Management of ischemic functional mitral valve regurgitation: Surgery, Devices or Medical therapy

Banff 2016
Differences between Primary vs Secondary M. Regurgitation

Primary

• Pathological abnormalities of the mitral apparatus

Secondary ("Functional")

• Normal or nearly normal mitral leaflets are prevented from proper coaptation by underlying LV dysfunction producing tethering, mitral annular dilation, or both
Mechanisms of Ischemic Mitral Regurgitation

- Increased tethering
- Bulging
- Decreased closing force
- Annular dilatation
- Papillary muscle traction
- MR
Clinical Significance of MR after MI

- 727 pts
- SAVE trial
- MI ≤16 days
- LVEF ≤40%

M. Regurg. on Angiography

141 pt 19.4%

Severity

1+ – 14.6%
2+ – 4.5%
3+ – 2 pts

Cumulative CV Survival

Days

Cardiovascular survival

Lamas: Circ, 1997
Ischemic MR: Outcomes Stratified by the Degree of MR

- 303 patients
- Prior (>16 days) QMI
- Mayo Clinic

### Survival Stratified by R. Vol

<table>
<thead>
<tr>
<th>RVol</th>
<th>Years</th>
<th>Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5</td>
<td>61±6</td>
</tr>
<tr>
<td>1-29</td>
<td>5</td>
<td>44±9</td>
</tr>
<tr>
<td>≥30</td>
<td>5</td>
<td>35±7</td>
</tr>
</tbody>
</table>

*P=0.002 on multivariate analysis

### Survival Stratified by ERO

<table>
<thead>
<tr>
<th>ERO</th>
<th>Years</th>
<th>Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5</td>
<td>61±6</td>
</tr>
<tr>
<td>1-19</td>
<td>5</td>
<td>47±8</td>
</tr>
<tr>
<td>≥20</td>
<td>5</td>
<td>29±9</td>
</tr>
</tbody>
</table>

**P>0.004 on multivariate analysis

Prigioni Circ, 2001
Therapeutic Considerations for Ischemic MR in Patients With LV Dysfunction

Guideline based medical therapy to address LV dysfunction
- Pharmacologic
- CRT

Coronary revascularization alone

*Clinical benefits well-documented

Beta blockers*
ACE/ARB*
Diuretics*
Isordil*
Aldosterone antagonists*

Indications
Extensive ischemia
Angina
Viability

Inconsistent effect on severity of MR

MV Replacement/Repair

?

LVAD/Cardiac transplantation
Effect of Mitral Valve Annuloplasty in Patients With LVEF ≤30%

- 419 patients
- Retrospective analysis
- Consecutive series

Survived Free of Death/VAD/Cardiac Transplant

Event-free survival

0.00 0.20 0.40 0.60 0.80 1.00

0 500 1,000 1,500 2,000 2,500

Days

No MVA (surgical candidate)
MVA

P=NS

Effectiveness of surgical Mitral Valve Repair Versus Medical Treatment for People With Significant Mitral Regurgitation and Non-Ischemic Congestive Heart Failure (SMMART-HF)

This study has been terminated (unable to recruit sufficient numbers of patients)

Clinical Trials.gov NCT 00608140
Durability of Ischemic Mitral Valve Repair

- 78 patients
- Ischemic MR
- Mean follow-up 28 mo

Recurrent MR (2+) – 32%
Severe MR (3-4+) – 20%

Recurrence of Severe MR After CABG ± Annuloplasty in Ischemic MR

- Recurrent severe MR lower with annuloplasty, but still 20% at 5 years

Jerri: JTCVS, 2006
## Randomized Trials of Surgical Treatment in Moderate Functional MR

<table>
<thead>
<tr>
<th>Trial</th>
<th>Pt (no.)</th>
<th>F-U</th>
<th>Outcomes (CABG + MVR vs CABG alone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fattouche et al</td>
<td>102</td>
<td>5 yr</td>
<td>(\uparrow) EF &lt;br&gt; (\downarrow) Volumes &lt;br&gt; Improved NYHA class</td>
</tr>
<tr>
<td>Chan (RIME Trial)</td>
<td>73</td>
<td>1 yr</td>
<td>(\downarrow) LV reverse remodeling &lt;br&gt; (\uparrow) Peak O(_2) consumption &lt;br&gt; (\downarrow) M regurgitation &lt;br&gt; (\downarrow) BNP</td>
</tr>
<tr>
<td>Smith (CST Network)</td>
<td>301</td>
<td>1 yr</td>
<td>No change in LVESV &lt;br&gt; (\downarrow) Moderate (\rightarrow) severe MR &lt;br&gt; (\uparrow) Bypass time and hospital stay &lt;br&gt; (\uparrow) Perioperative neurologic events</td>
</tr>
</tbody>
</table>

*No trial powered for major clinical outcomes*

*Mitral annuloplasty

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JTCVS, 2009  
Circ, 2012  
NEJM, 2014
Mitral Annuloplasty vs Replacement for Functional MR

↑ Periop. mortality and morbidity in some centers

Higher risk of persistent MR

Replacement

Repair

Impact on long-term clinical outcomes
Mitral Valve Repair vs Replacement for Severe Ischemic MR
CTSN Trial – 2-Year Outcomes (251 Patients)

Decrease in LVESV from Baseline

- Replacement: 6.5 mL/m²
- Repair: 9.0 mL/m²

Mortality

- Replacement: 23.2
- Repair: 19.1

Moderate → Severe MR Recurrence

- Replacement: 1.3
- Repair: 31.3

Repair patients - higher rate of serious heart failure, 24% vs 15% (P=0.05) and more CV readmissions 48.3 vs 32.2 (P=0.01)

Goldstein: NEJM, 2015
Critique of the CTSN Trials

Critique
• Patients randomized irrespective of the prediction of successful MV repair including measurements of valve-tethering forces
  • Regurgitation was severe not moderate (ERO 0.20)
  • High rate of residual MR
  • Simple mitral annuloplasty ring technique is inadequate

Defense
• Large number screened vs randomized

  Does this not imply “equipoise” in those enrolled?

  • Measurements of MV tethering were performed but not reported and not predictive of recurrent MR
  • Trial examined currently established techniques for mitral valve repair
  • Enrollment criteria that included a population seen in clinical practice thereby increasing the generalization of the results
Impact of Functional MR

... a marker of a sicker LV
- and/or –
... a contributor to a sicker LV?

Is it a target for therapy?

Medical  Surgical/MitraClip

Therapies that produce beneficial reverse remodeling also reduce severity of functional MR but probably not survival
Should Moderate to Severe Functional MR be Corrected?

Intuitively– Yes

Caveats

• No concrete evidence that surgery alters natural history
• High risk of recurrence after MV Repair
• Significant morbidity and mortality with MV replacement in some series

Ongoing trials are important for both approaches

- Surgery vs Medical
- Percutaneous vs Medical
- Percutaneous vs Surgery
## Ongoing Randomized Trials of MitraClip in Patients With HF and Secondary MR

<table>
<thead>
<tr>
<th></th>
<th>COAPT</th>
<th>RESHAPE-HF</th>
<th>MITRA-FR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No pt</strong></td>
<td>430</td>
<td>800</td>
<td>288</td>
</tr>
<tr>
<td><strong>Sites</strong></td>
<td>US/Canada</td>
<td>Europe</td>
<td>France</td>
</tr>
<tr>
<td><strong>LVEF</strong></td>
<td>≥20-50%</td>
<td>≥15-40%</td>
<td>≥15-40%</td>
</tr>
<tr>
<td><strong>Primary efficacy endpoint</strong></td>
<td>HF hospitalization</td>
<td>Death or HF hospitalization</td>
<td>Death or recurrent HF hospitalization</td>
</tr>
<tr>
<td><strong>F-U</strong></td>
<td>1 yr</td>
<td>1 yr</td>
<td>1 yr</td>
</tr>
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</table>
Short-Term Results of Transapical Transcatheter Mitral Valve Implantation for Mitral Regurgitation

Anson Cheung, MD, John Webb, MD, Stefan Verheyen, MD, PhD, Robert Moss, MD, Robert Boone, MD, Jonathan Leipsic, MD, Ron Ree, MD, Shmuel Banai, MD

• 2 patients
• Tiara system
• 2 months successful outcomes

TEE showing a normally functioning mitral valve prosthesis with no significant paravalvular leak, a low transvalvular gradient, and no LV outflow obstruction
Surgery for Ischemic MR

Conclusions

No evidence of a survival benefit

Explanation – Majority do not have severe regurgitation

Patients with symptomatic CHF

Symptomatic benefits in some but whether survival is improved remains unproven
Why is the Benefit of MR Reduction so Hard to Prove?

• MR recurrence ≥20%; perioperative mortality 1.5-15%

• The benefit may be limited to specific pt subgroups that have not been pre-defined in CV datasets

• Perhaps there is no benefit? – *MR is a surrogate not causally related to outcome?*

• “Things may not be as they seem”

_Gersh And Frye NEJM 2008_
Functional Mitral Regurgitation – Conclusions

- FMR is primarily a disorder of the LV
- FMR is common in CHF and after MI
- FMR predicts increased mortality in a graded fashion
- Medical therapy including beta-blockers, ACE-1 ARB are effective
- CRT may be effective in some patients
- CABG alone can reduce FMR acutely in some patients – results unpredictable
Functional (Secondary) MR
“Evidence and Uncertainties”

• Does correcting FMR prolong or improve the quality of life?
  May depend upon presence of CHF symptoms

• Trials with Mitraclip / devices will help inform the field

• If correcting FMR is demonstrated to help:
  then providing the most complete and durable correction
  is desirable

Predictors of recurrences after repair
• Severe tethering
• Inferobasal aneurysm
• Severe LV dilatation

Valve-sparing mitral valve replacement
should be used more liberally in these patients