The Relationship between the Magnitude of Reduction in Mitral Regurgitation Severity and Left Ventricular and Left Atrial Reverse Remodeling after MitraClip® Therapy

Running title: Grayburn et al.; Reverse remodeling post percutaneous mitral repair

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Abstract

Background—MitraClip has been shown to reduce mitral regurgitation (MR) severity safely but to a lesser degree than surgery. No data exist on the magnitude of MR reduction necessary to reverse left ventricular (LV) and left atrial (LA) dilation in patients with severe MR. Therefore, an analysis was performed to evaluate the relationship between MR reduction and LV and LA volumes after MitraClip therapy.

Methods and Results—A total of 801 patients treated with MitraClip and 80 patients treated surgically were included. All patients had severe (3-4+) MR. MR severity, LV volumes at end-diatole (LVEDV) and end-systole (LVESV) and LA volumes were measured at baseline, discharge, 30 days, 6 months and 1 year by an independent echocardiographic core laboratory. A linear repeated measures model was developed to determine the relationship between MR severity and time of measurement post-index procedure on longitudinal LV and LA volumes. Separate models were fit for functional (FMR) and degenerative MR (DMR). In both DMR and FMR, reduction in LVEDV was associated with degree of residual MR at 12 months (p<0.0001). LVESV was significantly reduced in FMR but not DMR. LA volumes were significantly related to reduction of MR severity in both groups.

Conclusions—Reduction of LVEDV and LA volumes, but not LVESV in DMR is consistent with correction of volume overload from primary MR. Reduction of all three measurements in FMR demonstrates reverse remodeling when MR severity is reduced to either 1+ or 2+ by MitraClip therapy.

Clinical Trial Registration Information—www.clinicaltrials.gov. Identifier: NCT00209274.

Key words: percutaneous mitral valve repair, mitral regurgitation, reverse remodeling
Chronic severe mitral regurgitation (MR) imposes a pure volume overload on the left heart,\(^1\) which in turn causes dilation of the left ventricle (LV) and left atrium (LA). Clinical manifestations of uncorrected severe MR include heart failure, pulmonary hypertension, atrial fibrillation and death.\(^2\) When MR is due to a primary leaflet abnormality, surgical repair or chord-sparing valve replacement usually eliminates MR, resulting in prevention or regression of LV and LA dilation.\(^1,2\) Current guidelines recommend surgery for severe primary MR when accompanied by symptoms, LV dysfunction, atrial fibrillation, or pulmonary hypertension.\(^3,4\)

Surgery is also indicated in asymptomatic patients with severe MR if the likelihood of valve repair is at least 90%.\(^3,4\) In centers of excellence, degenerative MR (DMR) due to mitral valve prolapse or flail leaflet can almost always be repaired with elimination of MR.\(^5\) However, when MR is secondary to underlying LV dysfunction, the need for surgery is uncertain. Although secondary or functional MR (FMR) is associated with an adverse prognosis,\(^6-10\) it is not clear that mitral valve annuloplasty or replacement reverses the underlying LV dysfunction. MR may also recur after mitral annuloplasty due to continuing LV remodeling with tenting of the mitral leaflets.\(^11,12\) Therefore, current guidelines recommend surgery for FMR only in patients scheduled to undergo coronary bypass surgery.\(^3,4\)

The development of percutaneous device therapy for MR offers the potential to reduce MR severity without sternotomy/thoracotomy or cardiopulmonary bypass. The MitraClip System (MitraClip) is a first-of-a-kind transcatheter mitral valve repair system design to reduce significant MR by clipping together the leaflets of the mitral valve. In a randomized trial of MitraClip versus surgery, MitraClip reduced MR safely, but to a lesser degree than surgery.\(^13\) Both MitraClip and surgery improved LV volumes and quality of life measures. Subsequent non-randomized studies of MitraClip have consistently shown clinically meaningful
improvements in hemodynamic, echocardiographic and quality of life measures, even with moderate residual MR present. These findings imply that even modest reduction of MR is beneficial. However, it is not clear how much improvement in MR severity is necessary to result in reverse remodeling of the LV or LA. Therefore, this study was performed to explore the relationship between the magnitude of reduction in MR severity and reduction in LV and LA volumes in patients treated with MitraClip or surgery in the EVEREST clinical trials program. The relationship between change in MR severity and reduction in left heart volumes was also examined by etiology. A statistical modeling approach was used to take advantage of the large amount of repeated echocardiographic measures of MR severity, LV and LA volumes over time in the same patients.

Methods

Patient population

The EVEREST (Endovascular Valve Edge-to-Edge Repair Study) II clinical studies were designed to assess the safety and effectiveness of the MitraClip device in patients with severe MR (3+ or 4+ as per ACC/AHA Guidelines). The EVEREST II randomized controlled trial compared the safety and effectiveness of the MitraClip to surgery in non-high risk patients who were surgical candidates. A total of 178 patients were treated with the MitraClip and 80 patients treated with surgery in this study; these data have been reported in detail. In the single-arm EVEREST II High Risk Study, 78 patients who were poor operative candidates due to high surgical risk were treated with the MitraClip. In a continued access study of EVEREST II (REALISM), 273 high-risk patients and 272 non-high risk patients received the MitraClip and had one-year follow up echocardiography analyzed by the core laboratory. This analysis
included the 801 patients treated with MitraClip and the 80 patients treated surgically in these studies, for a total of 881 patients. The trials are registered at www.clinicaltrials.gov (number NCT00209274).

Data Collection

Echocardiograms were collected at baseline, 30 days, 6 months and 12 months using a standardized protocol and were assessed by an independent core laboratory (University of California San Francisco or MedStar Research Institute, Washington, DC). MR severity was graded per American Society of Echocardiography (ASE) guidelines using an integrative method that incorporated both quantitative and qualitative criteria. Quantitative measurements included vena contracta width, effective regurgitant orifice area, regurgitant volume, and regurgitant fraction. Qualitative measures included jet size and eccentricity, mitral inflow pattern, and pulmonary venous flow patterns. Details of MR grading pre- and post-MitraClip have been previously reported. LV volumes and ejection fraction were measured using the biplane method of disks. LA volumes were measured by biplane method.

Statistical Analysis

Baseline demographics and clinical characteristics were summarized for each cohort using means and standard deviations for continuous measures and counts and proportions for categorical measures. MR severity and left heart volume measures were analyzed in patients treated with MitraClip or MV surgery to evaluate the association between MR severity and measures of LV end-diastolic volume (LVEDV), end-systolic volume (LVESV), and left atrial volume (LAV). Specifically, echocardiographic core lab measures of MR, LVEDV, LVESV, and LAV were analyzed over time, and linear mixed effect models were fit to examine the various associations. Repeated measures from individual patients were used to generate the
models; a compound symmetric covariance structure was assumed to account for repeated measures within subject. Models were then used to estimate changes in measures of LV and LA volumes associated with changes in MR severity between baseline and 12 months. For each measure, the model included MR severity as measured by the core lab and the follow up time period (days) as independent variables. Separate models were fit for DMR and FMR, and for MitraClip and surgery. Model fit was evaluated by analyzing residuals; there was no evidence of lack of fit.

Data on all patients, including those with missing values at one or more time points, were included in the models. Predicted mean changes and their standard errors were derived using Proc Mixed in SAS version 9.2. Data presented graphically are shown as predicted mean change together with 95% confidence intervals.

Results
Demographic and clinical variables for the study population are shown in Table 1; the high risk cohort combines patients from the EVEREST II High Risk and REALISM High Risk studies. Patients in the high risk cohort were approximately 10 years older than those in the randomized clinical trial. They also had more severe comorbidities, as demonstrated by a mean STS score of 11.3%, roughly 3-fold higher than in the randomized clinical trial. LVEF was lower and LVESV higher in the high risk cohort, which was predominantly FMR, whereas the randomized clinical trial was predominantly DMR. Table 2 shows demographic and clinical variables at baseline and one year according to etiology of MR. As expected, patients with FMR tended to have lower LVEF and larger LV dimensions than patients with DMR. Table 3 shows demographic and clinical variables at baseline and one year according to degree of residual MR severity one
year after MitraClip therapy. Blood pressure and heart rate were similar for patients with different degrees of residual MR severity. Reduction in LV and LA volumes from baseline to 12 months were similar in patients with residual MR severity of ≤ 1+ or 2+ at one year. In contrast, there was no clinically important changes in LV or LA volumes in patients with residual MR severity of 3-4+ at one year, nor was there an increase in forward stroke volume.

This analysis included 3,368 evaluable echocardiograms from 881 patients who were enrolled as described previously. Of these, there were 855 echocardiograms at baseline, 1,146 at discharge or 30 days, 719 at 6 months, and 648 at one year. MitraClip was implanted in 745 of the 801 patients (93%) who underwent the MitraClip procedure, all of whom had severe (3-4+) site-assessed MR at baseline. Reduction of MR severity to ≤ 2+ at discharge was achieved in 657 of 801 patients (82%) treated with MitraClip and in all 80 surgically treated patients. There was no difference in the proportion of patients achieving discharge MR severity ≤ 2+ for patients with DMR (81%) and FMR (84%).

Figure 1 shows the model-predicted mean change in LVEDV together with the 95% CI at one year for patients treated with MitraClip (left panels) and surgery (right panels). For patients with DMR treated with MitraClip, there is a progressive decrease in predicted mean change in LVEDV at one year for each level of MR reduction. Predicted mean change in LVEDV at one year is -30ml for ≤1+ residual MR, -21ml for 2+, and -10 for 3-4+ MR. This relationship is statistically significant (p<0.0001). A similar relationship is presented for patients treated surgically, with even larger predicted mean change in LVEDV for ≤ 1+ residual MR (p<0.0001). Confidence intervals are wider for the surgery group because of small numbers of patients, particularly in the 2+ residual MR (n=57 with MR ≤=1+, n=18 with MR=2+). For patients with FMR treated with MitraClip, the relationship between mean change in LVEDV and
MR reduction was similar to that of DMR patients. Predicted mean LVEDV at one year was -24ml for ≤ 1+ residual MR, -18ml for 2+, and -7ml for 3-4+ MR (p<0.0001). Similar results are shown in the surgery group, but wide confidence intervals are present because of the small numbers of patients (n=16 with MR<1+, 13 with MR=2+ for FMR), thus precluding statistical comparison between MitraClip and surgery models.

**Figure 2** shows the model-predicted mean change in LVESV at one year together with the 95% CI for patients treated with MitraClip (left panels) and surgery (right panels). For patients with DMR treated with MitraClip, the association between LVESV and MR is not statistically significant. Predicted mean change in LVESV at one year is -5ml for 1+ residual MR, -4ml for 2+, and -4ml for 3-4+ MR (p=0.2693). For patients treated surgically, the relationship is statistically significant (p=0.0005), however confidence intervals are wide due to small numbers.

For patients with FMR treated with MitraClip, the relationship between LVESV and MR is statistically significant (p<0.0001). Predicted mean change in LVESV at one year is -12ml for ≤ 1+ residual MR, -9ml for 2+, and -4ml for 3-4+ MR (p<0.0001). Similar magnitudes of predicted change are shown in the surgery group, but wide confidence intervals are present due to small patient numbers, and the relationship between MR and LVESV did not reach significance (p=0.4553).

**Figure 3** shows the model-predicted mean change in LAV at one year together with the 95% CI for patients treated with MitraClip (left panels) and surgery (right panels). There is a significant decrease in mean LAV with greater magnitude of MR reduction for DMR treated with MitraClip. Predicted mean change in LAV at one year was -13ml for ≤ 1+ residual MR, -8ml for 2+, and -2 for 3-4+ MR (p<0.0001). Surgically treated DMR patients also have a statistically significant relationship between MR severity and mean change in LAV (p<0.0001),
with a larger decrease in LAV for patients with ≤ 1+ residual MR. The confidence intervals for surgery patients are again wide due to small numbers of patients. For patients with FMR treated with MitraClip, the relationship between mean change in LAV and MR is statistically significant (p<0.0001). Predicted mean change in LAV at one year is -9ml for ≤ 1+ residual MR, -7ml for 2+, and -3ml for 3-4+ MR. For patients with FMR treated surgically, there is no difference in LA volumes between patients with ≤ 1+ or 2+ residual MR, but wide confidence intervals are present because of the small patient numbers.

Discussion

Treatment with the MitraClip System

This is the first study to systematically estimate the effect of improved MR severity on LV and LA volumes after percutaneous mitral valve repair. The results demonstrate convincing evidence that reduction of MR severity with MitraClip is associated with reverse LV and LA remodeling. In general, greater remodeling was observed with a greater degree of MR reduction. Importantly, even reduction of MR severity to moderate (2+) is associated with LV and LA reverse remodeling. Some slight differences in response were evident in DMR versus FMR patients, as will be discussed.

Response in DMR

In patients with DMR, model-predicted LVEDV improved proportionally to the degree of MR reduction at one year. In contrast, model-predicted LVESV was slightly reduced for all degrees of MR reduction, but this difference was not statistically significant in DMR patients treated with MitraClip. This is what one would anticipate for correction of the pure volume overload of primary MR since LVEDV is a rough surrogate for pre-load and LVESV a rough surrogate for
afterload. Additionally, since LVESV was not increased at baseline in the DMR subgroup, no improvement would be expected. Further support for relief of volume overload associated with MR reduction by MitraClip is manifested by acute hemodynamic changes during implant, including increased forward stroke volume and reduction in LVEDV and LV end-diastolic pressure. Model-predicted LAV also decreased in a proportional fashion, again as one would expect for correction of the volume overload of MR.

Two prior studies have retrospectively reported the results of surgery for DMR in reducing LV dimensions by echocardiography. Suri, et al reported on 1,063 patients who underwent surgery for DMR at the Mayo Clinic. Repair was performed in 924 (87%), 95% of whom had MR reduced to none or mild (1+). LVEDV was not reported, but LV end-diastolic diameter was reduced from 60 to 51 mm at one year. LV end-systolic diameter was reduced to a lesser degree from 37 to 35 mm, and LVEF declined from 62 to 55%. Shafii, et al reported similar findings in 2,778 patients operated at the Cleveland Clinic. LV end-diastolic diameter declined from 57 to 49 mm, LV end-systolic diameter from 34 to 31 mm, and LVEF from 58 to 53%. Both of these studies demonstrated greater LV reverse remodeling in patients with normal LV size and LVEF pre-operatively. In the present study, DMR patients had normal LVEF and LV size.

Reduction in LAV after surgical repair of DMR has been previously reported. The current findings confirm that MR reduction is associated with LA reverse remodeling in DMR. The direct relationship of LA remodeling after surgical or percutaneous reduction of MR and outcomes is not known. However, a dilated LA is a marker of adverse outcomes in MR patients.

Response in FMR
In patients with FMR, LVEDV improved proportionally to the degree of MR reduction at one year, and these results were of similar magnitude as seen in DMR patients. Unlike DMR patients, FMR patients also exhibited a proportional decrease in LVESV at one year. This implies that in FMR, not only is the volume overload state of MR improved, but salutary effects on LV wall stress might also occur. However, this remains speculative since we did not directly measure preload, afterload, or LV mass in this study. However, similar findings were observed in the mitral valve surgery arm of the Acorn Clinical Trial. In that study of mostly non-ischemic cardiomyopathy patients randomized to mitral surgery with or without the CorCap ventricular support device, LVEDV was reduced by roughly 35 ml at one year and LVESV reduced by roughly 25 ml. Further reductions were observed over time, and the results remained stable out to 5 year follow up. These changes were associated with improved measures of symptom status and quality of life, as were reported in both EVEREST II and EVEREST High Risk patients. While the general results of ACORN and the present study show similar findings with regard to LV remodeling, there are important differences in patient characteristics. Patients in ACORN all had LVEF < 35% and LV end-diastolic diameter > 6.0 cm. In contrast, the mean LVEF in the FMR group was 43±12% and mean LV end-diastolic diameter was 5.8±0.7 cm. Patients with LVEF <20% or LV end-systolic diameter > 5.5 cm (EVEREST II) or > 6.0 cm (High Risk) were excluded because of concern that the MitraClip could not grasp both mitral leaflets in markedly dilated ventricles. Larger decreases in LV chamber volumes are expected when the baseline chamber dimensions are larger, as they were in the ACORN trial.

**Comparison to Surgery**

In patients treated surgically in the EVEREST II study, similar patterns of reduction in LVEDV and LVESV were observed for both DMR and FMR, but with a greater magnitude of reverse
remodeling. This is likely due to the fact that surgery resulted in greater reduction of MR severity than MitraClip, as previously reported. For example, surgery often eliminates MR (especially DMR), such that the ≤1+ MR group contains a large number of patients with no MR. In contrast, the ≤1+ MR group for MitraClip is predominantly comprised of mild residual MR, as MitraClip rarely completely eliminates MR. The surgical data are presented as validation of the modeling results. It is not appropriate to directly compare the 80 surgical patients to the 801 MitraClip patients because most of the latter group were not randomized. Nevertheless, MR reduction with the MitraClip appears to be independent of risk status, as roughly 80-85% of patients in non-high risk and high risk studies have reduction of MR severity to moderate (2+) or less. Additionally, in contrast to analysis of surgical results, the analyses of patients treated percutaneously does provide insight into the relationship between the effect of various degrees of MR reduction on LV reverse remodeling without the confounding effects of sternotomy or cardiopulmonary bypass.

**Limitations**

The development of 3-dimensional echocardiographic (3D) technology has offered more precise and accurate quantification of LV volumes and MR severity. Despite the use of expert core laboratory facilities and a standardized guidelines-based approach, MR quantification can be challenging after MitraClip placement. It is possible that the small decrease in LV volumes seen even in patients with residual 3-4+ MR reflects a small decrease in regurgitant volume that is sufficient to reduce LV volumes without changing MR grade to 2+ or better. The assessment of MR severity after distortion of the mitral orifice by placement of 1 or 2 MitraClip devices is further complicated. Future studies with 3D echocardiographic measurement of regurgitant volume and regurgitant orifice area may shed further light on this issue. This study used a
statistical model to estimate changes in LV and LA volumes based on MR grading as assessed by a core laboratory. Although one might prefer actual volumes, the model is advantageous in that it 1) includes all available data from all patients, including data from expired or withdrawn patients through their last available follow-up echo prior to death (e.g., discharge, 30 days and/or 6 months as applicable) and 2) smooths out measurement error in MR grade and/or volume measurements by utilizing the large amount of longitudinal data available. It is possible that patients who died prior to a 12-month echo may have had higher LV and LA volumes than survivors in our model with 12-month data. It is well established that severe MR is associated with increased mortality. Reverse remodeling is not expected to occur with ongoing severe MR. The exclusion of 12 month data for these expired patients may explain the slight improvement from baseline in volumes observed in patients with 3+ or 4+ MR at 12 months. However, this potential survivors’ bias if anything, represents a conservative analysis and would not be expected to alter the conclusions.

Finally, MitraClip implantation is limited to patients who have severe MR and are anatomically suitable for device placement. Patients with markedly dilated LV are generally excluded and were not represented in this model.

Conclusions

Reduction of LVEDV and LA volumes, but not LVESV in DMR is consistent with correction of volume overload from primary MR. Reduction of all three measurements in FMR demonstrates reverse remodeling that appears to be similar in magnitude whether MR severity is reduced to 1+ or 2+ by the MitraClip.
Disclaimer: MitraClip is an investigational device only in the U.S. Not available for sale in the U.S.


References:


Table 1. Baseline demographic and clinical variables.

<table>
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<th></th>
<th>High Risk Cohort MitraClip (n=351)</th>
<th>Non-High Risk Cohort MitraClip (n=272)</th>
<th>EVEREST II Randomized Trial MitraClip (n=178)</th>
<th>Surgery (n=80)</th>
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<tr>
<td>Age (years)</td>
<td>76 ± 11</td>
<td>74 ± 11</td>
<td>67 ± 13</td>
<td>65 ± 13</td>
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<tr>
<td>Male</td>
<td>61%</td>
<td>53%</td>
<td>64%</td>
<td>66%</td>
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<td>Body Surface Area (m²)</td>
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<td>Prior Cardiac Surgery</td>
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<td><strong>Echocardiography</strong></td>
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<tr>
<td>LVEF (%)</td>
<td>47 ± 14</td>
<td>56 ± 11</td>
<td>60 ± 10</td>
<td>61 ± 11</td>
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<td>LVEDV (mL)</td>
<td>159.2 ± 53.8</td>
<td>130.4 ± 42.8</td>
<td>157.5 ± 38.9</td>
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<td>LVESV (mL)</td>
<td>87.4 ± 45.7</td>
<td>59.2 ± 29.8</td>
<td>64.1 ± 25.5</td>
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<td>LA Volume (mL)</td>
<td>87.4 ± 42.6</td>
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<td>85.9 ± 28.8</td>
<td>84.4 ± 30.5</td>
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<td>LVIDd (cm)</td>
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<td>3.7 ± 0.9</td>
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<td>LVIDs (cm)</td>
<td>5.6 ± 0.8</td>
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<tr>
<td>Etiology of MR (%FMR)</td>
<td>70%</td>
<td>31%</td>
<td>27%</td>
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Table 2. Patient demographics and clinical variables at baseline and 12 months according to etiology. *(individual n’s at 12 months may vary based on availability of data)

<table>
<thead>
<tr>
<th>Clinical Measures and Outcomes</th>
<th>Degenerative MR (n=422)</th>
<th>Functional MR (n=379)</th>
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<tr>
<td></td>
<td>Baseline</td>
<td>12 months*</td>
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<tr>
<td>Blood Pressure – Systolic (mm Hg)</td>
<td>128 ± 19</td>
<td>125 ± 20</td>
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<tr>
<td>Blood Pressure – Diastolic (mm Hg)</td>
<td>71 ± 12</td>
<td>70 ± 11</td>
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<tr>
<td>Heart Rate (beats/min)</td>
<td>70 ± 13</td>
<td>68 ± 12</td>
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<td>Core Lab MR grade ≤1+ (%)</td>
<td>0.3%</td>
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<td>Core Lab MR grade 2+ (%)</td>
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<td>46.5%</td>
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<td>Core Lab MR grade 3+/4+ (%)</td>
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Echocardiography

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<th></th>
<th>Degenerative MR (n=422)</th>
<th>Functional MR (n=379)</th>
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<tbody>
<tr>
<td>LVEF (%)</td>
<td>62 ± 8</td>
<td>59 ± 8</td>
</tr>
<tr>
<td>LVEDV (mL)</td>
<td>139.6 ± 40.5</td>
<td>119.6 ± 35.5</td>
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<tr>
<td>LVESV (mL)</td>
<td>52.9 ± 21.2</td>
<td>49.5 ± 19.9</td>
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<tr>
<td>LVIDd (cm)</td>
<td>5.2 ± 0.7</td>
<td>4.9 ± 0.7</td>
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<tr>
<td>LVIDs (cm)</td>
<td>3.4 ± 0.7</td>
<td>3.3 ± 0.7</td>
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<tr>
<td>LA Volume (mL)</td>
<td>90. ± 34.5</td>
<td>82.2 ± 33.2</td>
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Table 3. Demographic and clinical variables according to degree of residual MR at 12 months. (presented for survivors with interpretable or available data at both baseline and 12 months; individual paired n’s denoted in parentheses)

<table>
<thead>
<tr>
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<th>≤ 1+ MR</th>
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<th>2+ MR</th>
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<th>3-4+ MR</th>
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<td></td>
<td>Baseline</td>
<td>12 mo</td>
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<td><strong>Clinical Measures and Outcomes</strong></td>
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<tr>
<td>Blood Pressure – Systolic (mm Hg)</td>
<td>124 ± 19 (168)</td>
<td>125 ± 21 (168)</td>
<td>125 ± 19 (192)</td>
<td>123 ± 18 (192)</td>
<td>126 ± 20 (77)</td>
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<td>Blood Pressure – Diastolic (mm Hg)</td>
<td>70 ± 11 (168)</td>
<td>69 ± 12 (168)</td>
<td>70 ± 13 (192)</td>
<td>69 ± 11 (192)</td>
<td>70 ± 12 (77)</td>
<td>69 ± 11 (77)</td>
</tr>
<tr>
<td>Heart Rate (beats/min)</td>
<td>72 ± 13 (201)</td>
<td>69 ± 11 (201)</td>
<td>72 ± 15 (241)</td>
<td>70 ± 12 (241)</td>
<td>73 ± 11 (93)</td>
<td>69 ± 11 (93)</td>
</tr>
<tr>
<td><strong>Echocardiography</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>54 ± 14 (185)</td>
<td>52 ± 12 (185)</td>
<td>54 ± 13 (221)</td>
<td>52 ± 12 (221)</td>
<td>55 ± 13 (92)</td>
<td>55 ± 13 (92)</td>
</tr>
<tr>
<td>LVEDV (mL)</td>
<td>152.4 ± 46.9 (186)</td>
<td>124.6 ± 42.1 (186)</td>
<td>143.2 ± 48.8 (221)</td>
<td>133.3 ± 43.9 (221)</td>
<td>160.9 ± 45.9 (92)</td>
<td>151.5 ± 48.3 (92)</td>
</tr>
<tr>
<td>LVESV (mL)</td>
<td>72.9 ± 37.1 (185)</td>
<td>63.0 ± 35.6 (185)</td>
<td>69.9 ± 38.8 (221)</td>
<td>66.8 ± 35.2 (221)</td>
<td>74.6 ± 38.0 (92)</td>
<td>71.8 ± 39.0 (92)</td>
</tr>
<tr>
<td>LVIDd (cm)</td>
<td>5.5 ± 0.8 (198)</td>
<td>5.1 ± 0.8 (198)</td>
<td>5.4 ± 0.7 (242)</td>
<td>5.2 ± 0.7 (242)</td>
<td>5.6 ± 0.7 (94)</td>
<td>5.4 ± 0.7 (94)</td>
</tr>
<tr>
<td>LVIDs (cm)</td>
<td>4.0 ± 1.0 (191)</td>
<td>3.8 ± 1.0 (191)</td>
<td>3.9 ± 1.0 (230)</td>
<td>3.8 ± 1.0 (230)</td>
<td>4.0 ± 1.0 (90)</td>
<td>3.9 ± 1.0 (90)</td>
</tr>
<tr>
<td>LA Volume (mL)</td>
<td>89.6 ± 34.3 (184)</td>
<td>76.5 ± 32.6 (184)</td>
<td>87.0 ± 34.0 (214)</td>
<td>81.4 ± 29.0 (214)</td>
<td>89.9 ± 32.4 (82)</td>
<td>90.3 ± 33.7 (82)</td>
</tr>
<tr>
<td>Etiology of MR (%FMR)</td>
<td>48.8% (104/213)</td>
<td></td>
<td>42.7% (109/255)</td>
<td></td>
<td>42.7% (41/96)</td>
<td></td>
</tr>
</tbody>
</table>
**Figure Legends:**

**Figure 1.** Relation of predicted change in LVEDV to residual MR severity. Model-predicted mean change in left ventricular end-diastolic volumes (LVEDV) from baseline to 12 months with the 95% CI by residual mitral regurgitation severity at one year for patients treated with MitraClip (left panels) and surgery (right panels). Data is presented separately for patients with degenerative mitral regurgitation (DMR; top panels) and functional mitral regurgitation (FMR; bottom panels).

**Figure 2.** Relation of predicted change in LVESV to residual MR severity. Model-predicted mean change in left ventricular end-systolic volumes (LVESV) from baseline to 12 months with the 95% CI by residual mitral regurgitation severity at one year for patients treated with MitraClip (left panels) and surgery (right panels). Data is presented separately for patients with degenerative mitral regurgitation (DMR; top panels) and functional mitral regurgitation (FMR; bottom panels).

**Figure 3.** Relation of predicted change in LA volumes to residual MR severity. Model-predicted mean change in left atrial (LA) volumes from baseline to 12 months with the 95% CI by residual mitral regurgitation severity at one year for patients treated with MitraClip (left panels) and surgery (right panels). Data is presented separately for patients with degenerative mitral regurgitation (DMR; top panels) and functional mitral regurgitation (FMR; bottom panels).
Figure 1

Change in LVEDV, DMR MitraClip

Change in LVEDV, DMR Surgery

Change in LVEDV, FMR MitraClip

Change in LVEDV, FMR Surgery

MR Severity at 12 Months
Figure 2
Figure 3

Change in LA vol, DMR MitraClip

Change in LA vol, DMR Surgery

Change in LA vol, FMR MitraClip

Change in LA vol, FMR Surgery
The Relationship between the Magnitude of Reduction in Mitral Regurgitation Severity and Left Ventricular and Left Atrial Reverse Remodeling after MitraClip® Therapy
Paul A. Grayburn, Elyse Foster, Chithra Sangli, Neil J. Weissman, Joseph Massaro, Donald G. Glower, Ted Feldman and Laura Mauri

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