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Left Ventricular Function After Valve Repair for Chronic Mitral Regurgitation: Predictive Value of Preoperative Assessment of Contractile Reserve by Exercise Echocardiography

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Objectives. We evaluated the value of preoperative assessment of left ventricular contractile reserve in predicting ventricular function after valve repair for minimally symptomatic mitral regurgitation.

Background. The optimal timing for operation in minimally symptomatic patients with significant mitral regurgitation is controversial. Accurate preoperative assessment of left ventricular function is difficult, and the ability to predict postoperative function is limited. Previous studies in patients undergoing mitral valve replacement may not be applicable in the present era of valve repair.

Methods. We performed exercise echocardiography in 139 patients with isolated mitral regurgitation and no coronary disease, 74 of whom subsequently underwent uncomplicated valve repair. We measured rest left ventricular end-systolic dimension, end-systolic wall stress and positive first derivative of left ventricular pressure (dP/dt). End-diastolic and end-systolic volumes and ejection fraction were measured preoperatively at rest, immediately after exercise and postoperatively.

Results. Ejection fraction decreased postoperatively to 55 ± 10% from a rest preoperative value of 64 ± 9% ($p < 0.001$). Compared with patients with a postoperative ejection fraction ≥50% (n = 56), patients with postoperative ejection fraction <50% (n = 18) had a significantly lower preoperative exercise ejection fraction (57 ± 11% vs. 73 ± 9%, $p < 0.0005$), a larger exercise end-systolic volume index (32 ± 8 vs. 18 ± 7 cm^3/m^2, $p < 0.0005$) and a lower change in ejection fraction with exercise (−4 ± 8% vs. 9 ± 10%, $p < 0.005$). Preoperative rest indexes, including dP/dt, end-systolic wall stress and end-systolic volume index were less predictive, whereas exercise capacity, rest ejection fraction and end-systolic dimension were not predictive of post-repair ejection fraction. An exercise end-systolic volume index >25 cm^3/m^2 was the best predictor of postoperative dysfunction, with a sensitivity and specificity of 83%.

Conclusions. In minimally symptomatic patients with mitral regurgitation, latent ventricular dysfunction may be indicated by a limited contractile reserve, manifest at exercise as an inadequate increase in ejection fraction and a larger end-systolic volume. These variables may also be used to predict left ventricular function after repair.

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The development of irreversible left ventricular dysfunction is a major concern in the management of asymptomatic patients with significant mitral regurgitation. Early detection of subclinical dysfunction may permit timely intervention, thereby forestalling further deterioration. However, the accurate assessment of left ventricular performance is difficult in the presence of significant mitral regurgitation. Left ventricular ejection fraction, augmented by increased preload, frequently remains normal despite the presence of significant dysfunction.

Surgical treatment of mitral regurgitation, by removing the low impedance outlet for the left ventricle, increases ventricular afterload and may precipitate development of overt dysfunction. The response of ventricular function to mitral valve surgery has been difficult to predict. Various measurements of left ventricular size and function (1–5) have been used with limited success in predicting outcome after mitral valve replacement. Moreover, these measurements may not be applicable in patients undergoing mitral valve repair, which is now the preferred operation for most patients.

Preoperative latent dysfunction may be unmasked by stimuli to increase contractility such as exercise. The effects of exercise on left ventricular performance in patients with mitral regurgitation in the absence of ischemia have not been well studied. Exercise echocardiography is already established as an effective tool for detection of exercise-induced systolic dysfunction and wall motion abnormalities in the setting of myocardial ischemia (6). It may also be useful in unmasking latent ventricular dysfunction preoperatively and in predicting ventricular function after mitral valve repair. The purpose of this study was to examine, in asymptomatic or minimally symptom-

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Abbreviations and Acronyms

dP/dt	=	positive first derivative of left ventricular pressure
ECG	=	electrocardiogram
ROC curve	=	receiver operating characteristic curve

atic patients with chronic mitral regurgitation, the left ventricular response to exercise and the value of rest and exercise variables in predicting ventricular function after mitral valve repair.

Methods

Study patients. We studied a total of 139 patients with chronic nonrheumatic mitral regurgitation referred for evaluation. The study patients were carefully selected to involve only those with pure mitral regurgitation in New York Heart Association functional class I or II. Patients with coronary artery disease, previous cardiac surgery, coexisting aortic valve disease, mitral stenosis and suboptimal echocardiographic images were excluded.

Eighty-two patients subsequently underwent mitral valve repair. To ensure that changes in ventricular variables reflected the response to valve repair alone, we excluded patients with more than mild mitral regurgitation postoperatively (n = 1), intraoperative or postoperative myocardial infarction (defined as new Q waves on the electrocardiogram [ECG] or a twofold increase in the creatine kinase MB fraction [n = 1]) or any perioperative complication that might adversely affect ventricular function (systolic anterior motion of the mitral valve leaflets with outflow obstruction [n = 1] and significant postoperative pericardial effusion [n = 1]). Four more patients were excluded because of inability to obtain follow-up echocardiography or suboptimal postoperative echocardiographic images.

The 74 study patients included 55 men and 19 women with a mean age of 54 ± 13 years. Fifty-four patients (73%) were in functional class I and 20 in functional class II. Sixty-six patients (92%) were in sinus rhythm and 8 in well controlled atrial fibrillation. All patients had either moderately severe (n = 24) or severe mitral regurgitation (n = 50). The mechanism of mitral regurgitation was prolapse or flail posterior mitral leaflet in 47 patients (64%), prolapse of the anterior leaflet in 3, bileaflet prolapse in 22 and an isolated congenital cleft anterior leaflet in 2.

Preoperative rest and exercise echocardiography. All patients underwent symptom-limited exercise testing before mitral valve repair with the use of either a treadmill (Bruce or modified Bruce protocol, n = 52) or an upright exercise bicycle protocol (2-min stages with 25-W increments, n = 22) selected according to the cardiovascular and physical state of each patient. Symptoms and the ECG were monitored continuously during exercise, and blood pressure was measured noninvasively at rest and every 3 min during and after exercise. Peak heart rate, blood pressure, rate–pressure product and estimated exercise capacity were recorded. Patients achieved a work load of 7.9 ± 2.2 metabolic equivalents with a maximal rate–pressure product of $28.8 \pm 7.2 \times 10^3$. All but four patients achieved ≥85% of the age-predicted maximal heart rate with exercise. The maximal heart rate achieved (as percent of age-predicted maximum) was not significantly different between the two exercise protocols (92 ± 16% for bike protocol vs. 96 ± 11% for treadmill protocol, p = 0.29). Exercise was terminated because of fatigue in 71 patients and because of shortness of breath in 3.

All patients underwent transthoracic echocardiography in a supine position at rest and immediately after exercise. Echocardiographic examinations were performed with commercially available equipment (Hewlett-Packard Sonos 1000 or 1500) using standard views. Echocardiographic images were recorded on 0.5-in. VHS videotapes and also captured (gated to the R wave of the ECG) and digitized on-line into a quad-screen, cine-loop format (ImageVue, Nova Microsonics). All digitized images were stored on 5.25-in. optical disks. At rest, the left ventricular end-diastolic and end-systolic dimension, thickness of the interventricular septum and posterior wall were measured according to the recommendations of the American Society of Echocardiography (7). Left ventricular end-systolic dimension was normalized to body surface area to give the end-systolic dimension index. The mechanism of mitral regurgitation was carefully examined, and its severity was assessed semiquantitatively by color and continuous wave Doppler (8). The positive first derivative of left ventricular pressure (dP/dt) at rest was measured from the continuous wave Doppler signal of the mitral regurgitant jet obtained from the apical four-chamber view according to previously described methods (5,9). The average of three to five measurements was taken.

Mitral valve repair. Patients underwent mitral valve repair at 27 ± 73 days after exercise echocardiography. Mitral valve repair was performed in the standard fashion (10,11), with quadrilateral resection of posterior leaflet (n = 69), chordal shortening or transfer (n = 9), repair of anterior leaflet (n = 3) and insertion of annuloplasty ring (n = 73). Both anterograde and retrograde cardioplegia were used for myocardial protection. The mean duration of cardiopulmonary bypass was 70.4 ± 25.6 min, and mean aortic cross-clamp time was 52.3 ± 17.9 min. There were no intraoperative complications.

Postoperative echocardiography. Patients underwent rest transthoracic echocardiography 8 ± 14 days after mitral valve repair and was performed and recorded as described for preoperative echocardiography. Patients were classified into two groups according to their postoperative ejection fraction. On the basis of previous data (12), patients with a postoperative ejection fraction <50% were considered to have impaired systolic function.

Measurements and calculations. Left ventricular end-systolic and end-diastolic volumes were measured by two experienced observers (T.W.M., D.Y.L.) from the apical four-chamber view according to the modified Simpson's rule. Only representative cycles were measured, and the average of at least three measurements was taken. The endocardial border was traced excluding the papillary muscles. The frame captured at the R wave of the ECG was considered the end-diastolic frame, and the frame with the smallest left ventricular cavity was considered the end-systolic frame. The end-diastolic and end-systolic volumes were normalized to the body surface area to give the respective index. Ejection fraction was calculated from the left ventricular end-systolic and end-diastolic volumes. The left ventricular volumes and ejection fraction were measured at rest, immediately after exercise and after mitral valve repair. Left ventricular end-systolic wall stress (ESWS) at rest was calculated noninvasively according to previously validated methods (13) using the equation:

$$\text{ESWS (dynes/cm}^2) = 334 \times \text{BPsys} \times \frac{\text{LVESD}}{\text{PWsys} \times \left(1 + \frac{\text{PWsys}}{\text{LVESD}}\right)},$$

where BPsys = rest systolic blood pressure measured by a sphygmomanometer in mm Hg; LVESD = left ventricular end-systolic dimension, and PWsys = posterior left ventricular wall thickness measured at end-systole. The average of three measurements of end-systolic wall stress was taken.

Interobserver and intraobserver variability. To determine the interobserver variability in measuring left ventricular volumes, we randomly selected 10 studies each from the rest, immediate postexercise and postoperative phases. Two experienced observers (T.H.M., D.Y.L.) measured left ventricular end-systolic and end-diastolic volumes. The interobserver variability was measured by the mean difference of the two measurements ±SD. Correlation between the two measurements was also calculated. To determine the intraobserver variability, a single observer (D.Y.L.) measured the ventricular volumes on 10 randomly selected sets of images on two occasions. The intraobserver variability was measured by the mean difference of the two measurements ±SD. Correlation between the two measurements was also calculated.

Statistical analysis. Results are expressed as mean value ±SD, unless otherwise stated. The chi-square test and Fisher exact test as appropriate were used to compare categoric variables and the paired or unpaired Student *t* test to compare continuous variables. Simple linear regression analysis was used to estimate correlations between continuous variables. A stepwise multiple linear regression model was used to identify preoperative predictors of postoperative left ventricular function; variables were centered where appropriate before entering into the model to mitigate the problems of multicollinearity (14). The statistical package SPSS for Windows (Release 6.0, SPSS Inc.) was used for statistical analysis. For continuous variables, diagnostic cutoffs with the most favorable sensitivities and specificities were determined from the receiver operating characteristics (ROC) curves of the respective variables. The areas under the ROC curves of different variables were compared with the methods described by Hanley and McNeil (15). Statistical significance was defined as a two-tailed p value <0.05.

Results

Preoperative rest and exercise echocardiography. At rest, the mean left ventricular end-systolic dimension was 34 ± 7 mm, corresponding to a mean end-systolic dimension index of 18 ± 4 mm/m^2. The mean left ventricular end-diastolic and end-systolic volumes were 145 ± 39 and 52 ± 20 cm^3, respectively, corresponding to an end-diastolic volume index of 76 ± 20 cm^3/m^2 and an end-systolic volume index of 27 ± 10 cm^3/m^2. The mean ejection fraction at rest was 64 ± 9%. Immediately after exercise, the end-diastolic volume decreased slightly to 135 ± 32 cm^3 (index 71 ± 16 cm^3/m^2, p = 0.002), and end-systolic volume decreased to 41 ± 17 cm^3 (index 21 ± 9 cm^3/m^2, $p < 0.001$), resulting in an increase in ejection fraction to 70 ± 12% ($p < 0.001$).

The rest left ventricular dP/dt could not be measured in seven patients (9%) because of the eccentricity of the mitral regurgitant jets and in another two patients because of the midsystolic timing of the mitral regurgitation. The mean dP/dt in the remaining 65 patients was 1,183 ± 587 mm Hg/s, with 23 patients (35%) having a rest dP/dt < 1,000 mm Hg/s. The mean rest left ventricular end-systolic wall stress was 55 ± 26 × 10^3 dynes/cm^2.

Postoperative transthoracic echocardiography. Postoperatively, left ventricular end-diastolic volume decreased significantly to 112 ± 35 cm^3 ($p < 0.001$), whereas end-systolic volume remained unchanged at 52 ± 22 cm^3 (p = 0.67), resulting in a significantly lower ejection fraction of 55 ± 10% (range 28% to 77%, $p < 0.001$). Eighteen patients (24%) had a postoperative ejection fraction <50%. The duration of cardiopulmonary bypass and aortic cross-clamp time was not significantly different between these 18 patients and the 56 patients with normal postrepair left ventricular function (80 ± 36 vs. 68 ± 22 min for duration of cardiopulmonary bypass, p = 0.2; 55.5 ± 21.6 vs. 51.3 ± 16.8 min for aortic cross-clamp time, p = 0.43).

Preoperative measures of ventricular function and postoperative ventricular dysfunction. The relation between measures of preoperative rest left ventricular function and postoperative left ventricular ejection fraction is summarized in Table 1. The preoperative left ventricular end-systolic wall stress and end-systolic volume index at rest were significantly higher and dP/dt significantly lower in patients with postoperative ventricular dysfunction. However, rest left ventricular ejection fraction, end-systolic wall stress/end-systolic volume ratio and end-systolic dimension were not different between the two groups.

Table 2 summarizes the relation between exercise variables of preoperative ventricular function and postoperative left ventricular ejection fraction. Patients with normal postoperative left ventricular function (ejection fraction ≥50%) had a significantly higher exercise ejection fraction, a greater increase in ejection fraction with exercise and a lower exercise end-systolic volume index than patients with postoperative dysfunction. The maximal heart rate, maximal rate–pressure product and exercise capacity during preoperative exercise and

Table 1. Relation Between Preoperative Rest Left Ventricular Function Variables and Postoperative Ejection Fraction

Variable	Postop EF <50% (mean ± SD) (n = 18)	Postop EF ≥50% (mean ± SD) (n = 56)	p Value
Rest LV dP/dt (mm Hg/s)	831 ± 405	1,315 ± 594	0.003
$ESVI_{REST}$ (cm^3/m^2)	32 ± 10	26 ± 10	0.03
EF_{REST} (%)	61 ± 10	64.7 ± 9	0.14
$EDVI_{REST}$ (cm^3/m^2)	83 ± 18	74 ± 20	0.08
ESDI (mm/m^2)	20 ± 5.4	17.3 ± 3.5	0.06
ESWS ($\times 10^3$ $dynes/cm^2$)	70.6 ± 36.7	49.5 ± 18.8	0.03
ESWS/ESV ratio ($\times 10^3$ dynes m^2/cm^5)	2.2 ± 0.8	2.1 ± 1	0.9

EF = ejection fraction; EF_{REST} = ejection fraction at rest; ESDI = left ventricular end-systolic dimension index; ESV = end-systolic volume; $ESVI_{REST}$ = end-systolic volume index at rest; ESWS = left ventricular end-systolic wall stress; LV dP/dt = positive first derivative of left ventricular pressure; Postop = postoperative.

exercise left ventricular end-diastolic index were not different between the two groups.

Bivariate correlation coefficients between postoperative left ventricular ejection fraction and the various preoperative rest and exercise indexes of systolic function are shown in Table 3. Figure 1 is a scatterplot showing the relation between preoperative end-systolic volume index at exercise and the postoperative ejection fraction. Stepwise multiple linear regression was performed with the seven significant variables as explanatory variables. Only exercise ejection fraction ($p = 0.03$) and exercise end-systolic volume index ($p = 0.003$) had significant independent value in predicting postoperative ejection fraction (multiple $R = 0.78$, $p < 0.0005$). None of the rest indexes was significant in the multiple regression model.

Table 2. Relation Between Exercise Variables and Postoperative Left Ventricular Ejection Fraction

Variable	Postop EF <50% (mean ± SD) (n = 18)	Postop EF ≥50% (mean ± SD) (n = 56)	p Value
$ESVI_{EXE}$ (cm^3/m^2)	32 ± 7.6	18.1 ± 6.6	< 0.0005
EF_{EXE} (%)	57.4 ± 10.7	73.4 ± 9.4	< 0.0005
ΔEF_{EXE} (%)	−3.7 ± 7.8	8.7 ± 10.4	< 0.0005
$EDVI_{EXE}$ (cm^3/m^2)	76.1 ± 13.5	69.4 ± 16.8	0.13
Exercise capacity (METS)	8 ± 2.9	7.9 ± 2	0.89
Peak RPP ($\times 10^3$)	26 ± 6.6	29.7 ± 7.2	0.06
Peak heart rate (beats/min)	150.9 ± 26	153.5 ± 23	0.78

$EDVI_{EXE}$ = left ventricular end-diastolic volume index immediately after exercise; EF_{EXE} = ejection fraction immediately after exercise; $ESVI_{EXE}$ = end-systolic volume index immediately after exercise; METS = metabolic equivalents; RPP = rate–pressure product; ΔEF_{EXE} = change in ejection fraction with exercise; other abbreviations as in Table 1.

Table 3. Correlation Between Postoperative Left Ventricular Ejection Fraction and Preoperative Variables of Left Ventricular Function

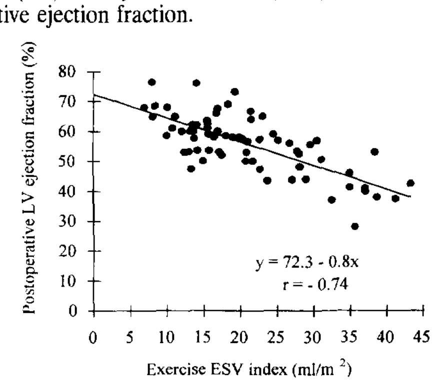
Preoperative Index	Correlation Coefficient (p value)
$ESVI_{EXE}$ (cm^3/m^2)	−0.74 (<0.0005)
EF_{EXE} (%)	0.72 (<0.0005)
ΔEF_{EXE} (%)	0.57 (<0.0005)
LV dP/dt (mm Hg/s)	0.39 (0.002)
ESWS ($dynes/cm^2$)	−0.4 (0.001)
$ESVI_{REST}$ (cm^3/m^2)	−0.33 (0.007)
EF_{REST} (%)	0.26 (0.03)

Abbreviations as in Tables 1 and 2.

Predictors of postoperative left ventricular dysfunction. To establish threshold levels of these variables for use in clinical decision-making regarding the referral of patients for operation, ROC curves were drawn to express the sensitivities and specificities of the various criteria for the prediction of postoperative left ventricular dysfunction (Table 4). Figure 2 shows the ROC curves of the significant predictors of postrepair left ventricular dysfunction. The area under the curve of exercise left ventricular end-systolic volume index was significantly larger than those for all resting indexes (all $p < 0.001$). The areas under the curves of exercise ejection fraction and change in ejection fraction with exercise were significantly larger than those for rest ejection fraction and rest end-systolic volume index ($p = 0.01$) and were marginally larger than that for dP/dt ($p = 0.09$).

Interobservability and intraobserver variability. Interobserver variability in the measurement of rest left ventricular end-diastolic and end-systolic volumes was 3 ± 8.5 cm^3 ($r = 0.98$) and 0.7 ± 8.2 cm^3 ($r = 0.94$), respectively, corresponding to a variability in rest ejection fraction of $0 \pm 5\%$. Immediately after exercise, the variability was 1.2 ± 14.5 cm^3 for end-diastolic volume ($r = 0.94$), -1.8 ± 4.7 cm^3 for end-systolic volume ($r = 0.96$) and $1 \pm 3\%$ for ejection fraction. After operation, variability was -1.5 ± 5.7 cm^3 for end-diastolic

Figure 1. Scatterplot showing the relation between preoperative left ventricular (LV) end-systolic volume (ESV) index at exercise and postoperative ejection fraction.



JACC Vol. 28, No. 5
November 1, 1996:1198–205

Table 4. Sensitivity and Specificity of Diagnostic Cutoff Values of Preoperative Rest and Exercise Indexes of Left Ventricular Function (as determined by receiver operating characteristic curves) in Predicting Early Postoperative Left Ventricular Dysfunction

Variable	Optimal Diagnostic Cutoff Value	Specificity	Sensitivity
$ESVI_{EXE}$	25 cm^3/m^2	83%	83%
EF_{EXE}	68%	80%	81%
ΔEF_{EXE}	4%	75%	79%
LV dP/dt	1,000 mm Hg/s	73%	65%
$ESWS_{REST}$	52.4 × 10^3 $dynes/cm^2$	65%	64%
$ESVI_{REST}$	29 cm^3/m^2	63%	66%
EF_{REST}	66%	51%	67%

Abbreviations as in Tables 1 and 2.

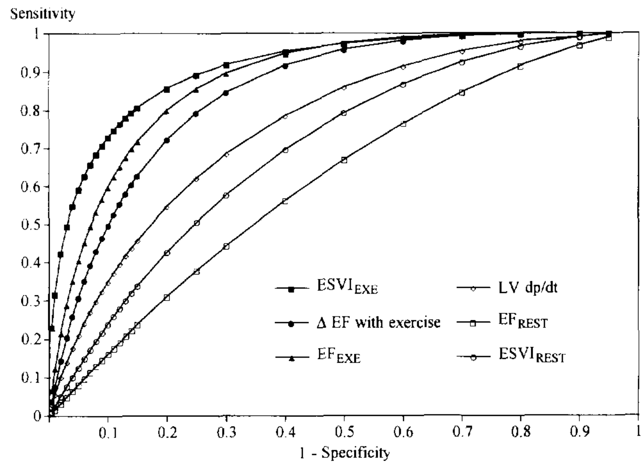


Figure 2. Receiver operating characteristic curves of the various significant predictors of early postoperative left ventricular dysfunction. EF_{EXE} = ejection fraction immediately after exercise; EF_{REST} = ejection fraction at rest; $ESVI_{EXE}$ = end-systolic volume index immediately after exercise; $ESVI_{REST}$ = end-systolic volume index at rest; LV dP/dt = peak rate of change in left ventricular pressure; ΔEF with exercise = change in ejection fraction with exercise.

volume (r = 0.99), 2 ± 9.2 cm^3 for end-systolic volume (r = 0.97) and 0 ± 5% for ejection fraction.

Intraobserver variability in the measurement of rest left ventricular end-diastolic and end systolic volumes was 4.9 ± 10.4 cm^3 (r = 0.97) and −0.9 ± 3.5 cm^3 (r = 0.99), respectively, corresponding a variability in ejection fraction of −2 ± 4%. Immediately after exercise, variability was −0.8 ± 9.5 cm^3 for end-diastolic volume (r = 0.98), −0.9 ± 3.2 cm^3 for end-systolic volume (r = 0.99) and −1 ± 2% for ejection fraction. Postoperatively, it was −2.4 ± 6.3 cm^3 for end-diastolic volume (r = 0.99), −1.2 ± 4.1 cm^3 for end-systolic volume (r = 0.99) and 1 ± 3% for ejection fraction.

Discussion

In patients with isolated, minimally symptomatic mitral regurgitation, the use of exercise echocardiography to examine the response of the left ventricle to dynamic exercise is useful in detecting latent ventricular dysfunction and predicting left ventricular function after mitral valve repair. Specifically, the decrease in left ventricular ejection fraction early after mitral repair may be reliably predicted preoperatively by measuring the postexercise left ventricular end-systolic volume index and ejection fraction, as well as the change in ejection fraction with exercise. In contrast, rest variables of left ventricular systolic function (including dP/dt, end-systolic wall stress, end-systolic volume index, ejection fraction and end-systolic dimension index) were less predictive of postoperative function. Indexes of exercise capacity, including maximal rate–pressure product or work load, were not useful predictors of postrepair ventricular function in these patients.

Assessment of rest left ventricular function in mitral regurgitation. Left ventricular function has been shown (12,16–18) to be a principal determinant of morbidity and mortality in both uncorrected and surgically corrected mitral regurgitation. Therefore, accurate assessment of ventricular function is important in these patients so that appropriate, timely intervention can be recommended and postoperative ventricular function predicted. Previous studies have focused on the related problem of assessment of rest left ventricular dysfunction in patients before mitral valve replacement. Various indexes of left ventricular size and function have been used with varying success in predicting outcome after mitral valve replacement. A rest end-systolic dimension index >2.6 cm/m^2 or a fractional shortening <31% by echocardiography has been suggested (3) to be associated with an adverse postoperative outcome. Rest left ventricular end-systolic volume, a relatively preload-independent measurement of systolic function, was found to be correlated with the left ventricular fractional shortening after valve replacement, and an end-systolic volume index >60 cm^3/m^2 was associated with a higher risk of perioperative cardiac mortality (1). This finding was confirmed by Nakano et al. (2) who found that a left ventricular end-systolic volume index >100 cm^3/m^2 was associated with higher mortality after valve replacement. Left ventricular end-systolic wall stress (3) and its ratio to end-systolic volume (19) were also predictive of outcome after valve replacement. Patients who died perioperatively had a significantly lower end-systolic wall stress/end-systolic volume index ratio (19). A more recent retrospective study (12) that included patients with coronary artery disease also suggested that preoperative rest left ventricular ejection fraction was correlated with postoperative ejection fraction. However, the majority of these studies used symptomatic improvement (3,19) or perioperative or postoperative mortality (2,19,20) as outcome measure. The use of these end points as outcome measures may not be applicable in the current setting, where many patients with mitral regurgitation undergoing operation are asymptomatic or only minimally symptomatic and surgical mortality is generally low.

Left ventricular dP/dt has recently been studied (5) as another load-independent index of ventricular function. In the presence of mitral regurgitation, continuous wave Doppler echocardiography provides an accurate, yet noninvasive way to measure rest left ventricular dP/dt (9). Pai et al. (5) showed in patients with mitral regurgitation that preoperative dP/dt correlated with ejection fraction after surgical correction of the regurgitant lesion. However, in the presence of severe mitral regurgitation, dP/dt cannot be measured in the true isovolumetric phase of left ventricular contraction. Additionally, noninvasive measurement of left ventricular dP/dt requires proper alignment of the continuous wave Doppler beam with the mitral regurgitant jet, which is not always possible in the presence of an eccentric regurgitant jet, as is associated with mitral valve prolapse. This is illustrated by the fact that rest dP/dt could not be measured in seven of our patients because of the eccentricity of the mitral regurgitant jet. Therefore, the accuracy of the measurement, and hence the utility of the technique in patients with mitral valve prolapse, cannot be ensured in all cases.

Left ventricular response to exercise in mitral regurgitation. Latent ventricular dysfunction may be manifest as limited contractile reserve in response to stimuli (such as exercise) that increase contractility. Isometric exercise, which causes an increase in afterload, is associated with a decrease in left ventricular ejection fraction in patients with mitral regurgitation, the extent of which correlates with the change in rest ejection fraction after valve replacement (21). Isometric exercise performed during cardiac catheterization has also been used to predict symptomatic improvement and ventricular function after aortic valve replacement (22). In contrast, isotonic exercise in normal subjects results in increased global ventricular function and cardiac output with a decrease in end-systolic volume, whereas end-diastolic volume remains relatively unchanged (23–26). Isotonic exercise produces a much greater stimulus to left ventricular contractility than does isometric exercise (23,25,26) and may be more suited to detecting latent ventricular dysfunction.

Exercise radionuclide ventriculography has been used to quantitate mitral regurgitation and to assess ventricular response to isotonic exercise (27–34). Rosen et al. (33) performed exercise radionuclide ventriculography in patients with asymptomatic or minimally symptomatic mitral regurgitation and found that the change in right ventricular ejection fraction with exercise was predictive of symptomatic deterioration. Hochreiter et al. (18) also suggested that left and right ventricular ejection fraction at rest and at exercise provided valuable information on prognosis. Although exercise radionuclide ventriculography is also a valuable tool for examining ventricular response to exercise, few studies have systemically examined the prediction of left ventricular function after mitral valve surgery in a large series of patients.

Ginzton et al. (26) used exercise echocardiography with an upright bicycle protocol and found that left ventricular end-systolic volume index, ejection fraction and the ratio of peak systolic blood pressure to end-systolic volume at peak exercise accurately identified patients with a previous myocardial infarction from normal patients. In the present study, we extended the observation to patients with mitral regurgitation without coronary artery disease and found that exercise ejection fraction, exercise end-systolic volume index and the change in ejection fraction with exercise detected latent ventricular dysfunction and reliably predicted ventricular function after mitral valve repair. That the exercise variables are superior to the rest variables in predicting ventricular function after mitral valve repair is perhaps not surprising considering the value of the left ventricular pressure–volume relation in assessing ventricular function and the way that relation changes with exercise (35). In normal subjects, the slope of the end-systolic pressure–volume relation increases with isotonic exercise. The decrease in end-systolic volume with a relatively unchanged end-diastolic volume leads to an increase in stroke volume. In contrast, in patients with overt or latent ventricular dysfunction, the flatter end-systolic pressure–volume relation will be manifest by either a higher end-systolic volume or a lower end-systolic pressure and smaller increase in stroke volume that can readily be detected by exercise echocardiography.

Study limitations. Surgical treatment of mitral regurgitation usually leads to a decrease in left ventricular ejection fraction and often precipitates development of left ventricular dysfunction. However, the natural history of such early postoperative dysfunction is unclear, and few studies have examined its reversibility. Starling (36) suggested that preoperative latent left ventricular dysfunction may be reversible after mitral valve surgery. The follow-up period in the present study was short, and further studies are needed to examine serially the change in ventricular function after mitral repair over a longer period of time and to evaluate the role of exercise echocardiography. By the study design, our study patients were a relatively small and selected group and the inferiority of rest indexes of left ventricular function in predicting postrepair function may have been due to the selection of relatively low risk patients in the study. In the present study, left ventricular volumes were measured from the apical four-chamber view because the apical two-chamber views immediately after exercise were often foreshortened, and the anterior wall was often not well seen because of hyperventilation. However, because patients with coronary artery disease were excluded, and left ventricular enlargement in mitral regurgitation is usually symmetric, the use of a single apical four-chamber view would be unlikely to be responsible for inaccuracies in volume measurement due to chamber asymmetry (37). In the present study, the severity of mitral regurgitation was graded semiquantitatively according to the color Doppler regurgitant jet areas. Recently developed proximal convergence methods of quantification were not used. It was technically very difficult to adequately visualize the proximal flow convergence area immediately after exercise. Moreover, because mitral valve prolapse was the mechanism of regurgitation in the majority of patients, the proximal convergence area was heavily constrained by the left ventricular wall. Accurate quantification of mitral regurgitant volume requires special angle correction, which would be difficult to apply in this situation.

Conclusions. Mitral valve repair is associated with better preservation of left ventricular function than valve replacement (38,39). However, there is still a substantial decrease in ejection fraction after surgical repair, as shown in the present study. We showed that in minimally symptomatic patients, conventional indexes of rest left ventricular function are of inferior value in predicting left ventricular function after mitral valve repair. Preoperative latent left ventricular dysfunction may be indicated by a limited contractile reserve, manifest as an inadequate increase or a decrease in ejection fraction with isotonic exercise and a higher exercise end-systolic index. By detecting a limited contractile reserve in the presence of "normal" ventricular function, exercise echocardiography may enable selection of at-risk patients for early operation. The role of exercise echocardiography in determining the optimal timing of operation and in improving long-term outcome needs to be addressed by further studies.

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