Restrictive Annuloplasty and Coronary Revascularization in Ischemic Mitral Regurgitation Results in Reverse Left Ventricular Remodeling

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Background—Data on combined coronary artery bypass grafting (CABG) and restrictive annuloplasty in patients with ischemic cardiomyopathy are scarce, and the effect on reverse left ventricular (LV) remodeling is unknown.

Methods and Results—51 patients with ischemic LV dysfunction (LV ejection fraction 31±8%) and severe mitral regurgitation (grade 3 to 4+) underwent CABG and restrictive annuloplasty with stringent downsizing of the mitral annulus (by 2 sizes, Physio-ring, mean size 28±2). Serial transthoracic echocardiographic studies were performed (before surgery and within 3 months and 1.5 years after surgery) to assess mitral regurgitation, transmitral gradient, leaflet coaptation, and left atrial and LV reverse remodeling. Clinical follow-up (New York Heart Association [NYHA] class, survival, events) was assessed at 2-year follow-up. Early operative mortality was 5.6%; at 2-year follow-up, all patients were free of endocarditis and thromboembolism, and 1 needed re-operation for recurrent mitral regurgitation; 2-year survival was 84%. NYHA class improved from 3.4±0.8 to 1.3±0.4 (P<0.01), with all patients in class I/II. Intraoperative transesophageal echo showed minimal (grade 1+) mitral regurgitation in 8 patients and none in 43, without stenosis. Leaflet coaptation was 0.8±0.2 cm. These values remained unchanged; all patients had no or minimal (grade 1+) mitral regurgitation at 2-year follow-up. LV end-systolic and end-diastolic dimensions decreased from 51±10 to 43±12 mm (P<0.001) and from 64±8 to 58±11 mm (P<0.001). Left atrial dimension decreased from 53±8 to 47±7 mm (P<0.001).

Conclusion—Excellent results of combined restrictive annuloplasty and CABG were obtained. Residual mitral regurgitation was absent/minimal at 2-year follow-up, associated with a significant reduction in left atrial dimension and LV reverse remodeling. (Circulation. 2004;110[suppl II]:II-103–II-108.)

Key Words: ischemic mitral regurgitation ▪ restrictive annuloplasty ▪ heart failure ▪ surgical revascularization

Mitral regurgitation is frequently observed in patients with ischemic left ventricular (LV) dysfunction and can be related to dysfunction of the posterior mitral leaflet in patients with previous infarction of the inferior, posterior, or lateral wall, or can be related to annular dilatation and altered geometry in LV dilatation. Ischemic mitral regurgitation results in LV volume overload, resulting in further LV remodeling with progressive mitral regurgitation. This condition is associated with a high morbidity and mortality when treated conservatively. Alternatively, surgical correction of ischemic mitral regurgitation (in combination with coronary artery bypass grafting [CABG]) may be preferred. In particular, when CABG is considered, Aklog et al have recently demonstrated that revascularization alone does not resolve mitral regurgitation. However, cardiac surgery is associated with a relatively high (peri)operative morbidity and mortality. Currently, data on combined CABG and surgical correction of mitral regurgitation in patients with ischemic LV dysfunction are scarce. Bolling et al have initially reported on the feasibility of restrictive mitral annuloplasty in patients with ischemic cardiomyopathy. In addition, the authors have reported on the short-term and mid-term survival after restriction of mitral annuloplasty. The same group has also reported on reverse LV remodeling in 26 patients without coronary artery disease after mitral annuloplasty. At present, however, not much information (in large patient populations) is available on the feasibility and outcome after CABG and restrictive mitral annuloplasty in patients with ischemic LV dysfunction. Accordingly, we have evaluated 51 patients with ischemic LV dysfunction and severe mitral regurgitation who underwent CABG and restrictive annuloplasty with stringent undersizing of the mitral annulus (by 2 sizes). From these data, operative morbidity and mortality and 2-year outcome...
The baseline characteristics are presented in Table 1. All patients had New York Heart Association (NYHA) class III and 9 (18%) were in class IV.

**TABLE 1. Patient Characteristics (n=51)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64±8</td>
</tr>
<tr>
<td>Gender, M/F</td>
<td>43/8</td>
</tr>
<tr>
<td>DM</td>
<td>11 (22%)</td>
</tr>
<tr>
<td>HT</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Severe COPD</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>Previous CVA</td>
<td>0</td>
</tr>
<tr>
<td>Previous MI</td>
<td>42 (82%)</td>
</tr>
<tr>
<td>Inferior, posterior, lateral</td>
<td>32 (76%)</td>
</tr>
<tr>
<td>Anterior</td>
<td>5 (12%)</td>
</tr>
<tr>
<td>Both</td>
<td>5 (12%)</td>
</tr>
<tr>
<td>Infarct &gt;3 mo</td>
<td>37 (88%)</td>
</tr>
<tr>
<td>Infarct &lt;6 wk</td>
<td>5 (12%)</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>NYHA</td>
<td>3.4±0.8</td>
</tr>
<tr>
<td>CCS</td>
<td>2.4±0.3</td>
</tr>
<tr>
<td>VD</td>
<td>2.6±0.8</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>31±8</td>
</tr>
</tbody>
</table>

CVA indicates cerebrovascular accident; CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Score; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HT, hypertension; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; VD, vessel disease.

are presented. In addition, serial transthoracic echocardiographic studies were performed (1 echocardiogram before surgery, and 2 echocardiograms after surgery within 3 months after surgery and at 1.5-year follow-up), allowing for assessment of left atrial and LV reverse remodeling and also to determine the time-course of reverse remodeling.

**Methods**

**Patients and Study Protocol**

The study population existed of 51 patients with ischemic cardiomyopathy and severe mitral regurgitation (grade 3 to 4+). The patients presented with heart failure and 58% had accompanying symptoms of heart failure) and the Canadian Cardiovascular Society (CCS) classification (for angina pectoris). Symptoms were evaluated in random order by 2 combined readers, blinded to the clinical and the timing of the echocardiogram.

**CABG and Mitral Valve Surgery**

The procedures were performed with the use of cardiopulmonary bypass with antegrade warm blood cardioplegia for myocardial protection. After median sternotomy, patients underwent conventional multivessel CABG, and internal mammary arteries were used if possible. Next, the right atrium was opened, and after a transseptal approach, mitral valve repair was performed. All patients underwent restrictive anuloplasty with implantation of an undersized semirigid ring (aiming at stringent downsizing of the mitral annulus by 2 sizes).

**Echocardiography**

The clinical echocardiographic evaluation was as follows. A transthoracic (TTE) and transesophageal echocardiogram (TEE) were performed within 5 days before surgery. The TTE and TEE were performed without general anesthesia to avoid underestimation of the severity of the mitral regurgitation. For the TTE, patients were imaged in the left lateral decubitus position using a commercially available system (Vingmed Vivid Seven; General Electric–Vingmed). Images were obtained using a 3.5-MHz transducer at a depth of 16 cm in the parasternal and apical views (standard long-axis, 2-chamber, and 4-chamber images). The left atrial diameter and LV dimensions (end-systolic and end-diastolic diameter) were determined from parasternal M-mode acquisitions. The severity of mitral regurgitation was graded semiquantitatively from color-flow Doppler in the conventional parasternal long-axis and apical 4-chamber images. Mitral regurgitation was characterized as: mild, 1+ (jet area/left atrial area <10%); moderate, 2+ (jet area/left atrial area 10% to 20%); moderately severe, 3+ (jet area/left atrial area 20% to 45%); and severe, 4+ (jet area/left atrial area >45%). Immediately after the TTE, a TEE was performed. The severity and precise mechanism of the mitral regurgitation were confirmed from the TEE images.

When the severity of the mitral regurgitation was less than 3+, a loading test (as described by Byrne et al) was performed just before surgery during anesthesia. Briefly, a preload test is performed by rapid infusion of volume until the pulmonary artery capillary wedge pressure reaches 15 to 18 mm Hg, whereas afterload testing includes administration of intravenous phenylephrine until the mean arterial pressure reaches 100 mm Hg. After these provocative tests, the severity of mitral regurgitation is reassessed, and patients with 3 to 4+ mitral regurgitation underwent mitral valve repair.

Immediately after surgery, the TEE was repeated to assess residual mitral regurgitation, transmural diastolic gradient (determined from continuous-wave Doppler), mitral valve area (by direct planimetry), and length of coaptation of the mitral leaflets. Serial TTEs were performed after surgery. The first TTE was performed within 3 months (average 2.7±0.3) and the second TTE was performed 1.5 years after surgery. From these TTEs, the severity of mitral regurgitation, transmural diastolic gradient, length of coaptation, left atrial diameter, and LV dimensions were assessed. All TTEs were analyzed in random order by 2 combined readers, blinded to the clinical status and the timing of the echocardiogram.

**Assessment of Functional Status and Long-Term Follow-Up**

Functional status was assessed according to the NYHA criteria (for symptoms of heart failure) and the Canadian Cardiovascular Society (CCS) classification (for angina pectoris). Symptoms were evaluated within 1 week before surgery and at 2-year follow-up. The long-term follow-up was performed by an independent physician at the outpatient clinic. In all patients, follow-up data (events) were (according to the protocol) assessed to maximum 2-year follow-up. Events included cardiac death, myocardial infarction, cerebrovascular accident, and endocarditis. Moreover, the number of days the patient stayed in the intensive care unit was noted. The need for intra-aortic balloon pumping to sustain adequate hemodynamic status, dialysis, and reoperation for bleeding were also noted.

**Statistical Analysis**

Continuous data were expressed as mean±SD and compared using the Student t test for paired and unpaired data when appropriate. Comparison of proportions was performed using χ² analysis. Repeated measurements were compared by 1-way ANOVA analysis. Survival over time was analyzed by the method of Kaplan–Meier. P<0.05 was considered significant.

**Results**

**CABG, Mitral Valve Surgery, and Outcome**

In 41 (80%) patients, severe (grade 3 to 4+) mitral regurgitation was confirmed by TTE and TEE performed within 5 days before surgery. In 10 (20%) patients, grade 2+ mitral regurgitation was observed during the TTE and TEE performed within 5 days before surgery. In these patients,
provocative testing was performed in the operating room, resulting in grade 3 to 4+ mitral regurgitation in all patients. None of the patients had primary organic valvular disease. The mechanism underlying the mitral regurgitation was systolic retraction with annular dilatation in 43 patients (resulting in a central regurgitant jet) and restriction and isolated dysfunction of the posterior leaflet in 8 patients (resulting in a slightly eccentric jet toward the lateral wall of the left atrium).

Mean cardiopulmonary bypass time was 168±21 minutes and mean ischemic time was 121±32 minutes. On average, 3.3±0.8 grafts were placed. In 84% of patients, left and/or right mammalian arteries were used. For the mitral valve repair, semirigid rings (Carpentier–Edwards, Physio-ring) were used; the mean ring size was 28±2 (range, 24 to 30). In 16% of patients with severe tricuspid regurgitation, a concomitant DeVega tricuspid annuloplasty was performed.

The mean stay in the intensive care unit was 5±3 days, with a mean total hospital stay of 12±4 days. The early operative mortality (<30 days) was 5.9% with 1 arrhythmic death (day 3) and 2 deaths caused by multi-organ failure (day 3 and day 9). Perioperative and postoperative complications included 1 myocardial infarction, 4 patients requiring an intra-aortic balloon pump, 3 patients requiring re-operation for bleeding, and 4 patients requiring temporary dialysis. During the 2-year follow-up, there were 4 heart failure deaths and 1 noncardiac death, resulting in 84% survival (Figure 1). One patient needed re-operation (at 9 months) for recurrent severe (3+) mitral regurgitation; endocarditis and cerebrovascular/thromboembolic events were not observed.

At 2-year follow-up, NYHA class had improved from 3.4±0.8 to 1.3±0.4 (P<0.01), and all surviving patients were in NYHA class I or II (Figure 2). The mean CCS score had improved from 2.4±0.3 to 1.2±0.5 (P<0.01). During the 2-year follow-up period, 2 patients required hospitalization for heart failure; 1 of these patients had recurrent mitral regurgitation (see previous) and needed re-operation. After re-operation, the patient was in NYHA class II.

**Echocardiography**

All transthoracic echocardiography within 5 days before surgery demonstrated severe (grade 3 to 4+) mitral regurgitation in 80% of patients. In the remaining 20% of patients, provocative testing during TEE in the operating room (just before surgery) increased the mitral regurgitation, resulting in severe mitral regurgitation in all of these patients. On average, the patients had grade 3±0.6 mitral regurgitation (with 24 patients having grade 4+).

On the baseline TTE, the mean left atrial dimension was 53±8 mm (range, 38 to 75 mm). The LV end-diastolic and end-systolic dimensions were 64±8 mm (range, 45 to 88 mm) and 51±10 mm (range 38 to 75 mm).

TEE immediately after surgery showed minimal residual mitral regurgitation (grade 1+) in 8 (16%) patients, whereas the remaining 43 (84%) patients had no residual mitral regurgitation. On average, the patients had grade 0.2±0.4 mitral regurgitation. The mean length of coaptation was 0.8±0.2 cm (range, 0.5 to 1.1 cm). The mean transmural diastolic gradient was 2.7±0.6 mm Hg (range, 1.8 to 4.3 mm Hg). No systolic anterior movement of the anterior leaflet was observed in any patient. The mitral valve area (assessed by direct planimetry) was 2.6±0.8 cm2 (range, 2.1 to 3.4 cm2).

The first follow-up TTE (<3 months after surgery) showed similar results. The mean mitral regurgitation grade was 0.4±0.3; the mean transmural diastolic gradient was 2.5±0.4 mm Hg; the mean length of coaptation was 0.8±0.1 cm. Comparable results were obtained from the second follow-up TTE, obtained at 1.5 years after surgery. The mean mitral regurgitation grade was 0.8±0.8 (1 patient had grade 2+ mitral regurgitation and 10 patients had grade 1+ mitral regurgitation); the transmural diastolic gradient was 2.4±0.6 mm Hg, and the length of coaptation was 0.8±0.2 cm.

The mean left atrial dimension decreased gradually from 53±8 mm at baseline to 51±8 mm at early follow-up to 47±7 mm at late follow-up (P<0.001; Figure 3). The mean LV end-systolic dimension decreased significantly from 51±10 mm at baseline to 48±10 mm at early follow-up to 43±12 mm at late follow-up (P<0.001; Figure 4). Of interest, when 10% reduction in dimension was considered indicative of significant reverse remodeling, 33% of patients demonstrated reverse remodeling at early follow-up, 40% at late follow-up, and 27% did not exhibit reverse remodeling at early follow-up, 40% at late follow-up, and 27% did not exhibit reverse remodeling.
remodeling. The patients without reverse remodeling had a significantly larger LV end-systolic dimension as compared with the patients with early or late remodeling (62 ± 8 mm versus 48 ± 8 mm versus 47 ± 5 mm, \(P < 0.05\)).

The mean LV end-diastolic dimension decreased significantly from 64 ± 8 mm at baseline to 61 ± 9 mm at early follow-up to 58 ± 11 mm at late follow-up (\(P < 0.001\); Figure 5); 22% of patients demonstrated reverse remodeling at early follow-up, 36% at late follow-up, and 42% did not exhibit reverse remodeling. The patients without reverse remodeling had a significantly larger LV end-diastolic dimension as compared with the patients with early or late remodeling (69 ± 8 mm versus 61 ± 6 mm versus 60 ± 5 mm, \(P < 0.05\)).

**Discussion**

The number of patients presenting with heart failure and a severely dilated LV is increasing exponentially,\(^{13}\) with the majority having coronary artery disease as the underlying cause.\(^ {14}\) Data from the Duke Cardiovascular Database\(^ {1}\) have demonstrated that mitral regurgitation is observed frequently in these patients, with 30% having severe mitral regurgitation. In these patients, conservative management is associated with a poor prognosis, with a 1-year survival of 30% to 40%.\(^ {15}\) Moreover, Grigioni et al\(^ {16}\) have demonstrated that the mortality risk is directly related to the severity of mitral regurgitation. In addition, further analysis from the data from the Duke Cardiovascular Databank demonstrated that in patients with ischemic mitral regurgitation, CABG with mitral valve surgery is associated with an improved survival as compared with medical therapy.\(^ {6}\)

Still, surgical interventions in patients with ischemic cardiomyopathy are associated with a relatively high mortality, and CABG procedures alone do not reduce the severity of mitral regurgitation in these patients.\(^ {5}\) However, recent data from Bolling et al\(^ {7}\) have demonstrated the feasibility of mitral valve repair by downsizing the mitral annulus using a flexible ring. Using their initial results, the authors have demonstrated a 1- and 2-year survival of 82% and 71%, respectively, in 48 patients (with \(\sim 50\%\) having ischemic cardiomyopathy) undergoing restrictive mitral valve annuloplasty.\(^ {9}\) More recently, Szalay et al\(^ {17}\) reported an early mortality of 6.6% with an 85% survival at 2 years in 91 patients with ischemic cardiomyopathy and moderate–severe mitral regurgitation undergoing CABG and mitral valve repair. In addition, Gummert et al\(^ {18}\) reported a 1-year survival of 86% (although

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**TABLE 2. Echocardiographic Results**

<table>
<thead>
<tr>
<th></th>
<th>Baseline (51 pts)</th>
<th>Intraoperative TEE (51 pts)</th>
<th>3 mo TTE (48 pts)</th>
<th>1.5 y TTE (45 pts)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR, grade</td>
<td>3.4 ± 0.6</td>
<td>0.2 ± 0.4</td>
<td>0.4 ± 0.3</td>
<td>0.8 ± 0.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LA, mm</td>
<td>53 ± 8</td>
<td>--</td>
<td>51 ± 8</td>
<td>47 ± 7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LVEDD, mm</td>
<td>64 ± 8</td>
<td>--</td>
<td>61 ± 9</td>
<td>58 ± 11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LVESD, mm</td>
<td>51 ± 10</td>
<td>--</td>
<td>48 ± 10</td>
<td>43 ± 12</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Coaptation, cm</td>
<td>--</td>
<td>0.8 ± 0.2</td>
<td>0.8 ± 0.1</td>
<td>0.8 ± 0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Transmirtal grade (mm Hg)</td>
<td>--</td>
<td>2.7 ± 0.6</td>
<td>2.5 ± 0.4</td>
<td>2.4 ± 0.6</td>
<td>NS</td>
</tr>
<tr>
<td>MVA (cm²)</td>
<td>--</td>
<td>2.6 ± 0.8</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

LA indicates left atrium; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; MR, mitral regurgitation; MVA, mitral valve area; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; transmirtal, mean diastolic transmitral gradient.

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**Figure 3.** Scatter plot showing the mean left atrial (LA) dimension at baseline, and at early (within 3 months after surgery) and late (1.5 years after surgery) follow-up.

**Figure 4.** Scatter plot showing the mean left ventricular end-systolic dimension (LVESD) at baseline, and at early (within 3 months after surgery) and late (1.5 years after surgery) follow-up.
the majority [80%] of the 66 patients in that study had dilated cardiomyopathy and only 20% had ischemic cardiomyopathy). The results in the current study are in line with these results: the early mortality was 5.9% with an 84% survival at 2-year follow-up, and all surviving patients had minimal heart failure symptoms and were in NYHA class I or II at 2-year follow-up. Finally, the truly restrictive annuloplasty resulted in virtually no recurrence of mitral regurgitation at late follow-up, with restoration of leaflet coaptation, without inducing mitral valve stenosis. Only 1 (2%) patient needed re-operation for recurrent mitral regurgitation. In addition, no endocarditis or thromboembolic events occurred.

In these patients, serial echocardiographic studies were performed, allowing evaluation of LV reverse remodeling after surgery. The results demonstrated that significant reverse remodeling occurred after surgery, in line with results of Szalay et al. Bolling et al hypothesized that stabilization of the mitral annulus and unloading of the LV may be responsible for the reverse remodeling. It is well-known that a reduction in LV dimensions is associated with a favorable prognosis.

A novel aspect of the current study is the serial echocardiographic assessment of LV dimensions after surgery. The results showed that reverse remodeling of the LV is a gradual and time-dependent process. A regression in LV end-systolic dimension was observed in 73% of patients, with 33% occurring at early follow-up. In contrast, a decrease in LV end-diastolic dimension was observed less frequently (56% of patients), with 22% occurring at early follow-up. Moreover, in 27% and 42% of patients, no reductions in LV end-systolic and end-diastolic dimensions were observed. These patients were characterized by larger LV dimensions at baseline; this finding may suggest that extensive LV dilation may be an irreversible process and surgery should preferably be performed before extensive dilatation has occurred.

Finally, the left atrium also exhibited reverse remodeling over time; the clinical value of this phenomenon is not entirely clear, although some studies have suggested that an enlarged left atrium was independently predictive of worse long-term outcome.

Limitations
In the current study, only patients with severe (grade 3 to 4+) mitral regurgitation were included, and additional studies are needed in patients with ischemic cardiomyopathy and mild-to-moderate mitral regurgitation.

In 16% of patients, a concomitant repair of the tricuspid valve was performed; this may have influenced results.

Although reverse remodeling was demonstrated in the current study, identification of patients who will benefit from surgery remains difficult. The patients without reverse remodeling had significantly larger LV end-diastolic and end-systolic dimensions, suggesting that severe dilatation will prevent reverse remodeling. Larger studies are needed to further evaluate this issue. Moreover, viability testing was not routinely performed in these patients and LV reverse remodeling may be partially related to improvement of function of hibernating myocardium after CABG. Inclusion of viability assessment may further optimize selection of patients who may benefit most from combined revascularization and mitral valve repair.

Conclusion
CABG and truly restrictive mitral annuloplasty in patients with ischemic cardiomyopathy and severe mitral regurgitation corrected mitral regurgitation in virtually all patients, with a 2-year survival of 84%. Leaflet coaptation was restored without inducing mitral stenosis. Significant reverse LV remodeling appeared over time, with a reduction in LV end-systolic dimension occurring earlier and more frequently as compared with LV end-diastolic dimension.

References


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