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Left Ventricular Geometry and Operative Mortality in Patients Undergoing Mitral Valve Replacement

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Summary

Background: Distortion of left ventricular (LV) shape is often associated with LV dysfunction and is thought to be an independent predictor of survival in patients with coronary disease.

Hypothesis: The purpose of this study was to examine the relationship between LV geometry and hospital mortality in patients with mitral regurgitation (MR) undergoing mitral valve surgery.

Methods: A consecutive series of patients (aged 68 ± 12 years, 47% men) (n = 149) with MR who underwent cardiac catheterization, left ventriculography, and mitral valve surgery from 1995 to 1996 at Mount Sinai Medical Center was studied. Left ventriculograms, clinical records, and hemodynamics were reviewed. Left ventricular volumes and ejection fraction were calculated using standard techniques. Left ventricular shape in diastole and systole was evaluated using the sphericity index, which is defined as the end-systolic LV volume (× 100) divided by the volume of a sphere whose diameter is equal to the LV long axis.

Results: In the patients studied, the etiology of mitral insufficiency was mitral valve prolapse in 40.9%, ischemic heart disease in 40.3%, rheumatic heart disease in 11.4%, and prosthetic valvular dysfunction in 7.4%. The average ejection fraction was 65% ± 17. Systolic sphericity index (SSI) was 36% ± 15 in patients who died, compared with 25% ± 11 in patients who lived ($p < 0.001$). A multivariate model was constructed using hemodynamic and angiographic indices derived during preoperative cardiac catheterization. Systolic sphericity index (odds ratio = 1.6 for each point increase, $p < 0.01$) was found to be an independent predictor of postoperative survival in the global population, as well as in patients with coronary disease ($p < 0.01$).

Conclusion: Left ventricular geometry is an independent angiographic risk factor for survival following mitral valve replacement. Sphericity index is a simple method for assessing LV geometry which should be calculated in patients as part of risk stratification.

Key words: mitral regurgitation, mitral valve, ventricular remodeling, cardiac surgery

Introduction

Mitral valve surgery for mitral regurgitation (MR) places an acute hemodynamic burden on the left ventricle (LV) due to the sudden increase in afterload that accompanies closure of the low resistance path for ejection of blood into the left atrium.[1] A low surgical mortality and a good hemodynamic result require not only impeccable surgical technique, but also an LV with sufficient reserve to withstand this inevitable increase in afterload. Several indices of LV structure and function have been found to be predictive of surgical mortality following mitral valve surgery. These ventricular factors include high end-systolic volume[2] or end-systolic dimension, and low ejection fraction.[3,4]

Recently there has been an appreciation of the importance of LV geometry, independent of size or systolic function, on functional class and prognosis.[5–7] Patients with MR have been found to have more spherical chamber geometry both in systole and diastole.[8–10] Transformation of the LV from a typical ellipsoidal shape to one that more closely approximates a sphere has been described as causal in the development of MR in patients with low ejection fraction.[11] Furthermore, wall tension is inversely proportional to curvature. Thus, an increase in

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the sphericity of the LV inevitably leads to a redistribution of regional wall tension and stress. The present study was designed to assess the clinical relevance of these physiologic concepts and to determine whether LV shape was a predictor of operative risk for patients undergoing mitral valve surgery for MR.

Methods

We studied 149 consecutive patients with MR who underwent cardiac catheterization, left ventriculography, and mitral valve surgery for chronic mitral regurgitation at Mount Sinai Medical Center between January 1, 1995, and December 31, 1996. Patients were excluded if they presented with acute MR or had associated obstructive hypertrophic cardiomyopathy. The study cohort consisted of 120 (79.9%) patients who had mitral valve replacement and 29 (20.1%) who had mitral valve repair. Coronary bypass surgery was simultaneously performed on 77 (52%). The primary endpoint of the study, hospital mortality, was defined as death occurring at any time during surgical hospitalization.

All patients had undergone cardiac catheterization with hemodynamic measurements, left ventriculography, and selective coronary angiography using standard techniques. Pressures were measured using a conventional fluid-filled catheter/transducer system, and cardiac output was determined by the Fick method immediately before LV contrast angiography.

Single-plane left ventriculography was performed in the 30° right anterior oblique projection. End-diastolic and end-systolic frames were selected and traced by hand. The areas at end diastole and end systole were measured with a digital planimeter. Premature beats and postextrasystolic beats were excluded from the analysis. Left ventricular volumes were calculated by the area-length method[12] and were normalized for body surface area. Ejection fraction was calculated as the difference between end-diastolic and end-systolic volume divided by end-diastolic volume. The presence and extent of MR was graded qualitatively using Sellers' classification.[13] Regurgitant fraction was calculated as the difference between angiographic stroke volume and the forward stroke volume divided by angiographic stroke volume.[14]

Left ventricular shape was expressed as sphericity index in end systole and end diastole.[5] Sphericity index does not require magnification correction and is defined as the end-systolic LV volume (× 100) divided by the volume of a hypothetical sphere whose diameter is equal to the length of the LV long axis. Thus, the sphericity index of a sphere is 100%. The normal range is 29% ± 7 for diastolic sphericity index and 15% ± 8 for systolic sphericity index. We also measured other indices of LV shape, including eccentricity[8] and the long/short axis ratio of the LV.[11]

Statistical Analyses

Baseline characteristics were compared by the presence or absence of the primary endpoint using the chi-square statistic for categorical variables and one-way analysis of variance for continuous variables. Multivariate analyses to determine independent predictors of mortality were carried out using logistic regression analysis. The variables included in the logistic regression model were based on significance in univariate analyses and included prior infarction, number of diseased coronary arteries, ejection fraction, end-systolic volume, end-diastolic volume, diastolic and systolic sphericity index, and aortic pressure. Similar analyses were performed independently in the group of patients with ischemic disease. For all comparisons, statistical significance was defined as $p < 0.05$ (2-tailed).

Results

Baseline Characteristics

The study cohort consisted of 149 patients (47% men, average age of 68 ± 12 years, range 25–90 years, Table I). The etiology of MR was mitral valve prolapse in 41%, ischemic heart disease in 40%, rheumatic heart disease in 11%, and mitral prosthetic dysfunction in 8%. Although 20% of patients had sustained a prior infarction, the average ejection fraction for

TABLE I Patient characteristics

Age (years)	68 ± 12
Male sex (%)	47
Etiology	
Mitral valve prolapse (%)	41
Ischemic heart disease (%)	40
Rheumatic heart disease (%)	11
Prosthetic valvular dysfunction (%)	7
NYHA	
II (%)	24 (16)
III (%)	82 (55)
IV (%)	43 (28)
Sinus rhythm (%)	70
Previous AMI (%)	20
CABG previous (%)	12
Pacemaker (%)	12
LBBB (%)	15
Mitral calcification (%)	16
Mitral regurgitation	
1+ (%)	6 (4)
2+ (%)	23 (15)
3+ (%)	45 (30)
4+ (%)	75 (50)
Surgery	
Replacement (%)	50 (34)
Replacement and CABG (%)	70 (47)
Repair (%)	20 (13)
Repair and CABG (%)	9 (6)

When applicable, data are reported as mean ± standard deviation.
Abbreviations: AMI = acute myocardial infarction, CABG = coronary artery bypass graft, LBBB = left bundle-branch block, NYHA = New York Heart Association.

the group was within the normal range (64% ± 16). The angiographic severity of mitral regurgitation was: 1 + in 6 (4%), 2 + in 23 (15.4%), 3 + in 45 (30.2%), and 4 + in 75 (50.3%). There were 12 hospital deaths (8.1%), which were all due to cardiovascular causes. The extent of LV shape abnormality did not differ based on the severity of MR (SSI by MR severity: 1 +: 17 ± 10; 2 +: 26 ± 10; 3 +: 28 ± 12; 4 +: 26 ± 12; p = 0.22). In contrast, patients with coronary artery disease had more spherical ventricles in systole, but not in diastole, than did patients without coronary disease (SSI in patients with coronary disease: 30 ± 12 vs. 24.6 ± 11 in patients without coronary disease; p = 0.012).

Comparison of Measurements of Left Ventricular Shape

Three measurements of LV shape—axis ratio, eccentricity, and sphericity index—were taken on each ventriculogram. There was an excellent correlation among all three measurements: sphericity index with eccentricity ($r = -0.99$, $p < 0.001$), sphericity index with long/short axis ratio ($r = 0.89$, $p < 0.001$), and eccentricity with long/short axis ratio ($r = 0.85$, $p < 0.001$). All three methods demonstrated that patients who died had more spherical ventricles than those who lived (Table II).

Clinical Correlates of In-Hospital Mortality

The presence of ischemic MR ($p < 0.001$), a prior infarction ($p = 0.001$), more diseased vessels ($p = 0.002$), and combined coronary and mitral surgery (Table III) were each associated with higher in-hospital mortality. No other baseline clinical characteristics were significantly different between survivors and nonsurvivors.

TABLE II Ventriculographic variables and indices of geometry by survival

Characteristic	Dead (n = 12)	Alive (n = 137)	p Value[a]
Ejection fraction (%)	0.51 ± 0.08	0.65 ± 0.16	0.004
Regurgitation fraction (%)	0.65 ± 0.34	0.60 ± 0.20	0.469
LV volumes			
End diastolic (ml/m^2)	115 ± 54	116 ± 39	0.955
End systolic (ml/ m^2)	55 ± 18	43 ± 35	0.256
LV sphericity			
Diastolic sphericity index (%)	47 ± 20	41 ± 10	0.042
Systolic sphericity index (%)	36 ± 15	25 ± 11	0.001
Change (%)	11 ± 8	15 ± 9	0.117
Eccentricity systolic	0.77 ± 0.11	0.85 ± 0.06	0.007
Eccentricity diastolic	0.72 ± 0.10	0.75 ± 0.07	0.139
Ratio long axis/short axis, systolic	1.7 ± 0.31	2 ± 0.49	0.009
Ratio long axis/short axis, diastolic	1.48 ± 0.22	1.57 ± 0.19	0.134

Plus-minus values are means ± standard deviation.
[a] P values were calculated by one-way analysis of variance.
Abbreviation: LV = left ventricular.

Hemodynamic and Ventriculographic Correlates of Mortality

Survival was associated with the highest aortic pressures measured during cardiac catheterization (systolic $p = 0.041$, diastolic $p = 0.016$, and mean $p = 0.02$). The remainder of the hemodynamic variables were similar in both groups (Table II). An analysis of ventriculographic variables showed that survivors had a higher ejection fraction than nonsurvivors ($p = 0.004$). Although there were no differences in LV volumes between groups, diastolic ($p = 0.042$) and systolic ($p = 0.001$) sphericity index were both lower in patients who lived than in those who died. Similarly, measurements of systolic eccentricity ($p = 0.007$) and systolic axis ratio ($p = 0.009$) confirmed that patients who died had the most spherical ventricles.

Multivariate Analyses

In the overall patient population, a logistic regression analysis was constructed to determine the independent angiographic and hemodynamic predictors of postoperative survival. The model included prior infarction, number of diseased coronary arteries, ejection fraction, end-systolic volume, end-diastolic volume, diastolic and systolic sphericity indices, and mean aortic pressure. Systolic sphericity index ($p = 0.02$) and prior infarction ($p = 0.01$) were the only two variables found to be independent predictors of in-hospital mortality. Multivariate

TABLE III Ventriculographic variables and indices of geometry in survival

Characteristic	Dead (n = 12)	Alive (n = 137)	p Value[a]
Age (years)	72 ± 10	68 ± 12	0.281
Male sex (%)	33.3	48	0.323
Sinus rhythm (%)	75	69	0.682
Previous AMI (%)	58	17	0.001
CABG previous (%)	25	11	0.152
Q waves	0.7	0.4	0.198
Vessels >70 %	2.5	1.1	0.002
NYHA >II (%)	8	84	0.956
Pacemaker (%)	17	12	0.611
LBBB (%)	25	15	0.338
RBBB (%)	17	7	0.199
Mitral calcification (%)	17	19	0.844
Mitral stenosis (%)	8	12	0.677
Mitral regurgitation III–IV (%)	67	82	0.205
Ischemic etiology (%)	83	42	0.006
CABG (%)	83	50	0.027

Plus-minus values are means ± standard deviation.
[a] P values were calculated by one-way analysis of variance for age, vessels > 70%, and Q waves, and by the chi-square test for categorical variables.
Abbreviations: AMI = acute myocardial infarction, CABG = coronary artery bypass graft, NYHA = New York Heart Association, LBBB = left bundle-branch block, RBBB = right bundle-branch block.

analyses were performed on the subgroup of patients with ischemic MR. The multivariate model included prior infarction, ejection fraction, diastolic and systolic sphericity index, and mean aortic pressure. Systolic sphericity index ($p = 0.039$) and mean aortic pressure ($p = 0.047$) were the only two variables found to be independent predictors of hospital mortality in patients with ischemic MR.

Discussion

Mitral valve surgery for mitral insufficiency is an excellent model to test whether LV shape is a clinically important correlate of cardiac reserve. In chronic MR, the apparent preservation of LV systolic performance and paucity of clinical symptoms during the course of the disease may be attributed to ejection into a low-pressure, high-compliance chamber, the left atrium.[1, 19] Consequently, ejection phase indices such as ejection fraction may appear falsely normal in patients with severe MR. When mitral valve replacement or repair takes place, the LV has to have sufficient contractile reserve to withstand both the temporary loss of contractility caused by cardiopulmonary bypass and cardiac surgery, as well as the sudden increase in afterload caused by eliminating systolic flow into the left atrium. We assessed the hemodynamic and angiographic predictors of in-hospital mortality in patients with MR who were undergoing mitral valve surgery, and found that aortic pressure and LV shape predicted postoperative outcome.

Patients with MR have more spherical ventricles, both in diastole and in systole, than do patients without MR. In different patient populations, both Kono *et al.*[11] and Lamas *et al.*[10] have reported these findings. Furthermore, Sabbah *et al.*[15] and Kono *et al.*[11, 17] have postulated that LV shape change might be the primary determinant of functional MR in patients with heart failure, and that these associated geometric alterations may be etiologic both to the presence of MR and to the attendant clinical consequences. In the present study, in-hospital mortality was low (8.1%) and similar to that reported by other centers[17, 18] for mitral valve replacement. However, a propos of the above hypothesis linking LV shape with outcome in patients with MR, LV systolic shape proved to be an independent predictor of postoperative survival. Systolic LV shape measured with sphericity index proved to be an even better predictor of postoperative outcome than were LV volumes, ejection fraction, or even the extent of underlying coronary disease.

There are physiologic reasons why alterations in LV shape are related to the adequacy of cardiovascular adaptation to hemodynamic stress, and ultimately to clinical outcome. Although a spherical shape leads to a more uniform distribution of LV wall tension, differences in LV wall thickness may lead to unfavorable distribution of LV wall stress. In a normal LV, wall tension should be lowest at the apex, the site with the smallest radius of curvature. As the ventricle becomes more spherical, the apex typically becomes less sharply curved, with a longer radius of curvature. Without a commensurate increase in wall thickness, apical stress will increase. Gould *et al.*[9] have reported that as ventricular dilatation occurs and the LV becomes more spherical, myocardial fiber orientation changes and wall stress is distributed more toward the meridional plane. This is quite different from the normal circumstance, in which circumferential wall stress generally predominates. Thus, maldistribution of local wall stress is a potential cause for associated adverse clinical consequences. Subclinical contractile abnormalities have also been reported in ventricles with geometric abnormalities. Borow *et al.* reported that patients with the greatest distortion of the LV had the most severely depressed contractility, as demonstrated by an attenuated response to infusions of inotropes.[19]

Although LV shape and volume are correlated variables, our data show that for any LV volume there is a large range of associated LV shapes. This was described by Kass *et al.*[20] who, using more complex methodology, noted that shape changes cannot be predicted from diastolic and systolic cavity volume alone but also depend upon the nature of ventricular loading during ejection. In their study, detailed cavity geometry was assessed by a Fourier analysis and general shape by eccentricity and circularity indices. The lack of a close correlation between LV volume, ejection fraction, and LV shape provides the statistical foundation for sphericity to be an independent predictor of outcome.

Previous studies have emphasized the importance of LV geometry to cardiac function and clinical outcome. Lamas *et al.* reported that LV sphericity index was an independent predictor of exercise duration and of the development of heart failure symptoms in patients with a recent anterior myocardial infarction (MI).[5] Tischler *et al.* performed a similar study in patients with idiopathic dilated cardiomyopathy and found a strong correlation between ventricular sphericity and exercise capacity.[7] These studies brought to light the potential importance of LV shape independent of volume, since neither ventricular volume nor ejection fraction correlated with exercise duration in either study.

Left ventricular shape is a predictor of mortality in patients with a variety of diagnoses. In dilated cardiomyopathy, those patients with the most spherical ventricles demonstrate decreased survival.[6] Lamas *et al.* analyzed LV shape in 699 patients following MI, and noted that systolic sphericity index predicted mortality independent of ejection fraction.[21] In another study, the same investigators postulated that the unexpected importance of hemodynamically mild mitral regurgitation was due to associated, unmeasured abnormalities in LV shape.[10] The present study is consistent with other studies that emphasize the importance of LV shape, and extends these results to the preoperative assessment of cardiac surgical risk.

Survival is decreased in patients with ischemic MR.[1, 19] This may be attributed to the coexistence of valvular and myocardial disease, as well as to the older age of this population and attendant comorbidities. Furthermore, ischemic MR may present a particularly severe hemodynamic stress for healthy, nonischemic ventricular myocardium. The maladaptive response by which LV remodeling and dilatation begets more LV remodeling and dilatation,[3] ultimately leading to heart failure, may be particularly severe in ischemic MR, since there is an actual loss of myocytes due to coronary ischemia and infarction. We separately analyzed the ischemic population and found results consistent with those of the overall study. Only systolic LV shape and aortic pressure were independent predictors of postoperative mortality in patients with ischemic heart disease undergoing mitral valve replacement. Unfortunately, the number of events in patients with nonischemic MR was low, and a similar analysis for patients with nonischemic etiologies was not conclusive.

Notwithstanding this finding, however, patients with ischemic MR had more spherical ventricles than those with nonischemic MR. Vokonas *et al.*[8] studied normal patients and patients with nonischemic MR with normal or decreased ejection fractions. Those with MR and a normal ejection fraction demonstrated well-preserved LV shape. The group with reduced ejection fraction had changes in spherical chamber geometry. The investigators suggested that an adaptive geometric change may have compromised pump function or contraction pattern.

Patients who undergo mitral valve replacement may have a higher sphericity postoperatively than do patients undergoing mitral valve repair.[22] Our study did not assess postoperative LV geometry and volumes, so this finding could not be confirmed. Nevertheless, preoperative sphericity did not differ among patients undergoing mitral repair or replacement.

The weight of clinical evidence now suggests that LV shape should be measured routinely in patients undergoing LV angiography. In contrast to LV volumes, which require careful correction for magnification and pincushion distortion, sphericity index is easy to measure. Sphericity index does not require magnification correction, nor is it rendered inaccurate by the presence of regional wall motion abnormalities. Ejection fraction has retained its universal applicability as the standard of reference measurement of LV function because of ease of calculation and clinical relevance. However, these analyses, as well as the evidence of other studies reviewed above, all conclude that systolic sphericity index does not require magnification correction and yields equivalent or superior information about the patient's prognosis. Moreover, in the patient with severe MR, ejection fraction may be falsely preserved until late in the clinical course, reducing its prognostic utility. Thus, although ejection fraction has been shown to be clinically relevant in many different circumstances, measurements of LV shape now have also been shown to predict clinical outcomes in patients who are post MI, who have cardiomyopathy, and now, in those with mitral insufficiency.

Study Limitations

The most important limitation of this study stems from the relatively small sample size and the excellent and low in-hospital mortality. These two factors lead to fewer overall endpoints to analyze, decreasing the statistical power for subgroup analyses. Consequently, only broad statements may be made about the various subgroups of the study population, such as patients without coronary disease and patients with valve repair compared with valve replacements. The present study is also limited by the selection of in-hospital mortality as the primary endpoint because of limited availability of long-term survival data. However, short-term survival does offer some benefits in measuring the importance of LV geometry. The hemodynamic stresses exacerbated by abnormalities of LV geometry are greatest at the time of mitral valve surgery. In the present database, all deaths were cardiovascular in nature and not primarily due to confounders such as renal failure or sepsis. Thus, although the long-term implications of LV geometry in patients following mitral valve surgery will need to await larger long-term reports, the present analyses support the importance of LV geometry in the acute setting. There are additional limitations that may restrict the applicability of our findings. Since this was an attempt to assess preoperative predictors of postoperative outcome, intraoperative variables, such as crossclamp time, were not studied. Also, not all previously described[3] predictors of postoperative outcome, particularly left atrial size, were available to be analyzed. Finally, the variables analyzed here were purposely kept simple in order to increase the potential clinical applicability of our findings. More complex studies, such as end-systolic pressure–volume relationship, were avoided.

The present study also emphasizes the close correlation of the three principally reported measures of LV shape: sphericity index, eccentricity index, and long/short axis ratio. There was insufficient statistical power to permit an accurate analysis of the relative value of each of these measurements. Therefore, the proper interpretation of this study is to emphasize the added value of measuring LV shape in various clinical circumstances.

Conclusions

Thus, the present study demonstrates that patients with MR have more spherical LVs than do normals, and that LV sphericity, particularly in systole, independently predicts survival following mitral valve surgery. Clinicians and cardiac surgeons should consider the use of this simple measurement to assess operative risk in their patients.

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