

Left Atrial Mechanical Function Predicts Postoperative AF in Patients with Rheumatic Mitral Valve Disease Who Underwent Mitral Valve Surgery

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ABSTRACT

Objective: Postoperative atrial fibrillation (PoAF) is a common complication after surgical mitral valve replacement. Late PoAF is independently associated with long-term mortality. This study aimed to test the utility of preoperative left atrial mechanical function as a predictor of early and late PoAF in clinical practice.

Methods: Patients (N = 150) with a rheumatic mitral valve who underwent mitral valve replacement with or without tricuspid valvuloplasty and who were in stable sinus rhythm were included. Baseline characteristics and transthoracic echocardiographic assessment information on the day before surgery were collected. Em, Em', and Ei indicate early diastolic peak velocity of the mitral valve, early diastolic velocity at the lateral wall of the mitral annulus, and early diastolic velocity at the interventricular septal annulus, respectively.

Results: Early PoAF was present in 59 of 150 patients (39.3%), and 32 of 150 patients (21.3%) developed late PoAF within 1 year after surgery. Among all of the variables examined, age, diabetes, early mitral filling velocity (Mitral E), left atrial mechanical function (Mitral A), Em/Em', Em/Ei', and mitral transvalvular gradient showed a significant correlation with PoAF. Only age, Mitral A, and mitral transvalvular gradient showed strong, significant correlations with the occurrence of late PoAF. In a multivariate analysis, predictors of late PoAF recurrence included early PoAF and Mitral A.

Conclusion: Routine evaluation of Mitral A is feasible and useful to predict early and late PoAF in patients with a rheumatic mitral valve undergoing surgical mitral valve replacement.

INTRODUCTION

Atrial fibrillation (AF) is a common complication after cardiac surgery and is associated with significantly increased morbidity, mortality, and total treatment costs [El-Chami 2010]. Reported incidences of early postoperative AF (PoAF) range from 10% to 65% [Mathew 2004; Zhang 2017; Zhang 2018]. Furthermore, early PoAF is known to increase the risk of late PoAF [Lanters 2018; Lee 2014], which has a high mortality rate [Park-Hansen 2018; Kawamoto 2018; Magruder 2016]. Patients who undergo surgical mitral valve replacement (MVR) for rheumatic mitral disease are at risk for developing PoAF, even after valve replacement [Park-Hansen 2018]. It is well documented that enlargement of the left atrium is associated with AF and its recurrence in patients with rheumatic mitral disease [Zhang 2017; Wang 2019; Wang 2018; Xu 2017]. However, the relationship between left atrial mechanical function and late PoAF is seldom investigated in patients undergoing mitral valve surgery. Left atrial mechanical function can be estimated by noninvasive techniques, including pulse wave Doppler across the mitral valve, during diastole in patients in sinus rhythm, with the transmitral A wave (Mitral A) corresponding to late diastolic filling of the left ventricle, associated with atrial contraction [Mottram 2005]. Therefore, the aim of this study was to explore the utility of evaluating left atrial mechanical function before surgery in predicting the risk of early and late PoAF among patients undergoing surgical MVR.

Methods

Eligibility Criteria

From January 2012 to December 2016, we retrospectively enrolled consecutive patients with a severe isolated rheumatic mitral valve who underwent MVR with or without tricuspid valvuloplasty at the Department of Cardiovascular Surgery, General Hospital of Northern Theater Command, Liaoning, China. The patients were evaluated the day before surgery and had to be in stable sinus rhythm as documented by 12-lead electrocardiography (ECG) and Holter. Patients were excluded from the study if they had (1) emergent surgery; (2) other, more than moderate aortic valvular disease or a valvular prosthesis; (3) a history of cardiac surgery; (4) a history of congenital cardiac abnormalities or cardiac tumors; (5)

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significant coronary artery disease; or (6) a history of arrhythmia, including atrial fibrillation (AF) and ventricular tachycardia. Finally, 150 patients met the criteria. Ethics approval was obtained from the Ethics Committee of the General Hospital of Northern Theater Command. Our research is in compliance with the Declaration of Helsinki.

Surgical Procedure

The surgical mitral valve replacement procedure was performed as described previously [Wang 2018; Jin 2013]. Briefly, all operations were performed by the same cardiac anesthesiologist, perfusionist, and surgical team. Under standard cardiopulmonary bypass with mild hypothermia (34°C), mitral valve replacement was performed using an atrial septal approach. Antegrade cold potassium (16 mmol/L) cardioplegia was applied for regular repeated perfusion. Mitral valve replacement used mitral anterior leaflet resection and posterior leaflet preservation. Tricuspid valvoplasty was performed according to the pathological changes of the tricuspid valve. After cardiopulmonary bypass, transesophageal echocardiography was used to monitor the mean mitral transvalvular pressure difference (3–8 mmHg).

Early Postoperative AF

The early PoAF monitoring was as described previously [Zhang 2017; Zhang 2018; Xu 2017]. Briefly, postoperative cardiac rhythms were continuously recorded during the first 4 to 5 days. Telemetry recordings, ECGs, and patient records were all manually evaluated for the presence of AF episodes. Early PoAF was defined as irregular RR intervals in the absence of distinct P waves, with a duration of ≥ 1 minute, or for any length of time requiring an intervention for hemodynamic compromise, occurring within 14 days after the surgery.

Late Postoperative AF

AF that occurred or lasted beyond the first 12 months after surgery was considered late PoAF. Late PoAF was detected on either ECGs or 24-hour Holter recordings. If applicable, additional rhythm registrations obtained during the follow-up period were requested from the referring hospital [Lanters 2018].

Echocardiography

All patients underwent a 2-dimensional Doppler echocardiogram using PHILIPS IE33 (Andover, MA) 5-1 MHz probes. The early and late diastolic peak velocities of the mitral valve (Em and Am, respectively) and tricuspid valve (Et and At) was collected by pulse-wave tissue Doppler imaging (PW-TDI). Measurements of the mean mitral transvalvular pressure difference were used with the PW-TDI. Two-dimensional area trace or Pt1/2 of the early-diastolic blood flow of the mitral valves was used to measure the mitral valve area (MVA). PW-TDI was used to measure the early diastolic, late diastolic, and systolic peak velocities at the lateral wall of the mitral annulus (Em', Am', and Sm'), the interventricular septal annulus (Ei', Ai', and Si'), and the lateral wall of the tricuspid annulus (Et', At', and St'), and then Em/Em', Em/Ei', and Et/Et' were calculated. The extent of stenosis

and regurgitation at the mitral, aortic, and tricuspid valves were judged by pulsed, continuous, and color Doppler echocardiography [Joint Task Force 2012; Nishimura 2014] and classified as slight (grade 1), mild (grade 2), moderate (grade

Table 1. Analysis of Echocardiographic Data of Early PoAF Patients*

Variable	Early PoAF		P Value
	No (n = 91)	Yes (n = 59)	
LAD (mm)	46.5 \pm 5.8	46.2 \pm 5.8	.731
LVEDD (mm)	43.6 \pm 5.3	45.2 \pm 5.3	.084
RVOTd (mm)	25.1 \pm 5.2	25.5 \pm 4.3	.635
PAD (mm)	23.7 \pm 4.5	23.6 \pm 5.0	.934
LVEF (%)	58.5 \pm 2.8	58.2 \pm 3.8	.558
Em (m/s)	2.02 \pm 0.68	1.80 \pm 0.58	.043
Am (m/s)	1.94 \pm 0.63	1.72 \pm 0.48	.023
Et (m/s)	0.47 \pm 0.13	0.47 \pm 0.13	.871
At (m/s)	0.44 \pm 0.14	0.43 \pm 0.14	.565
Em' (cm/s)	5.06 \pm 1.76	5.37 \pm 1.78	.299
Am' (cm/s)	7.80 \pm 2.97	7.29 \pm 2.69	.299
Sm' (cm/s)	7.35 \pm 2.01	7.41 \pm 1.55	.855
Et' (cm/s)	8.89 \pm 2.87	9.21 \pm 3.16	.527
At' (cm/s)	14.08 \pm 4.34	14.48 \pm 4.05	.566
St' (cm/s)	12.39 \pm 2.70	12.38 \pm 2.68	.976
Em/Em'	45.7 \pm 24.1	36.9 \pm 18.9	.016
Ei' (cm/s)	4.38 \pm 1.76	4.53 \pm 1.42	.603
Ai' (cm/s)	6.54 \pm 1.81	7.03 \pm 2.30	.155
Si' (cm/s)	6.67 \pm 1.47	6.84 \pm 1.54	.509
Em/Ei'	50.1 \pm 27.8	43.5 \pm 20.1	.024
Et/Et'	10.07 \pm 3.63	9.65 \pm 4.42	.527
PASP (mmHg)	50.5 \pm 18.7	47.6 \pm 18.5	.363
Mitral transvalvular gradient (mmHg)	11.5 \pm 8.3	8.6 \pm 5.3	.019
MVA (m ²)	1.12 \pm 0.44	1.04 \pm 0.34	.768
MR grade	2.29 \pm 0.91	2.32 \pm 0.97	.865
TR grade	2.16 \pm 0.53	2.13 \pm 0.51	.702

*Data are mean \pm standard deviation.

Em, Am, Et, and At indicate peak early and late inflow peak velocity of the transmitral and transtricuspid valves, respectively; Em', Ei', Et', Am', Ai', At', Sm', Si', and St' indicate early and late diastolic and systolic peak velocities at the lateral mitral valve, interventricular septum, and lateral tricuspid of the annulus, respectively; LAD, left atrial diameter; LVEDD, left ventricular end-diastolic internal diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MVA, mitral valve area; PAD, peripheral arterial disease; PASP, pulmonary artery systolic pressure; RVOTd, right ventricular outflow tract end diastolic diameter; TR, tricuspid regurgitation.

3), or severe (grade 4). An MVA $<1.5 \text{ cm}^2$ was diagnosed as severe mitral stenosis. Based on the tricuspid regurgitation spectrum, right ventricular systolic pressure (RVSP) was calculated with the following equation: $\text{RVSP} = 4V^2 + \Delta P$, where V is the tricuspid regurgitation peak velocity and ΔP is the right atrial pressure (10 mmHg). If the pulmonary valve has no stenosis, RVSP can be considered to be the pulmonary artery systolic pressure (PASP).

Statistical Analysis

All statistical calculations were carried out using SPSS 18.0 software (IBM, Chicago, IL). Differences in the distribution of host characteristics between cases and controls were evaluated by Pearson's χ^2 test for categorical variables. To compare the characteristics of the 2 patient groups, independent Student's t test and Mann–Whitney U test were used. χ^2 test was applied to compare sex and atrial fibrillation presence. Independent risk factors of PoAF were identified using multiple logistic regression analysis from the variables of $P < .1$. $P < .05$ was considered significant in all comparisons.

Results

Study Population

A total of 150 patients (age 54.7 ± 9.2 years, 27 male [18%]) with no history of preoperative atrial fibrillation met the study inclusion criteria and underwent mitral valve replacement between January 2012 and December 2016. Their baseline characteristics are summarized in Table 4. Early PoAF occurred in 59 patients (39.3%). The patients with early PoAF were significantly older than the patients without early PoAF ($P = .001$) (Table 4). Additionally, patients with diabetes mellitus were more likely to have early PoAF ($P = .037$) (Table 4).

There were no patients lost to follow-up and deaths within the 1-year period. Thirty-two patients (21.3%) developed late PoAF during follow-up. Age was strongly associated with the occurrence of late PoAF ($P = .009$) (Table 5).

Echocardiographic Parameters and PoAF

Table 1 shows all of the preoperative echocardiographic parameters. Among the analyzed variables, early mitral filling

velocity (Mitral E), Mitral A, and mean mitral transvalvular pressure were significantly associated with early PoAF (Table 1). There was no significant difference between the measures of mitral valve area, pulmonary artery systolic pressure, or

Table 2. Analysis of Echocardiographic Data of Late PoAF Patients*

Variable	Late PoAF		P Value
	No (118)	Yes (32)	
LAD (mm)	46.2 ± 5.9	47.0 ± 5.3	.515
LVEDD (mm)	43.9 ± 5.3	45.5 ± 5.1	.141
RVOTd (mm)	25.0 ± 4.7	26.3 ± 5.3	.194
PAD (mm)	23.4 ± 4.6	24.3 ± 4.9	.374
LVEF (%)	58.3 ± 2.9	58.7 ± 4.4	.511
Em (m/s)	2.02 ± 0.68	1.74 ± 0.62	.060
Am (m/s)	1.94 ± 0.59	1.57 ± 0.41	.001
Et' (m/s)	0.47 ± 0.13	0.47 ± 0.13	.422
At (m/s)	0.44 ± 0.14	0.43 ± 0.14	.500
Em' (cm/s)	5.11 ± 1.73	5.45 ± 1.87	.330
Am' (cm/s)	7.74 ± 3.03	7.06 ± 2.08	.243
Sm' (cm/s)	7.31 ± 1.85	7.58 ± 1.78	.475
Et' (cm/s)	9.15 ± 3.03	8.52 ± 2.78	.297
At' (cm/s)	14.35 ± 4.30	13.81 ± 3.55	.517
St' (cm/s)	12.36 ± 2.74	12.48 ± 2.52	.823
Em/Em'	44.0 ± 22.4	35.6 ± 17.2	.055
Ei' (cm/s)	4.53 ± 1.74	4.08 ± 1.11	.170
Ai' (cm/s)	6.72 ± 2.04	6.79 ± 1.98	.856
Si' (cm/s)	6.74 ± 1.54	6.74 ± 1.34	.985
Em/Ei'	50.1 ± 26.0	46.4 ± 23.2	.487
Et/Et'	10.16 ± 4.05	8.94 ± 3.44	.126
PASP (mmHg)	49.7 ± 18.2	48.3 ± 20.3	.725
Mitral transvalvular gradient (mmHg)	11.0 ± 7.64	7.97 ± 5.84	.042
MVA (m^2)	1.03 ± 0.39	1.02 ± 0.44	.863
MR grade	2.25 ± 0.87	2.52 ± 1.12	.150
TR grade	2.13 ± 0.49	2.24 ± 0.62	.266

*Data are mean \pm standard deviation.

Em, Am, Et, and At indicate peak early and late inflow peak velocity of the transmitral and transtricuspid valves, respectively; Em', Ei', Et', Am', Ai', At', Sm', Si', and St' indicate early and late diastolic and systolic peak velocities at the lateral mitral valve, interventricular septum, and lateral tricuspid of the annulus, respectively; LAD, left atrial diameter; LVEDD, left ventricular end-diastolic internal diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MVA, mitral valve area; PAD, peripheral arterial disease; PASP, pulmonary artery systolic pressure; RVOTd, right ventricular outflow tract end diastolic diameter; TR, tricuspid regurgitation.

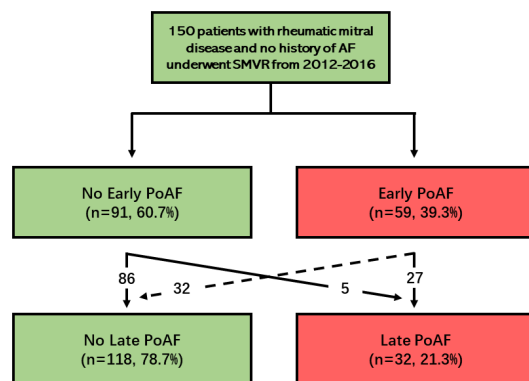


Figure 1. Rhythm outcomes for patients undergoing mitral valve replacement. SMVR indicates surgical mitral valve replacement.

left atrial diameter in our cohort (Table 1). Interestingly, there was a significant reduction in Mitral A wave and mitral transvalvular pressure among patients who developed late PoAF (Table 2).

Relationship between Early PoAF and Late PoAF

Rhythm outcomes are shown in Figure 1. Twenty-seven of 59 patients (45.7%) with early PoAF developed late PoAF

after mitral valve replacement (Figure 1). Consequently, there was a strong correlation between early PoAF and late PoAF ($P < .001$) (Table 6).

Prediction of Late PoAF

Univariate and multivariate logistic regression analyses for the prediction of late PoAF are summarized in Table 3. Multivariate logistic analysis showed that Mitral A and early

Table 3. Univariable and multivariable logistic regression analysis of risk factors of late PoAF

Factor	Univariable Logistic Regression			Multivariable Logistic Regression		
	OR	95% CI	P value	OR	95% CI	P Value
Age (y)	0.935	0.888 to 0.985	.011	0.957	0.896 to 1.023	.196
Em	2.017	1.007 to 4.039	.048	1.561	0.225 to 10.85	.652
Am	4.069	1.693 to 9.777	.002	20.128	2.811 to 144.12	.003
Em/Em'	1.022	0.999 to 1.046	.060	1.005	0.970 to 1.042	.781
Mitral transvalvular gradient	1.088	1.006 to 1.176	.034	0.805	0.631 to 1.027	.081
Early PoAF	14.51	5.145 to 40.93	<.001	15.607	4.925 to 49.46	<.001

OR indicates odds ratio; CI, confidence interval.

Table 4. Demographic and Clinical Characteristics by Presence of Early PoAF*

Characteristic	Early PoAF		P Value
	No (n = 91)	Yes (n = 59)	
Age (y)	52.73 ± 9.66	57.93 ± 7.67	.001
Male sex	17 (18.6)	10 (16.9)	.787
BSA (m ²)	1.73 ± 0.16	1.75 ± 0.15	.523
BMI (kg/m ²)	22.75 ± 2.70	22.69 ± 2.91	.925
Hypertension	19 (20.8)	10 (16.9)	.551
Diabetes mellitus	2 (2.2)	7 (11.8)	.037
Heart rate (bpm)	78.96 ± 11.34	78.82 ± 14.60	.954
Smoking	20 (21.9)	12 (20.3)	.811
Blood glucose (mmol/L)	5.42 ± 1.71	5.31 ± 1.09	.722
Albumin (mg/dL)	40.65 ± 5.99	39.82 ± 5.82	.438
Creatinine (μmol/L)	63.57 ± 20.04	64.19 ± 18.32	.857
Cardiopulmonary bypass time (min)	99.3 ± 36.7	104.9 ± 59.1	.594
Aortic clamp time (min)	62.2 ± 34.5	58.68 ± 27.1	.602
Blood product transfusion	47 (51.6)	35 (59.3)	0.546
Combined TVP	21 (23.0)	14 (23.7)	0.927

*Data are mean ± standard deviation or n (%).

BMI indicates body mass index; BSA, body surface area; TVP, tricuspid valvuloplasty.

Table 5. Demographic and Clinical Characteristics by Presence of Late PoAF*

Characteristic	Late PoAF		P Value
	No (n = 118)	Yes (n = 32)	
Age (y)	53.76 ± 9.41	58.53 ± 7.72	.009
Male sex	28 (23.7)	4 (12.5)	.361
BSA (m ²)	1.75 ± 0.17	1.72 ± 0.12	.418
BMI (kg/m ²)	22.68 ± 2.90	22.84 ± 2.48	.807
Hypertension	23 (19.5)	6 (18.7)	.925
Diabetes mellitus	7 (5.93)	2 (6.25)	.724
Heart rate (bpm)	78.71 ± 11.69	79.50 ± 15.23	.768
Smoking	26 (22.0)	6 (18.7)	.291
Blood glucose (mmol/L)	5.32 ± 1.48	5.56 ± 1.53	.468
Albumin (mg/dL)	40.45 ± 6.01	39.89 ± 5.65	.652
Creatinine (μmol/L)	63.90 ± 20.72	63.57 ± 13.82	.936
Cardiopulmonary bypass time (min)	100 ± 38.3	103.3 ± 64.9	.826
Aortic clamp time (min)	60.6 ± 28.3	58.04 ± 34.9	.735
Blood product transfusion	63 (53.8)	19 (59.3)	.356
Combined TVP	29 (24.5)	6 (18.7)	.489

*Data are mean ± standard deviation or n (%).

BMI indicates body mass index; BSA, body surface area; TVP, tricuspid valvuloplasty.

PoAF were significant and independent risk factors for late PoAF (Table 3).

Discussion

Among a group of patients with severe rheumatic mitral valve disease who underwent mitral valve replacement, we observed that early PoAF affected nearly 40% of the cohort. We also assessed the correlation between left atrial mechanical function (Mitral A) before surgery and late PoAF. Preoperative Mitral A and early PoAF after surgery are independent factors in the prediction of late PoAF. It has been reported that late PoAF is independently associated with long-term mortality [Kawamoto 8; Park 2017]. In accordance with previous findings, our data also suggest that early PoAF was the most powerful predictor of late mortality.

Meanwhile, the incidence of early PoAF in valve surgery is different from that of isolated coronary artery bypass grafting [Zhang 2017; Zhang 2018; Lanter 2018]. This may indicate that the mechanisms of PoAF are diverse. Factors promoting the development of early PoAF after cardiothoracic surgery include, for example, an inflammatory response, sympathetic activation, and oxidative stress [Lanter 2018]. In patients with rheumatic mitral valvular disease, the arrhythmogenic substrate is present and extensive. Owing to the mitral valve disease, atrial alterations at the structural, electrical, and contractile levels create higher vulnerability to the development of AF [Wijffels 1995]. Therefore, strategies for the prevention of PoAF should be precise.

In our study, multivariate analysis also found that a significant reduction in Mitral A was an independent characteristic of the late PoAF patients with sinus rhythm and rheumatic mitral valve disease; that is, those rheumatic mitral valve disease patients whose preoperative left atrial systolic function was significantly reduced were more prone to late AF after surgery. A greater left atrium size increases the surface area, leading to AF, as previously well documented by our group and others [Zhang 2017; Damiano 2011]. However, in our cohort, the left atrium size of patients with rheumatic mitral valve disease did not predict PoAF. One explanation is that the mean left atrium size was large (>45 mm) in our cohort, owing to the longstanding underlying rheumatic mitral valve disease, which likely influenced the data.

The assessment of left atrium function provides further insights into the consequences of left atrium structural remodeling [Delgado 2017]. The A peak is the left ventricular end diastolic blood flow through the atrioventricular valve, caused by atrial contractions. Clinical measurements of the E peak, A peak, and mitral annular tissue Doppler velocity can be used to evaluate changes in ventricular diastolic function [Nagueh 2009; Rudski 2010]. The A peak and the P wave on ECG are the mechanical and electrical activities of the left atrial contraction, respectively. The maximum velocity and time velocity integral of the A peak at the mitral valve are related to the contractile function of the left atrium. For patients with mitral valve disease, especially rheumatic mitral stenosis, the A peak at the mitral valve can reflect changes in left atrial function. The dynamic changes of these data can be used to quantitatively assess the changes in atrial function

Table 6. Relation between Early PoAF and Late PoAF*

Early PoAF	Late PoAF		P Value
	No (n = 118)	Yes (n = 32)	
No (91)	86 (72.9)	5 (15.6)	<.001
Yes (59)	32 (27.1)	27 (84.4)	

*Data are n (%).

and ventricular diastolic function. When atrial fibrillation occurs, left atrial systolic function decreases, and the Mitral A wave disappears or is reduced [Akilli 2019]. In our data, the preoperative Mitral A wave decreased before the AF and predicted AF after surgery. In addition, measurements of the E peak, A peak, and mitral annular tissue Doppler velocity are characterized by good repeatability, easy operation, and easy data quantification, and they should be well applied in routine follow-up observations of patients.

Limitations

This was a single-center retrospective analysis of a small patient cohort. In addition, the relatively small sample size in this study limited the statistical capacity to detect interactions between left atrial mechanical function and other major risk factors. Further prospective studies are needed to confirm these findings with a larger sample size. The greatest limitation of this study is the absence of atrial strain measurements, which is an emerging modality for the assessment of left atrial function [Pathan 2018]. This has grounds for future study.

Conclusion

According to our study conducted on a population of patients with rheumatic mitral valve disease, increased Mitral A has an independent role in predicting early and late PoAF. Furthermore, preoperative left atrial function (Mitral A) could also enable us to more accurately detect patients who are at risk and thereby improve the effects of prophylactic treatments.

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