Percutaneous Versus Surgical Revascularization in Patients With Ischemic Mitral Regurgitation

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Background—The proper way of revascularization remains controversial in patients with ischemic mitral regurgitation (IMR). We sought to compare the long-term results of percutaneous coronary intervention (PCI) and surgical revascularization in IMR.

Methods and Results—From 1996 to 2008, 185 consecutive patients (132 men; age, 63±9 years) with significant IMR underwent PCI (PCI group) (n=66) or coronary artery bypass graft surgery (OP group) (n=119). In the OP group, 68 (57%) patients also underwent concomitant mitral annuloplasty. Significant IMR was defined as functional MR occurring >1 week after myocardial infarction with an effective regurgitant orifice area ≥0.2 cm². During a median follow-up of 54 months, there were 2 operative mortalities, 26 cardiac deaths, and 11 heart failure hospitalizations in the OP group and 22 cardiac deaths and 10 heart failure hospitalizations in the PCI group. The survival and cardiac mortality rates were not significantly different between the 2 groups, but event-free survival rates were significantly higher in the OP group. For the 45 propensity score-matched pairs, the risk of cardiac events was significantly lower in the OP group than in the PCI group (hazard ratio, 0.499; 95% CI, 0.251 to 0.990; P=0.043). Compared with patients who underwent coronary artery bypass graft surgery alone, event-free survival rates were significantly higher in those who underwent additional mitral annuloplasty.

Conclusions—Compared with PCI, surgical revascularization is associated with an improved long-term event-free survival, and concomitant mitral annuloplasty should be considered in patients with significant IMR. (Circulation. 2011;124[suppl 1]:S156–S162.)

Key Words: myocardial infarction ■ mitral valve regurgitation ■ mitral valve annuloplasty ■ revascularization

Ischemic mitral regurgitation (IMR) is frequently noted in the acute and chronic phases of myocardial infarction and carries an adverse prognosis with a graded relationship between IMR severity and reduced survival.1-3 Percutaneous or surgical revascularization has been associated with improved survival compared with medical therapy in patients with IMR,3,4 but the proper way of revascularization remains controversial. Surgical revascularization has potential benefits of achieving more complete revascularization and improving IMR more effectively by addition of a mitral valve (MV) procedure at the time of coronary artery bypass graft (CABG) surgery. However, surgical revascularization has a higher procedural risk compared with percutaneous coronary intervention (PCI), and it is unclear whether IMR is merely a marker for more advanced left ventricular (LV) dysfunction or whether IMR itself should be a target for therapy.5 In previous studies, MV surgery in addition to CABG was not associated with an incremental reduction in mortality beyond PCI and CABG alone.6,7 To date, no prospective trial has addressed the impact of therapies intended to reduce MR on symptoms, LV function, and clinical end points.5,8 Using our prospectively collected registry data on patients with IMR, we sought to compare the long-term outcomes of percutaneous versus surgical revascularization and to evaluate the impact of additional mitral annuloplasty on clinical and echocardiographic outcomes.

Methods

Study Patients
A prospective registry that commenced in 1996 and uses a standard case report form has included all consecutive patients with IMR undergoing echocardiography at our hospital. Case report forms, including patient demographics, clinical presentation, and echocardiographic data, were stored in an electronic database.9 Clinical and echocardiographic follow-up data on study patients were collected annually and entered into the database. From 1996 to 2008, 185 patients (132 men; age, 63±9 years) with significant IMR who...
underwent percutaneous or surgical revascularization were consecutively enrolled in the present study. Significant IMR was defined as MR occurring >1 week after myocardial infarction with (1) global or regional LV systolic dysfunction; (2) significant coronary artery disease; (3) no evidence of primary valvular, chordal, or papillary muscle pathology; and (4) effective regurgitant orifice area (ERO) ≥0.2 cm². Revascularization was performed only in patients with symptoms and signs of myocardial ischemia or viability, and adenosine stress thallium single-photon emission CT was performed to confirm myocardial ischemia and viability in 98 (53%) patients without typical angina. Patients with organic MV disease, including prolapse of mitral leaflets, ruptured chordae, or rupture of papillary muscles; those who presented with ST-elevation myocardial infarction and required direct PCI; and those who had prior CABG or significant aortic valve disease were excluded. Patients requiring surgical ventricular restoration for large apical aneurysm also were excluded. The decision to perform percutaneous or surgical revascularization was the choice of the physician and patient, and the decision of whether to perform mitral annuloplasty at the time of CABG was at the discretion of the surgeon. Whereas PCI was chosen for 66 patients (PCI group), surgical revascularization was performed in 119 (OP group). After patients were assigned to a treatment group, they were maintained in that group, regardless of treatment crossovers. Treatment crossover occurred in 6 patients in the PCI group and 2 in the OP group. Informed consent was obtained from each patient, and the study protocol was approved by the Ethical Committee of our institution.

### Procedures

PCI procedures were performed with standard interventional techniques as previously described. Stent implantation was performed in 61 (92%) patients in an attempt to fully cover the diseased segment and to ensure complete stent apposition. The choice of bare-metal stents (n=32) or drug-eluting stents (n=29) was left to the discretion of the operator. After the procedure, aspirin was continued indefinitely. Clopidogrel was prescribed to patients treated with bare-metal stents for at least 1 month and to those with drug-eluting stents for at least 6 months.

Surgical procedures were performed with the use of a standard cardiopulmonary bypass (n=103) or an off-pump (n=16) method. After median sternotomy, patients underwent conventional multivesel CABG surgery, using internal mammary arteries whenever possible. Complete revascularization was performed when possible, using arterial conduits or saphenous vein grafts as follows: internal mammary arteries in 107 (90%) patients, radial arterial conduits in 72 (61%), gastroepiploic arteries in 9 (8%), and saphenous vein grafts in 79 (66%). Surgical ventricular reconstruction was not performed in conjunction with CABG. In patients undergoing MV repair, mitral annuloplasty was performed with an undersized rigid or semirigid complete annuloplasty ring placement, and 2 patients underwent additional repair procedures (commissuroplasty in 1 and Alfieri method in the other). Intraoperative transesophageal echocardiography was routinely performed during the MV repair procedure.

### Echocardiographic Evaluation

Echocardiographic evaluation was performed before revascularization and annually during follow-up. Comprehensive 2D and Doppler echocardiographic examinations using a Hewlett-Packard Sonos 2500 or 5500 imaging system equipped with a 2.5-MHz transducer (Hewlett-Packard; Andover, MA) were performed in all patients. End-systolic dimension, end-diastolic dimension, and end-diastolic interventricular septal and posterior wall thickness of the LV were measured from parasternal M-mode acquisitions. End-systolic volume, end-diastolic volume, and ejection fraction (EF) of the LV were obtained using the biplane Simpson method. Regional wall motion abnormalities were analyzed using a 16-segment model. The ERO was determined by dividing the regurgitant flow rate (calculated as 2πr²halling velocity, where r is the radius of proximal isovelocity surface area) by peak MR velocity, and the degree of MR was graded as moderate (0.2 cm² ≤ERO <0.4 cm²) or severe (ERO ≥0.4 cm²). An improvement in MR was defined as a decrease of ERO to <0.2 cm² and functional recovery of LV as an increase of EF ≥5% with improvement of the regional wall motion score on 6-month follow-up echocardiography. Changes in LV volumes and severity of MR were evaluated on annual follow-up echocardiographic examinations, and a recurrence of MR was defined as reappearance of MR with ERO ≥0.2 cm².

### Follow-Up

Data were collected until December 2009 during annual visits to the echocardiographic laboratory or by telephone interviews and by a detailed review of all medical records. Functional status during follow-up was assessed according to New York Heart Association criteria. Deaths were classified as cardiac or noncardiac on the basis of medical records. For the 3 (1.6%) patients lost to follow-up, data on vital status and dates and causes of death were obtained from the Korean national registry of vital statistics. The primary end point of the study was defined as the composite of in-hospital death, cardiac death, and hospitalization due to congestive heart failure (CHF) during follow-up, and the secondary end point was death from any cause. A CHF hospitalization was defined as an unplanned, urgent admission for the management of CHF. A patient admitted for CHF had to show resting dyspnea and radiological signs of pulmonary edema and require intravenous diuretics.

### Statistical Analysis

Categorical variables are presented as numbers and percentages and were compared using the χ² test and Fisher exact test. Continuous variables are expressed as mean±SD, and were compared using the Student t test or Wilcoxon signed rank test as appropriate. The paired t test was used for analysis of echocardiographic follow-up data. To reduce the effect of treatment selection bias and potential confounding in this observational study, we performed rigorous adjustment for the differences in the baseline characteristics by using propensity score matching. Propensity scores were estimated without regard to outcome variables with multiple logistic regression analysis. All prespecified covariates were included in the full nonparsimonious models for treatment with percutaneous versus surgical revascularization (Table 1). The discrimination and calibration ability of the propensity score model was assessed by means of the C statistic and the Hosmer-Lemeshow statistic. For development of propensity score-matched pairs without replacement (a 1:1 match), the Greedy 5 5 1 digit match algorithm was used. After propensity score matching, the baseline covariates were compared between the 2 groups with the paired t test or the Wilcoxon signed rank test for continuous variables and the McNemar test or marginal homogeneity test for categorical variables.

The analysis of clinical end points was done on an intention-to-treat basis and included all patients. Event-free survival curves were constructed with Kaplan-Meier estimates and compared using the log-rank test. For Kaplan-Meier estimates, we analyzed all clinical events by time to first event. In the propensity score-matched cohort, the risks of clinical end points were compared using Cox regression models with robust SEs that accounted for the clustering of matched pairs. Cox proportional hazards models were used to examine the association of baseline characteristics with all-cause mortality, cardiac mortality, and cardiac events. Covariates considered for inclusion in the models included all variables presented in baseline demographics and echocardiographic findings. All reported P values were 2-sided, and a value of P<0.05 was considered statistically significant. SAS version 9.1 (SAS Institute Inc; Cary, NC) software was used for statistical analyses.

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

### Results

#### Baseline Characteristics

A comparison of the baseline clinical and echocardiographic characteristics of the OP and PCI groups is shown in Table 1.
There were no significant differences between the groups in terms of age, sex, body mass index, smoking, diabetes mellitus, hypertension, atrial fibrillation, New York Heart Association class, percentage of patients with acute coronary syndrome, drug therapy, LV dimensions, or ERO of MR, but EF was significantly lower in the OP group than in the PCI group (P=0.05).

Comparison of Outcomes Between the OP and the PCI Groups

Clinical Outcome
There were 2 (1.7%) deaths in the OP group and 2 (3.0%) deaths in the PCI group within 30 days of the index procedure or before hospital discharge (P=0.62). The median follow-up was 1613 days (interquartile range, 972 to 2365 days) in the OP group and 1612 days (interquartile range, 624 to 2774 days) in the PCI group. Including 4 in-hospital deaths, there were 28 (24%) cardiac and 10 (8%) noncardiac deaths in the OP group and 22 (33%) cardiac and 6 (9%) noncardiac deaths in the PCI group during follow-up (P=0.15) (Table 2). The estimated actuarial 5- and 7-year survival rates, respectively, were 75±5% and 60±6% in the OP group and 66±6% and 55±7% in the PCI group (P=0.021) (Figure 1A). The 7-year cardiac mortality rate of the OP group was 31±6% and not significantly different from that of the PCI group (36±7%, P=0.21). Using unadjusted Cox proportional hazards analysis, we found that baseline correlates of all-cause mortality and cardiac mortality were age, male sex, presence of chronic renal failure, EuroSCORE, and decreased EF.

During follow-up, 11 patients in the OP group and 10 in the PCI group required hospitalization for CHF without cardiac mortality, and 2 patients among them underwent heart transplantation because of progressive heart failure. Thus, 39 (33%) patients in the OP group and 32 (48%) in the PCI group attained the primary composite end point, and the estimated actuarial 5- and 7-year event-free survival rates, respectively, were 75±5% and 58±6% in the OP group and 55±7% and 50±7% in the PCI group (P=0.034) (Figure 1B). The event-free survival rates were not significantly different between the groups (P=0.51) (Figure 1C).
different between patients with moderate MR and those with severe MR (52±5% versus 59±10% at 7 years, \(P=0.53\)). Baseline correlates of end points were age, male sex, EuroSCORE, decreased EF, and PCI group on unadjusted Cox proportional hazards analysis. The PCI group (hazard ratio, 1.846; 95% CI, 1.135 to 3.001) was independently associated with cardiac events in the multivariable-adjusted Cox proportional hazard models. For the 45 propensity score-matched pairs, the risk of cardiac events was significantly lower in the PCI group patients had significantly longer bypass (183±97 versus 113±49 minutes, \(P<0.001\)) and aortic clamp (97±49 versus 113±47 minutes, \(P<0.001\)) times.

**Impact of Additional Mitral Annuloplasty on Outcomes**

Of the 119 patients in the OP group, 51 underwent CABG alone, and 68 underwent additional mitral annuloplasty (Table 3). The 2 groups were similar in terms of age, sex, incidence of diabetes mellitus, atrial fibrillation, baseline New York Heart Association class, EuroSCORE, baseline EF, ERO, and number of bypass grafts. At surgery, repair group patients had significantly longer bypass (183±64 versus 113±47 minutes, \(P<0.001\)) and aortic clamp (97±49 versus 68±23 minutes, \(P<0.001\)) times.

At 6 months after the surgery, the symptoms improved significantly in both the CABG and MV repair groups by an average of 0.6 and 1.0 classes, respectively (\(P<0.001\) for each). However, changes in symptoms from baseline were significantly different between the 2 groups (\(P=0.023\), and functional status at 6 months after surgery was significantly better in the MV repair than in the CABG group (\(P=0.011\)). During follow-up, there were 15 cardiac deaths and 8 CHF hospital admissions in the CABG group and 15 cardiac deaths and 3 CHF hospital admissions in the MV repair group, with the event-free survival rates being significantly lower in the CABG group than in the MV repair group (\(P=0.042\) (Figure 1).
Compared with the MV repair group, CABG group was significantly associated with cardiac events (hazard ratio, 1.907; 95% CI, 1.012 to 3.593; \( P < 0.05 \)) in the Cox proportional hazard models. Although the increase in EF was similar between the CABG (5.6\% to 9.9\%) and the MV repair (7.8\% to 11.2\%) groups (\( P < 0.309 \)), the improvement rate of IMR was significantly higher in the MV repair than in the CABG group (95\% versus 57\%, \( P < 0.001 \)) on 6-month follow-up echocardiographic examination. On late echocardiographic follow-up performed at a median interval of 1549 days (interquartile range, 503 to 2282 days) after surgery, recurrence of MR was observed in 2 patients in the CABG group and 1 patient in the MV repair group, whereas LV volume was significantly increased during follow-up in the CABG group only (Table 4).

**Discussion**

The present study demonstrates that in patients with significant IMR, surgical revascularization combined with mitral annuloplasty is associated with a higher event-free survival through improving MR and LV dysfunction more effectively compared with PCI. Mortality increases even when IMR is only mild and with a graded relationship to the severity of IMR. In a community-based study of 1331 patients, a graded positive association was observed between the presence and severity of MR and heart failure or death. Another study of 303 patients with recent myocardial infarction showed that the risk of mortality was directly related to the severity of regurgitation as defined by ERO. However, it is still disputed whether MR causes a poor outcome or merely indicates advanced LV dysfunction. A recent study of 390 patients with moderate or severe IMR found that mitral annuloplasty combined with CABG did not improve survival, and myocardial factors, rather than MR, were the primary determinants of outcome. Because IMR may be a surrogate marker for severe LV dysfunction, correction of MR may not have an impact on survival if the underlying LV dysfunction is not improved. Alternatively, MV repair may primarily affect other important end points, such as heart failure and adverse remodeling of the LV. Our findings agree with the results of previous studies showing that percutaneous and surgical revascularization had comparable long-term survival and that MV repair was insufficient to improve long-term survival. However, to our knowledge, the present study is the first prospective study to demonstrate that compared with revascularization alone, additional mitral annuloplasty significantly improved functional status and long-term event-free survival by decreasing the incidence of persistent and recurrent IMR to 6%.

The choice of percutaneous or surgical revascularization depends on several factors, particularly the location and number of coronary vessels involved, and CABG usually is the revascularization procedure of choice for patients with left main disease and diffuse 3-vessel disease. About 90%

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**Table 4. Follow-Up Echocardiographic Results in Patients Who Underwent PCI, CABG Alone, and Additional MV Repair**

<table>
<thead>
<tr>
<th></th>
<th>PCI Group (n=57)</th>
<th>CABG Group (n=51)</th>
<th>Repair Group (n=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>6 mo</td>
<td>Late</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>39±11</td>
<td>41±12</td>
<td>40±11</td>
</tr>
<tr>
<td>Improved MR</td>
<td>...</td>
<td>31 (54)</td>
<td>30 (53)</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>138±40</td>
<td>141±52</td>
<td>146±56</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>39±11</td>
<td>41±12</td>
<td>40±11</td>
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<td>Improved MR</td>
<td>...</td>
<td>31 (54)</td>
<td>30 (53)</td>
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Data are presented as mean±SD or n (%). LVEF indicates left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume. Other abbreviations as in Tables 1 and 3. 
*\( P < 0.05 \) baseline vs 6-mo follow-up. 
†\( P < 0.05 \), 6-mo vs late follow-up.
of our patients had multivessel coronary artery disease, and CABG was the preferred treatment option for patients with 3-vessel disease. However, there is increasing evidence of favorable clinical outcomes associated with drug-eluting stents in patients with multivessel disease, and we recently reported that PCI with drug-eluting stent implantation showed equivalent long-term mortality to CABG for the treatment of multivessel disease.10 Future studies are needed to compare clinical outcomes in patients with IMR who undergo multivessel PCI combined with percutaneous MV repair and in those who undergo CABG with surgical MV repair.

The remaining question is how to define significant IMR for which mitral annuloplasty is indicated. Contrary to organic MR, even modest regurgitation is associated with increased mortality.1,2 Although the presence of mild MR will have little if any impact on treatment decisions, the optimal management of moderate IMR remains controversial. Quantification of the severity of MR is strongly recommended in the guidelines13 because measurements of ERO and regurgitant volume have important prognostic value. The ERO cutoff of 0.20 cm² in the present study was lower than the 0.40 cm² used in organic MR20 and qualitatively classified as moderate or severe MR.13 The adjusted relative risk of CHF or cardiac death was 4.4 when ERO was ≥0.2 cm², suggesting that IMR of ERO ≥0.2 cm² imposes severe clinical consequences related to poor LV tolerance to MR.21 Our findings suggest that mitral annuloplasty is indicated for patients with moderate IMR defined as ERO >0.2 cm² if MV surgery does not increase the operative risk of CABG.

Restrictive mitral annuloplasty currently is considered the standard surgical therapy for IMR,8 but long-term failures of mitral annuloplasty are increasingly recognized.22,23 Progressive ventricular remodeling in ischemic heart disease can increase tethering and render initial successful repair ineffective.22 Myocardial viability and LV size are important variables related to ventricular remodeling after revascularization and mitral annuloplasty.24,25 Because all study patients showed evidence of myocardial ischemia or viability and preoperative LV volumes were smaller than those of previous studies,21 LV remodeling was attenuated in the present study. These findings that LV volumes did not increase during follow-up and that late postoperative LV volume was maintained significantly lower than preoperative volume might contribute to the lower rate of recurrent MR observed in the present study. Braun et al25 recently reported that in patients in whom LV reverse remodeling had occurred in 74% and was sustained at late follow-up, 85% of patients had less than grade 2+ MR at a mean echocardiographic follow-up of 3.8 years, and their 5-year survival rate (71±5.1%) was similar to that (75±5%) of the present OP group. The results of the present study support the conclusion of Braun et al that restrictive mitral annuloplasty with CABG provides a cure for IMR and heart failure in patients with a preoperative LV end-diastolic dimension of ≤65 mm and suggest that even optimal management of IMR does not improve survival because survival of such patients is primarily dictated by the extent of ischemic cardiomyopathy and recurrence of coronary artery disease.16

**Study Limitations**

Comparison of treatment strategies for IMR is subject to the limitations inherent to nonrandomized assignment, and such limitations may have significantly affected our results because of selection bias and unmeasured confounders. However, all study patients were enrolled consecutively in a prospectively designed registry for annual clinical and echocardiographic follow-up, and all baseline characteristics except EF and the incidence of triple-vessel disease were not significantly different between the OP and the PCI groups. To minimize selection bias and confounding, we used propensity score matching, which has been shown to eliminate a greater proportion of baseline differences than stratification or covariate adjustment. In the propensity score-matched cohort, the OP group consistently showed a significantly lower rate of end points.

The present study targeted a homogenous population with IMR for whom revascularization therapy was clearly indicated and excluded patients requiring surgical ventricular restoration. The results are not applicable to patients with functional MR of other causes or to those with large apical aneurysms. Further clinical studies are needed to determine the optimal management of IMR in patients with significant LV dilatation.

**Conclusions**

Although percutaneous and surgical revascularization showed comparable long-term survival, surgical revascularization improved IMR more effectively by adding mitral annuloplasty at the time of CABG and is associated with better functional status and improved long-term event-free survival. Consideration for concomitant mitral annuloplasty is warranted in patients with significant IMR and indications for revascularization therapy.

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**Disclosures**

None.

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