Percutaneous Mitral Valve Repair in the Initial EVEREST Cohort

Evidence of Reverse Left Ventricular Remodeling

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Background—Percutaneous repair of mitral regurgitation (MR) permits examination of the effect of MR reduction without surgery and cardiopulmonary bypass on left ventricular (LV) dimensions and function. The goal of this analysis was to determine the extent of reverse remodeling at 12 months after successful percutaneous reduction of MR with the MitraClip device.

Methods and Results—Of 64 patients with 3 and 4+ MR who achieved acute procedural success after treatment with the MitraClip device, 49 patients had moderate or less MR at 12-month follow-up. Their baseline and 12-month echocardiograms were compared between the group with and without LV dysfunction. In patients with persistent MR reduction and pre-existing LV dysfunction, there was a reduction in LV wall stress, reduced LV end-diastolic volume, LV end-systolic volume and increase in LV ejection fraction in contrast to those with normal baseline LV function, who showed reduction in LV end-diastolic volume, LV wall stress, no change in LV end-systolic volume, and a fall in LV ejection fraction.

Conclusions—Patients with pre-existing LV dysfunction demonstrate reverse remodeling and improved LV ejection fraction after percutaneous mitral valve repair.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifiers: NCT00209339, NCT00209274.

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Key Words: echocardiography ■ left ventricular dysfunction ■ mitral regurgitation ■ percutaneous mitral valve repair ■ reverse left ventricular remodeling

Left ventricular (LV) remodeling associated with mitral regurgitation (MR) is adaptive in that forward stroke volume (FSV) is preserved, but may eventually become mal-adaptive, leading to irreversible LV dysfunction and adverse late outcomes even after correction of MR. Several studies have raised the specter of a point of no return, prompting the recommendation for intervention in asymptomatic patients with hemodynamically significant MR when the LV ejection fraction falls below 60% or the LV end-systolic dimension exceeds 40 mm.1 A concern that surgery itself may contribute to postoperative LV dysfunction has led to modifications of surgical technique, with a strong preference for mitral valve repair over replacement.

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Percutaneous repair of MR with the MitraClip system (Abbott Vascular, Menlo Park) offers a potential therapy for patients with 3 to 4+ MR. Safety and effectiveness outcomes in these patients have been previously reported from the Endovascular Valve Edge-to-Edge Repair Study (EVEREST) Clinical Trial, including a single-arm feasibility study,2 a randomized controlled trial comparing the treatment with mitral
valve surgery,\textsuperscript{3} and in a high surgical risk single-arm study.\textsuperscript{4} Percutaneous reduction of MR with the MitraClip procedure provides a unique opportunity to examine the extent of reverse LV remodeling in the absence of surgical intervention.

We hypothesized that sustained MR reduction would be associated with significant reversal in LV remodeling and sought to investigate the impact of pre-existing LV dysfunction on the extent of reverse remodeling. The primary aim of this analysis was to determine the extent of reverse remodeling at 12 months after successful percutaneous reduction of MR (acute procedural success [APS]) with the MitraClip device. We compared changes in indices of LV remodeling at baseline, and at 12 months, in APS patients with and without sustained 12-month MR reduction. In addition, we compared the extent of remodeling associated with sustained MR reduction in APS patients with and without baseline LV dysfunction. The patients in the EVEREST I safety and feasibility study and those in the roll-in phase of the EVEREST II randomized controlled trial form the basis of the current study.

Patients in these studies were followed with echocardiography at prespecified time points, and all of the echo studies were evaluated in a core laboratory as previously described.\textsuperscript{5}

\section*{Methods}

\textbf{Study Design}

The study includes 55 patients from EVEREST I, a prospective multicenter, single-arm feasibility study and 52 patients from the roll-in
Patients were selected if they met class I indications for mitral valve surgery.\textsuperscript{1,6} Patients with moderate to severe (2+) or severe (3+) functional or degenerative MR, or asymptomatic with compromised LV function (ejection fraction 25\%–60\% or end-systolic dimension ≥40 mm) were candidates for inclusion. After the core laboratory analysis of baseline MR, it was determined that 9 enrolled subjects had mild (n=2) or moderate MR (n=7). In addition, all patients were candidates for MV surgery, in the event surgery was required for complications.

**MitraClip System and Procedure**

The MitraClip system (Figure 1A) uses a triaxial catheter system with an implantable clip. The guide catheter is 24-French proximally, and a 22-French at the atrial septum, and is delivered with a tapered dilator. The clip delivery system has the MitraClip device attached to its distal end. The MitraClip device (Figure 1B) is a 4-mm wide cobalt–chromium implant with 2 arms. Each leaflet is independently secured between their respective edges.

The procedure is performed under general anesthesia using an arm and a gripper. The procedure has previously been described in detail.\textsuperscript{7} The procedure was performed in the cardiac catheterization laboratory under fluoroscopy and transesophageal echocardiographic guidance. The goal was to reduce MR to mild to moderate (1+ or 2+) or less with optimal placement of 1 or 2 MitraClip devices.

### Table 1. Baseline Characteristics of the Patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Subjects (n=107)</th>
<th>Group 1 Continued Success (n=49)</th>
<th>Group 2 Recurrent MR (n=15)</th>
<th>P-Value Between Groups 1 and 2</th>
<th>Group 1a Continued Success Pre-existing LV Dysfunction (n=20)</th>
<th>Group 1b Continued Success Pre-existing LV Dysfunction (n=29)</th>
<th>P-Value Between Groups 1a and 1b</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Sex, female, %</td>
<td>38.3% (41/107)</td>
<td>36.7% (18/49)</td>
<td>46.7% (7/15)</td>
<td>0.55</td>
<td>35.0% (7/20)</td>
<td>37.9% (11/29)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Age, y</td>
<td>67.2±14.2 (107)</td>
<td>69.0±13.9 (49)</td>
<td>66.5±16.3 (15)</td>
<td>0.56</td>
<td>68.8±15.5 (20)</td>
<td>69.1±12.9 (29)</td>
<td>0.93</td>
</tr>
<tr>
<td>Body surface area</td>
<td>1.87±0.23 (96)</td>
<td>1.90±0.23 (43)</td>
<td>1.76±0.17 (14)</td>
<td>0.048</td>
<td>1.95±0.26 (18)</td>
<td>1.87±0.21 (25)</td>
<td>0.28</td>
</tr>
</tbody>
</table>

### Patient Selection

Patients were enrolled at 33 centers in the EVEREST II randomized controlled trial, representing the prerandomization start-up experience. Each site performed ≤ 3 MitraClip procedures in the roll-in phase of the EVEREST II randomized controlled trial. Thirty-one sites enrolled the 107 patients that comprise the study cohort. The EVEREST Clinical study was approved by the Food and Drug Administration, Health Canada, the participating local institutional review boards/independent ethics committees, and all patients signed informed written consent. The trials are registered at www.clinicaltrials.gov (numbers: NCT00209339, NCT00209274).

FSV indicates forward stroke volume; LV, left ventricular; LVEDD, LV end-diastolic dimension; LVEDV, LV end-diastolic volume; LVEF, LV ejection fraction; LVESD, LV end-systolic dimension; LVESV, LV end-systolic volume; MR, mitral regurgitation; NYHA, New York Heart Association Class; RF, regurgitant fraction; and RV, regurgitant volume.
Echocardiography

Transcatheter echocardiograms were performed using a prespecified protocol at baseline, predischarge, and at 1, 6, 12, 18, 24 months, and yearly ≤5 years. All echocardiograms were reviewed by a core laboratory (UCSF, San Francisco, CA). MR was graded according to the criteria of the American Society of Echocardiography guidelines using quantitative (regurgitant volume, regurgitant fraction, and regurgitant orifice area) and qualitative criteria (color Doppler and pulmonary venous flow). To be included, moderate to severe (3+) or severe (4+) MR using the integrative approach per the American Society of Echocardiography guidelines was required. Key anatomic inclusion criteria included a regurgitant jet origin associated with the A2-P2 segment of the mitral valve, and for patients with functional MR, a coaptation depth of not >11 mm, and for patients with mitral valve surgery, a flail gap <10 mm and a flail width <15 mm.9

Statistical Analysis

Continuous data are presented as means±SD, whereas categorical data are presented as n (%). Baseline comparisons between groups were performed with t tests for continuous data and Fisher exact test for dichotomous data. Within group comparisons (eg, from baseline and 12 months) were performed using a paired t test (all variables being continuous). Between-group comparisons on relative change from baseline were performed using an ANOVA (all variables being continuous). Bonferroni correction was used for multiple variables and a P<0.0042 was considered statistically significant.

Results

Baseline Demographics and Echocardiographic Variables

Group 1 Versus Group 2

Sixty-four patients with APS were available for the analysis at 12 months. Seventy-seven percent (49/64) of the APS patients had sustained MR reduction (MR≤2) at 12 months (group 1), and 23% (15/64) had recurrent MR (MR>2) at 12 months (group 2). Baseline demographics and echocardiographic variables are presented in Table 1 for the overall patient group (n=107) and for patients in groups 1 and 2. No significant baseline differences were noted between patients in groups 1 and 2. For the overall cohort, mean age was 67 years, 38% were women, 70% had congestive heart failure, 19% had prior cardiac surgery, and 48% presented with New York Heart Association Class III or IV symptoms. Seventy-nine percent of patients (n=85) had degenerative mitral valve disease and 21% of patients (n=22) had functional MR. MR severity was moderate to severe (3+) in 54% and severe (4+) in 38%. LV measures were similar for the overall cohort and for groups 1 and 2. At baseline, there was no difference in LV end-diastolic volume (LVEDV; group 1: 171±41 mL versus group 2: 168±35 mL; P=0.81), LV endsystolic volume (LVESV; group 1: 70±29 mL versus group 2:
68±28 mL; \( P = 0.77 \)), ejection fraction (group 1: 59.9±9.2 versus group 2: 60.2±8.8; \( P = 0.92 \)) and LV mass (group 1: 180±57 g versus group 2: 205±40 g; \( P = 0.14 \)), and peak wall stress (group 1: 216±56 dynes/cm\(^2\); \( P = 0.15 \)) between those patients with sustained MR reduction (MR≤2) at 12 months compared with those patients with recurrent MR (MR>2) at 12 months. Patients with sustained MR reduction at 12 months had a significantly smaller baseline sphericity index in the 2-chamber view than patients with recurrent MR at 12 months. There was no difference in the overall baseline MR grade (\( P = 0.73 \)), regurgitant volume (\( P = 0.31 \)), and regurgitant fraction (\( P = 0.67 \)) between the 2 groups.

**Group 1a Versus Group 1b**

Of the 49 patients with sustained MR reduction (MR≤2) at 12 months available for the analysis, 41% (20/49) had existing baseline LV dysfunction (group 1a) and 59% (29/49) did not have baseline LV dysfunction (group 1b). Baseline demographics and echocardiographic variables for patients in groups 1a and 1b are presented in Table 1. Baseline demographics, comorbidities, and MR grade were similar between the 2 groups. Significant differences in baseline echocardiographic variables were noted among the patients with and without baseline LV dysfunction. Those with pre-existing LV dysfunction were more likely to have functional MR (group 1a: 40% functional mitral regurgitation (FMR) versus group 1b: 10% FMR; \( P = 0.033 \)) and had lower ejection fractions (group 1a: 51.8±8.1% versus group 1b: 65.9±4.0%; \( P < 0.0001 \)). All measures of LV remodeling were significantly greater, including LVEDV (group 1a: 196±36 mL versus group 1b: 152±35 mL; \( P = 0.0001 \)), LVESV (95±25 mL versus 52±13 mL; \( P = 0.0001 \)) LV mass (209±55 g versus 158±48 g; \( P = 0.0021 \)), and sphericity indices (2 chamber: 0.63±0.09 versus 0.59±0.05; \( P = 0.028 \) and 4 chamber: 0.65±0.08 versus 0.56±0.17; \( P = 0.032 \)) in patients with pre-existing LV dysfunction. Peak systolic wall stress was, however, no different at baseline.

**12-Month MR Reduction and LV Remodeling**

**Group 1 Versus Group 2**

In group 1, there was significant improvement in overall MR grade at 12 months (51% mild and 49% moderate; Figure 3A), regurgitant volume (baseline: 45±18 mL versus 12 months: 21±10 mL) and regurgitant fraction (baseline: 42±11% versus 12 months: 23±10%). In group 2, 80% had moderate to severe MR compared with 53% at baseline and 20% had severe MR compared with 40% at baseline, suggesting modest improvement. However, there were no significant changes in regurgitant volume and regurgitant fraction. Group 1 exhibited significant reductions in diastolic and systolic LV dimensions and volumes (Figure 4), LV mass, LV peak wall stress, and sphericity indices from baseline to 12 months, whereas those in group 2 demonstrated no significant changes except in sphericity in the 4-chamber view. FSV increased in group 1, although there was no observed change in LV ejection fraction. Group 2 did not demonstrate an improvement in FSV, or a change in ejection fraction (Table 2).

**Group 1a Versus Group 1b**

At 12 months, there were similar reductions in MR by overall grade (Figure 3B), regurgitant volume, and regurgitant fraction among those with (group 1a) and without (group 1b) baseline LV dysfunction. However, patients in group 1a (baseline LV dysfunction) exhibited significantly greater reductions in LVEDV (−41±30 mL; \( P < 0.0001 \)), LVESV (−24±17
mL; \( P<0.0001 \), left ventricular end-diastolic dimension (-0.5±0.6 cm; \( P=0.0045 \)), and left ventricular end-systolic dimension (-0.5±0.5; \( P=0.0004 \)) from baseline to 12 months, whereas those in group 1b exhibited a significant reduction in only LVEDV (-21±21 mL; \( P<0.0001 \)) and left ventricular end-diastolic dimension (-0.3±0.3 cm; \( P=0.0001 \); Figure 5). FSV (7.3±15.0; \( P=0.055 \)) and LV ejection fraction increased (4.1±4.9; \( P=0.0019 \)) in group 1a, whereas in group 1b, FSV increased (10.6±11.5; \( P=0.0002 \)) and LV ejection fraction decreased (-4.9±6.3; \( P=0.0004 \)). Significant decreases in LV mass, left ventricular peak wall stress, and sphericity indices were observed in group 1a. In group 1b, significant changes were observed in LV mass, left ventricular peak wall stress but not in sphericity indices (Table 3). Although the degree of MR reduction did not differ between groups 1a and 1b (change in regurgitant volume and regurgitant fraction; \( P=\text{not significant} \)), the extent of reduction in LVESV, LVSDs, and improvement in ejection fraction was significantly greater in group 1a.

The present analysis was also performed by removing 2 patients who were deemed to have baseline MR >2+ based on the sites’ assessment but who were later reclassified as having MR ≤2+ by the echocardiography core laboratory. Both of these patients were in group 1 (1 each in groups 1a and 1b). The inclusion of these 2 patients in the analysis does not impact the results and conclusions presented herein.

**Discussion**

In a careful analysis of 64 of 107 patients enrolled in EVEREST I feasibility and safety trial and the roll-in phase of the EVEREST II pivotal trial who had both APS after MitraClip therapy and echo analysis at 12 months, we demonstrate that reduction of MR is associated with sustained reverse remodeling of the left ventricle. These data are the first to demonstrate that mechanical correction of MR using a percutaneous approach is associated with improved LV function. In addition, we examined the association of pre-existing LV dysfunction with the extent of reverse remodeling and found that the reduction in LVESV, improvement in LV ejection fraction, and reduced sphericity were found only in those patients who had evidence of LV dysfunction at baseline as defined by LV ejection fraction <60% or LV end-systolic dimension >4.0 cm. The patients with pre-existing LV dysfunction were more likely to have functional MR. Nevertheless, both groups of patients demonstrated a slight but significant decline in peak wall stress, which is anticipated with the alleviation of the volume overload condition of isolated MR. In patients without LV dysfunction at baseline, the LV ejection fraction declined slightly but remained within normal limits. This finding was associated with a reduction in LVEDV without a change in LVESV or sphericity.

We recently reported the acute hemodynamic effects of MR reduction with the MitraClip device in the same cohort of patients described in this article. Successful MitraClip treatment resulted in immediate increases in FSV and cardiac output with a decrease in systemic vascular resistance and in LV end-diastolic pressure. However, the predischarge echocardiogram performed 24 hours after the procedure showed a reduction in ejection fraction by ≈4% points. The observed reduction in ejection fraction was no longer present at 12 months, although echocardiograms were not available in the entire cohort that was studied at 24 hours. Nevertheless, the current study demonstrates that the favorable changes in hemodynamics persisted in patients with sustained reduction in MR but not in those with recurrent MR. The current analysis also examines the differences in those with and without pre-existing LV dysfunction.

Until recently, the treatment of MR has required surgery, with the exception of a small minority of patients with functional MR who respond to medical therapy or cardiac resynchronization...
therapy. Percutaneous treatment for MR is now under investigation and has for the first time opened the door to nonsurgical treatment of MR through a mechanical correction. During the course of the past 40 years, earlier intervention with improved criteria for patient selection and major advances in surgical treatment and myocardial preservation have improved the outlook for patients with MR. However, ≤20% of patients with degenerative MR still demonstrate an early postoperative decline in ejection fraction. A number of studies have demonstrated that there is an early decline in LV ejection fraction after surgery that is associated with a decrease in LV diastolic volume with no change in LV systolic volume. Some investigators have demonstrated a postoperative increase in LV wall stress because of elimination of LV ejection into the lower pressure left atrium, but others have shown that there is no net increase in LV afterload. However, LV reverse remodeling is likely to be important prognostically.

Prospective studies examining the extent of reverse remodeling after surgical correction of MR are not available. In a study by Suri et al, the recovery of LV function was investigated in 1063 patients undergoing surgical correction of MR who had 2488 echocardiograms available for the analysis. After the initial decline in ejection fraction immediately postoperatively, there was a progressive increase in ejection fraction as the left ventricular end-systolic volume declined to a greater extent than the end-diastolic volume. Predictors of late normalization of the ejection fraction were valve repair as compared with replacement, greater preoperative ejection fraction, and smaller LV dimensions. Other studies have linked late mortality, late ventricular dysfunction, and lack of reverse remodeling to the presence of preoperative LV dysfunction. The degree of LV dysfunction among patients in our cohort was relatively mild compared with those in previous surgical studies. Nevertheless, in 1 study of 27 patients, those with preoperative LV dysfunction who underwent mitral valve repair, there was an initial decline in fractional shortening, which improved during the course of 1 year, such that it returned to normal levels but remained lower than those without preoperative LV dysfunction, although the differences at 1 year did not remain statistically significant. In this small study, a preoperative LV end-systolic dimension >40 mm was the best predictor of early LV dysfunction. In our study of percutaneous mitral valve, the patients with pre-existing LV dysfunction, as defined by a left ventricular end-systolic dimension >40 mm or LV ejection fraction <60%, showed significant reverse remodeling and an improvement in ejection fraction. The recently published mitral surgery cohort of the Acorn study demonstrated a progressive decline in LV volumes and improvement in LV ejection fraction >5 years of follow-up. There was an ≈40-mL decrease in LVEDV among the 91 patients who received mitral valve replacement or repair without cardiac restraint, despite recurrent MR in ≈20%. There are significant differences between this study and the EVEREST cohort. The mean ejection fraction in the Acorn study was 24% compared with 52% in our patients with pre-existing LV dysfunction. Another difference is that we report only matched data, whereas the Acorn study reported results in the entire cohort. Given the 30% mortality at 5 years, it is likely that there was a survivor bias in the data reported at years 3, 4, and 5, exaggerating the impact of MR reduction on LV volumes. Finally, core laboratory analysis of MR in the Acorn study showed 3+ or 4+ MR in only 59% of the enrolled patients compared with 87% of our cohort.

The most salient difference between our study of patients treated with a percutaneous device and previous reports after surgery is that our patients were not subjected to the potentially

Figure 5. Changes of echocardiographic parameters in patients with sustained mitral regurgitation reduction at 12 months (groups 1, 1a, and 1b). A, Changes in left ventricular ejection fraction (LVEF); B, left ventricular end-diastolic volume (LVEDV); and C, left ventricular end-systolic volume (LVESV) between baseline and 12 months.
adverse effects of cardiopulmonary bypass that causes ischemic injury and can lead to impaired systolic and diastolic function. Furthermore, the percutaneous procedure has minimal likelihood of disrupting the subvalvular apparatus. Potential explanations for the differences in reverse remodeling that we observed between the cohort with normal function and those with pre-existing dysfunction can be related to changes in wall stress and the greater hemodynamic impact of a similar degree of MR on a compromised ventricle. The results of this study suggest that patients with mild pre-existing LV dysfunction in the setting of both functional and degenerative MR demonstrated improved LV systolic function and significant reverse remodeling ≤1 year after percutaneous repair. By comparison with data from the surgical literature, it seems that this mechanism of reverse remodeling in subjects with baseline LV dysfunction may be unique to percutaneous treatment. The study is also unique as one of the first reports to include a multiple clinical centers with prospective data collection, an echocardiographic core laboratory, and the American Society of Echocardiography measures of MR severity.

Limitations
The limitations of the current analysis are the relatively small size of the subgroups available for the analysis. The patients included in this study did not have severe LV dilatation or severe reductions in LV ejection fraction. Therefore, the findings of this study cannot be extrapolated to patients with severe dilated cardiomyopathy. The group of patients with pre-existing LV dysfunction included those with both functional and degenerative MR, and specific conclusions cannot be drawn between these 2 subgroups. We did not have complete data available on changes in medication between the 2 time points. Finally, we cannot exclude a floor effect in the group without pre-existing LV dysfunction (group 1b) below which there can be no further reduction in LV volumes.

Conclusions
The current study demonstrates significant reverse remodeling at 12 months after percutaneous correction of hemodynamically significant MR if there is sustained reduction in regurgitation. Significant improvements in LV volumes, shape, and ejection fraction were most pronounced in those patients with echocardiographic evidence of mild pre-existing LV dysfunction. Long-term follow-up of percutaneously treated patients will determine whether the favorable impact of percutaneous treatment of MR on LV remodeling is sustained, and long-term follow-up of the randomized cohort will elucidate whether this benefit is unique to the percutaneous treatment.

Sources of Funding
This work was funded by Abbott Vascular.

Disclosures
Dr Foster reports receiving grant funding and consulting fees from Abbott Vascular and being on the speakers’ bureau for Pri-Med; Dr Feldman receiving research grants and honoraria from Abbott, BSC, and Edwards Lifesciences; Dr Weissman receiving research grant from Abbott Vascular; Dr Grayburn receiving research grant and consulting fees from Abbott Vascular; Dr Kar receiving research grant and consulting honoraria from Abbott Vascular; Dr Fail being a member of CardioSolutions advisory board and having ownership interests in Objective Medical Systems; Dr Hermiller receiving consulting honoraria from Abbott

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**Table 3. Change in Echocardiographic Variables From Baseline to 12 Months in Patients With Mitral Regurgitation ≤2+ at 12 Months With and Without Pre-existing Left Ventricular Dysfunction**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group 1a: Continued Success+Pre-existing LV Dysfunction (n=20)</th>
<th>Group 1b: Continued Success+No Pre-existing LV Dysfunction (n=29)</th>
<th>P Value* Groups 1a and 1b Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV, mL</td>
<td>Baseline: 40.5±13.8 (17) 12 mo: 19.1±8.0 (17)</td>
<td>49.9±19.9 (18) 12 mo: 22.3±11.5 (18)</td>
<td>&lt;0.0001 0.29</td>
</tr>
<tr>
<td>RF, %</td>
<td>Baseline: 38.9±10.4 (17) 12 mo: 22.4±9.4 (17)</td>
<td>45.1±11.4 (18) 12 mo: 24.2±11.4 (18)</td>
<td>&lt;0.0001 0.35</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>Baseline: 195.5±36.2 (20) 12 mo: 155.0±31.6 (20)</td>
<td>152.2±34.7 (27) 12 mo: 131.0±32.9 (27)</td>
<td>&lt;0.0001 0.013</td>
</tr>
<tr>
<td>LVESD, mL</td>
<td>Baseline: 94.5±25.3 (20) 12 mo: 70.2±22.3 (20)</td>
<td>51.8±12.8 (27) 12 mo: 51.8±18.0 (27)</td>
<td>0.99 &lt;0.0001</td>
</tr>
<tr>
<td>LVEDDD, cm</td>
<td>Baseline: 5.8±0.7 (19) 12 mo: 5.4±0.7 (19)</td>
<td>5.2±0.5 (25) 12 mo: 5.0±0.5 (25)</td>
<td>0.0001 0.24</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>Baseline: 51.4±8.1 (19) 12 mo: 55.5±8.0 (19)</td>
<td>65.9±4.0 (27) 12 mo: 60.9±6.3 (27)</td>
<td>0.0004 &lt;0.0001</td>
</tr>
<tr>
<td>FSV, mL</td>
<td>Baseline: 61.8±16.0 (18) 12 mo: 69.1±16.6 (18)</td>
<td>58.2±13.7 (24) 12 mo: 68.7±15.7 (24)</td>
<td>0.0002 0.43</td>
</tr>
<tr>
<td>Sphericity index (2C)</td>
<td>Baseline: 0.63±0.09 (20) 12 mo: 0.57±0.06 (20)</td>
<td>0.59±0.05 (24) 12 mo: 0.58±0.06 (24)</td>
<td>0.88 0.007</td>
</tr>
<tr>
<td>Sphericity index (4C)</td>
<td>Baseline: 0.65±0.08 (20) 12 mo: 0.59±0.08 (20)</td>
<td>0.56±0.17 (29) 12 mo: 0.55±0.18 (29)</td>
<td>0.44 0.03</td>
</tr>
<tr>
<td>LV mass indexed (Devereaux equation)</td>
<td>Baseline: 209.2±55.3 (19) 12 mo: 173.3±39.2 (19)</td>
<td>158.3±47.7 (25) 12 mo: 145.0±32.8 (25)</td>
<td>0.035 0.05</td>
</tr>
<tr>
<td>LV peak wall stress, dynes/cm²</td>
<td>Baseline: 229.2±69.7 (15) 12 mo: 197.6±56.5 (15)</td>
<td>205.2±41.4 (20) 12 mo: 175.9±29.4 (20)</td>
<td>0.0003 0.88</td>
</tr>
</tbody>
</table>

FSV indicates forward stroke volume; LV, left ventricular; LVEDD, LV end-diastolic dimension; LVEDV, LV end-diastolic volume; LVEF, LV ejection fraction; LVESD, LV end-systolic dimension; and LVEF, LV end-systolic volume; RF, regurgitant fraction; and RV, regurgitant volume.

*The columns of P values are not corrected for multiple testing. To be statistically significant after correction for multiple testing because of the 12 outcomes in a column, a P value needs to be <0.05/12=0.0042.
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CLINICAL PERSPECTIVE

Percutaneous repair of mitral regurgitation offers a potential therapy for patients with 3 to 4+ mitral regurgitation, avoiding the potential adverse impact of surgery especially in patients with pre-existing left ventricular (LV) dysfunction. This analysis demonstrates that reduction in mitral regurgitation through percutaneous repair is associated with reverse remodeling and improved LV ejection fraction in patients with pre-existing LV dysfunction. Although the patients in this analysis had relatively mild LV dysfunction, they constitute a group deemed to be at higher risk for surgery based on previous studies. This group of patients with pre-existing LV dysfunction comprised patients with either functional or degenerative mitral regurgitation. The relatively small numbers of each subset do not permit comparisons by the category of mitral regurgitation. We also cannot compare the results to surgical reduction of mitral regurgitation in this population. The major finding in this study is, that at 1 year, higher risk patients with mitral regurgitation, as defined by LV ejection fraction <60% or left ventricular end-systolic dimension >40 mm, had improvements in ejection fraction and reductions in LV volumes and mass, which were greater than those without pre-existing LV dysfunction. This study shows that the previously reported improvements in clinical status in this cohort of patients were accompanied by structural and functional long-term changes that potentially impact long-term outcomes in patients with mitral regurgitation.
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