Determinants of early decline in ejection fraction after surgical correction of mitral regurgitation

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Objective: We sought to echocardiographically examine the early changes in left ventricular size and function after mitral valve repair or replacement for mitral regurgitation caused by leaflet prolapse.

Methods: Preoperative and early postoperative echocardiograms of 861 patients with mitral regurgitation caused by leaflet prolapse who underwent mitral valve repair or replacement (with or without coronary revascularization) were studied. Among the patients, 625 (73%) were men and 779 (90%) had mitral valve repair.

Results: The rate of valve repair increased from 78% in the first decade of the study to 92% in the second decade. At early echocardiography (mean, 5 days postoperatively), we observed significant decreases in left ventricular ejection fraction (mean, -8.8) and left ventricular end-diastolic dimension (mean, -7.5). The magnitude of the early decline in ejection fraction was similar in patients who had mitral valve repair and replacement. The decrease in postoperative ejection fraction was independently associated with a lower preoperative ejection fraction, the presence of atrial fibrillation, advanced New York Heart Association functional class, greater left ventricular end-diastolic and end-systolic dimensions, and larger left atrial size.

Conclusion: Surgical correction of mitral regurgitation results in an early decrease in ejection fraction, particularly in symptomatic patients with increased left heart dimensions.

Surgical correction of mitral regurgitation may lead to an early postoperative decline in left ventricular ejection fraction,¹⁻³ but studies addressing this phenomenon are limited to echocardiographic data obtained several weeks to years⁴ postoperatively. Few data characterize the changes in cardiac size and function in the early postoperative period. Furthermore, there is uncertainty about the magnitude of these changes and how soon they occur after mitral valve surgery,^{5,6} together with the predisposing clinical and hemodynamic variables. Also, many of the reports from studies of ejection fraction change after mitral valve surgery have used data collected from patients who had mitral valve replacement. Whether a similar decrease occurs after mitral valve repair is controversial.^{1,4,7-12} Finally, it has been suggested that maintenance of chordal continuity between the left ventricular wall and the leaflets during mitral valve replacement is essential to attenuate this decrease¹³⁻¹⁵ or even increase postoperative ejection fraction.

The objective of this study was to examine the changes in left ventricular size and function that occur early after mitral valve surgery for correction of mitral regurgitation caused by leaflet prolapse.

Materials and Methods

We reviewed the clinical and echocardiographic data of patients who underwent primary surgical correction (repair or replacement) for mitral regurgitation caused by leaflet prolapse. The study was approved by the Mayo Clinic Institutional Review Board. The primary inclusion criterion was the availability of measurements of left ventricular ejection fraction preoperatively

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Abbreviations and Acronyms

LVEDD = left ventricular end-diastolic dimension
LVESD = left ventricular end-systolic dimension

(within 6 months of surgery) and early postoperatively. We included patients who had concomitant coronary artery bypass graft surgery or closure of a secundum atrial septal defect or patent foramen ovale. The study population included patients with mitral disease caused by fibroelastic deficiency and patients with myxomatous degeneration. We excluded patients who declined involvement in clinical research, who had previous mitral valve surgery or concomitant cardiac procedures, and who had a primary diagnosis of mitral regurgitation caused by congenital or ischemic heart disease or by other forms of cardiomyopathy. Also excluded were patients with significant mitral valve stenosis and patients with endocarditis causing leaflet destruction or subvalvar abscess at the time of primary mitral valve repair.

Between January 1, 1980, and December 31, 2000, a total of 2219 patients underwent surgical correction of mitral regurgitation at Mayo Clinic in Rochester, Minnesota. Among these patients, 861 met the study criteria. The mean ($\pm$ standard deviation) period between surgery and postoperative echocardiography was 5 ± 1.8 days. Of the 861 patients, 779 underwent mitral valve repair and 82 underwent mitral valve replacement.

Surgical Procedure

During the 20-year study period, the indications for operation and the surgical methods evolved. During the second decade of the study, a strategy of earlier mitral valve repair for mitral regurgitation caused by leaflet prolapse was adopted on the basis of quantitative echocardiographic criteria.¹⁶ The lesion for which patients most frequently underwent surgical correction of mitral regurgitation at Mayo Clinic was isolated posterior leaflet prolapse of the middle scallop, caused by chordal elongation or chordal rupture. The most common repair that was performed was triangular partial resection and suture repair of the involved portion of the posterior leaflet, supplemented by a standard length (63 mm) of flexible posterior annuloplasty band.^{17,18} In the first decade of the study, anterior leaflet prolapse was corrected by various techniques, including chordal shortening, chordal transfer, and commissural annuloplasty. In the current era (1990s and beyond), we have preferred the insertion of artificial neo-chordae (expanded polytetrafluorethylene; Gore-Tex; WL Gore & Associates, Flagstaff, Ariz) for repair of anterior leaflet prolapse.^{19,20}

Among the 82 patients who underwent mitral valve replacement, 46 (56%) received a mechanical valve and 36 (44%) received a bioprosthesis. During valve replacement, chordal preservation of the posterior leaflet was documented in 77 patients (94%).

Statistical Analysis

Group statistics were expressed as the mean $\pm$ 1 standard deviation. Categorical variables were compared between the groups using the chi-square test for independence. Two-sample *t* tests or Wilcoxon rank-sum tests were used to compare continuous variables between the groups. Univariate and multivariate predictors of predissmissal ejection fraction were determined using linear regression models. Multivariate models were constructed in 2 stages. In the first stage,

only clinical variables and preoperative ejection fraction were included as possible predictors, and a stepwise selection technique was used to construct the final model. In the second stage, the importance of echocardiographic variables was analyzed; this analysis was necessary to account for the inability to collect all measurements from each study. Each of the second-stage variables was forced into the final clinical model to determine importance. *P* values of less than .05 were considered significant.

Results

Baseline characteristics are shown in Table 1 for all 861 patients and the 2 treatment groups (mitral valve repair and mitral valve replacement). Compared with patients who had mitral valve replacement, the patients who underwent mitral valve repair were younger, had a lower incidence of preoperative atrial fibrillation, and were more likely male. The repair group was also slightly less symptomatic and less likely to have significant coronary artery disease but more likely to have isolated posterior leaflet prolapse. Preoperative ejection fraction and left heart dimensions were similar between the 2 groups.

Comparing preoperative and early postoperative data, we found significant decreases in left ventricular ejection fraction, left ventricular end-diastolic dimension (LVEDD), and left atrial dimensions (Table 2). A statistically significant decrease in both left ventricular ejection fraction and LVEDD was seen early after surgery overall; however, there was no demonstrable change in left ventricular end-systolic dimension (LVESD). The mean decrease in left ventricular ejection fraction in patients who had mitral valve repair was similar to that in patients who had mitral valve replacement (-8.8 vs -8.9 ; $P = .071$).

To determine the factors that might predict a greater decline in postoperative ejection fraction, univariate and multivariate models were constructed (Table 3). Independent predictors of a lower postoperative ejection fraction included the presence of preoperative atrial fibrillation ($P = .05$), poorer New York Heart Association functional status ($P = .008$), and lower ejection fraction ($P < .001$) before surgery. After adjustment for these predictors, larger preoperative left heart dimensions (LVEDD, $P < .001$; LVESD, $P < .001$; and left atrial size, $P < .001$) were also independently associated with a lower postoperative ejection fraction.

Discussion

This study clearly demonstrates that left ventricular ejection fraction declines soon after surgical correction of mitral regurgitation and occurs to a similar extent whether patients undergo mitral valve repair or mitral valve replacement. Our data suggest that the early decrease in ejection fraction is more pronounced in patients with larger left heart dimensions, depressed preoperative ejection fraction, and advanced symptoms preoperatively. Preservation of postoperative left ventricular systolic function after mitral valve surgery may be ensured by earlier referral for surgical correction.

TABLE 1. Baseline characteristics of patients*

Variable	Overall (N = 861)	MV repair (n = 779)	MV replacement (n = 82)	P value
Age, y	64	63	68	.002
Male sex	625 (73)	574 (74)	51 (62)	.03
Preoperative atrial fibrillation	100 (12)	80 (10)	20 (24)	<.001
NYHA class				<.001
I	101 (12)	99 (13)	2 (2)	
II	215 (25)	207 (27)	8 (10)	
III	458 (53)	402 (52)	56 (68)	
IV	87 (10)	71 (9)	16 (20)	
Operation decade (1990s vs 1980s)	102 (12)	80 (10)	22 (27)	<.001
Preoperative EF, % (N = 861)	62	62	57	<.001
Preoperative LVEDD, mm (n = 462)	60	60	58	.13
Preoperative LVESD, mm (n = 427)	37	37	37	.41
Preoperative left atrial size, mm (n = 517)	52	52	55	.05
Preoperative myocardial infarction	89 (10)	67 (9)	22 (27)	<.001
Type of prolapse				<.001
Anterior leaflet	130 (15)	101 (13)	29 (35)	
Posterior leaflet	488 (57)	472 (61)	16 (20)	
Bileaflet	243 (28)	206 (26)	37 (45)	
CABG	243 (28)	209 (27)	34 (41)	.005

CABG, Coronary artery bypass graft; EF, ejection fraction; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; MV, mitral valve; NYHA, New York Heart Association. *Categorical data are expressed as number of patients and percentage of sample; continuous data are expressed as mean.

This series analyzed a relatively homogeneous population of patients who had surgical correction of mitral regurgitation solely caused by isolated degenerative mitral leaflet prolapse. Although other studies have also reported that ejection fraction is diminished after correction of mitral regurgitation, there has been considerable variability in the timing of the studies that documented the change in left ventricular ejection fraction. Also, there has been debate on whether the postoperative decrease in left ventricular ejection fraction is influenced by the type of procedure performed.⁷⁻¹¹ In our study, the mean interval between operation and echocardiography before dismissal was 5 days. Ren and colleagues⁸ analyzed intraoperative echocardiograms in 50 patients and found that ejection fraction was better preserved after mitral valve repair than after mitral valve replacement. However, if

the assumption is made that forward stroke volume remained constant before and after surgery, the reported change in left ventricular end-diastolic and end-systolic volumes suggests that preoperative mitral regurgitation in patients who had mitral valve repair was not severe (ie, >60 mL/beat), which may partially explain the difference between our two studies. In addition, our assessment of ventricular function occurred at a mean of 5 days after surgery, and normalization of hemodynamic and neurohumoral imbalances may have occurred since the time of operation. Le Tourneau and colleagues⁷ studied patients who underwent mitral valve repair or mitral valve replacement for myxomatous or rheumatic heart disease at a mean of 216 days after surgery and found that left ventricular ejection fraction was preserved by repair but not by replacement. Corin and colleagues⁹ reported similar findings at a mean of 22 months after surgery.

Several other studies have reported that mitral valve replacement is associated with a decrease in left ventricular ejection fraction of approximately 10 units postoperatively⁷⁻¹¹ and suggested that the magnitude of this decrease might be attenuated by chordae-sparing valve replacement.^{13-15,21} Goldman and colleagues¹¹ suggested that intraoperative left ventricular ejection fraction remained stable after mitral valve repair. Harpole and colleagues²² suggested that partial resection of the subvalvar apparatus during mitral replacement did not significantly diminish early left ventricular function. In our study, the decrease in left ventricular ejection fraction after mitral valve replacement for mitral regurgitation was similar to that reported by other investigators

TABLE 2. Echocardiographic changes in the early postoperative period

Variable	Preoperative*	Postoperative*	Overall change*	P value
LVEF, %	62.9 ± 9.9	53.1 ± 11.3	-8.8 ± 10.7	<.001
LVEDD, mm	69.9 ± 7.6	53.1 ± 7.7	-7.5 ± 7.3	<.001
LVESD, mm	36.9 ± 7.1	36.6 ± 8.2	-0.5 ± 6.5	.26
Left atrial size, mm	52.3 ± 9.2	48.0 ± 8.7	-5.0 ± 7.4	<.001

LVEDD, Left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension. *Expressed as mean ± standard deviation.

TABLE 3. Univariate and multivariate predictors of predissmissal ejection fraction

Variable	Univariate		Multivariate	
	Slope	P value	Slope	P value
Female sex	1.32	.12	NA	NA
MV repair vs MV replacement	4.30	.001	NA	NA
Preoperative atrial fibrillation	-4.61	<.001	-2.12	.05
NYHA class	-2.38	<.001	-1.11	.008
Operation decade, 1980s	-0.91	.44	NA	NA
Age	-0.01	.73	NA	NA
CABG	-1.61	.06	NA	NA
Myocardial infarction	-7.95	<.001	NA	NA
Type of prolapse				
Anterior leaflet vs posterior leaflet	-5.57	<.001	NA	NA
Bileaflet vs posterior leaflet	-0.87	.32	NA	NA
Preoperative EF	0.56	<.001	0.54	<.001
LVEDD (n = 462)	-0.49	<.001	-0.37	<.001*
LVESD (n = 427)	-0.69	<.001	-0.43	<.001*
Left atrial size (n = 517)	-0.22	<.001	-0.16	<.001*

CABG, Coronary artery bypass graft; EF, ejection fraction; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; MV, mitral valve; NA, not applicable; NYHA, New York Heart Association. *Model includes echocardiographic parameters after adjustment for clinical factors; not all parameters are in the model at the same time.

despite the fact that chordal preservation was documented in 94% of patients, and a similar decrease was seen after mitral valve repair.

Our data suggest that considerable early reverse cardiac remodeling occurs early after correction of mitral regurgitation (Figure 1). We observed, as have others,²³ that LVEDD

significantly decreased early after correction of mitral regurgitation, whereas LVESD remained relatively unchanged.^{5,24} Other investigators have also shown that left atrial dimension decreased early after mitral valve surgery,²⁵⁻²⁷ as we found. We have no mechanistic data in this study to indicate whether cellular or molecular alterations accompany early reverse geometric remodeling. However, other investigators have suggested that these changes may occur.²⁸ This question will be the subject of future investigations.

Although the type of correction of mitral regurgitation did not seem to influence the early postoperative decline in left ventricular ejection fraction, our multivariate analysis did identify important clinical and echocardiographic factors. For example, the decrease in early postoperative left ventricular ejection fraction was greater in patients with preoperative atrial fibrillation and poorer functional class, and these variables likely reflect more advanced cardiac decompensation.²⁹

Further, we found that greater degrees of left heart dilatation (ie, LVEDD, LVESD, and left atrial size) were associated with lower postoperative left ventricular ejection fraction. Prior investigations have also established that left ventricular enlargement is associated with both diminished ejection fraction^{4,5,23} and poorer long-term survival.^{1,4,12,30} However, the current study is the first documentation of the early postoperative change in ejection fraction in a population of patients with mitral regurgitation caused by isolated leaflet prolapse. The independence of left ventricular systolic and diastolic dimensions and left atrial size in predicting postoperative ejection fraction is interesting and requires further study.

On the basis of the data we have collected in this study, we cannot comment specifically as to whether left ventricular contractility is also affected by these clinical factors,

Figure 1. Early ventricular remodeling. Diagrammatic representation of early changes in left ventricular (LV) volume and ejection fraction (EF) after surgical correction of severe chronic mitral regurgitation (MR). **A**, Normal heart ejecting typical stroke volume of 60 mL. LV end-diastolic volume (LVEDV) of 100 mL and LV end-systolic volume (LVESV) of 40 mL generate an observed EF of 60%. LVEDD of normal heart (solid line). **B**, Severe chronic MR leads to increase in left heart dilatation and LV capacity to maintain forward stroke volume of 60 mL per beat while losing an additional 60 mL per beat into left atrium. Increases in LVEDV to 180 mL and LVESV to 60 mL lead to apparent preservation of EF at 66%. LVEDD with increased dimension (dotted line) caused by severe chronic MR (LVEDD + x). **C**, Early after correction of MR (leaflet repair plus posterior annuloplasty band), atrial runoff is eliminated. To maintain normal forward stroke volume of 60 mL per beat, LVEDV decreases while LVESV remains constant. Because LVEDV is still increased compared with normal volume, EF declines to limit stroke volume. LVEDD + x (dashed line) that has been decreased because of early postoperative remodeling (LVEDD + x - y). (Used with permission of Mayo Foundation for Medical Education and Research.) LVEDV, Left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; EF, ejection fraction.

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recognizing that contractility correlates poorly with static ejection fraction measurements. Several historic reports have addressed contractile function after surgery, however Kouchoukos³¹ found that the elimination of severe chronic, simulated mitral regurgitation led to an increase in left ventricular afterload and elevated end-diastolic pressure in dogs. He suggested that similar changes after the elimination of chronic mitral regurgitation in humans may predispose patients with impaired preoperative left ventricular contractility to cardiac dysfunction postoperatively. Rankin and colleagues³² further developed this concept, proposing that the acute increase in afterload after the surgical procedure may be responsible for impaired postoperative ventricular function in patients with a “chronically depressed left ventricle.” Spratt and colleagues³³ suggested that the decrease in cardiac output after surgical correction of mitral regurgitation might not be fully explained by the increase in afterload, proposing that myocardial fibrosis and intraoperative injury might also be important. Starling⁶ demonstrated that left ventricular contractility (measured by left ventricular chamber elastance) may actually increase despite a decrease in ejection fraction after correction of mitral regurgitation. He concluded that early mitral valve repair before ejection fraction decline or left ventricular dilation is important to allow improvement in contractility after surgery.

We propose that the early postoperative decline in ejection fraction may be explained as a volumetric adjustment to the elimination of mitral regurgitation in patients with left ventricular dilatation. With severe chronic mitral regurgitation, ventricular enlargement compensates for regurgitant volume into the left atrium; left ventricular capacity increases, expanding LVEDD and LVESD while maintaining normal left ventricular ejection fraction. Soon after the surgical correction of mitral regurgitation and the elimination of regurgitant volume, increased efficiency of antegrade cardiac pumping could as much as double the stroke volume if ejection fraction was preserved and cardiac volumes were unchanged. To maintain near-normal forward aortic stroke volume, left ventricular diastolic volume decreases, but not enough to preserve left ventricular ejection fraction in the early postoperative period.

Limitations

Our study has the typical limitations associated with retrospective reviews. Patients in this study were selected because of the availability of early postoperative echocardiograms. Those patients who did not survive to have postoperative echocardiography are obviously missing from the series.

Clinical Implications

Our data suggest that the early change in left ventricular ejection fraction after surgical correction of mitral regurgitation can be explained by compensatory alterations in left ventricular volume and dimension. The fear that surgery might result

in a prohibitively large decline in ejection fraction postoperatively should not be used as justification to deny patients an operation. Rather, it is likely that patients who undergo early surgical correction of mitral regurgitation with favorable clinical and echocardiographic characteristics are more likely to have optimal recovery of normal left ventricular geometry and function in the early postoperative period.

Conclusions

Left ventricular ejection fraction decreases early after correction of mitral regurgitation caused by leaflet prolapse, and this decrease occurs to a similar extent in patients who have mitral valve repair or mitral valve replacement. Preoperative predictors of a decrease in ejection fraction after correction of mitral regurgitation include 1) significant symptoms or atrial fibrillation and 2) larger left heart dimensions (ie, LVESD, LVEDD, and left atrial size).

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