	.25
Beta-blockers, n (%)	16 (84)	55 (75)	.61
Calcium channel blockers, n (%)	5 (26)	15 (20)	.50
Lipid-lowering drugs, n (%)	14 (74)	56 (77)	.27
ACE inhibitors, n (%)	6 (32)	27 (37)	.31
Number of bypasses >2, n (%)	9 (47)	28 (38)	.51
Graft, n (%)			.86
IMA	4 (21)	14 (19)	
Saphenous	4 (21)	12 (16)	
Both	11 (58)	47 (65)	
On-pump time, min	85 (21.4)	84 (27)	.93
Ischemia time, min	42 (18.2)	44 (20.6)	.62
Lactate at end of on-pump, mmol/L	1.9 (0.6)	1.7 (0.7)	.21
Mortality, n (%)	1 (5)	3 (4)	.88

ACE inhibitors indicates angiotensin-converting enzyme inhibitors; BMI, body mass index; COPD, chronic obstructive pulmonary disease; IMA, internal mammary artery; LVEF, left ventricular ejection fraction; PAF, new-onset postoperative atrial fibrillation.

\*Student *t* or Mann-Whitney *U* test for quantitative variables.  $\chi^2$  test for qualitative variables.

Data are expressed as the mean (SD) except where otherwise indicated.

**TABLE 2. Echocardiographic Parameters**

Variable	PAF (n=19)	No PAF (n=73)	P
Ventricular septum, mm	13.2 (2.7)	13.3 (2.8)	.92
LV end-diastolic diameter, mm	49.6 (0.8)	48.9 (0.8)	.81
LV end-systolic diameter, mm	34.9 (0.9)	38.4 (1.2)	.71
LA parasternal long-axis diameter, cm	4.6 (0.55)	4.5 (0.69)	.94
Diastolic mitral annulus-to-LA roof distance, cm	4.9 (0.79)	4.2 (0.9)	.02
Transmitral E wave, cm/s	75 (21)	69 (18)	.23
Transmitral A wave, cm/s	66 (17)	75 (22)	.15
E/A ratio	1.28 (0.75)	0.98 (0.36)	.18
Deceleration time, ms	211 (75)	182 (55)	.12
Transmitral A wave duration, ms	146 (73)	134 (63)	.58
Isovolumetric relaxation time, ms	99 (29)	97 (27)	.82
Lateral mitral annulus e wave, cm/s	6.4 (1.8)	5.9 (1.7)	.40
Lateral mitral annulus a wave, cm/s	7.1 (2.1)	8.7 (2.2)	.01
e/a ratio	0.96 (0.3)	0.7 (0.2)	.01
Lateral mitral annulus s wave, cm/s	6.8 (1.2)	7.7 (1.9)	.20
E/e ratio	9.1 (3.6)	8.8 (2.4)	.75
Lateral mitral annulus A wave duration, ms	114 (55)	118 (63)	.85
Pulmonary vein S wave, cm/s	45 (14)	49 (13)	.40
Pulmonary vein D wave, cm/s	44 (16)	40 (15)	.33
Pulmonary vein S/D ratio	1.13 (0.4)	1.33 (0.4)	.12
Pulmonary vein A wave, cm/s	30 (10)	27 (6)	.22
Pulmonary A wave duration, ms	127 (53)	113 (40)	.28

LA indicates left atrium; LV, left ventricle; PAF, new-onset postoperative atrial fibrillation.

**TABLE 3. Construction of the Model of Variables Independently Associated With New-Onset Postoperative Atrial Fibrillation**

	OR	95% CI	P
Simple logistic regression analysis of the independent variables			
Age	1.07	1.01-1.13	.024
Left atrial size	2.14	1.06-4.32	.024
Mitral annulus A wave	0.67	0.48-0.94	.011
Mitral annulus e/a ratio	40.21	3.27-493.7	.002
Multivariate logistic regression			
Left atrial size	2.23	1.05-4.76	.033
Mitral annulus A wave	0.7	0.50-0.99	.034
Constant	0.273		.001

CI indicates confidence interval; OR, odds ratio.

always in sinus rhythm before the procedure.<sup>17</sup> None of the other medical risk factors analyzed (hypertension, diabetes mellitus, obesity, and dyslipidemia) were associated with the development of PAF. Although these factors are presented in the literature as predisposing to PAF, an association is not always seen in the related clinical studies<sup>7,14</sup>; the same is true for the present study. We have seen something similar with the use of beta-blockers and statins prior to the procedure, which has not been associated with the development of PAF. The known protective role of beta-blockers has been firmly established in recent recommendations for PAF prophylaxis. Although there was no defined prophylactic protocol in the present study, patients who were receiving beta-blockers continued to take them up to the time of surgery. The percentage of patients using these agents was high in both groups and this fact may have had an influence on the lack of relationship with the development of PAF, as has occurred in other studies.<sup>7,14</sup> The recently described protective role of statins against the development of PAF<sup>7,18,19</sup> may also have played a part. Preoperative use of statins in our series was also high in both groups (74% and 77%), and this may have masked the protective role of these agents against PAF. In a study by Arribas-Leal et al<sup>7</sup> only 39% of patients who developed PAF were using statins compared to 66% of patients who did not develop PAF.<sup>7</sup>

Several studies in recent years have examined the role of the left atrium in conditions such as atrial fibrillation, stroke, and heart failure, and it has also been the subject of extensive review articles.<sup>20,21</sup> Determination of the left atrial volume has been found to provide a more precise measure than conventional M mode measurement.<sup>12</sup> Advances have also been made in the study of atrial function, which is usually carried out noninvasively by determining

the transmitral blood flow with conventional pulsed Doppler, incorporating imaging techniques such as tissue Doppler. This method records systolic and diastolic flow velocities within the myocardium and has been validated as reliable for measuring filling pressures and diastolic function.<sup>11,22</sup> Pérez-Paredes et al<sup>23</sup> analyzed the left atrial wall velocities by tissue pulsed Doppler and found a wave pattern that correlated with the various phases of atrial function. Hesse et al<sup>9</sup> validated tissue Doppler to assess left atrial systolic function and concluded that peak atrial systolic mitral annular velocity correlates well with left atrial contractile function evaluated by other more complex methods. Similarly, Yu et al<sup>8</sup> described the presence of left atrial dysfunction in coronary patients with tissue Doppler imaging and reported that contractile function can be altered even when transmitral flow values are normal.

Two recent studies have specifically assessed the value of preoperative tissue Doppler images for predicting PAF.<sup>14,24</sup> In one of them, Benedetto et al<sup>24</sup> expressly evaluated preoperative atrial systolic function by tissue Doppler and the relationship of this parameter with the development of atrial fibrillation in the postoperative period of patients undergoing coronary revascularization. In keeping with the present study, the authors found that slower A'm wave velocities, that is, greater left atrial dysfunction, predicted the development of PAF. In contrast, parameters indicating left ventricular diastolic dysfunction, such as those derived from transmitral filling or the E/e ratio, were not related with the development of PAF. Along this line, we found no association in the wave study of the pulmonary veins. In the other study, however, Açil et al<sup>14</sup> reported that tissue Doppler was not suitable for predicting the appearance of PAF. Left atrial enlargement was another factor related to PAF.<sup>14,24</sup>



The influence of atrial size on the development of atrial fibrillation is well recognized.<sup>12</sup> Our results are consistent with the reported findings, in which, additionally, no association was found between the atrial size and (a).<sup>8,9</sup>

This study has some limitations. The sample size may be small considering the large number of variables that can influence the development of PAF. We did not determine the left atrial area; however, the recordings were obtained as the mean of 5 consecutive beats. In addition, we only included episodes of atrial fibrillation occurring in the immediate postoperative period, and we have no information on the long-term clinical course of the patients. Future studies are needed to consolidate the role that LA contractile dysfunction assessed by tissue Doppler study of the mitral annulus has on a predisposition for PAF, since this has not been confirmed in all related studies.<sup>14</sup>

## CONCLUSIONS

Echocardiographic study with tissue Doppler imaging in patients about to undergo cardiac surgery is now common practice.<sup>25</sup> We believe that study of left atrial contractile function, a parameter that any examiner can easily obtain,<sup>9,23</sup> should be included in the routine preoperative workup of these patients, thereby providing another element to help us identify patients at risk of PAF.

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