Surgical Approach To Functional MR: One Size Does Not Fit All

Pavan Atluri, M.D
Associate Professor of Surgery
Director, Mechanical Circulatory Support and Heart Transplantation
Director, Minimally Invasive and Robotic Cardiac Surgery Program

Division of Cardiovascular Surgery
Department of Surgery
University of Pennsylvania
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• Principle Investigator: ENDURANCE, LATERAL, MOMENTUM III, CTSnet STEM CELL, CTSnet Hybrid Coronary
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  • Institute for Translational Medicine and Therapeutics
Severe Functional MR: Surgical Treatment Options

CABG + MV Repair

MV Replacement
**Mitral Valve Replacement/Heart Failure in IMR**

### Mitral Valve Replacement for Ischemic Mitral Insufficiency

<table>
<thead>
<tr>
<th>Series</th>
<th>No. of Patients</th>
<th>Hospital Mortality</th>
<th>Late Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gerbode et al [7]</td>
<td>41</td>
<td>48%</td>
<td>NA</td>
</tr>
<tr>
<td>Pinson et al [8]</td>
<td>28</td>
<td>38%</td>
<td>44% at 5 years</td>
</tr>
<tr>
<td>Lytle et al [9]</td>
<td>47</td>
<td>10%</td>
<td>NA</td>
</tr>
<tr>
<td>Connolly et al [10]</td>
<td>16</td>
<td>19%</td>
<td>85% at 5 years</td>
</tr>
<tr>
<td>Kay et al [11]</td>
<td>40</td>
<td>35%</td>
<td>35% at 5 years</td>
</tr>
<tr>
<td>Rankin et al [6]</td>
<td>42</td>
<td>45%</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>214</td>
<td>33%</td>
<td></td>
</tr>
</tbody>
</table>

NA = not available.

Historically associated with high mortality
With degenerative MR repair is clearly superior, how about in the case of functional MR?
MV Repair vs Replacement


Mayo Clinic: ICM -- no difference in survival between replacement and repair

Figure 3. Survival after surgical correction of MR in patients who underwent surgery for nonischemic MR (left) and ischemic MR (right). Graphs compare patients who had a valve repair with those who required a valve replacement. The 5-, 10-, and 15-year survival rates are indicated for each curve. Although in ischemic MR there is no clear benefit from valve repair overall, in nonischemic MR mitral valve repair is followed by a better survival rate than that seen after valve replacement.
Present study: 32.6 % and 58.8% at 1,2 years

Magne et al. Cardiology 2009;112:244-59
Mitral valve repair or replacement for ischemic mitral regurgitation? The Italian Study on the Treatment of Ischemic Mitral Regurgitation (ISTIMIR)


<table>
<thead>
<tr>
<th>Variable</th>
<th>Repair (n = 244)</th>
<th>Replacement (n = 244)</th>
<th>Standardized difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y; mean ± SD</td>
<td>66.0 ± 7.1</td>
<td>66.1 ± 8.0</td>
<td>0.036</td>
</tr>
<tr>
<td>Sex, male/female; n (%)</td>
<td>178/66 (72.9/27.1)</td>
<td>169/75 (69.2/30.8)</td>
<td>0.081</td>
</tr>
<tr>
<td>BSA, kg/m²; mean ± SD</td>
<td>1.79 ± 1.2</td>
<td>1.78 ± 1.2</td>
<td>0.022</td>
</tr>
<tr>
<td>NYHA functional class, mean ± SD</td>
<td>2.8 ± 1.2</td>
<td>2.8 ± 1.3</td>
<td>0.000</td>
</tr>
<tr>
<td>EuroSCORE, mean ± SD</td>
<td>12.9 ± 4.0</td>
<td>13.0 ± 3.0</td>
<td>0.057</td>
</tr>
<tr>
<td>Family history, n (%)</td>
<td>131 (53.6)</td>
<td>137 (56.1)</td>
<td>0.090</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>101 (41.3)</td>
<td>99 (40.5)</td>
<td>0.016</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>89 (36.4)</td>
<td>86 (35.2)</td>
<td>0.022</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>44 (18.6)</td>
<td>51 (20.9)</td>
<td>0.032</td>
</tr>
<tr>
<td>CRD, n (%)</td>
<td>68 (27.8)</td>
<td>72 (29.5)</td>
<td>0.037</td>
</tr>
<tr>
<td>CVD, n (%)</td>
<td>19 (7.7)</td>
<td>22 (9.0)</td>
<td>0.046</td>
</tr>
<tr>
<td>PVD, n (%)</td>
<td>12 (4.9)</td>
<td>13 (5.3)</td>
<td>0.018</td>
</tr>
<tr>
<td>AF, n (%)</td>
<td>30 (12.2)</td>
<td>32 (13.1)</td>
<td>0.027</td>
</tr>
<tr>
<td>Pulmonary hypertension, n (%)</td>
<td>21 (8.6)</td>
<td>23 (9.4)</td>
<td>0.028</td>
</tr>
<tr>
<td>History of CHF, n (%)</td>
<td>123 (50.4)</td>
<td>127 (52.0)</td>
<td>0.032</td>
</tr>
<tr>
<td>IABP, n (%)</td>
<td>78 (31.9)</td>
<td>75 (30.7)</td>
<td>0.025</td>
</tr>
<tr>
<td>MI localization, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>62 (25.5)</td>
<td>64 (26.2)</td>
<td>0.015</td>
</tr>
<tr>
<td>Lateral</td>
<td>60 (24.5)</td>
<td>61 (25.0)</td>
<td>0.011</td>
</tr>
<tr>
<td>Inferior</td>
<td>122 (50.0)</td>
<td>119 (48.8)</td>
<td>0.024</td>
</tr>
<tr>
<td>Left main CAD</td>
<td>56 (22.9)</td>
<td>56 (21.9)</td>
<td>0.000</td>
</tr>
<tr>
<td>Echocardiographic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF, %; mean ± SD</td>
<td>35.0 ± 3.2</td>
<td>34.9 ± 2.9</td>
<td>0.057</td>
</tr>
<tr>
<td>EDD, mm; mean ± SD</td>
<td>55.0 ± 7.2</td>
<td>55.2 ± 6.9</td>
<td>1.075</td>
</tr>
<tr>
<td>ESD, mm; mean ± SD</td>
<td>42.0 ± 7.0</td>
<td>42.2 ± 7.3</td>
<td>0.074</td>
</tr>
<tr>
<td>EDD, ml.; mean ± SD</td>
<td>173 ± 25.3</td>
<td>173 ± 27.2</td>
<td>0.000</td>
</tr>
<tr>
<td>ESV, ml.; mean ± SD</td>
<td>108 ± 16.6</td>
<td>108 ± 18.7</td>
<td>0.000</td>
</tr>
<tr>
<td>MR, grade; mean ± SD</td>
<td>2.8 ± 0.5</td>
<td>2.8 ± 0.5</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**FIGURE 2.** A. Actuarial survival in mitral valve repair (MVP) and mitral valve replacement (MVR). B. Actuarial survival in MVP and MVR by left ventricular ejection fraction (LVEF).
Is the Best Repair a Replacement?

- Preservation of entire MV apparatus has been demonstrated to preserve ventricular geometry, decrease wall stress, improve systolic and diastolic function
- Must maintain chordal, annular and subvalvular continuity

Comparisons of results to Era where subchordal apparatus was excised not valid; Mortality in current era for MVR <5%
AHA/ACC and ESC Guidelines

• Class I Ib Level C evidence for severe secondary MR

Guidelines on the management of valvular heart disease (version 2012)

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Aloc Yahayaian (Chairperson) (France), Ottavio Alfieri (Chairperson) (Italy), Felicia Andreotti (Italy), Manuel J. Arrieta (Portugal), Gonzalo Barro-Espinar (Spain), Heike Baumgartner (Germany), Michael Andrew-Bergner (Germany), Thierry P. Carrel (Switzerland), Michel De Bonis (Italy), Arturo Evangelista (Spain), Volker Seiler (Switzerland), Bernard Ung (France), Patrizio Lancellotti (Belgium), Luc Pierard (Belgium), Basques Prat (UK), Hans-Joachim Schulze (Germany), Gerhard Schuler (Germany), Janina Sipuscola (Poland), Karl Swedenborg (Sweden), Johanna Takkunen (The Netherlands), Ulrich Otto Von Oppell (UK), Stephan Windhager (Switzerland), Jose Luis Zamora (Spain), Mariam Zimbalta (Poland)

• Class I Ib Level C evidence for severe secondary MR

European Journal of Heart Failure 13: 241-246

No conclusive evidence for superiority of repair or replacement

• Class I Level C evidence for IMR patients undergoing CAB w/ EF > 30%
• Class IIa Level C evidence for IMR patients undergoing CAB w/ EF < 30%
• Class IIb Level C evidence for IMR patients not undergoing CAB
Two-Year Outcomes of Surgical Treatment of Severe Ischemic Mitral Regurgitation


At 1 Year:

- No difference in reverse remodeling - LVESVI
- No difference in clinical end points; Mortality; MACCE
- No difference in QOL metrics

251 pts MV repair vs replacement for severe MR
Change in LVESVI at 2 Years

Z = -1.32, p = 0.19 (All Patients)

Median with 95% CI for change in LVESVI (2 Year – baseline)
Mortality

1 Year Mortality: 14% (Repair) vs. 18% (Replacement), p = 0.47

2 Year Mortality: 19% (Repair) vs. 23% (Replacement), p = 0.42

30 Day Mortality: 1.6% (repair) vs. 4.0% (replacement), p = 0.26

Hazard Ratio, 0.79 (95% CI, 0.46-1.35) P=0.39
Hazard Ratio = 0.97 (95% CI, 0.66-1.42)
P = 0.88

<table>
<thead>
<tr>
<th>Months</th>
<th>MV Repair</th>
<th>MV Replacement</th>
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<tbody>
<tr>
<td>0</td>
<td>126</td>
<td>125</td>
</tr>
<tr>
<td>6</td>
<td>96</td>
<td>87</td>
</tr>
<tr>
<td>12</td>
<td>84</td>
<td>83</td>
</tr>
<tr>
<td>18</td>
<td>77</td>
<td>76</td>
</tr>
<tr>
<td>24</td>
<td>48</td>
<td>50</td>
</tr>
</tbody>
</table>
Moderate/severe MR by TTE assessment in surviving pts at 30 days, 6, 12 and 24 months.
Cumulative Failure Over Time
(failure = death, ≥ mod MR or MV reoperation)

68% vs. 29% overall incidence of failure at 2 years
(RR = 2.3; 95% CI: (1.69-3.22)
\(p<0.001\)
Rates of Serious Adverse Events

- Heart Failure: p=0.19
- Stroke: p=0.41
- Bleeding: p=0.19
- Renal Failure: p=0.31
- Resp Failure: p=0.18
- All Events: p=0.049
## Hospitalizations

<table>
<thead>
<tr>
<th></th>
<th>Repair (n=126)</th>
<th>Replacement (n=125)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Readmissions (#events ppy)</td>
<td>152 (78.9)</td>
<td>121 (66.0)</td>
<td>0.14</td>
</tr>
<tr>
<td>CV Readmissions (#events ppy)</td>
<td>93 (48.3)</td>
<td>59 (32.2)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Reason for CV Readmissions:
Repair: CHF (30.3%), ICD/PPM (8.6%)
Replacement: CHF (24.0%), ICD/PPM (7.4%)
MLHF Scores
Don’t give up on repair yet.....
Post Hoc Analysis: Recurrence vs. No Recurrence in Repair Arm

<table>
<thead>
<tr>
<th>LVESVI (ml/m²)</th>
<th>Repair</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Recurrence</td>
</tr>
<tr>
<td>62.6 ± 26.9</td>
<td>42.7 ± 26.4</td>
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</tbody>
</table>

(replacement patients 60.6)

\[ p < 0.001 \]
Predictors of Recurrence

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TTE/TEE</th>
<th>Cutoff value</th>
<th>Sensitivity/specificity, %</th>
<th>Ref.</th>
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</thead>
<tbody>
<tr>
<td>Valvular parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral annulus diameter</td>
<td>TEE</td>
<td>≥37 mm</td>
<td>84/76</td>
<td>85</td>
</tr>
<tr>
<td>Tenting area</td>
<td>TEE</td>
<td>≥2.5 cm²</td>
<td>64/95</td>
<td>23</td>
</tr>
<tr>
<td>Coaptation distance</td>
<td>TEE</td>
<td>≥1.6 cm²</td>
<td>80/54</td>
<td>85</td>
</tr>
<tr>
<td>Coaptation distance</td>
<td>TEE</td>
<td>≥10 mm</td>
<td>64/90</td>
<td>23</td>
</tr>
<tr>
<td>Posterior leaflet angle</td>
<td>TTE</td>
<td>&gt;45°</td>
<td>100/95</td>
<td>23</td>
</tr>
<tr>
<td>Posterior leaflet tethering distance</td>
<td>TEE</td>
<td>≥40 mm</td>
<td>...</td>
<td>78</td>
</tr>
<tr>
<td>MR grade</td>
<td>TEE</td>
<td>≥3.5</td>
<td>42/81</td>
<td>85</td>
</tr>
<tr>
<td>MR jet</td>
<td>TEE</td>
<td>Central or complex</td>
<td>...</td>
<td>77</td>
</tr>
<tr>
<td>Ventricular parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV end-systolic volume</td>
<td>TTE</td>
<td>≥145 ml</td>
<td>90/90</td>
<td>87</td>
</tr>
<tr>
<td>Systolic sphericity index</td>
<td>TEE</td>
<td>≥0.7</td>
<td>100/100</td>
<td>87</td>
</tr>
<tr>
<td>Myocardial performance index</td>
<td>TTE</td>
<td>&gt;0.9</td>
<td>85/84</td>
<td>87</td>
</tr>
<tr>
<td>Wall motion score index</td>
<td>TTE</td>
<td>≥1.5</td>
<td>80/82</td>
<td>87</td>
</tr>
<tr>
<td>Interpapillary muscle distance</td>
<td>TTE</td>
<td>≥20 mm</td>
<td>96/97</td>
<td>86</td>
</tr>
<tr>
<td>Diastolic function</td>
<td>TTE</td>
<td>Restrictive filling pattern</td>
<td>...</td>
<td>89</td>
</tr>
</tbody>
</table>

TTE = Transthoracic echocardiography; TEE = transesophageal echocardiography.

Figure 1. Quantification of mitral valve geometry. ALA, Anterior leaflet angle; ALCA, anterior leaflet concavity area; PLA, posterior leaflet angle; CD, coaptation distance; BD, bending distance; PLL, posterior leaflet length; ALBD, anterior leaflet bending distance; LA, left atrium; LV, left ventricle.

Magne et al. Cardiology 2009;112:244-59
Kron et al. JTCVS 2015;149:752-61
2016 update to The American Association for Thoracic Surgery (AATS) consensus guidelines: Ischemic mitral valve regurgitation

• Patients with severe IMR

In the presence of basal aneurysm/dyskinesis, significant echo evidence of leaflet tethering and/or moderate to severe LV remodeling (LVEDD >70), patients should have MV replacement (COR IIa LOE A)—(less than 70 yo mechanical MVR; >70yo tissue MVR)

In the absence of basal aneurysm/dyskinesis, echo evidence of significant leaflet tethering or moderate to severe LV remodeling patients (LVEDD < 70), patients should have MV repair with an undersized, complete, rigid ring (COR IIb LOE B).
Repair can be bad, if not appropriately sized
Restrictive mitral valve annuloplasty versus mitral valve replacement for functional ischemic mitral regurgitation: A
n exercise echocardiographic study

Carlo Fino, MD,* Attilio Lacovoni, MD,† Paolo Ferrero, MD,‡ Michele Senni, MD,§ Maurizio Merlo, MD,§ Diego Cugola, MD,§ Paolo Ferrazzi, MD,§ Massimo Caputo, MD,§ Antonio Miceli, MD, PhD,§ and Julien Magne, PhD§

Objective: Mitral valve annuloplasty and mitral valve replacement are common strategies for the manage-
ment of functional ischemic mitral regurgitation with ischemic cardiomyopathy. However, mitral valve annu-
loplasty may create some degree of functional mitral stenosis. The purpose of this study was to compare the
mitral valve hemodynamics in patients with functional ischemic mitral regurgitation undergoing mitral valve
annuloplasty or mitral valve replacement, using exercise echocardiography.

Methods: We performed resting and exercise echocardiography in 70 patients matched for indexed effective
orifice area, systolic pulmonary arterial pressure, and left ventricular ejection fraction after mitral valve annu-
loplasty or mitral valve replacement with coronary artery bypass grafting.

Results: There was no significant difference between the 2 groups regarding baseline demographic and
clinical data. Exercise systolic pulmonary arterial pressure was higher in the mitral valve annuloplasty
replacement group compared with the mitral valve replacement group (from 36.3 ± 8.1 mm Hg to 35 ± 12 mm Hg,
vs mitral valve replacement: 33 ± 6 mm Hg to 42 ± 6.2 mm Hg, P = .0001). Exercise-induced improvement in
effective orifice area and indexed effective orifice area was better in the mitral valve annuloplasty replacement
vs mitral valve replacement: 0.24 ± 0.04 vs mitral valve annuloplasty: 0.14 ± 0.03 cm², P = .001, for effective
orifice area; mitral valve replacement: 0.27 ± 0.07 vs mitral valve annuloplasty: 0.20 ± 0.05 cm², P = .03, for
indexed effective orifice area). Exercise indexed effective orifice area was correlated with exercise systolic
pulmonary arterial pressure (r = −0.45, P = .01). In a multivariable analysis mitral valve annuloplasty,
postoperative indexed effective orifice area and resting mitral peak gradients were independent predictors of
elevated systolic pulmonary arterial pressure during exercise.

Conclusions: In patients with functional ischemic mitral regurgitation, mitral valve annuloplasty may cause
functional mitral stenosis, especially during exercise. Mitral valve annuloplasty was associated with poorer
exercise mitral hemodynamic performance, lack of mitral valve opening reserve, and markedly elevated
postoperative exercise systolic pulmonary arterial pressure compared with mitral valve replacement. (J Thorac

FIGURE 1. Absolute (A) and relative (B) exercise-induced changes in SPAP according to surgical technique (MVA vs MVR). MV, Mitral valve; 
SPAP, systolic pulmonary arterial pressure.
In patients with functional IMR, MV annuloplasty with small ring may cause Functional MS especially during exercise. MV annuloplasty was associated with poor MV hemodynamic performance, lack of MV opening reserve, and markedly elevated post operative post exercise pulmonary arterial systolic pressures compared to MV replacement.

**FIGURE 2.** Mitral valve opening reserve assessed as the individual exercise-induced changes in EOA for MVA (A) and MVR (B) groups. EOA, Effective orifice area; SD, standard deviation.

Greater increase in SPAP during exercise

Repair vs MVR

Indexed orifice area during exercise greater for MVR compared to repair

Improved 6 min walk with exercise with MVR
Is subvalvular repair worthwhile in severe ischemic mitral regurgitation? Subanalysis of the Papillary Muscle Approximation trial.

TABLE 3. Recurrence of moderate-to-severe mitral regurgitation at 5 years

<table>
<thead>
<tr>
<th></th>
<th>RA group, N = 34</th>
<th>PMA group, N = 37</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>19/34 (55.9%)</td>
<td>10/37 (27.0%)</td>
<td>.013</td>
</tr>
<tr>
<td>Tethering</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symmetric</td>
<td>7/12 (58.3%)</td>
<td>4/14 (28.6%)</td>
<td>.126</td>
</tr>
<tr>
<td>Asymmetric</td>
<td>12/22 (54.5%)</td>
<td>6/23 (26.1%)</td>
<td>.051</td>
</tr>
<tr>
<td>Regional wall motion abnormality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior</td>
<td>12/21 (57.1%)</td>
<td>5/23 (21.7%)</td>
<td>.016</td>
</tr>
<tr>
<td>Inferoposterior</td>
<td>4/8 (50.0%)</td>
<td>3/9 (33.3%)</td>
<td>.486</td>
</tr>
<tr>
<td>Anterolateral</td>
<td>3/5 (60.0%)</td>
<td>2/5 (40.0%)</td>
<td>.527</td>
</tr>
</tbody>
</table>

RA, Restrictive annuloplasty; PMA, papillary muscle approximation.
Repair Techniques for Ischemic Mitral Regurgitation

Damien J. LaPar, MD, MSc, and Irving L. Kron, MD

A: Anterior leaflet
B: Coaptation leaflets
C: Cerise with reduced tension
D: Papillary muscle
E: Posterior papillary muscle
F: Traction suture through posterior papillary muscle and pledgeted mitral annulus

Operative Techniques in Thoracic and Cardiovascular Surgery
Although it is clear that the advent of secondary MR is associated with a worse prognosis, it is unclear whether the worse outcome stems from MR itself or whether MR is simply a marker for worsening heart failure or that its correction will improve symptoms or survival. (Doug Mann)

- Robbins (AJC 2003; 91: 360) increased mortality with MR
- Trichon (AJC 2003; 91: 538) 1 and 5 year survival rates lower in moderate to severe MR
- Koelling (AHJ 2002; 144: 524) Prognosis is worse if MR present
Randomized trials that have demonstrated a benefit to MV surgery for heart failure
Conclusion

- Replacement confers most durable correction of severe IMR.
- Greatest reverse remodeling seen in repair patients w/o MR recurrence. Identification of predictors essential
- Individualize therapy, MV repair may still be an option in appropriately selected patients
- Long-term effect of MV surgery on heart failure therapy is unproven
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Jessica Howard
Eva Laverty- Wilson
Alysse Ameer

Students:
Jacob Goldenring
Andrew Acker
Jonathan Gordan
Bryan Auvil
Murray Skolnick
Rohith Thaiparambil
Alexander Zhou
Cody Fowler

Collaborators:
Jason Burdick, PhD
Robert Gorman, MD
Joseph Gorman, MD
Sergei Vinogradov, PhD
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