Predicting early left ventricular dysfunction after mitral valve reconstruction: The effect of atrial fibrillation and pulmonary hypertension

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Objective: The preoperative ejection fraction (EF) and left ventricular (LV) end-systolic dimension are known predictors of postoperative LV dysfunction after mitral valve repair. We investigated the effect of a preoperative history of atrial fibrillation and moderate pulmonary hypertension (defined as pulmonary artery systolic pressure >50 mm Hg) on early postoperative LV dysfunction.

Methods: From 2003 to 2010, 632 patients who had undergone successful mitral valve repair surgery for degenerative disease were included in the present study. The preoperative and postoperative echocardiographic data and postoperative outcomes were collected retrospectively. We analyzed the demographic, hemodynamic, and echocardiographic parameters to assess the predictors of early postoperative LV dysfunction, defined as an LVEF <50%.

Results: The mean age of the cohort was 57 ± 13 years. All patients had less than mild mitral regurgitation on postoperative echocardiography. After mitral valve repair, a significant decrease in the LVEF ($60\% \pm 8\%$ to $54\% \pm 9\%$), LV end-systolic diameter (36 ± 7 mm to 33 ± 7 mm), and LV end-diastolic dimension (56 ± 8 mm to 48 ± 7 mm) was observed at early postoperative echocardiography ($P < .001$). On multivariate regression analysis, preoperative atrial fibrillation, pulmonary hypertension, and LV end-systolic dimension were independent predictors of the postoperative LVEF ($P = .035$ and $P < .001$, respectively). Preoperative atrial fibrillation (odds ratio, 1.97; 95% confidence interval, 1.28-3.02; $P = .002$) and pulmonary artery systolic pressure >50 mm Hg (odds ratio, 1.82; 95% confidence interval, 1.11-2.97; $P = .017$) increased the risk of postoperative LV dysfunction by almost twofold.

Conclusions: In addition to the established predictors of postoperative LV dysfunction, the presence of preoperative pulmonary hypertension and a history of atrial fibrillation in patients undergoing mitral valve repair surgery increased the risk of early postoperative LV dysfunction by almost twofold. (J Thorac Cardiovasc Surg 2014;148:422-7)

Mitral valve repair is the recommended treatment for patients with severe degenerative mitral valve disease. Despite having a preoperative preserved ejection fraction (EF), a number of patients will develop early left ventricular (LV) dysfunction after valve reconstruction. A number of studies have examined the echocardiographic predictors of LV dysfunction after valve replacement.¹ However, some have examined this question in a mixed cohort of valve repair and valve replacement,^{2,3} and others have examined a mixed cohort of mitral valve disease

(degenerative, ischemic, and rheumatic).⁴ None have thoroughly examined the nonechocardiographic predictors of early postoperative LV dysfunction. Furthermore, whether early postoperative LV dysfunction after mitral valve reconstruction affects morbidity and mortality has not been examined.

In the present large series, we sought to examine the echocardiographic and nonechocardiographic predictors of early postoperative LV dysfunction after mitral valve repair for degenerative valve disease and its effects on surgical outcomes.

METHODS

Study Population

From June 2003 to December 2010, we retrospectively analyzed the data from 646 consecutive patients who underwent mitral valve surgery for degenerative mitral valve regurgitation by a single surgical team. Patients were excluded from the present study if they had undergone mitral valve replacement (1 patient) or had not undergone a complete pre-discharge echocardiogram (13 patients). Patients with concomitant tricuspid valve repair or coronary artery bypass grafting for incidental coronary disease found during preoperative catheterization were included

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Abbreviations and Acronyms

AF	= atrial fibrillation
EF	= ejection fraction
LV	= left ventricular
LVEF	= left ventricular ejection fraction
PHT	= pulmonary hypertension

in the present study. After the exclusions, 632 patients were included in the present analysis.

The Mount Sinai School of Medicine institutional review board approved the present research protocol.

The patients underwent a variety of techniques in repairing the mitral valve using a lesion-specific approach, as described previously.^{5,6} These techniques included quadrangular or triangular resection, leaflet sliding plasty, neochordal replacement, and commissuroplasty. Most patients received a complete annuloplasty ring; a small percentage received an incomplete annuloplasty ring. Tricuspid valve repair was undertaken if more than mild regurgitation or annular dilatation was present. Complete left sided or biatrial ablation was undertaken for all patients in persistent or permanent atrial fibrillation (AF).

During valve repair, myocardial protection was maintained using an induction dose of antegrade blood cardioplegia, with maintenance cardioplegia given mostly in a retrograde manner by way of a catheter in the coronary sinus. Cold blood cardioplegia was administered at 4°C and consisted of a 4:1 ratio of blood to cardioplegia. The doses were administered approximately every 20 to 25 minutes. Before removal of the crossclamp, a dose of warm blood was administered through the retrograde catheter.

Echocardiographic Parameters

All patients had a preoperative transthoracic echocardiogram documenting severe mitral valve regurgitation. The degree of regurgitation was measured using a variety of techniques according to the guidelines of the American Society of Echocardiography. If doubt was present regarding the degree of mitral valve regurgitation on an echocardiogram from an outside institution, the echocardiogram was repeated at our hospital using proximal isovelocity surface area (effective regurgitant orifice area, effective regurgitant volume) and qualitative measurements such as reversal of flow in the pulmonary veins to assess mitral regurgitation. Transthoracic echocardiograms were performed in all patients after valve repair and before discharge from the hospital. The mean interval to echocardiography was 4.1 days. Postoperative LV dysfunction was defined as an LVEF < 50%. Other echocardiographic parameters such as the LV end-systolic diameter (LVESD), LV end-diastolic diameter (LVEDD), and left atrial diameter were also measured using the American Society of Echocardiography guidelines. Preoperative pulmonary artery systolic pressures were obtained from preoperative catheterization if available and, if not, by echocardiography using the simplified Bernoulli's equation [pulmonary artery systolic pressure = $4 \times (\text{peak tricuspid regurgitant velocity})^2 + \text{mean right atrial pressure}$]. Pulmonary hypertension (PHT) was defined using the American Heart Association/American College of Cardiology guideline of 50 mm Hg. AF was defined as permanent, persistent, and paroxysmal AF. All patients with permanent or persistent AF underwent ablation. All but 1 patient with paroxysmal AF underwent ablation. That patient had a history of 1 brief episode of paroxysmal AF and did not undergo ablation.

Statistical Analysis

Continuous variables are presented as the mean $\pm$ standard deviation, if normally distributed, and the median and interquartile range, if not normally distributed. Categorical variables are presented as proportions

and absolute numbers. For continuous variables, the normality test was performed using the combination of the Kolmogorov-Smirnov test and a visual assessment of the histograms. The differences between the 2 groups were detected using the chi-square test or Fisher's exact test for categorical variables and unpaired and paired Student *t* tests or the Mann-Whitney *U* test for continuous variables. Logistic and linear regression analyses were performed to identify the univariate and multivariate predictors of postoperative LV dysfunction and LVEF, respectively. Variables with $P < .25$ on univariate analysis were included in the final multivariate model. In logistic regression analysis, the model fit and predictive power were validated using the Hosmer-Lemeshow goodness-of-fit test and c-statistic. Before multivariate analysis, a correlation analysis between each variable was performed (Pearson or Spearman, as appropriate) to ensure no violation of the assumption of multicollinearity (cutoff correlation coefficient < 0.7). The results are presented as odds ratios, with the corresponding 95% confidence intervals. $P < .05$ was considered statistically significant. All *P* values are the results of 2-tailed tests. The statistical analysis was performed using IBM SPSS Statistics for Windows, version 20.0 (SPSS, Inc, IBM Corp, Armonk, NY).

RESULTS

The baseline characteristics of the patients are listed in Table 1. Of the 646 patients, 242 (38.3%) developed postoperative LV dysfunction. We observed that 68% of the patients in the series had a preoperative LVEF > 60% and 85.3% of patients had a preoperative LVEF > 50%. On average, the patients who developed LV dysfunction were 2.7 years older. More than one half of the patients (57.9%) in the series were symptomatic. The preoperative comorbidities were otherwise similar in both groups. The mean preoperative LVEF was slightly lower in the patients who developed postoperative LV dysfunction compared with those who did not (59.3% vs 61.5%). The patients who developed postoperative LV dysfunction were more likely to have a dilated ventricle, PHT, and AF. The etiology of the degenerative disease was not different, and the repair techniques used were similar in both groups (Table 2). Barlow's disease was evident in 339 patients (53.6%), and posterior leaflet prolapse was the most common lesion noted (475 patients; 75.2%). Tricuspid annuloplasty was undertaken in 413 patients (65.3%).

The mean cardiopulmonary bypass times and crossclamp times were not significantly different between the 2 groups (Table 2).

Figure 1 illustrates the preoperative and postoperative cardiac chamber sizes in the entire series. The mean postoperative LVEF changed in the entire cohort by a mean of $-7.3\% \pm 10.8\%$. After valve repair, a significant decrease was seen in the LVESD, LVEDD, and left atrial diameter.

Tables 3 and 4 list the independent predictors of postoperative LV dysfunction after mitral valve repair, including LVESD, preoperative AF, and preoperative PHT. The preoperative LVEF showed a trend toward predicting postoperative LV dysfunction but the difference was not statistically significant. We observed that in patients with a preoperative LVEF of <60%, 34.2%

TABLE 1. Baseline demographic data

Variable	All patients (n = 632)	Postoperative LV dysfunction		
		No (n = 390)	Yes (n = 242)	P value
Demographics and comorbidity				
Age (y)	57.0 ± 13.2	56.0 ± 13.1	58.7 ± 8.1	<.001
Female gender	229 (36.2)	148 (37.9)	81 (33.5)	.255
Body surface area (m ²)	1.90 ± 0.25	1.89 ± 0.24	1.92 ± 0.25	.193
Hypertension	290 (45.9)	179 (45.9)	111 (45.9)	.994
Hypercholesterolemia	163 (25.8)	105 (26.9)	58 (24.0)	.409
Diabetes mellitus	20 (3.2)	8 (2.1)	12 (5.0)	.042
Coronary artery disease	74 (11.7)	38 (9.7)	36 (14.9)	.051
Obstructive lung disease	19 (2.9)	1 (0.8)	4 (2.9)	.234
Peripheral vascular disease	7 (1.1)	6 (1.5)	1 (0.4)	.288
Renal failure	2 (0.3)	2 (0.5)	0 (0)	.260
Cerebrovascular accident	14 (2.2)	6 (1.8)	8 (3.3)	.225
Symptomatic	366 (57.9)	228 (58.5)	138 (57.0)	.722
Preoperative echocardiographic parameters				
LVEF (%)	60.7 ± 7.5	61.5 ± 6.7	59.3 ± 8.4	<.001
LVEF < 50%	65 (10.3)	28 (7.2)	37 (15.3)	.001
LVESD (mm)	35.8 ± 6.8	34.6 ± 6.2	37.8 ± 7.3	<.001
LVESD > 40 mm	159 (25.2)	74 (19.0)	85 (35.1)	<.001
PA systolic pressure (mm Hg)	34.6 ± 13.3	32.3 ± 11.6	38.0 ± 14.5	<.001
LVEDD (mm)	56.0 ± 7.9	54.9 ± 7.4	58.0 ± 8.1	<.001
PASP > 50 mm Hg	82 (13.0)	39 (10.0)	43 (17.8)	.005
AF	124 (19.6)	58 (14.9)	66 (27.3)	<.001

Data presented as mean ± standard deviation or n (%). LV, Left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; PA, pulmonary artery; LVEDD, left ventricular end-diastolic diameter; PASP, pulmonary artery systolic pressure; AF, atrial fibrillation.

developed postoperative LV dysfunction. When the preoperative LVEF was <60%, the LVESD was >40 mm, and AF and PHT were present, the incidence of postoperative LV dysfunction increased to 66.7% (Table 5).

We examined the mortality and morbidity between the 2 groups (Table 6). One patient in the entire series died (0.2%) but that patient had not developed postoperative LV dysfunction. When comparing major postoperative morbidity, we found no significant differences between the 2 groups. The incidence of major morbidity and/or mortality was 5.7%. Respiratory failure, defined as mechanical ventilation for >48 hours (for any reason), occurred in 4% of patients without LV dysfunction and

3.6% of patients with LV dysfunction ($P = .549$). The cause in most of these cases was related to postoperative right ventricular dysfunction in those with longer crossclamp times, and the patients required inotropic support for the right ventricle.

DISCUSSION

Postoperative LV dysfunction after mitral valve surgery has been shown to occur in a number of studies.^{2,7} Similar to these series, the incidence of postoperative LV dysfunction after mitral valve repair in our series was significant, despite 85.3% of our patients having a preoperative LVEF of >50%. Understanding the

TABLE 2. Operative data

Variable	All patients (n = 632)	Postoperative LV dysfunction		
		No (n = 390)	Yes (n = 242)	P value
Crossclamp time (min)	131 ± 48	132 ± 46	130 ± 52	.848
Cardiopulmonary bypass time (min)	167 ± 77	162 ± 51	176 ± 111	.269
Barlow's disease	339 (53.6)	206 (52.8)	133 (55.0)	.600
Anterior leaflet prolapse	27 (4.3)	18 (4.6)	9 (3.7)	.588
Posterior leaflet prolapse	475 (75.2)	289 (74.1)	186 (76.9)	.436
Bileaflet prolapse	123 (19.5)	78 (20.0)	45 (18.6)	.665
Concomitant CABG	58 (9.2)	30 (7.7)	28 (11.6)	.101
Concomitant TVR	413 (65.3)	249 (63.8)	164 (67.8)	.314
Concomitant maze procedure	123 (19.5)	58 (14.9)	65 (26.9)	<.001

Data presented as mean ± standard deviation or n (%). LV, Left ventricular; CABG, coronary artery bypass grafting; TVR, tricuspid valve repair.

FIGURE 1. The preoperative and postoperative cardiac chamber sizes for all patients. *LVESD*, Left ventricular end-systolic diameter; *LVEDD*, left ventricular end-diastolic diameter; *MVR*, mitral valve repair.

predictive factors provides insight into the postoperative treatment of patients with degenerative mitral valve disease. In our study, the LVESD and the presence of PHT and AF independently predicted postoperative LV dysfunction (LVEF < 50%). In a series of 861 patients, Suri and colleagues² examined the predictors of LV dysfunction after mitral valve surgery and also found that increased LV size, worsening heart failure symptoms, preoperative LVEF, and AF predicted postoperative LV dysfunction. Their series consisted of a mixed population of patients undergoing either valve repair or replacement. Tribouilloy and colleagues⁷ examined the predictors of LV dysfunction at 10.8 months after mitral valve repair. At 10 months after surgery, they continued to find a decrease in the mean LVEF of 9%. The largest incidence of postoperative LV dysfunction (33%) was found in those patients with a preoperative LVEF < 64% and LVESD ≥ 37 mm. Our study is unique in that it examined early postoperative LV dysfunction (mean, 4.1 days) in patients who had only undergone mitral valve repair for degenerative disease.

TABLE 3. Predictors of postoperative left ventricular ejection fraction (continuous variables)

Variable	Univariate		Multivariate	
	β	P value	β	P value
Age (y)	−0.092	.021	—	.793
LVEF (%)	0.209	<.001	0.076	.057
ESD (mm)	−0.337	<.001	−0.299	<.001
PASP (mm Hg)	−0.205	<.001	−0.167	<.001
Left atrial diameter (mm)	−0.185	<.001	—	.407*
Crossclamp time (min)	−0.006	.652	—	—

LVEF, Left ventricular ejection fraction; *ESD*, end-systolic diameter; *PASP*, pulmonary artery systolic pressure. *Multivariate analysis using left atrial diameter was performed separately because of a larger number of missing cases.

Our study did not find that the preoperative LVEF predicted postoperative LV dysfunction, in contrast to previous published studies. On multivariate analysis, the *P* value for this measurement was .057. Although it showed a trend toward significance, the preoperative LVEFs were very similar in both groups and, hence, led to a type 1 error in our study, because we did not have a sufficient sample size to elicit a difference between the 2 groups.

We observed an overall decrease in the LVEF of 7.2% postoperatively. A number of explanations exist for this decrease in the postoperative LVEF. Starling and colleagues⁸ illustrated that the LVEF in the presence of mitral regurgitation is overestimated as a result of the increased ventricular preload (end-diastolic volume). After valve repair, this excess preload is removed, leading to a decrease in the end-diastolic volume and, subsequently, a decrease in the LVEF. They showed that the contractile reserve is a better indicator of LV function in the presence of severe mitral regurgitation. Their work has been

TABLE 4. Predictors of postoperative left ventricular dysfunction (categorical variables)

Variable	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (y)	1.02 (1.00-1.03)	.014	—	.667
Female gender	0.82 (0.59-1.15)	.255	—	—
Symptomatic	0.94 (0.68-1.30)	.722	—	—
History of AF	2.49 (1.66-3.75)	<.001	1.97 (1.28-3.02)	.002
PASP > 50 mm Hg	1.95 (1.22-3.10)	.005	1.82 (1.11-2.97)	.017
Concomitant CABG	1.57 (0.91-2.70)	.103	—	.176
Concomitant TVR	1.19 (0.85-1.67)	.314	—	—

In the final model, Hosmer-Lemeshow = 0.814; c-statistic = 0.680. *OR*, Odds ratio; *CI*, confidence interval; *AF*, atrial fibrillation; *PASP*, pulmonary artery systolic pressure; *CABG*, coronary artery bypass grafting; *TVR*, tricuspid valve repair.

TABLE 5. Prevalence of postoperative LV dysfunction according to presence of preoperative guideline parameters

Preoperative guideline parameters	Postoperative LV dysfunction (n)
LVEF < 60% only	26/76 (34.2)
LVEF < 60% + ESD > 40 mm	26/54 (48.1)
LVEF < 60% + ESD > 40 mm + AF or PHT	17/24 (70.8)
LVEF < 60% + ESD > 40 mm + AF + PHT	4/6 (66.7)

Data in parentheses are percentages. $P = .010$ for all. LV, Left ventricular; LVEF, left ventricular ejection fraction; ESD, end-systolic diameter; AF, atrial fibrillation; PHT, pulmonary hypertension.

supported by more recent evidence that measurements other than the LVEF, such as global strain and speckle tracking, can better assess ventricular function when severe mitral regurgitation is present.^{9,10} Other arguments for the early decrease in the LVEF could be the increased afterload in the ventricle after valve repair and the stress and/or myocardial injury that occurs after aortic crossclamping. A recent study found a similar decrease in the LVEF, in addition to global longitudinal and circumferential strain, on early postoperative echocardiograms at 7 days.¹¹

Our finding that preoperative PHT increased the incidence of postoperative LV dysfunction was likely a result of the severity and duration of mitral regurgitation. Enriquez-Sarano and colleagues¹² elegantly reported that as the severity of mitral regurgitation increased, a corresponding increase occurred in the pulmonary artery pressures. PHT also increased the incidence of right ventricular dysfunction and could subsequently lead to a decrease in LV preload and LVEF. In a recent multicenter registry, patients with PHT had an increased risk of operative mortality (hazard ratio, 2.15; $P = .01$) after mitral valve surgery.¹³ Furthermore, long-term survival was also diminished in the same study.

Just as with PHT, AF is a marker of the severity of regurgitation and portends a worse prognosis in patients

with severe mitral regurgitation.¹⁴ AF has also been shown to predict late survival after mitral valve repair.¹⁵ The greatest incidence of postoperative LV dysfunction was seen when patients presented with a combination of LV dysfunction, increased ventricular dimensions, PHT, and AF.

Postoperative LV dysfunction did not affect mortality or morbidity after valve repair. We believe this was because our threshold for defining LV dysfunction was 50%, and most patients who developed LV dysfunction still had a postoperative mean LVEF just <50%. One could postulate that if the threshold definition of LV dysfunction was moved toward 35% to 40%, a greater incidence of postoperative complications would likely be seen, given the potential for a longer intensive care unit and hospital stay; however, this was not examined in our study.

In the present study, the presence of symptoms did not increase the incidence of postoperative LV dysfunction. However, given the finding of a twofold increase in the risk of postoperative dysfunction in patients with preoperative AF or PHT, these results support close follow-up with a low threshold for surgical intervention for patients with severe degenerative mitral valve disease. We also believe that, in expert centers, early surgery in asymptomatic patients should be considered where mortality and morbidity remain low.

The strengths of the present study were the large sample size and a homogenous population of patients with only degenerative mitral valve disease. In addition, all patients in the present series underwent valve repair. The limitations of our study were its retrospective data collection. The preoperative echocardiograms were frequently performed at outside institutions; thus, an operator bias exists in the interpretation of the echocardiograms. Finally, the lasting implications of early postoperative ventricular dysfunction were not examined.

CONCLUSIONS

Early postoperative LV dysfunction occurs commonly after mitral valve repair for degenerative disease. The independent predictors of postoperative LV dysfunction were a large LV chamber size, PHT, and AF. Although no increase in perioperative mortality or morbidity was observed, patients who present with preoperative AF or PHT had a twofold increase risk of developing postoperative LV dysfunction.

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TABLE 6. Perioperative mortality and morbidity

Variable	All patients (n = 632)	Postoperative LV dysfunction		
		No (n = 390)	Yes (n = 242)	P value
30-d Mortality	1 (0.2)	1 (0.3)	0 (0)	1.000
Mortality and morbidity	36 (5.7)	22 (5.6)	14 (5.8)	.939
Stroke	9 (1.4)	6 (1.5)	3 (1.2)	.758
Myocardial infarction	0	0	0	
Sternal wound infection	5 (0.8)	4 (1.0)	1 (0.4)	.654
Bleeding	4 (0.6)	1 (0.3)	3 (1.2)	.159
Sepsis	7 (1.1)	2 (0.5)	5 (2.1)	.113
Gastrointestinal bleeding	1 (0.2)	1 (0.3)	0 (0)	1.000
Renal failure	3 (0.5)	2 (0.5)	1 (0.4)	1.000
Respiratory failure	25 (4.0)	14 (3.6)	11 (4.5)	.549
Reoperation	5 (0.8)	3 (0.8)	2 (0.8)	1.000

Data presented as n (%). LV, Left ventricular.

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