Usefulness of Preoperative Cardiac Dimensions to Predict Success of Reverse Cardiac Remodeling in Patients Undergoing Repair for Mitral Valve Prolapse

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Mitral valve repair for mitral regurgitation (MR) is currently recommended based on the degree of MR and left ventricular (LV) function. The present study examines predictors of reverse remodeling after repair for degenerative disease. We retrospectively identified 439 patients who underwent repair for myxomatous mitral valve degeneration and had both pre- and postoperative echocardiographic data available. Patients were categorized based on left atrial (LA) diameter and LV diameter standards of the American Society of Echocardiography. The outcome of interest was the degree of reverse remodeling on all heart dimensions at follow-up. Mean age was 57 ± 12 years, and 37% of patients were women. Mean preoperative LV end-diastolic diameter was 5.8 ± 0.7 cm, LV end-systolic diameter 3.5 ± 0.6 cm, LA 4.7 ± 0.7 cm, and median ejection fraction 60%. Median observation time was 81 months, and time to postoperative echocardiography was 38 months. Overall, 95% of patients had normal LV diastolic dimensions postoperatively, 93% normal LV systolic dimensions, and 37% normal LA dimensions. A Cox regression analysis showed that moderate (odds ratio [OR] 2.1, 95% confidence interval [CI] 1.3 to 3.4) or severe preoperative LA dilatation (OR 2.7, 95% CI 1.7 to 4.4), abnormal preoperative LV end-systolic dimensions (OR 1.3, 95% CI 1.1 to 1.5), and age in years (OR 1.02, 95% CI 1.01 to 1.03) were predictive of less reverse remodeling on follow-up. In conclusion, preoperative LV end-systolic dimensions and LA dilatation substantially affect the likelihood of successful LA remodeling and normalization of all heart dimensions after mitral valve repair for MR. These findings support early operation for MR before the increase in heart dimensions is nonreversible. **(Am J Cardiol 2014;113:1006−1010)**

The regurgitant jet of blood from mitral regurgitation (MR) overloads the left atrium (LA) and the left ventricle (LV).[1] LV loading is critical in understanding the remodeling process.[1] The remodeling due to MR is different from that seen in other left-sided valve diseases such as mitral stenosis, aortic stenosis, or aortic regurgitation in that it manifests with higher LV radius/thickness ratios and lower mass/volume ratios.[2] Reverse LA and LV remodeling may happen early after surgical correction of MR,[3−6] but long-standing MR left untreated leads to deterioration of LV function and impacts the potential for reverse remodeling. Thus, the degree of disease progression is an important consideration when weighing the value of surgical intervention. The present study evaluates long-term outcomes in a series of patients who underwent mitral valve repair for MR due to degenerative disease (prolapse). We sought to investigate whether preoperative echocardiographic data or other factors may predict the degree of reverse remodeling seen at long-term follow-up.

Methods

With approval from our internal review board, we identified all 824 patients who underwent minimally invasive mitral valve repair from August 1996 to November 2010. Our inclusion criteria were patients with MR due to myxomatous mitral valve degeneration, normal coronary arteries, availability of a preoperative echocardiogram within 1 year of the surgery date, and a follow-up echocardiogram at least 6 months after surgery. Subjects with previous mitral valve surgery or mitral stenosis were excluded; 439 patients met our inclusion criteria.

Clinical and surgical data were collected at the time of presentation, extracted from hospital electronic records or by chart review, and coded to Society of Thoracic Surgeons Adult Cardiac Database, version 2.52, specifications. Mortality data were collected during routine postoperative follow-up and supplemented by a query of the Social Security Death Index.

Our main outcome of interest was reverse remodeling of the heart, defined as each of the following being within

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normal parameters: LV end-diastolic diameter, LV end-systolic diameter, and LA diameter. These were collected by a manual review of the echocardiographic report. All echocardiographies were performed transthoracically. The preoperative echocardiography was the study most proximate to the surgery. If multiple echocardiographic studies existed, the latest normal or the earliest abnormal study was used. Only 1 preoperative and 1 postoperative echocardiogram for each patient was collected in the research data file. Grade of MR was assessed using color-flow Doppler as none or trivial (0), trace (1+), mild (2+), moderate (3+), and severe (4+).

We grouped patients based on the preoperative severity of abnormality of heart dimensions. For LV end-systolic diameter, the grouping was based on a preoperative value of ≤4 cm (normal) or >4 cm (abnormal). LV end-diastolic diameter and LA groupings were derived from the American Society of Echocardiography's recommendations for chamber quantification.[7] For men, normal LV end-diastolic diameter, 4.2 to 5.9 cm; mildly abnormal LV end-diastolic diameter, 6.0 to 6.3 cm; moderately abnormal LV end-diastolic diameter, 6.4 to 6.8 cm; severely abnormal LV end-diastolic diameter, ≥6.9 cm; normal LA, 3.0 to 4.0 cm; mildly abnormal LA, 4.1 to 4.6 cm; moderately abnormal LA, 4.7 to 5.2 cm; and severely abnormal LA, ≥5.3 cm. For women, normal LV end-diastolic diameter, 3.9 to 5.3 cm; mildly abnormal LV end-diastolic diameter, 5.4 to 5.7 cm; moderately abnormal LV end-diastolic diameter, 5.8 to 6.1 cm; severely abnormal LV end-diastolic diameter, ≥6.2 cm; normal LA, 2.7 to 3.8 cm; mildly abnormal LA, 3.9 to 4.2 cm; moderately abnormal LA, 4.3 to 4.6 cm; and severely abnormal LA, ≥4.7 cm. Successful postoperative remodeling for each of the heart dimensions was defined as measurements equal or the upper normal value; for men, LV end-diastolic diameter ≤5.9 cm and LA ≤4.0 cm, and for women, LV end-diastolic diameter ≤5.3 cm and LA ≤3.8 cm. Normal postoperative LV end-systolic diameter for all the samples was defined as ≤4.0 cm.

Our secondary outcome of interest was survival over the study observation period. Because we excluded reoperations and early mortality, the end point for survival was the time in months from operation until (1) the first postoperative echocardiography indicating heart abnormality, (2) death, or (3) alive at the end of the study observation period, with normal postoperative echocardiographic data. The study period ended on June 30, 2011.

Categorical data are expressed as numbers and percentages and were compared using Fisher's exact test. Continuous variables are presented as mean and SD or median and interquartile range for normally or nonnormally distributed continuous data, respectively, and were compared using *t* test with Levine test for homogeneity of variance or Mann-Whitney *U* test, as appropriate. Multivariate analysis of survival with complete reverse heart remodeling was estimated using a forward stepwise Cox regression model. An event was the first of either an echocardiogram showing any dimension abnormal or report of death. Tested variables were derived from available literature, clinical expertise, and variables that differed between groups on exploratory univariate analysis or could reasonably be expected to impact our outcomes. Interaction terms were examined, and colinearity diagnostics were evaluated. Statistical analyses were performed with SPSS, version 13.0 (SPSS Inc., Chicago, Illinois).

Table 1
Characteristics and operative and in-hospital outcomes of 439 patients with mitral valve repair

Characteristic		Study Cohort, n = 439
Preoperative characteristic		
Age (yrs)	Mean	57.0 ± 12.1
Age ≥65 yrs	n	121 (27.6)
Women	n	164 (37.4)
Body surface area	Mean	1.9 ± 0.2
New York Heart Association class III or IV	n	88 (20.0)
Diabetes mellitus	n	8 (1.8)
Chronic obstructive pulmonary disease	n	26 (5.9)
Renal failure	n	6 (1.4)
Atrial fibrillation	n	35 (8.0)
Echo data		
≥3+ MR	n	438 (99.8)
LV diameter/diastole	Mean	5.77 ± 0.7
	Median	5.73 (5.4−6.1)
LV diameter/systole	Mean	3.52 ± 0.6
	Median	3.50 (3.2−3.9)
LA dimension	Mean	4.69 ± 0.7
	Median	4.60 (4.2−5.0)
Ejection fraction (%)	Median	60 (55−65)
Operative data		
No ring used	n	5 (1.1)
Ring size	Median	34 (26−38)
Bypass time (minutes)	Median	115 (98−139)
Crossclamp time (minutes)	Median	81 (69−98)
Postoperative outcome		
Transfused with red cells	n	130 (29.6)
Units per transfused patient	Median	2.00 (1−3)
Renal failure	n	27 (6.2)
New-onset renal failure	n	22 (5.0)
Atrial fibrillation	n	137 (31.2)
New-onset atrial fibrillation	n	110 (25.1)
Died during follow-up	n	20 (4.6)
Follow-up time (mo)	Median	81 (53−116)

Number of cases presented with the percentage in parentheses. Means are presented with SDs and medians with interquartile ranges, except for ring size, which is a range.

Many cases had individual measures missing at random. Because deleting patients with missing values introduces biases that may not be identified or adequately controlled and affects generalizability of findings, we decided to impute missing data rather than conduct a complete-case analysis.[8,9] Preoperative LV end-diastolic diameter was missing for 89 patients (18%), LV end-systolic diameter missing for 107 (22%), and LA missing in 105 patients (21%). All patients had at least 2 of these data points present. Missing data were estimated using multiply imputed linear regression approach with random-error component; for each imputed measure, a minimum of 5 data sets (maximum of 20) were created until stability in the standard errors was achieved. The regression models included all covariates, including outcome variables.[10,11] Compared with known data, the correlation for imputed LV end-systolic diameter was $R^2 = 0.988$, LV end-diastolic diameter was $R^2 = 0.988$, and LA $R^2 = 0.993$. Imputed measures were only used when that variable was considered a covariate for that analysis. Outcome measures