Mitral Valve Repair Versus Revascularization Alone in the Treatment of Ischemic Mitral Regurgitation

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Background—For patients with ischemic mitral regurgitation (MR), it is not clear whether adjunctive mitral valve (MV) repair at the time of coronary artery bypass graft surgery (CABG) is beneficial. We sought to test the hypothesis that MV repair with CABG is superior to CABG alone in improving MR without increasing operative or long-term mortality.

Methods and Results—A total of 107 consecutive patients with moderate or severe ischemic MR, as determined by preoperative echocardiography, underwent CABG with concomitant MV repair (repair group, n=50) or CABG only (CABG group, n=57). Degree of MR was graded as none, mild, moderate, or severe by the proximal isovelocity surface area method. The groups were similar with respect to age, gender, baseline New York Heart Association class, ejection fraction, and number of bypass grafts. The repair group had a higher percentage of patients with atrial fibrillation or severe MR than the CABG group. The operative mortality was significantly higher for the repair group (12%) than the CABG group (2%), whereas the 5-year actuarial survival rate of the 2 groups was similar (88%±5% versus 87%±6%). On multivariate logistic regression analysis, older age, higher New York Heart Association class, and atrial fibrillation were independent predictors of operative mortality (P<0.05). Among patients with severe MR, ischemic MR was improved in all patients of the repair group and in 67% of patients in the CABG group (P<0.001), whereas improvement rates in patients with moderate MR were similar in the 2 groups (75% versus 67%, P=NS).

Conclusions—Although MV repair appears to be more effective at reducing ischemic functional MR, CABG alone may be a preferable treatment option for patients with moderate MR and high operative risk factors such as old age or atrial fibrillation. (Circulation. 2006;114[suppl I]:I-499–I-503.)

Key Words: ischemic mitral regurgitation ■ mitral valve repair ■ revascularization

The presence of ischemic mitral regurgitation (MR) has been shown to be a negative determinant of survival in patients with coronary artery disease.1–4 Unfortunately, the decision to intervene surgically for ischemic MR remains controversial. Although surgical correction of MR may be beneficial3,4 at the time of coronary artery bypass graft surgery (CABG), the clinical utility of mitral valve (MV) repair in ischemic MR still remains unproven because of the problems of prolonged surgical time, technical complexity, and patient selection.5,6 Surgical revascularization alone may improve ischemic MR,7,8 suggesting that long-term survival is dependent more on left ventricular (LV) function and relief of ischemia than on the presence of MR.9,10

We therefore examined the hypothesis that MV repair at the time of CABG is more effective than revascularization alone in reducing postoperative MR without an increase in operative mortality or long-term cardiac events. We also evaluated the impact of MV repair on ischemic MR and LV remodeling independent of revascularization.

Methods

Study Patients

From 1997 to 2003, a total of 107 consecutive patients with moderate to severe ischemic functional MR on preoperative echocardiography were treated with either CABG only (CABG group, n=57) or CABG in combination with MV repair (repair group, n=50), with the decision of whether to perform MV repair being at the discretion of the surgeon. The presence of concomitant aortic valve disease and the etiology and severity of MR were determined from preoperative echocardiographic examination. Patients with organic MV disease, including prolapse of mitral leaflets, ruptured chordae, and rupture of papillary muscles, and those with significant aortic valve disease were excluded.

Surgical Procedures

The procedures were performed with the use of standard cardiopulmonary bypass, using antegrade and retrograde cold blood cardioplegia. After median sternotomy, patients underwent conventional multivessel CABG with the use of internal mammary arteries whenever possible. All patients in the repair group also underwent ring annuloplasty with an undersized semirigid ring. Dor procedure was selectively performed in 7 patients with apical aneurysm.
Echocardiographic Evaluation
Echocardiographic imaging was performed using standard transthoracic windows with a Hewlett-Packard Sonos 2500 or 5500 imaging system equipped with a 2.5-MHz transducer. All echocardiographic studies stored on a digital network system were reviewed and interpreted by an experienced cardiologist blinded to clinical data. Ischemic MR was defined as functional MR associated with global or regional LV systolic dysfunction, with no evidence of primary valvular, chordal, or papillary muscle pathology. End-systolic and end-diastolic dimensions of the LV were measured from parasternal M-mode acquisitions, and end-systolic volume, end-diastolic volume, and ejection fraction (EF) of the LV were calculated using the biplane Simpson method. For analysis of regional wall motion abnormalities, a 16-segment model was used. Using the simplified proximal isovelocity surface area (PISA) method, the degree of MR abnormalities, a 16-segment model was used. Using the simplified proximal isovelocity surface area (PISA) method, the degree of MR was defined as 0 grade (radius of PISA < 2 mm); 1 grade, functional MR with no evidence of primary valvular, chordal, or papillary muscle pathology. End-systolic and end-diastolic dimensions of the LV were measured from parasternal M-mode acquisitions, and end-systolic volume, end-diastolic volume, and ejection fraction (EF) of the LV were calculated using the biplane Simpson method. For analysis of regional wall motion abnormalities, a 16-segment model was used. Using the simplified proximal isovelocity surface area (PISA) method, the degree of MR was defined as mild (1+, radius of PISA < 4 mm); moderate (2+, radius of PISA < 8 mm); or severe (3+, radius of PISA ≥ 8 mm). On follow-up echocardiographic examination, an improvement in MR was defined as decrease in severity ≥ 1 grade, and functional recovery of LV was defined as an increase of EF ≥ 5% with improvement of the regional wall motion score.

Thallium Scintigraphy
Because of unstable clinical presentation, adenosine stress thallium single photon emission computed tomography study could be performed in only 53 (50%) patients after stabilization. Conventional stress, 4-hour redistribution, and reinjection images were acquired and analyzed using a 14-segment model. A positive thallium study for the diagnosis of myocardial viability was defined as an improvement of thallium uptake in dysfunctional segments to mild or normal for the index procedure or before discharge.

Clinical Follow-Up
Functional status was assessed according to New York Heart Association (NYHA) criteria during follow-up. Clinical follow-up data were collected during patient visits to the department or by telephone interviews. Operative mortality was defined as death within 30 days of the index procedure or before discharge.

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Statistical Analysis
Numerical values were expressed as mean ± SD. Continuous variables were compared between 2 groups using the Student’s unpaired t test. The frequency ratios were compared between groups using the χ² test. LV remodeling was analyzed using the paired t test and Wilcoxon signed rank test. The Kaplan-Meier analysis was used to determine actuarial survival rates, and differences in survival rates between the 2 groups were examined by the log-rank test. Clinical and echocardiographic variables were evaluated by logistic regression analysis and Cox proportional hazards analysis to identify predictors of operative mortality and long-term survival. The variables included in the analysis were age, gender, incidence of diabetes mellitus, baseline NYHA class, cardiac rhythm, extent of coronary artery disease, LVEF, severity of baseline MR, and surgical procedure. A probability value < 0.05 was considered statistically significant.

Results
Baseline Characteristics
A comparison of the baseline clinical and surgical characteristics of patients undergoing combined CABG and MV repair (repair group, n = 50) or CABG alone (CABG group, n = 57) is shown in Table 1. The 2 groups were similar in terms of age, gender, incidence of diabetes mellitus, baseline NYHA class, baseline LVEF, and number of bypass grafts. The repair group had significantly more patients with severe MR

| TABLE 1.  Baseline Characteristics and Surgical Procedures |
|---------------------------------|-----------------|-----------------|
|                                | CABG Group       | Repair Group     |
| Age, y                         | 63 ± 9           | 61 ± 10          |
| Gender, male                   | 39 (68)          | 37 (74)          |
| Diabetes mellitus              | 32 (56)          | 26 (52)          |
| NYHA class                     | 3.1 ± 0.9        | 3.1 ± 0.8        |
| Ejection fraction              | 36 ± 9%          | 36 ± 11%         |
| Atrial fibrillation            | 0 (0)            | 6 (12)           |
| Severity of MR†                |                  |                  |
| Moderate                       | 33 (58)          | 14 (28)          |
| Severe                         | 24 (42)          | 36 (72)          |
| LIMA used                      | 49 (86)          | 45 (90)          |
| Graft vessels, n               | 3.8 ± 1.5        | 3.7 ± 1.5        |
| Bypass time†, min              | 145 ± 59         | 183 ± 85         |
| Cross-clamp time†, min         | 67 ± 59          | 107 ± 53         |

Values are expressed as mean ± SD or n (%). LIMA indicates left internal mammary artery.

†P < 0.01 vs CABG group.

(72% versus 42%, P < 0.01) at baseline. At surgery, repair group patients had significantly longer bypass (183 ± 85 minutes versus 145 ± 59 minutes, P < 0.01) and aortic clamp times (107 ± 53 minutes versus 67 ± 59 minutes, P < 0.01).

Clinical Follow-Up
There were 3 (6%) deaths within 30 days of the procedure and 3 (6%) in-hospital deaths occurring on postoperative day 42, 43, and 47 in the repair group, and 1 (2%) in-hospital death on postoperative day 84 in the CABG group (P = 0.03). The causes of operative mortality were low cardiac output syndrome in 3 patients and multiple organ failure, sepsis, aspiration pneumonia, and ticlopidine-induced pancytopenia in one patient each. On multivariate logistic regression analysis, patient age, atrial fibrillation, and higher preoperative NYHA class were found to be independent determinants of operative mortality (P < 0.05). In the repair group, 4 operative deaths occurred among 10 patients with the risk factor of atrial fibrillation or age ≥ 75 years, whereas 2 operative deaths occurred among 40 patients without either risk factor. The operative mortality rate was significantly higher in the patients with old age or atrial fibrillation in the repair group (P < 0.01), but the operative mortality in the CABG group was similar between patients with and without these risk factors (0/4 versus 1/53, P = NS). Gender, severity of MR, extent of coronary artery disease, and LVEF did not significantly affect operative mortality.

Clinical follow-up was completed with 106 (99%) patients, with a mean follow-up period of 40 ± 25 months. There were no late deaths in the repair group over a mean follow-up period of 37 ± 22 months, yielding an estimated actuarial 5-year survival rate of 88% ± 5%. NYHA class in this group improved from 3.1 ± 0.8 to 1.5 ± 0.6 during follow-up. There were 5 deaths in the CABG group over a mean follow-up of 41 ± 27 months, and NYHA class in this group improved from 3.1 ± 0.9 to 1.5 ± 0.7. The estimated actuarial 1- and 5-year survival rates in the CABG group (95% ± 3% and 87% ± 6%,
respectively) were not significantly different from those of repair group (Figure 1). Cox multivariate analysis identified baseline NYHA class and atrial fibrillation as independent predictors of long-term survival (P<0.05). Age, extent of coronary disease, LVEF, and severity of MR did not affect long-term survival.

Because the severity of MR was different in the 2 groups, we performed subgroup analysis of cardiac events according to baseline severity of MR. In patients with moderate MR, there were 2 in-hospital deaths and no late deaths in the repair group, compared with no in-hospital deaths and 2 late deaths in the CABG group. Thus, in patients with moderate MR, the operative mortality rate (14%) of the repair group was significantly higher than that of the CABG group (P=0.03). In patients with severe MR, there were 4 in-hospital deaths and no late deaths in repair group, compared with 1 in-hospital death and 3 late deaths in the CABG group during the follow-up. Thus, in patients with severe MR, the operative mortality and 5-year actuarial survival rates of the 2 groups did not differ significantly.

Impact on Ischemic MR and LV Remodeling
Follow-up transthoracic echocardiography was performed on all surviving patients 1 year after surgery. Ischemic MR was improved in 41 (93%) patients in the repair group, compared with 37 (66%) patients in the CABG group (P=0.001). Improvement rates among patients with severe MR were 100% in the repair group and 65% in the CABG group (P<0.001), whereas improvement rates in patients with moderate MR were similar between the 2 groups (75% versus 67%, P=NS). Functional recovery was observed in 54 patients after revascularization and the sensitivity and specificity of positive thallium study for predicting functional recovery was 69% (24/35) and 78% (14/18), respectively. To evaluate the effects of repair independent of revascularization, we performed subgroup analysis according to functional recovery of LV. In patients with functional recovery of the LV, the severity of MR and LV end-systolic dimension and volume and end-diastolic dimension and volume were significantly decreased in both groups (Table 2). In patients without functional recovery, the severity of MR and LV dimensions and volumes were not significantly changed after CABG alone, but the severity of MR was significantly decreased in repair group (Table 3). The independent effect of repair on LV remodeling in patients without functional recovery differed according to baseline severity of MR. In 15 patients with severe MR, improvements of MR after repair resulted in significant decreases in mean end-diastolic dimension (from 64±6 mm to 60±7 mm, P<0.01) and volume (from 160±56 mL to 128±37 mL, P<0.01) (Figure 2), whereas LV dimensions and volumes did not change significantly in patients with moderate MR.

**Discussion**
In the present study, the 5-year survival rates of each group of patients were higher than those previously reported.9,13–15 As the mechanism of ischemic MR is better understood,16,17 the surgical techniques have become more effective.18,19 Surgical timing is another important issue, because early intervention can prevent the irreversible myopathic changes consequent to remodeling. The lower survival rates reported in previous studies may be due to the performance of surgery in patients at the end stage of the disease process.14,18 We observed functional recovery in 54% of study patients, with significant reductions in end-diastolic and end-systolic volumes in patients who experienced functional recovery. These findings

**TABLE 2. Echocardiographic Results in Patients With Functional Recovery**

<table>
<thead>
<tr>
<th></th>
<th>CABG Group (n=32)</th>
<th>Repair Group (n=22)</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-Up</td>
</tr>
<tr>
<td>LVESD, mm</td>
<td>46.9±6.1</td>
<td>39.2±7.4</td>
</tr>
<tr>
<td>LVEDD, mm</td>
<td>59.2±4.9</td>
<td>53.7±5.9</td>
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<tr>
<td>LVESV, mL</td>
<td>84.1±33.8</td>
<td>57.9±25.3</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>133.0±41.3</td>
<td>106.5±36.4</td>
</tr>
<tr>
<td>MR grade†</td>
<td>2.5±0.5</td>
<td>0.9±0.6</td>
</tr>
<tr>
<td>LVEF, † %</td>
<td>36.2±10.0</td>
<td>47.3±8.8</td>
</tr>
</tbody>
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LVESD indicates left ventricular end-systolic dimension; LVEDD, left ventricular end-diastolic dimension; LVESV, left ventricular end-diastolic volume; and LVEDV, left ventricular end-diastolic volume.

†P<0.01 vs baseline.

**TABLE 3. Echocardiographic Results in Patients Without Functional Recovery**

<table>
<thead>
<tr>
<th></th>
<th>CABG Group (n=24)</th>
<th>Repair Group (n=22)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-Up</td>
</tr>
<tr>
<td>LVESD, mm</td>
<td>49.5±8.0</td>
<td>50.5±10.8</td>
</tr>
<tr>
<td>LVEDD, mm</td>
<td>62.9±5.7</td>
<td>61.7±8.2</td>
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<tr>
<td>LVESV, mL</td>
<td>91.0±38.4</td>
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<tr>
<td>LVEDV, mL</td>
<td>134.6±44.9</td>
<td>145.5±53.1</td>
</tr>
<tr>
<td>MR grade†</td>
<td>2.3±0.5</td>
<td>2.0±0.8</td>
</tr>
<tr>
<td>LVEF, † %</td>
<td>35.7±9.1</td>
<td>35.7±9.9</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 2.

†P<0.01 vs baseline.
indicate that the earlier surgery can improve long-term prognosis for patients with ischemic MR.

Moderate Versus Severe MR

The presence and severity of MR associated with myocardial infarction has been shown to be an important prognostic factor in ischemic heart disease. Lamas et al reported that the 3-year survival rate after myocardial infarction was significantly lower in patients with than without residual MR (71% versus 88%), and mortality risk has been shown to be directly related to the severity of ischemic MR. Because revascularization alone may not resolve ischemic MR, MV repair together with CABG may be preferable to CABG alone, but only if correction of MR can be performed safely. We have shown here that for patients with severe MR, MV repair was superior to CABG alone in reducing ischemic MR and LV size, without increasing operative or long-term mortality rates. In patients with moderate MR, however, the operative mortality rate of the combination of CABG and MV repair was significantly higher than that of CABG alone, whereas the MR improvement rates were similar in the 2 procedures. Even if MV repair was not independently related to operative mortality on multivariate analysis, the operative risk observed in this study was significant in MV repair group, suggesting that CABG alone might be a preferable treatment option in patients with moderate MR and high operative risk. In a case-controlled study comparing 58 patients with moderate MR undergoing CABG with 58 case-matched patients without MR, the long-term survival rates were very similar, suggesting that moderate ischemic MR need not be corrected at the time of CABG. Because ischemic MR may be a surrogate marker for severe dysfunction and adverse remodeling of LV, it may not be directly responsible for the poor prognosis, and correction of moderate MR may not have an impact on prognosis if the underlying LV function remains poor. Alternatively, MV repair in moderate MR may primarily affect other important end points, such as heart failure and progression of LV dysfunction. Thus, although CABG with MV repair was more effective than CABG alone at reducing ischemic MR, the effects of MV repair on clinical outcome were related to the severity of ischemic MR. Additional clinical studies are therefore required before wider application of MV repair in moderate ischemic MR.

Impact of MV Repair on Ischemic MR and LV Remodeling

In functional ischemic MR, the MV is structurally normal and MR is caused by dysfunction of the LV, resulting in incomplete leaflet closure. We found that in patients with functional recovery of the LV, the severity of MR and LV size were significantly decreased after surgery, because revascularization may improve LV dysfunction and geometry, restoring valvular coaptation and thereby improving ischemic MR. In patients without functional recovery, MV repair was significantly more likely to reduce MR than was revascularization alone, perhaps because a reduction in mitral annulus area by ring annuloplasty resulted in improved coaptation and decreased ischemic MR, independent of functional recovery. Because postoperative improvement of LV dysfunction by revascularization cannot be predicted reliably, the combination of CABG and MV repair may be a better treatment option to reduce ischemic MR.

Ischemic MR results in LV volume overload, resulting in further LV remodeling with progressive MR. It is not clear, however, whether improvement of ischemic MR by MV repair can have a favorable effect of LV remodeling. LV reverse remodeling has been observed after restrictive mitral annuloplasty, whereas recurrent MR can occur after CABG and MV repair, indicating that LV remodeling might be a progressive ventricular problem that cannot be treated by annuloplasty. In an experimental ovine model, prophylactic

Figure 2. Severe ischemic MR was significantly decreased by MV repair in a patient without functional recovery (from A to C). Improvement of MR after repair resulted in significant decreases of end-diastolic volume (from 157 mL to 126 mL) despite no change in EF (from B to D).
ventricular restraint attenuated adverse remodeling and reduced ischemic MR severity, whereas prevention of MR by ring annuloplasty did not influence remodeling. These findings have led to the development of novel surgical techniques, including infarct restraint and LV reconstruction, that can correct ischemic MR by favorably changing LV geometry. This study demonstrated that, in patients without functional recovery after CABG, improvement of ischemic MR by annuloplasty resulted in favorable LV remodeling. These results suggest that undersized simple annuloplasty may be clinically preferable, because it has favorable effects on LV remodeling, as well as a lower operative risk compared with more complex procedures.

Limitations
This study was subject to the limitations inherent to a nonrandomized study, including selection bias. The repair group had significantly more patients with severe MR and atrial fibrillation at baseline, and these differences in baseline characteristics might be related with the high operative mortality rate of the repair group. In this study, operative mortality included deaths of non-cardiac cause and in-hospital deaths occurring more than 30 days after the procedure. This broad definition of operative mortality may be another explanation to the relatively high operative mortality rate.

The issue of myocardial viability is also important in surgical management of ischemic MR. Because improvement of functional ischemic MR by CABG is closely related to the functional recovery of dysfunctional viable myocardium after revascularization, viability studies may provide useful information on improvements in LV dysfunction and ischemic MR. We did not routinely perform viability testing, and we did not examine the relation between viability test results and improvements in ischemic MR. Further clinical studies are needed to evaluate the clinical usefulness of viability studies in the management of ischemic MR.

Disclosures
None.

References
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