Ischemic Mitral Regurgitation

Did the surgical intervention change the natural history?

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DISCLOSURES

Conflicts of interest: none
Secondary MR: a rose by any other name....

- Functional MR (vs. Degenerative)
- Secondary MR (vs. Primary)
- Ischemic MR (vs. Non-Ischemic)

- Mitral regurgitation that occurs in the setting of left ventricular dysfunction with normal (or nearly normal) mitral leaflet and chordal structure
Pathology of FMR is Complex and Heterogeneous

- Coronary Artery Disease
  - Ischemic vs Nonischemic etiology
- Left Ventricle
  - Global vs regional wall motion abnormalities
  - Dilated or non-dilated
- Mitral Annulus
  - Normal, dilated, calcified
  - Symmetric or asymmetric dilation
- Electrical Activation
  - MR reduction occurs with CRT in some patients
- Dynamic
  - Preload and afterload sensitive
Functional MR Classification

Normal MV leaflet appearance and morphology, but annular dilation (DCM) or leaflet restriction (ischemic MR)

Type I: Normal
- Ring dilatation
- Perforation
- Cleft

Type II: Excessive
- Chordal or papillary muscle rupture / elongation

Type III: Restrictive
- Commissural fusion
- Thickening, calcification
- Leaflets
- Chords
- Chronic ischemic

Type IIIa: Structural during Systole and Diastole
- a structural during Systole and Diastole

Type IIIb: Functional during Systole
Moderate or Severe MR Is Common; Increases With Age

Mitral regurgitation is the most common type of heart valve insufficiency in the US$^{1,2}$

- Prevalence increases with increasing age, from 0.5% for 18-44 yr olds rising to 9.3% for ≥75 year olds ($p<0.0001$)

Prevalence of Valvular Heart Disease by Age

Chronic Ischemic MR

- IMR is associated with ↓ long term survival in post-MI and post revascularization patients

- IMR

- 70% of CHF in USA is due to ICM and half of them have IMR

- IMR
Mitral Regurgitation U.S.

Disease Prevalence

Total MR Patients
(MR ≥2+)

High-risk, MR≥3+

Annual incidence, MR≥3+

Annual MV surgery

4,100K

860K

260K

50K

Large and Growing Clinical Unmet Need
5 IMRs : 1696 adult cases
(2017 data)
## Indications for mitral valve intervention in chronic secondary mitral regurgitation

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
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<tr>
<td>Surgery is indicated in patients with severe secondary mitral regurgitation undergoing CABG and LVEF &gt;30%.</td>
<td>I</td>
<td>C</td>
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<tr>
<td>Surgery should be considered in symptomatic patients with severe secondary mitral regurgitation, LVEF &lt;30%, but with an option for revascularization and evidence of myocardial viability.</td>
<td>IIa</td>
<td>C</td>
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<tr>
<td>When revascularization is not indicated, surgery may be considered in patients with severe secondary mitral regurgitation and LVEF &gt;30% who remain symptomatic despite optimal medical management (including CRT if indicated) and have a low surgical risk.</td>
<td>IIb</td>
<td>C</td>
</tr>
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<td>When revascularization is not indicated and surgical risk is not low, a percutaneous edge-to-edge procedure may be considered in patients with severe secondary mitral regurgitation and LVEF &gt;30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have a suitable valve morphology by echocardiography, avoiding futility.</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>In patients with severe secondary mitral regurgitation and LVEF &lt;30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have no option for revascularization, the Heart Team may consider a percutaneous edge-to-edge procedure or valve surgery after careful evaluation for a ventricular assist device or heart transplant according to individual patient characteristics.</td>
<td>IIb</td>
<td>C</td>
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MV Repair for Ischemic MR

- Surgical gold standard for IMR is undersized mitral annuloplasty
- Undersized annuloplasty is associated with MR recurrence in high risk patients

Can we improve on results of undersized annuloplasty?
Restrictive Mitral Annuloplasty Cures Ischemic Mitral Regurgitation and Heart Failure

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Background. Restrictive mitral annuloplasty with revascularization is considered the best approach to ischemic mitral regurgitation with heart failure, but late results are controversial. We report late outcome in relation to preoperative left ventricular end-diastolic diameter (LVEDD) cutoff values, previously identified to predict intermediate-term left ventricular reverse remodeling.

Methods. One hundred consecutive ischemic mitral regurgitation patients underwent restrictive mitral annuloplasty (stringent downsizing by two ring sizes; median size, 26) and coronary revascularization. Survivors were clinically and echocardiographically assessed at intermediate (18 months) and late (mean, 46 months) follow-up.

Results. Early mortality was 8%, and late mortality was 18%. Actuarial 1-, 3-, and 5-year survival rates were 87% ± 3.4%, 80% ± 4.1%, and 71% ± 5.1%. Mortality predictors (Cox regression) were preoperative inotropic support (hazard ratio, 6.2; 95% confidence interval, 2.3 to 16.9) and preoperative LVEDD greater than 65 mm (hazard ratio, 4.5; 95% confidence interval, 1.9 to 10.9). Five-year survival rate for patients with LVEDD of 65 mm or less was 80% ± 5.2%, versus 49% ± 11% for LVEDD greater than 65 mm (p = 0.002). At 4.3 years' follow-up, New York Heart Association functional class had improved from 2.9 ± 0.8 to 1.6 ± 0.6 (p < 0.01). Mitral regurgitation grade was 0.8 ± 0.7, and was less than grade 2+ in 85% of patients. Left ventricular reverse remodeling was sustained with time for the LVEDD of 65 mm or less group. Late deaths did not show intermediate-term systolic left ventricular reverse remodeling, indicating a more extensive intrinsic left ventricular abnormality.

Conclusions. At 4.3 years' follow-up, intermediate-term cutoff values for left ventricular reverse remodeling proved to be predictors for late mortality. For patients with preoperative LVEDD of 65 mm or less, restrictive mitral annuloplasty with revascularization provides a cure for ischemic mitral regurgitation and heart failure; however, when LVEDD exceeds 65 mm, outcome is poor and a ventricular approach should be considered.

increased posterior leaflet tethering potentially caused by prosthetic ring implantation, which anteriorly displaces the posterior leaflet and reduces its mobility


Anterior Leaflet Strut Chordal Tethering Magnitude
Posterior Leaflet Intermediate Chordal Tethering Magnitude

Mitral Valve Annuloplasty and Anterior Leaflet Augmentation for Functional Ischemic Mitral Regurgitation: Quantitative Comparison of Coaptation and Subvalvular Tethering

Jean-Pierre M. Rabbah, Ph.D.1,3, Andrew W. Siefert, Ph.D.1,3, Steven F. Bolling, M.D.2, and Ajit P. Yoganathan, Ph.D.1
Limitations of Ring Annuloplasty

Is Undersized Annuloplasty the Answer?

Progression of 3+ or 4+ MR post-undersized annuloplasty
(n = 585)

McGee, Gillinov et al, JTCVS, 2004;128:916-24
Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation

CTS Net Trial
Repair vs. Replacement

- Repair > 30% recurrence of moderate MR
- Moderate MR did not progress
- Repair without MR, LVESVI improved

LVESVI

- non-inferiority MVrepair vs. MVR
- No difference in 12 month survival

- Repair > 30% recurrence of moderate MR
Two-Year Outcomes of Surgical Treatment of Severe Ischemic Mitral Regurgitation

Predicting recurrent mitral regurgitation after mitral valve repair for severe ischemic mitral regurgitation

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Annette C. Gelijns, PhD, b Alan J. Moskowitz, MD, e Pierre Voisine, MD, f Patrick T. O’Gara, MD, f
Michael Argenziano, MD, g Robert E. Michler, MD, b Marc Gillinov, MD, h John D. Puskas, MD, j
James S. Gammie, MD, b Michael J. Mack, MD, j Peter K. Smith, MD, b Chittoor Sai-Sudhakar, MD, n
Timothy J. Gardner, MD, g Gorav Ailawadi, MD, g Xin Zeng, MD, b Karen O’Sullivan, MPH, l
Michael K. Parides, PhD, d Roger Swayne, RN, BSN, b Vinod Thourani, MD, j Eric A. Rose, MD, c
Louis P. Perrault, MD, i and Michael A. Acker, MD, j for the CTSN Investigators

ABSTRACT

Objectives: The Cardiothoracic Surgical Trials Network recently reported no difference in the primary end point of left ventricular end-systolic volume index at 1 year postsurgery in patients randomized to repair (n = 126) or replacement (n = 125) for severe ischemic mitral regurgitation. However, patients undergoing repair experienced significantly more recurrent mitral regurgitation than patients undergoing replacement (32.6% vs 2.3%). We examined whether baseline echocardiographic and clinical characteristics could identify those who will develop moderate/severe recurrent mitral regurgitation or die.

Methods: Our analysis includes 116 patients who were randomized to and received mitral valve repair. Logistic regression was used to estimate a model-based probability of recurrence or death from baseline factors. Receiver operating characteristic curves were constructed from these estimated probabilities to determine classification cut-points maximizing accuracy of prediction based on sensitivity and specificity.

Results: Of the 116 patients, 6 received a replacement before leaving the operating room; all other patients had mild or less mitral regurgitation on echocardiogram after repair. During the 2-year follow-up, there were 13 mitral regurgitation recurrences and deaths. A model including age, body mass index, severity of ischemia, left ventricular area, basal aneurysm/dyskinesis, New York Heart Association class, history of coronary artery bypass grafting, percutaneous coronary intervention, and arrhythmias) yielded an area under the receiver operating characteristic curve of 0.82.

Conclusions: The model demonstrated good discrimination among patients who will survive 2 years without recurrent severe mitral regurgitation after repair. Although our results require validation, this putative risk score may be useful in selecting surgical candidates (Shuiyun Wang, MD; Bing Tang, MD. JTCVS 2017;153: 143-144 Letter to the Editor).
POINT: Efficacy of adding mitral valve restrictive annuloplasty to coronary artery bypass grafting in patients with moderate ischemic mitral valve regurgitation: A randomized trial

Khalil Fattouch, MD, PhD, Francesco Guccione, MD, Roberta Sampognaro, MD, Gaetano Panzarella, MD, Egle Corrado, MD, Emiliano Navarra, MD, Davide Calvaruso, MD, and Giovanni Ruvolo, MD

Objective: Surgical management of moderate chronic ischemic mitral valve regurgitation is still debated. The aim of this study was to evaluate the effect of adding mitral valve repair to coronary artery bypass grafting on clinical outcomes and left ventricular remodeling in patients who underwent coronary artery bypass grafting alone versus coronary artery bypass grafting plus mitral valve repair in a randomized trial.

Methods: Between February 2003 and May 2007, 102 patients were eligible for this study and were randomly assigned to one of 2 groups by means of cardioloigical criteria: coronary artery bypass grafting plus mitral valve repair (CABG plus MVR group; 48 patients, 47%) or coronary artery bypass grafting alone (CABG group; 54 patients, 53%). The 2 groups were similar regarding demographics, perioperative clinical data, and outcomes. There were differences regarding cardiopulmonary bypass (P < .0001) and aortic crossclamp (P < .0001) times. Exercise tests were performed for all survivors to evaluate tolerance to exercise and variability on grade of mitral regurgitation and systolic pulmonary arterial pressure. The study was blinded for physicians and nurses involved in postoperative care and clinical follow-up. The mean follow-up was 32 ± 18 months.

Results: Overall in-hospital mortality was 3% (3 patients). One (1.8%) patient died in the CABG group, and 2 (4.1%) patients died in the CABG plus MVR group. Survival rates ± standard error were 88.8% ± 3.2% and 93.7% ± 3.1% in the CABG and CABG plus MVR groups, respectively. A significant difference was found between the 2 groups with regard to mean New York Heart Association functional class (P < .01), left ventricular ejection fraction (P < .001), and left atrial size (P < .01). At follow-up, coronary artery disease was less likely to be revealed in patients with moderate mitral regurgitation grade and pulmonary artery pressure during exercise.

Conclusions: The efficacy of adding mitral valve repair to coronary artery bypass grafting in patients with moderate ischemic mitral valve regurgitation was assessed. In a randomized controlled trial, mitral valve repair significantly reduced mitral regurgitation grade, left ventricular end-systolic diameter, and left atrial size. More importantly, left ventricular ejection fraction was improved in patients with moderate mitral regurgitation grade. The results support the use of mitral valve repair in patients with moderate ischemic mitral valve regurgitation.
MODERATE IMR

Benefits of Additional MV Repair

- Less moderate or more MR during follow up:
  - 11% vs 32% at 2 years (CTS Net)
  - 4% vs 47% at 1 year (RIME)
  - 0% vs 60% at 2.5 years (Fattouch et al)

- Improved LV reverse remodeling (if no recurrent MR)

- Improved NYHA class / quality of life

- NO survival benefit
MODERATE IMR

Factors that ↑ Likelihood of Performing MV Repair for Moderate Ischemic MR

- Younger age (and longer life expectancy)
- More repairable MV (i.e. less severe tethering)
- ↑ LVEF (able to tolerate ↑ crossclamp time)
- ↓ reversibility in lateral / inferior walls (less likely to resolve with CABG alone)
- Less comorbidities (able to tolerate ↑ CPB time)
Surgical Repair of Moderate Ischemic Mitral Regurgitation—A Systematic Review and Meta-analysis

Mahesh Anantha Narayanan¹, Saurabh Aggarwal², Yogesh N. V. Reddy³, Venkata M. Alla², Janani Baskaran¹, Arun Kanmanthareddy², Rakesh M. Suri⁴

Two-Year Outcomes of Surgical Treatment of Moderate Ischemic Mitral Regurgitation

MV Repair for Ischemic MR

- Surgical gold standard for IMR is undersized mitral annuloplasty
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Patch Inflation

External Patch to Relieve Tethering and IMR

Figure 1. Patch placement and balloon inflation over the infarct region (highlighted) repositions the displaced PM toward the anterior annulus to relieve tethering and MR, monitored by ultrasound. Ao indicates aorta.

Hung et al, Circulation, 2002;106:2954-600
Initial results of the chordal cutting operation for ischemic mitral regurgitation

Michael A. Borger et al.
The Journal of Thoracic and Cardiovascular Surgery 2007; 133:1483-92
Combined papillary muscle sling and ring annuloplasty for moderate-to-severe secondary mitral regurgitation.


<table>
<thead>
<tr>
<th>Echocardiographic variables (6-10)</th>
<th>Preoperative</th>
<th>Follow-up</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral valve tenting height (cm, mean ± SD)</td>
<td>1.2 ± 0.4</td>
<td>0.6 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mitral valve tenting area (cm, mean ± SD)</td>
<td>2.8 ± 1</td>
<td>0.8 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mitral leaflet coaptation length (cm, mean ± SD)</td>
<td>0.4 ± 0.5</td>
<td>1 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anterior mitral leaflet tethering angle (degrees, mean ± SD)</td>
<td>42 ± 10</td>
<td>32 ± 7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Posterior mitral leaflet tethering angle (degrees, mean ± SD)</td>
<td>52 ± 14</td>
<td>72 ± 21</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Functional Mitral Regurgitation: Appraising the Evidence Behind Recommended Treatment Strategies
Samad Z, Velasquez EJ
Current Cardiology Reports 2016, 18:128
Therapeutic Approaches – Lots of Questions, Limited Answers

- What should we do about patients with moderate or severe FMR and LVSD going to CABG?
  - MV repair or MV replacement? Neither?

- What should we do about patients with severe FMR and LVSD but no CAD surgical indication?
  - MV repair/replacement? Continue medical therapy? MCSD?

- What should we do with patients with severe FMR and LVSD who are not otherwise CT surgical candidates?
  - MitraClip?
  - Medical therapy only?
Key points

- **In secondary mitral regurgitation**, there is **no conclusive evidence for a survival benefit** after mitral valve intervention. Mitral surgery is recommended concomitantly in patients with an indication for CABG and may be considered in patients who are symptomatic despite optimal medical therapy (including CRT if indicated) or who have a low surgical risk when revascularization is not indicated.

- Mitral valve repair is the **preferred** method, but mitral valve replacement should be considered in patients with unfavourable morphological characteristics.

- Outcomes of mitral valve repair depend on **surgeon experience** and centre related volume.

- Percutaneous edge-to-edge repair may be considered in patients at high surgical risk, avoiding futility.
Gaps in evidence

- The thresholds to define severe secondary mitral regurgitation are controversial and need to be evaluated with regards to their impact on prognosis after mitral valve intervention.

- The potential impact of mitral valve intervention (surgery and catheter intervention) on survival in patients with secondary mitral regurgitation needs to be evaluated.

- The new percutaneous valve repair and valve implantation techniques require further evaluation.
Do not blame the LV

- coaptation length of >8mm at the level A2-P2
- correct ring size to avoid stenosis
- semirigid or rigid rings
- appropriate adjunctive procedures
- trivial residual MReg with the patient awake
- costumized medical therapy
- close follow up
Thank you