Valvular Heart Disease

Echo-Guided Mitral Repair

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Background—Echocardiography is available in the most basic healthcare environments. Mitral repair is potentially curative and, when possible, recommended over replacement. The efficacy of echo-guided repair has not been established.

Methods and Results—We developed a succinct set of precisely defined images observed to be highly concordant with intraoperative findings. These images guided intervention on 237 consecutive patients. None were lost to follow-up, and serial echocardiography was obtained on all repairs. This analysis includes 2037 echocardiograms. The intent to repair or replace was documented preoperatively in 98.7%. Concordance was associated with successful repair (97.8% versus 57.1%; P=0.001). Three-dimensional concordance was higher than 2-dimensional (100% versus 94.4%; P=0.05). Echocardiography guided a graduated surgical approach for degenerative and myopathic repairs by quantifying segmental prolapse, anterior leaflet closing angles, and tenting for integration of secondary chord lysis (P<0.001) and commissural width (P<0.01). Repair rates increased from 46.5% to 77.6% (P<0.001). Concomitant Society of Thoracic Surgeons rates were 46.6% (versus unguided 46.5%; P=0.99) and 54.9% (versus echo guided 77.6%; P<0.001). Repair was successful in 91.5% of isolated echo-guided mitral operations (versus concomitant Society of Thoracic Surgeons 70.0%; P<0.001). Echo-guided repair rates for degenerative, myopathic, and inflammatory diseases were 99.0%, 97.1%, and 84.2% with linearized annual recurrent regurgitation of 0.63%, 2.19%, and 4.37%, respectively.

Conclusions—Echocardiography can reliably identify repairable mitral disease and guide intervention. Echo-guided repair is associated with a higher rate of initial success than unguided historical and concomitant national controls. Three-dimensional echo improves concordance. Secondary chord lysis is associated with durable repair and may prevent ventricular remodeling. (Circ Cardiovasc Imaging. 2014;7:132-141.)

Key Words: chordal-cutting ■ echocardiography ■ mitral valve insufficiency

Mitral regurgitation (MR) is a growing global health problem that affects millions worldwide.1,2 Severe regurgitation rarely resolves with medical therapy.3,4 Mitral repair is potentially curative and often provides excellent long-term event-free survival.5,7 When compared with repair, valve replacement increases operative mortality and, in the absence of maintenance anticoagulation or reintervention, eventually results in death from prosthetic failure.8 Even minor improvements in diagnosis and management of mitral disease would be expected to significantly reduce morbidity and mortality, especially for the medically underserved.1

Clinical Perspective on p 141

Mitrval valve repair is indicated for patients with symptomatic severe regurgitation and asymptomatic patients with evidence of left ventricular dysfunction.9 Repair may also be indicated for asymptomatic patients with severe regurgitation and normal ventricular function.4 Although repair is superior to replacement, repair is currently accomplished in <60% of mitral operations and no higher than 85% in the most optimally selected subgroups.8,10

Echocardiography is neither resource intensive nor invasive and is clinically available in even the most basic healthcare environments.1,11 Transesophageal echocardiography (TEE) is indispensible for optimal management of mitral disease.12 Recent reports indicate that TEE accurately and consistently demonstrates mitral leaflet dysfunction.13-17 However, the efficacy of echo-guided mitral repair has not been established.18,19

We developed a succinct set of precisely defined images observed to be highly concordant with intraoperative findings. These images were formally integrated into preoperative TEE and used to categorize the underlying disease, characterize lesions, describe leaflet dysfunction, identify repairable valves, and guide intervention. This study was designed to determine whether defined protocol-driven preoperative echocardiography would improve intraoperative concordance and thereby identify repairable mitral disease, guide intervention, and improve results. In addition, we sought to compare concordance between 2-dimensional (2D) and 3D TEE and evaluate secondary chord lysis in the management of myopathic regurgitation.
Methods

Study Design
Repair rates, freedom from recurrent regurgitation, and survival for mitral procedures using echo guidance were compared with unguided historical controls. In the echo-guided group, concordance between preoperative TEE and intraoperative findings was evaluated, as well as concordance between 2D and 3D TEE. To minimize hindsight bias, the operating surgeon reviewed the protocol-driven TEE preoperatively on each patient and provided written documentation of mitral dysfunction, associated lesions, and plan for intervention. Intraoperative findings, procedures, and outcomes were documented at the time of acquisition. Repair rates in both the unguided and echo-guided groups were compared with concomitant national controls. Institutional Review Board approval was obtained.

Echocardiography
A methodical search was made for well-defined, reproducible images that were highly predictive of intraoperative findings. This led to the observation that imaging parallel to the mitral-left ventricular apex axis ensured that the resultant planes were perpendicular to the annulus and subsequent measurements were not distorted by oblique orientation. These views are presented in Figure 1. They require specific landmark recognition and exceeded American Society of Echocardiography, Society of Cardiovascular Anesthesiologists, and European Association of Echocardiography guidelines.17,20,21

All echocardiograms were interpreted by board-certified cardiologists. The echocardiography facilities were certified by the Intersocietal Commission for the Accreditation of Echocardiography Laboratories. Echocardiography was performed in accordance with American Society of Echocardiography and Society of Cardiovascular Anesthesiologists guidelines.20,21 MR was graded using American College of Cardiology/American Heart Association guidelines as mild (1+), moderate (2+), or severe (3–4+).9 Data collection began on July 1, 2000. On July 1, 2004, the protocol-driven defined 2D TEE imaging protocol was initiated. The 3D TEE protocol was introduced on July 1, 2008, and used exclusively thereafter (Figure I in the Data Supplement). The 3D protocol included postacquisition matrix analysis (Philips Medical Systems, Bothell, WA). These defined images are presented in Figure 2A. The Carpentier systems for segmental nomenclature and dysfunction are also demonstrated.22,23

Disease Classification
Clinical data including echocardiographic and intraoperative findings were used to classify the primary disease leading to MR. The disease classification system was adopted with modification from Braunwald and Carpentier (Table I in the Data Supplement).24,25 Fibroelastic deficiency was characterized by thin leaflets with little redundancy. Annular dimensions were normal or slightly enlarged. Chordal rupture with subsegmental prolapse was common. Conversely, Barlow’s disease was characterized by billowing leaflets, dramatic annular enlargement, and mitral-ventricular dissociation.26,27 Extensive prolapse with or without chordal rupture was frequent. Forme fruste was used to describe a partial manifestation of Barlow’s disease. Myopathic disease from ventricular dilation, ischemia, or hypertrophic obstruction resulted in restricted leaflet motion during systole and secondary MR.28 Myopathies associated with dilation or decreased contractility resulted in functional regurgitation. Inflammatory lesions such as rheumatic disease resulted in leaflet immobility and restriction during diastole. The common diseases are presented in Figure 2B.

Surgical Strategy
The goal of mitral repair was to re-establish anatomically normal mitral geometry, dimensions, and function. This required sufficient but not excessive, freely mobile intact leaflet tissue with coaptative surfaces of adequate depth and located as close to the plane of the annulus as possible. The techniques used for degenerative and inflammatory reconstruction were as classically described by Carpentier.22,23,25 An image-guided graduated approach that integrated secondary chordal lysis was used for myopathic disease (Table II in the Data Supplement). Intraoperative TEE documentation of leaflet contour correction (elimination of the seagull sign) was required. The double orifice technique (Alfieri stitch) was never used.29

Postoperative systolic anterior motion is a well-recognized complication of mitral repair.30 With rare exception, only patients with Barlow’s disease or hypertrophic cardiomyopathy are at risk. Emerging evidence suggests that these 2 diseases may have other common elements.31,32 It was particularly important to recognize Barlow’s disease in association with ventricular dilation. The enlarging ventricle seemed to correct leaflet prolapse if the marginal chords remained intact (Carpentier dysfunction type II+IIIb=I).33 Recognition of these diseases, either alone or in combination, was important for the prevention of systolic anterior motion.

Statistical Analysis
Definitions jointly published by the Society of Thoracic Surgeons (STS), American Association for Thoracic Surgery, and European Association for Cardio-Thoracic Surgery were used for this analysis.34 Surgical mortality was all-cause mortality within 30 days or before hospital discharge. Reintervention was any surgical or percutaneous procedure on a previously repaired valve. Concordance required the preoperative TEE to correctly correlate both intraoperative assessment of segmental dysfunction and the major techniques used for repair. Pearson χ2 test was used to compare frequency counts for categorical variables with row frequencies ≥10, and the Fisher exact test was used when any cell frequency was <10. The t test was used to compare normally distributed continuous variables. All P values are for 2-sided tests. Freedom from recurrent regurgitation and survival curves were plotted using the Kaplan–Meier estimate. The Kruskal–Wallis ANOVA by ranks and the Mann–Whitney U test were used to compare New York Heart Association classifications between groups. The Newcombe–Wilson confidence interval compared differences between proportions for unguided versus guided procedures and for echo-guided versus STS mortality. Spearman rank order correlation was used to correlate procedural complexity with echocardiographic parameters. Statistica 9.1 (Statsoft, Inc. Tulsa, OK) was used for these analyses.

Figure 1. The mitral-left ventricular apex axis passes through the anterior leaflet such that the orthogonal long-axis and commissural planes traverse the 3 major coaptive surfaces. Extension of the intersection of these 2 planes through the ventricular apex creates an axial reference for subsequent mitral analysis. Imaging parallel or perpendicular to the mitral-left ventricular apex axis minimizes geometric distortion from oblique orientation.
Results

Study Population
From July 1, 2000, through June 30, 2010, 347 consecutive adult patients with mitral disease were referred for surgery (Figure II in the Data Supplement). Nine were excluded from further analysis because of previous mitral replacement or profound hemodynamic instability precluding complete evaluation. None of the excluded patients had isolated mitral operations or died within 30 days of surgery. In the 101 unguided controls, the decision to attempt repair was based on direct mitral evaluation in the arrested heart. Subsequently, 237 underwent protocol-driven echo-guided intervention. Results are presented in Figures 3 and 4.

All patients met American College of Cardiology/American Heart Association indications for surgery. In 2006, the American College of Cardiology/American Heart Association guidelines for repair expanded to include asymptomatic patients with normal ventricular function. As a result, patients with echo-guided procedures had lower New York Heart Association classifications and better left ventricular function than unguided controls (Figure 3).4,5

Repair was attempted in 81.0% of the echo-guided group compared with 51.5% of unguided controls (P < 0.001). Repair rates increased from 46.5% of unguided procedures to 77.6% (P < 0.001) with echo guidance. Table III in the Data Supplement presents the subgroup analysis of degenerative disease. Echo-guided secondary chord lysis was integrated into myopathic repair to increase coaptation and improve repair durability. The protocol and results are demonstrated in Tables II and IV in the Data Supplement.

In 45 echo-guided patients (19%), replacement was indicated or requested and repair was not attempted. Contraindications to repair often occurred in combination. Inflammatory lesions were present in 34, advanced rheumatic disease in 22, extensive nonrheumatic dystrophic calcification in 13, extensive endocarditis in 3, radiation necrosis in 1, and replacement was requested in 16 (Table V in the Data Supplement).

Using echo guidance, 234 (99%) of the 237 patients and their referring physicians were explicitly informed of the intent to repair or replace well in advance of surgery. Preoperative documentation confirmed that repair would be attempted in all 192 (100%) of the repair patients. In the 45 patients who received replacement, 42 (93%) were preoperatively informed that repair was unlikely or would not be attempted.

Concordance
Preoperative echo guidance was performed using 2D TEE on 157 patients (66%) and guided repair in 124. Repair was contraindicated and replacement was performed in the remaining 33 patients. Evaluation using 2D TEE was nonconcordant in 7 because of unrecognized deviation from the mitral-left ventricular apex axis and subtle variations in the anatomic relationship between the aortic and mitral valves.35 Three-dimensional TEE was used for the final 80 patients (34%) and guided repair in 68 patients. Two-dimensional TEE was concordant with intraoperative findings in 117 of 124 patients (94.4%), whereas 3D TEE was concordant in all 68 patients (100%; P = 0.05). Data collection on concordance through July 2013 (3D, 150/150) improved significance to P = 0.04.

Concordant patients were more likely to have successful repairs (97.8% versus 57.1%; P < 0.001) but did not differ from nonconcordant in operative mortality, recurrent regurgitation, reintervention, or late mortality. The low frequency of nonconcordance limited the statistical power to detect differences.

Commissional width and number of prolapsing segments were both independently correlated with complexity of degenerative repair (r = 0.41; P < 0.01 and r = 0.88; P < 0.001). Tenting area and A2 bending angle were both independently correlated with complexity of myopathic repair (r = 0.83 and r = −0.82; P < 0.001). These relationships are shown in Figure 5 and the Movie in the Data Supplement.

Preoperative TEE correctly identified potentially repairable mitral valve disease with sensitivity of 100%, specificity of 79%, positive predictive value of 94%, and negative predictive value of 100%. Exclusion of 3 inflammatory patients, who were informed preoperatively that repair was uncertain, improved specificity to 84% and positive predictive value to 96%.

Initial Results
Repair rates increased from 46.5% of unguided procedures to 77.6% with echo guidance (P < 0.001). Operative mortality, 5-year survival, and freedom from >2+ MR did not differ between unguided and echo-guided procedures. Echo-guided repair was successful in 99.0% of degenerative, 97.1% of myopathic, and 84.2% of inflammatory attempts. Unguided results were similar to the STS (46.5% versus STS 46.6%; P = 0.99), whereas echo guidance was superior (77.6% versus STS 54.9%; P < 0.001). Repair operative mortality was similar (echo guided 2.2% and concomitant STS 4.9%; P = 0.08).

Sixty-five echo-guided patients underwent isolated mitral repair. One hundred twenty-seven had additional procedures including coronary bypass grafting in 71, 31 tricuspid repairs, 19 aortic valve procedures, 3 ventricular septal defect closures and aneurysmectomies, and 2 tumor resections. Eight had previously had ≥1 open-heart procedure. Successful repair required cardiopulmonary bypass once for 174 (94.6%) and twice for 10 (5.4%) patients.

Post-bypass TEE demonstrated that 99.5% had 0 or 1+ MR. One hypertrophic patient had residual 2+ MR that completely resolved before hospital discharge. Transthoracic echocardiography (TTE) obtained near discharge demonstrated that 98.9% had 0 or 1+ MR. Two had 2+ MR on discharge TTE. Both had nonhypertrophic myopathies. One resolved with diuresis, and the second remained unchanged on TTE 22 months after surgery.

In the subgroup of isolated mitral operations without stenosis, shock, endocarditis, prior cardiac surgery, or concomitant tricuspid, aortic, pulmonic, or coronary procedures, echo guidance achieved repair in 65 of 71 (91.5%), which was superior to concomitant STS 19634 of 28143 (70.0%; P < 0.001).6 Subgroup operative mortality was similar (1.5% and 1.8%; P = 0.20).
Figure 2. Continued.
Late Results
No patients were lost to follow-up. All echo-guided repair survivors were followed echocardiographically for a minimum of 12 months after surgery with serial echocardiography at least biannually thereafter. All echo-guided repairs had TTE performed within 12 months of completion of the study or within 12 months of death. A total of 2037 echocardiograms were analyzed.

Linearized recurrence of ≥2+ MR was 1.45% per year for all echo-guided repairs, 0.63% per year for degenerative, 2.19% per year for myopathic, and 4.37% per year for inflammatory echo-guided repairs. Kaplan–Meier freedom from recurrent regurgitation and survival are presented in Figures 3 and 4 with composite comparisons in Figure III in the online-only Data Supplement. Table IV in the online-only Data Supplement demonstrates that secondary chord lysis was not associated with adverse perioperative events or diminished ventricular function. Survival following myopathic repair is compared with valve replacement in Figure IIIIB in the online-only Data Supplement.

Discussion
In 1674, Mayow36 carefully detailed the clinical deterioration of a young man in whom cardiac disease was suspected. Examination of the deceased revealed mitral stenosis. Open-heart analysis of the mitral valve has long been the standard for confirming diagnosis and planning surgical intervention. Mitral repair is generally superior to replacement, especially for degenerative and myopathic disease.8 Our findings demonstrate that carefully defined echocardiographic imaging allows identification of repairable mitral disease well in advance of open examination.

The 2009 State-of-the-Art review by Salcedo et al39 concluded that 3D TEE “has the potential to become the central imaging tool for guidance and follow-up of surgical and interventional procedures of the mitral valve.” Since then, numerous studies have documented that 3D TEE reliably identifies segmental dysfunction.12,16-17,39 In 2011, separate publications from Chandra et al40 and Chikwe et al39 retrospectively demonstrated that preintervention intraoperative 3D TEE was useful for predicting the complexity of surgical repair, and both concluded that TEE should be integrated into presurgical planning. Our analysis is the first to document that carefully defined TEE can directly guide surgical intervention. Protocol-driven echo guidance, performed well in advance of surgery, gives the patient, family, and referring physicians ample time to evaluate the proposed intervention and could serve as a basis for selective referral.

Echo-guided mitral repair was successful in 99.0% of those with degenerative disease, 97.1% with myopathic disease, and 84.2% with inflammatory disease. The repair rate for isolated mitral surgery was superior to even the most optimally selected STS subgroups. These early results compare favorably with other contemporary publications.6,7,41-44 Echo guidance was also associated with durable long-term results. The linearized recurrent regurgitation rate for degenerative disease was 0.6% per year, which compares favorably with 1.6% to 3.7% per year in other large degenerative series.6,41,43 In our analysis, recurrent regurgitation following myopathic repair was 2.2% per year over 5 years with 4.8% demonstrating ≥2+ MR on the latest TTE. This also compares favorably to recent reports of 20% to 44% repair failure at 5 years with ≥13% ≥2+ MR on the latest TTE.42,45,46

Echocardiography can reliably classify mitral valve disease.7,7,47 Accurate disease classification is important. The World Health Organization has long recommended screening for early rheumatic disease and secondary prophylaxis to prevent progression.1 Identification of degenerative disease, especially Barlow’s disease, is also important because of the high probability of durable repair.41 Treatments for early rheumatic disease and most degenerative disease are often curative and typically allow patients to return to a basic healthcare environment with reasonable expectation of long-term survival.

Although repair of myopathic dysfunction is not difficult, freedom from recurrent regurgitation is dependent on effective identification of repairable mitral disease well in advance of open examination.
prevention of further ventricular remodeling.\textsuperscript{28} It is unreasonable to conclude that replacement is equivalent to repair for all patients with myopathic regurgitation.\textsuperscript{7} Replacing the valve for simple ischemic annular dilation unnecessarily disrupts the subvalvular apparatus even if the chords are spared. It is equally inappropriate to attempt repair using only reductive ring annuloplasty when the tenting area is >2.0 cm\textsuperscript{2} because regurgitation will almost certainly recur.\textsuperscript{42} Therefore, an image-guided graduated approach to intervention is particularly valuable for myopathic disease.

\begin{table}
\centering
\begin{tabular}{|l|c|c|c|c|}
\hline
\textbf{Variable} & \textbf{Unguided Procedures} & \textbf{P} & \textbf{Echo-Guided Procedures} & \textbf{Proportional Difference (95\% CI)}* \\
\hline
\textbf{No. of patients (%)} & 101 & 237 &  &  \\
\hline
\textbf{Preoperative} & & & &  \\
\textbf{Age - years} & 66.6 ±10.797 & 0.38 & 64.8 ±11.5 & -1.19 (-3.83, 1.45) \\
\textbf{Male} & 59 (58.4) & 1.00 & 140 (59.1) & 0.66 (-10.97, 12.66) \\
\textbf{Hypertension} & 58 (57.4) & 0.54 & 146 (61.6) & 4.28 (-6.99, 15.60) \\
\textbf{Diabetes} & 24 (23.7) & 0.68 & 62 (26.2) & 2.40 (-8.13, 11.77) \\
\hline
\textbf{NYHA classification} & & & &  \\
\textbf{I} & 0 (0.0) & 0.002 & 22 (9.3) & 0.09 (0.04, 0.01) \\
\textbf{II} & 23 (22.8) & 0.06 & 78 (32.9) & 0.01 (-0.01, 0.20) \\
\textbf{III} & 51 (50.5) & 0.07 & 94 (39.7) & 0.01 (-0.01, 0.23) \\
\textbf{IV} & 27 (26.7) & 0.07 & 43 (18.1) & 0.09 (-0.01, 0.19) \\
\hline
\textbf{MRR 3.4+} & 91 (90.1) & 0.13 & 198 (83.5) & 6.55 (-1.92, 13.43) \\
\textbf{LVEF%} & 43.6 ±0.124 & <0.001 & 51.2 ±0.125 & 7.64 (4.72, 10.55) \\
\hline
\textbf{Intra-operative} & & & &  \\
\textbf{Degenerative} & 42 (41.6) & 0.91 & 101 (42.6) & 1.03 (-10.48, 12.10) \\
\textbf{Myopathic} & 36 (35.6) & 0.53 & 75 (31.6) & 4.00 (-6.63, 15.20) \\
\textbf{Inflammatory} & 21 (20.8) & 0.43 & 53 (22.4) & 1.57 (-8.57, 10.44) \\
\textbf{Other} & 2 (2.0) & 0.73 & 8 (3.4) & 1.40 (-3.83, 4.85) \\
\textbf{Repair attempts} & 52 (51.5) & <0.001 & 192 (81.0) & 29.53 (18.55, 40.14) \\
\textbf{Successful repairs/attempt} & 47/52 (90.4) & 0.16 & 184/192 (95.8) & 5.55 (-1.21, 16.63) \\
\textbf{Replacements} & 54 (53.5) & <0.001 & 53 (22.4) & 31.10 (19.86, 41.69) \\
\textbf{Repair rate**} & 47/101 (46.5) & <0.001 & 184/237 (77.6) & 31.10 (19.86, 41.69) \\
\textbf{P} & 0.99 & <0.001 & &  \\
\hline
\textbf{Proportional difference (95\% CI)} & 0.06 (-9.63, 9.49) & 22.74 (17.01, 27.59) & &  \\
\textbf{Concomitant STS† repair rate} & 35246/75649 (46.6) &  & 72805/132622 (54.9) &  \\
\hline
\textbf{Post-operative} & & & &  \\
\textbf{Operative mortality} & 1 (0.99) & 0.44 & 7 (2.95) & 1.96 (-2.70, 5.09) \\
\textbf{Repair operative mortality} & 0/47 (0.0) & 0.40 & 4/184 (2.17) & 2.17 (-5.50, 5.46) \\
\textbf{Replacement operative mortality} & 1/54 (1.85) & 0.30 & 3/55 (5.66) & 3.81 (-4.94, 13.64) \\
\textbf{Repair reintervention} & 1/47 (2.13) & 1.00 & 4/184 (2.17) & 0.05 (-9.04, 3.77) \\
\textbf{Kaplan-Meier analysis} & & & &  \\
\hline
\end{tabular}
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\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Unguided and echo-guided procedures are compared. Repair rates are also compared with concomitant 2000 to 2004 and 2004 to 2010 STS results. *Differences of proportion are demonstrated for all variables except age and left ventricular ejection fraction, which are mean differences. Other than age, differences are reported as percentages. CI indicates confidence intervals. †Plus-minus values are means±SD. New York Heart Association (NYHA). §Kruskal–Wallis ANOVA main effect. NYHA pairwise class comparisons are included but potentially increase the risk of type 1 error. #Mitral regurgitation. ‡Left ventricular ejection fraction. **Repair rate is repairs divided by the sum of repairs and replacements. ††Society of Thoracic Surgeons.}
\end{figure}
The anterior secondary chords are typically responsible for leaflet tenting associated with myopathic regurgitation. Szymanski et al observed that secondary chord lysis might reduce tethering and improve coaptation. Using animal models, they demonstrated the efficacy of chord lysis for relief of ischemic regurgitation and prevention of further ventricular remodeling.

### Table 1

<table>
<thead>
<tr>
<th>Disease Classification</th>
<th>All Echo-Guided Repairs</th>
<th>Degenerative Repairs</th>
<th>Myopathic Repairs</th>
<th>Inflammatory Repairs</th>
<th>P Group Main Effect</th>
<th>P Degenerative vs. Myopathic</th>
<th>P Myopathic vs. Inflammatory</th>
<th>P Inflammatory vs. Degenerative</th>
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<tbody>
<tr>
<td><strong>No. of patients (%)</strong></td>
<td>192 (100.0)</td>
<td>98 (51.0)</td>
<td>68 (35.4)</td>
<td>19 (9.9)</td>
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<td>Preoperative</td>
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<tr>
<td>Age - years*</td>
<td>64.2 ± 11.7</td>
<td>62.5 ± 12.0</td>
<td>67.4 ± 9.7</td>
<td>59.1 ± 14.8</td>
<td>0.005†</td>
<td>0.006</td>
<td>0.004</td>
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<td>Male</td>
<td>117 (60.9)</td>
<td>62 (63.3)</td>
<td>47 (69.1)</td>
<td>5 (26.3)</td>
<td>0.007‡</td>
<td>0.50</td>
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<td>0.005</td>
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<td>Hypertension</td>
<td>112 (58.3)</td>
<td>48 (49.0)</td>
<td>47 (69.1)</td>
<td>12 (63.2)</td>
<td>0.11‡</td>
<td>0.01</td>
<td>0.78</td>
<td>0.32</td>
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<td>Diabetes</td>
<td>45 (23.4)</td>
<td>10 (10.2)</td>
<td>26 (38.2)</td>
<td>5 (26.3)</td>
<td>0.001‡</td>
<td></td>
<td>0.42</td>
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<td>I</td>
<td>19 (9.9)</td>
<td>16 (16.3)</td>
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<td>66 (34.4)</td>
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<td>8 (42.1)</td>
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<td>0.02</td>
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<td>IV</td>
<td>31 (16.1)</td>
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<td>MR# 3-4+</td>
<td>163 (84.9)</td>
<td>95 (96.9)</td>
<td>49 (72.1)</td>
<td>17 (89.5)</td>
<td>&lt;0.001**</td>
<td>&lt;0.001</td>
<td>0.14</td>
<td>0.19</td>
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<td>LVEF†† %</td>
<td>51.4 ± 12.9</td>
<td>55.8 ± 8.3</td>
<td>42.1 ± 14.0</td>
<td>55.6 ± 12.1</td>
<td>&lt;0.001†</td>
<td>&lt;0.001</td>
<td>0.19</td>
<td>0.74</td>
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<td><strong>Intra-operative</strong></td>
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<tr>
<td>Concordance</td>
<td>185 (96.4)</td>
<td>97 (99.0)</td>
<td>67 (98.5)</td>
<td>15 (78.9)</td>
<td>&lt;0.001**</td>
<td>1.00</td>
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<td>2D TEE‡‡</td>
<td>117/124 (94.4)</td>
<td>53/54 (98.1)</td>
<td>9/13 (69.2)</td>
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<tr>
<td>P</td>
<td>0.05§§</td>
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<tr>
<td>3D TEE</td>
<td>68/68 (100.0)</td>
<td>44/44 (100.0)</td>
<td>14/14 (100.0)</td>
<td>6/6 (100.0)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Successful repair</td>
<td>184 (95.8)</td>
<td>97 (99.0)</td>
<td>66 (97.1)</td>
<td>16 (84.2)</td>
<td>0.03**</td>
<td>0.57</td>
<td>1.07</td>
<td>0.01</td>
</tr>
<tr>
<td>MR 0-1+</td>
<td>183/184 (99.5)</td>
<td>97/97 (100.0)</td>
<td>65/66 (98.5)</td>
<td>16/16 (100.0)</td>
<td>0.33**</td>
<td>0.40</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>MR 2+</td>
<td>1/184 (0.5)</td>
<td>0/97 (0.0)</td>
<td>1/66 (1.5)</td>
<td>0/66 (0.0)</td>
<td>0.31**</td>
<td>0.40</td>
<td>1.00</td>
<td>1.00</td>
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<tr>
<td>Post-operative inpatient</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Mortality</td>
<td>4/184 (2.2)</td>
<td>1/97 (1.0)</td>
<td>2/66 (3.0)</td>
<td>1/66 (6.3)</td>
<td>0.44**</td>
<td>0.57</td>
<td>0.53</td>
<td>0.30</td>
</tr>
<tr>
<td>MR 0-1+ at discharge</td>
<td>178/180 (98.9)</td>
<td>96/96 (100.0)</td>
<td>62/64 (96.9)</td>
<td>15/15 (100.0)</td>
<td>0.34**</td>
<td>0.16</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>MR 2+ at discharge</td>
<td>2/180 (1.1)</td>
<td>0/96 (0.0)</td>
<td>2/64 (3.1)</td>
<td>0/64 (0.0)</td>
<td>0.34**</td>
<td>0.16</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>LVEF at discharge %</td>
<td>51.2 ± 11.9</td>
<td>&lt;0.001†</td>
<td>54.8 ± 8.1</td>
<td>&lt;0.001</td>
<td>0.19</td>
<td>0.43</td>
<td>43.5 ± 14.2</td>
<td>56.9 ± 5.8</td>
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<td>Outpatient follow-up</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>Mitral reintervention</td>
<td>4/180 (2.2)</td>
<td>0/96 (0.0)</td>
<td>2/64 (3.1)</td>
<td>2/64 (13.3)</td>
<td>0.01**</td>
<td>0.16</td>
<td>0.16</td>
<td>0.02</td>
</tr>
<tr>
<td>MR &gt; 2+</td>
<td>5/175 (2.9)</td>
<td>1/96 (1.0)</td>
<td>3/62 (4.8)</td>
<td>1/62 (3.4)</td>
<td>0.27**</td>
<td>0.30</td>
<td>0.52</td>
<td>0.21</td>
</tr>
<tr>
<td>MR &gt; 2+ rate %/year</td>
<td>1.45</td>
<td>2.19</td>
<td>4.37</td>
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</tr>
<tr>
<td>LVEF latest TEE†† %</td>
<td>52.4 ± 12.9</td>
<td>&lt;0.001†</td>
<td>55.6 ± 9.2</td>
<td>&lt;0.001</td>
<td>0.006</td>
<td>0.006</td>
<td>0.006</td>
<td>0.85</td>
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<tr>
<td>Kaplan-Meier analysis</td>
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</tr>
</tbody>
</table>

**Figure 4.** Echo-guided repair results by disease classification including group main effect simultaneous comparisons of degenerative, myopathic, and inflammatory repairs. Subgroup pairwise comparisons are included but potentially increase the risk of type 1 error. The myopathic subgroup excludes isolated hypertrophic cardiomyopathy. *Plus-minus values are means±SD. †ANOVA. ‡Pearson χ² test of independence. §New York Heart Association. ‖Kruskal–Wallis ANOVA main effect. #Mitrail regurgitation. ‖‖Randomization test for goodness of fit. ††Left ventricular ejection fraction. ‡‡Transesophageal echocardiography. §§Data collection on concordance through July 2013 (3-dimensional [3D], 150/150) improved significance to P<0.04. ‧Transthoracic echocardiography.

The anterior secondary chords are typically responsible for leaflet tenting associated with myopathic regurgitation. Szymanski et al observed that secondary chord lysis might reduce tethering and improve coaptation. Using animal models, they demonstrated the efficacy of chord lysis for relief of ischemic regurgitation and prevention of further ventricular remodeling.
comitant national data. Automatic patients with normal ventricular function. This guidelines for repair were expanded to include asymp-
tic techniques necessary for repair. During the period of study,
concordance required that TEE correlated with all major
tion and consequently concordance. To reduce this effect,
tive echocardiography may have biased disease classifica-
results were used as controls. Familiarity with preopera-
Therefore, historical institutional and concomitant national
ventions are violations of equipoise.49
and prevent further ventricular remodeling.

Study Limitations
An observational rather than randomized design was nec-
ecessary because restricting the surgeon’s access to echocar-
diographic information or prolonging intraoperative cardiac
arrest for blinded evaluation are violations of equipoise.50
Therefore, historical institutional and concomitant national
results were used as controls. Familiarity with preopera-
tive echocardiography may have biased disease classifica-
tion and consequently concordance. To reduce this effect,
concordance required that TEE correlated with all major
 techniques necessary for repair. During the period of study,
guidelines for repair were expanded to include asympto-
tic patients with normal ventricular function. This
confound was managed by comparing each group with con-
comitant national data.

Conclusions
Echocardiography can reliably identify repairable mitral di-
ease and guide intervention. Echo-guided repair is associ-
ated with a higher rate of initial success than unguided and
concomitant national averages. Echo guidance is also associ-
ated with excellent long-term results. Concordance of 3D echo-
cardiography with intraoperative findings is superior to 2D
 echocardiography. Image-guided secondary chord lysis for
myopathic patients may be important for durable repair and
the prevention of further ventricular remodeling.

The historical gold standard of mitral repair based princ-
ally on surgical exploration is being transformed to a new
standard with shared contributions from both imaging and sur-
gery. Further studies evaluating a multidisciplinary approach
to intervention that include imaging protocols for screening,
disease severity stratification, and guidance are encouraged.

Acknowledgments
We thank Connie M. Bongiorno, MLS, Charles G. Drake, PE, David
M. Grix, CCP, Shenna A. Meredith, BSN, Virginia L. Noble, ST, and
Marcia L. Williams, MSMSI, for technical support and illustrations.

Disclosures
None.

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Mitrval regurgitation is an important health problem that affects millions worldwide. Severe regurgitation rarely resolves with medical therapy alone. Mitral repair generally provides excellent long-term event-free survival. Conversely, mitral valve replacement adds morbidity, and over time, the prosthesis may fail and result in the need for reoperation or potentially be associated with death. In addition, mechanical prostheses have the requirement of lifelong anticoagulation. Despite that, valve repair is currently accomplished in <60% of mitral procedures. Echocardiography is available in most healthcare environments, yet the efficacy of echo-guided repair has not been fully established. We developed a succinct set of defined images observed to be highly concordant with intraoperative findings. These images guided intervention on 237 consecutive patients. The intent to repair or replace was documented preoperatively in 98.7%. Three-dimensional concordance was higher than 2-dimensional. Repair rates increased from 46.5% to 77.6% \((P<0.001)\), whereas concomitant Society of Thoracic Surgeons rates were 46.6% (versus unguided 46.5%; \(P=0.99\)) and 54.9% (versus echo guided 77.6%; \(P<0.001\)). This is the first clinical series to formally integrate image-guided secondary chord lysis into the management of myopathic disease. Echo guidance was associated with excellent long-term results. The historical gold standard of repairability based solely on surgical exploration is being transformed into a new standard with shared contributions from both imaging and surgery. Echocardiography can reliably identify repairable mitral disease and guide successful intervention. Protocol-driven echocardiography, performed well in advance of surgery, gives the patient, family, and referring physicians the opportunity to evaluate the proposed intervention and could serve as a basis for selective referral. Disease classification, severity stratification, and a multidisciplinary approach are strongly encouraged.
Echo-Guided Mitral Repair

SUPPLEMENTAL MATERIAL

Daniel H. Drake, M.D., Karen G. Zimmerman, B.S., R.D.C.S. (A.E., P.E.), R.V.T.,
Anne M. Hepner, M.D., and Cynthia D. Nichols, Ph.D.
Online Data Supplement Table I. Classification of Principle Disease Resulting in Mitral Regurgitation

1. Primary Mitral Valve Disease
   1.1. Congenital
   1.2. Degenerative (myxomatous)
      1.2.1. Barlow’s disease including forme fruste
      1.2.2. Marfan’s disease
      1.2.3. Other genetic connective tissue disorders (Ehlers-Danlos, Loeys-Dietz, etc.)
      1.2.4. Fibroelastic deficiency (includes non-myopathic annular dilation)
      1.2.5. Other
   1.3. Inflammatory
      1.3.1. Endocarditis
      1.3.2. Rheumatic
      1.3.3. Immune mediated (excludes rheumatic and myopathic disease)
      1.3.4. Radiation
      1.3.5. Dystrophic calcification (as primary etiology)
      1.3.6. Other
   1.4. Neoplastic
      1.4.1. Primary cardiac
         1.4.1.1. Benign
            1.4.1.1.1. Papillary fibroelastoma
            1.4.1.1.2. Myxoma
            1.4.1.1.3. Other
         1.4.1.2. Malignant
            1.4.1.2.1. Sarcoma
            1.4.1.2.2. Other
      1.4.2. Extracardiac
         1.4.2.1. Carcinoid
         1.4.2.2. Metastatic
         1.4.2.3. Other
   1.5. Trauma
      1.5.1. Blunt
      1.5.2. Penetrating
      1.5.3. Iatrogenic
      1.5.4. Other
   1.6. Thrombotic
      1.6.1. Local
      1.6.2. Embolic
   1.7. Other

2. Mitral Dysfunction Secondary to Other Cardiac Disease
   2.1. Myopathy with decreased contractility and/or dilation resulting in functional regurgitation
      2.1.1. Regional (asymmetric)
      2.1.2. Global (symmetric)
   2.2. Myopathy with increased contractility and/or hypertrophy
      2.2.1. Hypertrophic obstructive cardiomyopathy
         2.2.1.1. Leaflets morphologically normal
         2.2.1.2. Degenerative leaflet morphology
         2.2.1.3. Other
      2.2.2. Semi-lunate obstructive myopathy
      2.2.3. Other
   2.3. Other

3. Other
1. Transthoracic and transesophageal echocardiographic evaluation performed well in advance of surgery. Following post-acquisition analysis, the findings are discussed with patient and, if necessary, multidisciplinary presentation. The surgeon provides written documentation of disease classification, dysfunction, intent to repair (or replace), and the major surgical techniques required for repair. The procedural checklist with representative views of mitral dysfunction is prepared.

2. General anesthesia, median sternotomy or right anterolateral thoracotomy, cardiopulmonary bypass, and cardioplegic arrest. Appropriate integration of concomitant surgical procedures.

3. Left atriotomy through interatrial approach followed by systematic evaluation of the segments, annulus, and subvalvular apparatus under direct vision.

A. Degenerative disease: The anterolateral segment of the posterior leaflet (P1) is typically used as reference.
   1) Type I dysfunction: No segmental prolapse
   2) Type II dysfunction: One or more segments prolapse above the plane of the annulus and are commonly associated with chordal elongation or rupture. Advanced Barlow’s demonstrates billowing leaflets with prolapse of all segments including P1.

B. Myopathic disease: Leaflet restriction is identified by saline ventricular insufflation to approximately 60 mmHg both before (if possible) and after ring annuloplasty.
   1) Type I dysfunction: No segmental restriction following insufflation
   2) Type IIIB dysfunction, non-hypertrophic: Insufflation demonstrates coaptation below the plane of the annulus. Tenting (dimpling) in the mid to distal anterior leaflet corresponding with secondary chord attachment is typically present. Coaptation is poor, even with partial insufflation.
   3) Type IIIB dysfunction, hypertrophic: Palpably thickened septum with or without abnormal papillary muscle insertion.

C. Inflammatory disease: Type IIIA dysfunction with restricted leaflet motion from fibrotic scar. Commisural fusion, thickened chords and scarring of the papillary muscles are common. The annular circumference is reduced and extensive calcification is often present.

4. Graduated protocols: The major techniques for each degenerative and myopathic disease are described. Minor adjunctive procedures such as stitch commissuroplasty and/or natural cleft closure are individualized based on echocardiographic and intra-operative findings. All mitral repairs completed with rigid or semi-rigid circumferential ring annuloplasty.

A. Degenerative disease: Graduated approach categorizes the spectrum from mild fibroelastic deficiency to advanced Barlow’s.
   1) Type I dysfunction from fibroelastic deficiency: Reductive (4 mm) ring annuloplasty only
   2) Type II dysfunction from fibroelastic deficiency or Forame Fruste with isolated anterior or posterior sub-segmental prolapse: Limited triangular, parabolic or quadrangular leaflet resection; or isolated neochordae
   3) Type II dysfunction from Barlow’s or Forame Fruste with extensive posterior segmental prolapse: Segmentectomy and sliding posteroplasty; or multiple neochordae
   4) Type II dysfunction from Barlow’s with extensive anterior or bileaflet prolapse: Unilateral or bilateral papillary muscle shortening with or without posterior segmentectomy and sliding posteroplasty; and/or multiple neochordae. Type I dysfunction from Barlow’s with secondary myopathic dysfunction (Type II + IIIB = I), intact marginal chords, and P2 width ≥1.5 cm: P2 segmentectomy and sliding posteroplasty; or multiple neochordae

B. Myopathic disease: Graduated surgical approach based on left ventricular contour and leaflet geometry.

Echocardiographic parameters of restriction measured exclusively in the long axis view.
   1) Type I or minimal IIIB dysfunction from myopathic restriction resulting in tenting area < 1.0 cm²: Reductive (4 mm) ring annuloplasty only
   2) Type IIIB dysfunction from myopathic restriction resulting in leaflet inversion >20 degrees (“seagull sign”) or tenting area of 1.0-2.0 cm² with the A2 closing angle ≥25 degrees, P2 closing angle ≤45 degrees, or the height of coaptation <1.0 cm below the plane of the annulus: Transatrial, trans-aortic or trans-mural (during septal defect repair) unilateral or bilateral secondary chord-lysis is based on preoperative echocardiographic assessment above; all anterior leaflet sub-segmental chords arising from the targeted papillary muscle are carefully identified and cut; always combined with rigid or semi-rigid circumferential 4 mm reductive ring annuloplasty
   3) Type IIIB dysfunction from myopathic restriction resulting in tenting area of >2.0 cm², A2 closing angle ≥25 degrees, P2 closing angle ≤45 degrees, and the height of coaptation ≥1.0 cm below the plane of the annulus: Complete bilateral secondary chord-lysis, leaflet augmentation, and 4 mm reductive ring annuloplasty
   4) Type IIIB dysfunction (systolic anterior motion) from hypertrophic cardiomyopathy: Septal myectomy with or without papillary mobilization and/or complete bilateral secondary chord-lysis.

5. Intraoperative transesophageal echocardiographic evaluation performed immediately following discontinuation of cardiopulmonary bypass for assessment of mitral function, transvalvular gradients, ventricular function, exclusion of systolic anterior motion, evaluation of concomitant procedures, and assessment of post-myectomy left ventricular outflow tract when indicated. Direct left ventricular outflow tract gradient measurement with simultaneously transduced 18 gauge needles in left ventricle and aorta for all myectomies. Document intraoperative findings and assess concordance.

6. Transthoracic echocardiography at or near the time of hospital discharge.
## Online Data Supplement Table III. Degenerative Echo-Guided Repair Subgroup Comparison

<table>
<thead>
<tr>
<th></th>
<th>Fibroelastic Deficiency (n = 28)</th>
<th>P</th>
<th>Barlow's Disease (n = 66)</th>
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</thead>
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</tr>
<tr>
<td>Age — years*</td>
<td>69.5 ± 12.3</td>
<td>&lt;0.001</td>
<td>59.7 ± 10.9</td>
</tr>
<tr>
<td>Male</td>
<td>20 (71.4)</td>
<td>0.27</td>
<td>41 (62.1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18 (64.3)</td>
<td>0.07</td>
<td>28 (42.4)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2 (7.1)</td>
<td>0.72</td>
<td>7 (10.6)</td>
</tr>
<tr>
<td>NYHA† classification</td>
<td></td>
<td>0.10‡</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3 (10.7)</td>
<td>0.49</td>
<td>13 (19.7)</td>
</tr>
<tr>
<td>II</td>
<td>13 (46.4)</td>
<td>0.97</td>
<td>31 (47.0)</td>
</tr>
<tr>
<td>III</td>
<td>9 (32.1)</td>
<td>0.71</td>
<td>18 (27.3)</td>
</tr>
<tr>
<td>IV</td>
<td>3 (10.7)</td>
<td>0.72</td>
<td>4 (6.1)</td>
</tr>
<tr>
<td>MR§ 3-4+</td>
<td>27 (96.4)</td>
<td>0.89</td>
<td>64 (97.0)</td>
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<td>LVEF</td>
<td></td>
<td>— %</td>
<td>53.6 ± 8.4</td>
</tr>
<tr>
<td>Anteroposterior width # — cm</td>
<td>3.14 ± 0.55</td>
<td>0.007</td>
<td>3.76 ± 0.57</td>
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<tr>
<td>Commissural width** — cm</td>
<td>3.69 ± 0.52</td>
<td>&lt;0.001</td>
<td>4.67 ± 0.48</td>
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<tr>
<td>Prolapsing segments††</td>
<td>0.78 ± 0.44</td>
<td>0.003</td>
<td>3.00 ± 2.01</td>
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<tr>
<td><strong>Intraoperative</strong></td>
<td></td>
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<tr>
<td>Concordance</td>
<td>27 (96.4)</td>
<td>0.30</td>
<td>66 (100.0)</td>
</tr>
<tr>
<td>Successful repair</td>
<td>27 (96.4)</td>
<td>0.30</td>
<td>66 (100.0)</td>
</tr>
<tr>
<td>MR 0-1+</td>
<td>27/27 (100.0)</td>
<td>1.00</td>
<td>66 (100.0)</td>
</tr>
<tr>
<td>MR 2+</td>
<td>0 (0.0)</td>
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<td>0 (0.0)</td>
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<td><strong>Postoperative inpatient</strong></td>
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<tr>
<td>Operative mortality</td>
<td>1/27 (3.7)</td>
<td>0.29</td>
<td>0 (0.0)</td>
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<tr>
<td>MR 0-1+ at discharge</td>
<td>26/26 (100.0)</td>
<td>1.00</td>
<td>66 (100.0)</td>
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<tr>
<td>MR 2+ at discharge</td>
<td>0 (0.0)</td>
<td>1.00</td>
<td>0 (0.0)</td>
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<tr>
<td>LVEF at discharge — %</td>
<td>55.8 ± 5.8</td>
<td>0.53</td>
<td>54.7 ± 7.9</td>
</tr>
<tr>
<td><strong>Outpatient follow-up</strong></td>
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<td></td>
</tr>
<tr>
<td>Mitral reintervention</td>
<td>0/26 (0.0)</td>
<td>1.00</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>MR &gt; 2+</td>
<td>0/26 (0.0)</td>
<td>1.00</td>
<td>1 (1.5)</td>
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<tr>
<td>MR &gt; 2+ rate — %/year</td>
<td>0.15</td>
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<td>0.10</td>
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<tr>
<td>LVEF on latest TTE‡‡ — %</td>
<td>56.7 ± 6.3</td>
<td>0.51</td>
<td>55.4 ± 9.2</td>
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* Variables are mean ± SD or n (%). † New York Heart Association. ‡ Kruskal-Wallis NYHA classification comparison for group main effect. NYHA pairwise class comparisons are included but potentially increase the risk of type 1 error. § Mitral regurgitation. || Left ventricular ejection fraction. # Anteroposterior width is the transesophageal echo measurement of the mitral annular width in the defined long axis view. ** Commissural width is the transesophageal echo measurement of the annular width in the defined commissural view. †† Prolapsing segments is the number of prolapsing segments (range 0-6) documented on the preoperative transesophageal echo. ‡‡ Transthoracic echocardiography.
### Preoperative

<table>
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<th>Annuloplasty Ring Only (n = 18)</th>
<th>Secondary Chord-Lysis and Ring (n = 24)</th>
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<tr>
<td>Age — years*</td>
<td>68.8±11.5</td>
<td>68.4±7.6</td>
<td>0.89</td>
</tr>
<tr>
<td>Male</td>
<td>13 (72.2)</td>
<td>18 (75.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hypertension</td>
<td>11 (61.1)</td>
<td>18 (75.0)</td>
<td>0.50</td>
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<tr>
<td>Diabetes</td>
<td>5 (27.8)</td>
<td>11 (45.8)</td>
<td>0.34</td>
</tr>
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<td>NYHA† classification</td>
<td></td>
<td></td>
<td>0.21</td>
</tr>
<tr>
<td>I</td>
<td>0 (0.0)</td>
<td>2 (8.3)</td>
<td>0.22</td>
</tr>
<tr>
<td>II</td>
<td>3 (16.7)</td>
<td>8 (33.3)</td>
<td>0.23</td>
</tr>
<tr>
<td>III</td>
<td>10 (55.6)</td>
<td>11 (45.8)</td>
<td>0.54</td>
</tr>
<tr>
<td>IV</td>
<td>5 (27.8)</td>
<td>3 (12.5)</td>
<td>0.22</td>
</tr>
<tr>
<td>MR§ 3-4+</td>
<td>10 (55.6)</td>
<td>17 (70.8)</td>
<td>0.24</td>
</tr>
<tr>
<td>LVEF</td>
<td></td>
<td>— %</td>
<td>47.4±12.6</td>
</tr>
<tr>
<td>LVIDD# — cm</td>
<td>5.32±0.78</td>
<td>5.53±0.88</td>
<td>0.43</td>
</tr>
<tr>
<td>LVIDS** — cm</td>
<td>3.97±0.79</td>
<td>4.30±1.10</td>
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### Intraoperative

<table>
<thead>
<tr>
<th></th>
<th>Annuloplasty Ring Only (n = 18)</th>
<th>Secondary Chord-Lysis and Ring (n = 24)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concordance</td>
<td>18 (100)</td>
<td>24 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>Successful repair</td>
<td>18 (100)</td>
<td>24 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>MR 0-1+</td>
<td>18 (100)</td>
<td>24 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>MR 2+</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

### Postoperative inpatient

<table>
<thead>
<tr>
<th></th>
<th>Annuloplasty Ring Only (n = 18)</th>
<th>Secondary Chord-Lysis and Ring (n = 24)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>0 (0.0)</td>
<td>1 (4.2)</td>
<td>0.22</td>
</tr>
<tr>
<td>MR 0-1+</td>
<td>18 (100)</td>
<td>23/23 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>MR 2+</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>LVEF — %</td>
<td>51.5±11.3</td>
<td>45.1±13.1</td>
<td>0.11</td>
</tr>
<tr>
<td>LVIDD — cm</td>
<td>4.88±0.50</td>
<td>5.24±0.82</td>
<td>0.11</td>
</tr>
<tr>
<td>LVIDS — cm</td>
<td>3.71±0.66</td>
<td>4.04±1.09</td>
<td>0.27</td>
</tr>
</tbody>
</table>

### Outpatient follow-up

<table>
<thead>
<tr>
<th></th>
<th>Annuloplasty Ring Only (n = 18)</th>
<th>Secondary Chord-Lysis and Ring (n = 24)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral reintervention</td>
<td>1 (5.6)</td>
<td>0/23 (0.0)</td>
<td>0.44</td>
</tr>
<tr>
<td>&gt;2+ MR</td>
<td>1 (5.6)</td>
<td>2/23 (8.7)</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt;2+ MR rate — %/year</td>
<td>1.68</td>
<td>3.73</td>
<td>0.15</td>
</tr>
<tr>
<td>LVEF on latest TTE†† − %</td>
<td>51.6±11.6</td>
<td>45.8±13.0</td>
<td>0.52</td>
</tr>
<tr>
<td>LVDD on latest TTE — cm</td>
<td>5.02±0.72</td>
<td>5.21±1.06</td>
<td>0.21</td>
</tr>
<tr>
<td>LVDS on latest TTE — cm</td>
<td>3.59±0.83</td>
<td>4.05±1.33</td>
<td>0.46</td>
</tr>
<tr>
<td>LVEF change‡‡ − %</td>
<td>1.3±21.5</td>
<td>0.1±17.3</td>
<td>0.46</td>
</tr>
<tr>
<td>LVDD change §§ − cm</td>
<td>-0.30±0.59</td>
<td>-0.53±1.22</td>
<td>0.91</td>
</tr>
<tr>
<td>LVDS change</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

This table compares patients with complete bilateral anterior secondary chord-lysis to those with no secondary chord-lysis whatsoever. Both groups had semirigid circumferential reductive ring annuloplasty. Postoperative TEE documentation of leaflet contour correction (elimination of “seagull sign”) was required in the secondary chord-lysis group. The interventional protocol is presented in Supplement Table 2.

* Variables are mean ± SD or n (%). † New York Heart Association. ‡ Kruskal-Wallis NYHA classification comparison for group main effect. NYHA pairwise class comparisons are included but potentially increase the risk of type 1 error. § Mitral regurgitation. || Left ventricular ejection fraction. # Left ventricular internal dimension at end diastole. ** Left ventricular internal dimension at end systole. †† Transthoracic echocardiography. ‡‡ LVEF change is the latest LVEF minus the preoperative LVEF. §§ LVDD change is the latest LVDD minus the preoperative LVDD. || || LVDS change is the latest LVDS minus the preoperative LVDS.
### Online Data Supplement Table V. Inflammatory Disease Prevalence in Echo-Guided Replacement and Repair

<table>
<thead>
<tr>
<th></th>
<th>Planned Replacements (n = 45)</th>
<th>P</th>
<th>Attempted Repairs (n = 192)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preoperative</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age — years*</td>
<td>67.5 ± 10.0</td>
<td>0.08</td>
<td>64.2 ± 11.7</td>
</tr>
<tr>
<td>Male</td>
<td>23 (51.1)</td>
<td>0.24</td>
<td>117 (60.9)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>34 (75.6)</td>
<td>0.04</td>
<td>112 (58.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>17 (37.8)</td>
<td>0.06</td>
<td>45 (23.4)</td>
</tr>
<tr>
<td>NYHA† classification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3 (6.6)</td>
<td>0.50</td>
<td>19 (9.9)</td>
</tr>
<tr>
<td>II</td>
<td>12 (26.7)</td>
<td>0.32</td>
<td>66 (34.4)</td>
</tr>
<tr>
<td>III</td>
<td>18 (40.0)</td>
<td>0.96</td>
<td>76 (39.6)</td>
</tr>
<tr>
<td>IV</td>
<td>12 (26.7)</td>
<td>1.00</td>
<td>31 (16.1)</td>
</tr>
<tr>
<td>MR§ 3-4+</td>
<td>35 (77.8)</td>
<td>0.27</td>
<td>163 (84.9)</td>
</tr>
<tr>
<td>LVEF ‖ — %</td>
<td>50.6 ± 10.8</td>
<td>0.71</td>
<td>51.4 ± 12.9</td>
</tr>
<tr>
<td><strong>Intraoperative</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concordance</td>
<td>45 (100.0)</td>
<td>0.35</td>
<td>185 (96.4)</td>
</tr>
<tr>
<td>2D TEE#</td>
<td>33/33 (100.0)</td>
<td>0.35</td>
<td>117/124 (94.4)</td>
</tr>
<tr>
<td>3D TEE</td>
<td>12/12 (100.0)</td>
<td>1.00</td>
<td>68/68 (100.0)</td>
</tr>
<tr>
<td>Degenerative disease</td>
<td>4 (8.9)</td>
<td>&lt;0.001</td>
<td>97 (50.5)</td>
</tr>
<tr>
<td>Myopathic disease</td>
<td>7 (15.6)</td>
<td>0.01</td>
<td>68 (35.4)</td>
</tr>
<tr>
<td>Inflammatory disease</td>
<td>34 (75.6)</td>
<td>&lt;0.001</td>
<td>19 (9.9)</td>
</tr>
<tr>
<td>Other disease</td>
<td>0 (0.0)</td>
<td>0.36</td>
<td>8 (4.2)</td>
</tr>
<tr>
<td><strong>Postoperative inpatient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operative mortality</td>
<td>3 (6.7)</td>
<td>0.13</td>
<td>4 (2.2)</td>
</tr>
</tbody>
</table>

* Variables are mean ± SD or n (%). † New York Heart Association. ‡ Kruskal-Wallis NYHA classification comparison for group main effect. NYHA pairwise class comparisons are included but potentially increase the risk of type 1 error. § Mitral regurgitation. ‖ Left ventricular ejection fraction. # Transesophageal echocardiography.
Two-Dimensional Transesophageal Echocardiography Acquisition Protocol

The defined images are acquired with careful demonstration of all diastolic landmarks. It is mandatory that all landmarks remain within view throughout the entire cardiac cycle. This is especially true for the mitral annulus. Magnified images will necessarily exclude the ventricular apex. Several cardiac cycles (approximately 5-10 beats in analog format or 3-5 beats in digital format) are acquired. Without moving the probe, each gray scale acquisition is followed by color flow Doppler of approximately the same acquisition length.

1. Long Axis View: The transesophageal probe is introduced into the mid esophagus and oriented at approximately 140 degrees. Images are acquired.

2. Long Axis Color Flow Doppler: Without moving the probe, color doppler images are obtained documenting the physiologic abnormalities associated with the anatomic findings.

3. Long Axis Magnified (Zoom): Again, without moving the probe, the image is magnified and several cardiac cycles are captured.

4. Long Axis Magnified (Zoom) Color Flow Doppler: Color flow Doppler is added to the magnified image and several cardiac cycles are acquired. Side by side color imaging is useful if available.

5. Commissural View: The probe is rotated to approximately 50 degrees and the defined commissural images are acquired.

6. Commissural Color Flow Doppler: Without moving the probe, color flow Doppler images are obtained.

7. Commissural Magnified (Zoom): The image is magnified and acquired.

8. Commissural Magnified Color Flow Doppler: Color flow Doppler is added and acquired. Side by side color compare is useful if available.

9. Study Completion: The study is completed using American Society of Echocardiography, European Association of Echocardiography and Society of Cardiovascular Anesthesiologists guidelines.

10. Transgastric Views: Modified transgastric-commissural views of the papillary muscles and subvalvular apparatus are acquired. Color imaging may be useful but is not mandatory.
Three-Dimensional Transesophageal Echocardiography Acquisition Protocol

Proper ECG lead placement with a high quality signal is essential for optimal imaging. Intra-operative studies usually require an ECG slave signal directly from the anesthesia monitors. Avoid overheating. The probe should be placed in the non-operative mode during insertion and 3D images should be obtained both early and expeditiously during the study.

The region of interest (ROI) images are as defined in the 2D protocol. Again, images are acquired with careful demonstration of all landmarks. Landmarks must remain within view throughout the entire cardiac cycle. This is especially true for the mitral annulus and left ventricular outflow tract. Biplane imaging ensures proper location of ROI’s. Magnified images will necessarily exclude the ventricular apex. Gain must be optimized to visualize the myocardium and leaflet tissue without dropout. The long axis and commissural views are obtained at approximately 140° and 50° respectively.

1. Live 3D Zoom: Adjust the sector height to include the entire annulus and outflow tract. Excessively close cropping will result in annular dropout with cardiac motion. The valve should be centrally located within the sector.

Adjust gain until leaflet tissue is appropriately opaque and image is otherwise optimal. Rotate the image until the aortic valve is located centrally above mitral valve. Tilt the image until the mitral annulus appears parallel to the viewing screen. This is the surgeons view. Acquire the image. During acquisition the patient and TEE probe should remain motionless. Several Live 3D Zoom acquisitions may be appropriate to insure capture of at least one high quality voxel.

2. Full Volume: The mitral valve and ventricular apex should be centrally located within the long axis sector. Adjust gains to optimize the appearance of the myocardium. Acquire the image. Several Full Volume acquisitions may be appropriate to insure capture of at least one high quality voxel.

3. Full Volume Color Flow Doppler: Adjust depth to the area of analysis and acquire long axis and commissural views. By using color suppress, preoperative full volume color can confirm the association between the observed anatomic abnormalities and physiologic regurgitation.

Reset crop and rotate the image until the aortic valve is located centrally above the mitral valve and the mitral annulus appears parallel to the viewing screen. This is the full volume color surgeons view. Acquire with color suppressed and in color. These images are particularly useful intraoperatively immediately following repair. The sonographer should be prepared to rapidly re-crop and rotate the full volume color images to guide correction of residual mitral regurgitation.

4. Study Completion: The study is completed using American Society of Echocardiography, European Association of Echocardiography and Society of Cardiovascular Anesthesiologists guidelines.

5. Transgastric Full Volume: Full volume modified transgastric-commissural views are acquired as above. Biplane imaging provides side by side orthogonal views of the subvalvular apparatus. Multiplane analysis is useful for evaluating the subvalvular apparatus. Color imaging may be performed but is not mandatory.
Online Data Supplement Figure I. Type I dysfunction (regurgitation despite normal leaflet motion) may result from fibroelastic deficiency and/or mild myopathies. Mild to moderate annular enlargement results in poor central coaptation which is demonstrated in the long axis and commissural views.

Type II dysfunction (excessive leaflet motion or leaflet prolapse during systole) from fibroelastic deficiency usually presents as a small isolated flail with one or two ruptured marginal chords. This can be appreciated in the atrial, long axis, and commissural views. Typically the remaining leaflet tissue, annulus, and ventricle appear normal.

Barlow’s disease typically results in Type II dysfunction from redundant billowing leaflet tissue which is obvious in all views. Multiple flail segments are common. The commissural view reveals dramatic enlargement of the annulus which appears to migrate into the atrium. Barlow’s disease occasionally results in Type I dysfunction when ventricular dilation is superimposed on prolapse and the marginal chords remain intact (II + IIIB = I).

The full volume view is diagnostic for hypertrophic disease and systolic anterior motion is usually evident in all views. Septal hypertrophy and an abnormal aortic-mitral angle are common in both hypertrophic cardiomyopathy and Barlow’s disease. Both abnormalities substantially increase the risk of systolic anterior motion.

Moderate to severe myopathies associated with dilation or decreased ventricular contractility result in Type IIIB dysfunction (leaflet motion restricted during systole). Ventricular pathology is easily appreciated in the full volume image. The degree of leaflet restriction (tenting area, height of coaptation relative to the annulus, and leaflet closing angles) should be measured in the long axis view. Leaflet dysfunction may result from either regional (ischemic) or global myopathic disease. Rarely, myocardial infarction will result in papillary muscle rupture and Type II dysfunction.

Rheumatic disease or radiation commonly result in Type IIIA dysfunction (leaflet motion restricted throughout diastole) which can be appreciated in all views. Asymmetric leaflet destruction and calcification are common.

Carpentier’s system for leaflet segment nomenclature is demonstrated in Figure 2. Ao denotes aorta, aortic com aortic valve commissure between the left and noncoronary cusps, ALPM anterolateral papillary muscle, AP anteroposterior, LA left atrium, LV left ventricle, and PMPM posteromedial papillary muscle.
Online Data Supplement Figure II. Study population, exclusions, imaging, and management.
Online Data Supplement Figure III. (A) Echo-guided repair composite Kaplan-Meier freedom from recurrent regurgitation by disease category. (B) Echo-guided repair composite Kaplan-Meier survival analysis including echo-guided mitral valve replacement.
Submitted in association with the manuscript entitled

Echo-Guided Mitral Repair

Daniel H. Drake, M.D., Karen G. Zimmerman, B.S., R.D.C.S. (A.E., P.E.), R.V.T.,
Anne M. Hepner, M.D., and Cynthia D. Nichols, Ph.D.

**Online Data Supplement Movie.** The movie demonstrates the mitral-left ventricular apex axis, elimination of parallax, and the resulting defined images. Disease classification is introduced with several echocardiographic examples. The disease based graduated surgical approach is clarified using a graphic depiction of echo images guiding operative management. Following a brief summary, the movie concludes with numerous examples of actual multiplanar imaging and the operative plans used to guide repair.