Importance of Mitral Valve Repair Associated With Left Ventricular Reconstruction for Patients With Ischemic Cardiomyopathy: A Real-Time Three-Dimensional Echocardiographic Study

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Background—Left ventricular (LV) reconstruction surgery leads to early improvement in LV function in ischemic cardiomyopathy (ICM) patients. This study was designed to evaluate the impact of mitral valve (MV) repair associated with LV reconstruction on LV function 1-year after surgery in ICM patients assessed by real-time 3-dimensional echocardiography (3DE).

Methods and Results—Sixty ICM patients who underwent the combination surgery (LV reconstruction in 60, MV repair in 30, and revascularization in 52 patients) were studied. Real-time 3DE was performed and LV volumes were obtained at baseline, discharge, 6-month and ≥12-month follow-up. Reduction in end-diastolic volumes (EDV) by 29% and in end-systolic volumes by 38% were demonstrated immediately after surgery and remained at subsequent follow-up (P<0.0001). The LV ejection fraction significantly increased by about 10% at discharge and was maintained ≥12-month (P<0.0001). Although the LV volumes were significantly larger in patients with MV repair before surgery (EDV, 235±87 mL versus 193±67 mL, P<0.05), they were similar to LV volumes of the patients without MV repair at subsequent follow-ups. However, the EDV increased from 139±24 mL to 227±79 mL (P<0.01) in 7 patients with recurrent mitral regurgitation (MR). Improvement in New York Heart Association functional class occurred in 81% patients during late follow-up.

Conclusion—Real-time 3DE demonstrates that LV reconstruction provides significant reduction in LV volumes and improvement in LV function which is sustained throughout the 1-year follow-up with 84% cardiac event free survival. If successful, MV repair may prevent LV redilation, while recurrent MR is associated with increased LV volumes. (Circulation. 2003;108[Suppl II]:II-241-II-246.)

Key Words: cardiomyopathy ■ ischemia ■ cardiac volume ■ surgery ■ echocardiography

Left ventricular (LV) reconstruction in ischemic cardiomyopathy (ICM) may reduce LV volume, increase LV ejection fraction and improve functional status. Despite early reports of high mortality with this technique, recent studies indicate a hospital mortality of <7% in patients with end stage ICM.1-4 In our previous studies, we demonstrated that LV reconstruction surgery combined with coronary revascularization for patients with ICM could significantly reduce symptoms in patients refractory to medical therapy and that an LV end-diastolic volume <150 mL after surgery predicted a favorable short term outcome.3,5 In contrast, persistent mitral regurgitation (MR) was found to be a strong predictor of poor long-term prognosis. Though repair of ischemic MR with a mitral ring annuloplasty and coronary revascularization may achieve immediate valve competence, a number of patients develop recurrent MR at intermediate follow-up.5-8 Furthermore, geometric changes in the LV cavity during reconstruction may result in MR not present preoperatively. Also, uncertainty remains as to the efficacy of coronary revascularization alone, without mitral valve (MV) repair or replacement, in patients with ischemic MR.5-17 Few studies have addressed the impact of MV repair on outcomes of combined LV reconstruction and/or coronary revascularization.18-19

The aim of this study was to evaluate the impact of MV repair associated with LV reconstruction and/or coronary revascularization in patients with ICM on LV function,
hemodynamics and clinical outcomes at 1 year follow-up at a single tertiary referral cardiac center. Because these patients have altered LV geometry with the presence of apical aneurysms, we used real-time 3-dimensional echocardiography (3DE) to quantify LV volumes without geometric assumptions.3,20

Methods

Patient Population

A total of 111 consecutive patients with ICM who were candidates for LV reconstruction surgery had baseline real-time 3DE at the Cleveland Clinic Foundation between May 1998 and April 2002. Sixty patients (46 males, mean age 61±9 years) who subsequently underwent LV reconstruction and had both pre- and postoperative real-time 3DE done were enrolled in this study. All patients had either akinesia or aneurysmal changes in the anterior wall, septum or apex of the LV and were in New York Heart Association (NYHA) functional class II or higher including 44 (73%) of patients in class III. Fourteen patients (23%) were on the waiting list for heart transplantation. Moderate to severe MR was present in 28 (47%) patients (23 detected by preoperative transthoracic echocardiography), while 35 (58%) patients had severe LV dysfunction, defined as LV ejection fraction <30% by real-time 3DE. Coronary angiography was performed before surgery in all patients. The study was approved by the Institutional Review Board of the Cleveland Clinic Foundation.

Real-Time 3-Dimensional Echocardiography

All real-time 3DE images were acquired transthoracically from the apical and parasternal windows using a real-time 3DE system (Volumetrics Medical Imaging Inc, Durham, NC) with a 2.5 MHz phased array hand-held transducer (14 mm in diameter) with the patient in a left lateral decubitus position. After the highest quality image was achieved, the digital LV volumetric data set was stored on an optical disc for off-line analysis. Care was taken to include the entire LV cavity in the real-time pyramidal volumetric data set during the entire cardiac cycle. Real-time 3DE was performed in all 60 patients at baseline, 52 patients before discharge, 23 patients at 6-month, and 21 patients at ≥12-month follow-up. Every patient had at least 1 real-time 3DE follow-up after surgery. No patient was excluded because of arrhythmia, a permanent pacemaker or difficulty with breath holding.

Quantitative Analysis of LV Function by Real-Time 3-Dimensional Echocardiography

Left ventricular volumes were determined by using a series of parallel short axis images. The cavity of the LV in each parallel slice that was orthogonal to the apical long axis (Figure 1) was manually traced and the cavity area calculated using software installed with the real-time 3DE system. After multiplying each cavity area by the slice thickness (8 to 10 mm), these segmental volumes were consecutively added to obtain an entire LV cavity volume, according to the Simpson’s rule. The end-diastolic volume (EDV) was defined as the volume occurring concurrently with the QRS wave or the largest LV silhouette, and end-systolic volume (ESV) was defined by the end of the T wave or the smallest LV silhouette. The total LV stroke volume, which included the LV forward stroke volume and MR volume when associated with MR, was calculated as the EDV minus the ESV. LV ejection fraction was calculated as stroke volume divided by EDV. For both diastolic and systolic measurements, LV trabeculations and papillary muscles were carefully excluded from the LV cavity contour. The area of mitral annulus and the interpapillary distance at end-diastole were also measured.

Two-Dimensional Echocardiography

A conventional echocardiographic study was obtained pre and post operatively including standard 2-dimensional images and spectral and color Doppler. MR severity was assessed qualitatively according to the recommendation of American Society of Echocardiography for each study, and MR volumes were quantified using the flow convergence method when possible.21 The forward stroke volume was calculated as the total LV stroke volume minus the MR volume.

Surgical Technique

Techniques of LV reconstruction have been described previously.1–3,22 Briefly, the procedure was performed with the use of cardiopulmonary bypass with both antegrade and retrograde cold blood cardioplegia for myocardial protection. Coronary revascularization, when needed, was performed with internal mammary artery and/or saphenous vein grafting in 52 patients (87%), including 11 with 1-vessel disease, 18 with 2-vessel disease and 23 with multivessel disease. The left atrium was then opened in the intra-atrial groove and the MV was repaired in 30 patients (50%), including 28 patients who had moderate to severe MR.

Figure 1. A real-time 3DE image to illustrate the measurement of left ventricular volume. The right panel is 2 orthogonal apical plane images (4-chamber on the top and 2-chamber image on the bottom). The left panel represents three C-scan (short axis) images that correspond to 3 green lines on the 4 and 2-chamber images, respectively. The left ventricular cavity area is traced manually on the C-scan images and the volume for each segment is then given automatically. The left ventricular volume is calculated as the sum of all segmental volumes (see text for detail).
before the surgery and 2 patients who had moderate to severe MR immediately after the isolated LV reconstruction. The MV was repaired with a Cosgrove-Edward ring (Baxter, Deerfield, IL) in 10 patients, a Carpenter-Edward ring (Baxter, Deerfield, IL) in 2 patients, an Alfieri stitch in 4 patients, and with both a Cosgrove-Edward ring and an Alfieri stitch in 14 patients. After revascularization and/or MV repair, the cross-clamp was removed and the LV reconstruction was performed on the beating heart for all 60 patients. The aneurysm was opened 2 cm left of the left anterior descending artery. A purse-string suture was placed along the border zone into the scarred tissue. Further purse-string suture was placed 5 mm above the first suture, and when tied, the neck was usually less than 2 cm. The LV was reconstructed to more of an ellipsoid shape (not globular), the residual chamber was reduced, and the infarcted anterior wall and septum were excluded. Palpation of akinetic region was used to define the border zone between infarcted and normal myocardium. Additional surgical procedures included cryoablation in 10 patients, tricuspid valve repair in 3 patients, and a ventricular septal defect repair in 1 patient.

Clinical Follow-Up
Following discharge, patients underwent periodic follow-up with assessment of clinical symptoms and a comprehensive physical examination. Phone interviews were also performed to assess end-points. The primary follow-up end-point was all cause mortality. Secondary end-points included hospitalization for decompensated heart failure, sudden cardiac death, percutaneous revascularization or need for repeat cardiac surgery.

Statistical Analysis
Statistical analysis was performed using SPSS 10.0 (SPSS Inc., Chicago, IL). Values for descriptive statistics are expressed as a mean±SD. Analysis of variance (ANOVA) with repeated measures was used to compare the values before, after, and at follow-up. Because of the varying number of patients at each time, paired Student’s t-test was used to compare preoperative and post-operative values with the utilization of a Bonferroni correction for multiple comparisons. Unpaired t-test with a Bonferroni correction was used to distinguish the difference in LV volumes between the patients with and without MV repair. An actuarial survival curve was constructed using the Kaplan-Meier method. A probability value <0.05 was considered statistically significant.

Results

Left Ventricular Volume and Function After Surgery
Left ventricular reconstruction resulted in a 29% reduction in EDV (214±80 mL at baseline to 153±68 mL at discharge, P<0.0001), which remained lower at 6-month and ≥12-month follow-up (166±73 mL and 163±53 mL, respectively, P<0.0001 for each versus baseline). A 38% reduction in ESV (156±72 mL at baseline to 98±53 mL at discharge, P<0.0001) was found with subsequent 6-month and ≥12-month follow-up (102±73 mL and 97±37 mL, respectively, P<0.0001 for each versus baseline). The LV ejection fraction increased from 29±10% to 38±11% (baseline versus discharge, P<0.0001) and remained higher at 6-month and ≥12-month follow-up (40±11% and 40±7%, respectively, P<0.0001 for each versus baseline).

The Left Ventricular Volume and Mitral Apparatus in Patients With or Without Mitral Valve Repair
Thirty patients had MV repair during LV reconstruction, which included all 28 patients with ≥Moderate MR before the surgery and 2 patients with ≥Moderate MR developed immediately after isolated LV reconstruction. Before surgery, both LV EDV and ESV were significantly larger in patients with MV repair than in those without MV repair. After surgery, the LV volume of patients with MV repair was similar to those patients without MV repair. The LV volume remained constant throughout 12 months after surgery in both groups (Table 1). The area of the mitral annulus at end-diastole before surgery was similar in patients with and without MV repair (14±4 cm² versus 14±3 cm², p=ns) and significantly reduced to 11±3 cm² and 11±2 cm², respectively, after surgery (both P<0.05). The interpapillary distance was also similar in patients with and without MV repair before surgery (3.1±0.5 cm versus 3.3±0.4 cm, p=ns) and remained so after surgery (3.3±0.5 cm versus 3.1±0.7 cm, respectively, versus baseline, both p=ns).

The Impact of Recurrent Mitral Regurgitation on Left Ventricular Function
Thirty-one patients had both real-time 3DE and 2-dimensional echocardiography done during ≥6-month follow-up. The severity of MR was significantly reduced in ≥Moderate MR patients following MV repair at discharge.

<table>
<thead>
<tr>
<th>Patients for 3DE (n)</th>
<th>Valve Repair</th>
<th>Baseline</th>
<th>Before D/C</th>
<th>6-Month F/U</th>
<th>12-Month F/U</th>
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<tr>
<td></td>
<td>MV repair</td>
<td>30</td>
<td>24</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>No MV repair</td>
<td>30</td>
<td>28</td>
<td>12</td>
<td>8</td>
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<tr>
<td>EDV (mL)</td>
<td>MV repair</td>
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<td>156±73</td>
<td>177±94</td>
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<td>193±67*</td>
<td>152±64</td>
<td>157±51</td>
<td>163±57</td>
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<tr>
<td>ESV (mL)</td>
<td>MV repair</td>
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<tr>
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<td>40±10</td>
<td>43±10</td>
<td>42±5</td>
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</tbody>
</table>

*No MV repair versus MV repair, P<0.05.
and subsequently increased at ≥ 6 months follow-up because of recurrent MR in 6 patients. No significant change in MR severity was found in patients with No MR and Mild MR following surgery except 1 patient with No MR (Figure 2).

Seven out of 31 patients were found to have recurrent MR, which was defined as ≥ moderate MR, at 6-month follow-up (Table 2). Redilation of the LV was demonstrated in these 7 recurrent MR patients with an increase in LV EDV from 139 ± 24 mL before discharge to 227 ± 79 mL at ≥ 6 month follow-ups (P < 0.01) and an increase in ESV from 80 ± 24 mL to 144 ± 60 mL (P < 0.01) during the same period. Both LV EDV and ESV at ≥ 6 month follow-up were larger in patients with (n = 7) than in patients without recurrent MR (n = 24) (227 ± 79 mL versus 147 ± 58 mL and 144 ± 60 mL versus 90 ± 42 mL, respectively, both P < 0.01). Although the LV ejection fraction was similar in patients with and without recurrent MR (38 ± 10% versus 40 ± 10%, p = NS), the net forward stroke volume was significantly smaller in patients with recurrent MR compared with those without MR, respectively (33 ± 12 mL versus 59 ± 22 mL, P < 0.01). A reoperation was required in 2 patients with recurrent MR at late follow-up using a pericardial tissue valve.

**Clinical Outcomes**

There were no operative deaths, though 3 (5%) patients died following discharge. Four patients living abroad were lost to follow-up. Fifty-three patients had a follow-up at a mean of 600 days (range from 101 to 1468 days), while 44 of 53 patients (83%) completed a full 1 year follow-up.

The NYHA functional class was improved at a last follow-up when compared with its pre-operative value (from 2.9 to 1.8, P < 0.0001, n = 53 patients). Forty-three patients (81%) had improvement of at least 1 NYHA functional class. In 3 patients NYHA class worsened, and 7 patients had no change in NYHA functional class (Figure 3). The NYHA functional class at clinical follow-up was similar in patients with and without MV repair (1.8 ± 0.7 versus 1.7 ± 0.8, p = NS). In 7 patients with recurrent MR, 4 were in NYHA functional class III. The functional class was significantly higher in patients with recurrent MR than in those without (2.3 ± 1.0 versus 1.5 ± 0.6, respectively, P = 0.01).

The overall survival at 6 months was 95% and stable thereafter. All 3 patients that died were in NYHA functional class IV with moderate to severe MR before surgery and were listed for heart transplantation. One patient had severe congestive heart failure and emergency surgery (pre-operative LV ejection fraction = 12%) and died 35 days after surgery. A second patient had sustained polymorphic ventricular tachycardia requiring emergency surgery (pre-operative LV ejection fraction = 30%), and died 81 days after surgery. A third patient (living abroad) died of unknown cause at 6 months after surgery. Cardiac events (ie, rehospitalization because of decompensation of congestive heart failure, arrhythmia, acute coronary syndrome, new cardiac surgery, or percutaneous coronary intervention) free survival was 84 ± 6% at 1 year (Figure 4).

**Discussion**

**Left Ventricular Reconstruction Procedure**

An LV aneurysm occurring following a myocardial infarction is an independent predictor of poor outcome. Based on the Law of Laplace, LV dilation produces a greater amount of...
stress and oxygen demand on contractile myocardium and aneurysmectomy and LV reduction has been introduced to improve LV function in patients with LV aneurysms since the early 1950’s.1,2,4 Several imaging modalities including biplane ventriculogram and 2-dimensional and 3DE have demonstrated a reduction in LV volume of about 28% to 39% by using the endoventricular circular patch plasty technique, which allows exclusion of all myocardial scar and reshaping of the remaining wall. An associated 60% to 80% life expectancy at 10 years is found with this surgical technique.1,3,4 In the present series, a modified LV reconstruction procedure. Whether the MV was repaired or not specifically determined intraoperatively by the LV reconstruction procedure. Whether the MV was repaired or not not may not have any impact on early postoperative LV size. Furthermore, the hospital mortality and 6 months mortality was 0 and 5%, respectively. The cardiac event-free survival at the first year was 84%. Redilation of the LV during follow-up is an important factor influencing prognosis and quality of life. Severe LV dysfunction prior to surgery, residual myocardial scar, residual or new onset MR, spherical shape of LV after surgery may all contribute to the LV redilation.1,2,4

Mitral Valve Repair in Ischemic Mitral Regurgitation
The type of surgical treatment of ischemic MR is controversial because of the high mortality in comparison with non-ischemic MR.3 Moderately severe ischemic MR may be normalized after myocardial revascularization alone in some patients, so it is often advocated that MV surgery should not be performed during revascularization in these patients.15,17 In the present study, however, we demonstrated that recurrent MR was one of essential correlate of LV redilation. In previous studies, pulmonary hypertension and high capillary wedge pressure were associated with recurrent MR and a re-dilated LV.25 Therefore, it is rational to prevent LV redilation by the elimination of MR and the potential to develop recurrent MR. Early MV repair may be beneficial in patients with ischemic MR because LV function prior to surgical treatments strongly correlates with mortality.19 In the present study, 30 patients had an MV repair and their LV volume and NYHA functional class at follow-up were similar to those patients without MR. Therefore, MV repair is recommended during the coronary revascularization and LV reconstruction.

Mechanism of Recurrent Mitral Regurgitation
Our data are consistent with the data on original endoventricular circular patch plasty repair series, which reported recurrent MR appearance in 39% of patients25 (23% in the present study). Possible mechanisms of recurrent MR are inadequate mitral repair procedures, LV shape change after surgical reconstruction, and continuing remodeling process. In the present study, 2 patients developed mitral regurgitation immediately after LV reconstruction probably because of the change of the LV geometry. MV repair with Alfieri stitch had been performed and could eliminate the mitral regurgitation after the second pump run in these 2 patients. Progressive LV dilation occurs in some patients after LV reconstruction and this dilation may result in MR because of leaflet tethering and eventual annular dilation. Annuloplasty or placement of a coaptation stitch does not affect local posterior mitral leaflet tethering which is a major determinant of ischemic MR.26,27 Therefore, the long-term durability of an annuloplasty or a coaptation stitch may be limited for treating the ischemic MR if the abnormal mitral leaflet stresses result from this procedure.8,28,29 Also, patient-to-patient variability of scarred area distribution may lead to reconstructed LV shape that is more spherical in some patients, which may adversely affect the competence of mitral valve closure and is a predictor of recurrent MR.25 These factors may interact with ongoing pathologic process and lead to mitral leaflet tethering despite normalized mitral annulus size. 35% patients had recurrent MR despite undergoing MV repair (physiological ring and/or Alfieri stitch) in the present study (Table 2), suggesting the use of complete remodeling ring or mitral prostheses for this procedure.

Advantages of Real-Time 3DE for Quantification of LV Volumes
The LV geometry frequently changes significantly after myocardial infarction or after cardiac surgery. The presence of an asymmetric LV cavity limits the accuracy of the two-dimensional methods for LV volume measurements because of the need of the geometrical assumptions, which are not always true. 3DE techniques have been demonstrated to be superior to the 2-dimensional methods and increase the accuracy for quantification of the LV volume in an asymmetric heart.20 Compared with the reconstruction techniques, real-time 3DE has retained many of the clinical advantages of 2DE. On-line adjustment of conventional echocardiographic planes can be performed to insure adequate quality 3D data sets and without need of EKG/or respiratory gating. Once the entire LV was included in the real-time 3DE data sets, the exact size and location of the LV aneurysm can be visualized easily. The quantification of LV volumes can be performed quickly when using a series of short axis views (about 10 mm apart from the mitral annulus to the apex), which covers the entire LV and aneurysm, without the need of extra computer workstation for the analysis.3,20

Limitations
This was a retrospective study with several limitations. First, there was no control group for patients with MR who were treated with MV repair, therefore, it is difficult to directly compare the LV function in ischemic MR patients treated with and without MV repair. However, the recurrence of MR with deterioration of LV function may indirectly illustrate the importance of successful MV repair in patients with ischemic MR. Second, since the follow-up period for real-time 3DE was variable, rigorous statistical matching with repeated ANOVA was not possible. Finally, one must acknowledge the limitation of image quality on the accuracy of measurements done with real-time 3DE.20

Conclusion
The combination of LV reconstruction, MV repair, and coronary revascularization provides significant reduction in
LV volumes and improvement in LV ejection fraction which is sustained for at least 1 year with a cardiac event-free survival of 84% at the first year. MV repair, if successful, may prevent LV redilation, as patients with recurrent MR demonstrate increases in LV volumes and less functional improvement, suggesting the importance of the mitral valve repair in patients with ischemic mitral regurgitation. Further studies are needed to address the causes and effects of recurrent MR in patients with LV reconstruction.

References

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