Mitral Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation

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Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation


BACKGROUND
Ischemic mitral regurgitation is associated with a substantial risk of death. Practice guidelines recommend surgery for patients with a severe form of this condition but acknowledge that the supporting evidence for repair or replacement is limited.

METHODS
We randomly assigned 251 patients with severe ischemic mitral regurgitation to undergo either mitral-valve repair or chordal-sparing replacement in order to evaluate efficacy and safety. The primary end point was the left ventricular end-systolic volume index (LVESVI) at 12 months, as assessed with the use of a Wilcoxon rank-sum test in which deaths were categorized below the lowest LVESVI rank.

RESULTS
At 12 months, the mean LVESVI among surviving patients was 54.6±25.0 ml per square meter of body-surface area in the repair group and 60.7±31.5 ml per square meter in the replacement group (mean change from baseline, −6.6 and −6.8 ml per square meter, respectively). The rate of death was 14.3% in the repair group and 19.6% in the replacement group (hazard ratio with repair, 0.79; 95% confidence interval, 0.42 to 1.47; P=0.45 by the log-rank test). There was no significant between-group difference in LVESVI after adjustment for death (P=0.33; F=0.18). The rate of moderate or severe recurrence of mitral regurgitation at 12 months was higher in the repair group than in the replacement group (52.6% vs. 22.9%, P=0.001). There were no significant between-group differences in the rate of a composite of major adverse cardiac or cerebrovascular events, in functional status, or in quality of life at 12 months.

CONCLUSIONS
We observed no significant difference in left ventricular reverse remodeling or survival at 12 months between patients who underwent mitral-valve repair and those who underwent mitral-valve replacement. Replacement provided a more durable correction of mitral regurgitation, but there was no significant between-group difference in clinical outcomes. (Funded by the National Institutes of Health and the Canadian Institutes of Health; ClinicalTrials.gov number, NCT00600704.)
Ischemic MR is not Degenerative MV Disease

- LV enlarges-loss of elliptical shape; more spherical
  - Mitral annulus dilates
  - Papillary muscles displace
  - Chordae tether leaflets
  - Valve leaflets are not in coaptation...

= Functional Mitral Regurgitation
AHA/ACC and ESC Guidelines

No conclusive evidence for superiority of repair or replacement

• Class IIb Level C evidence for severe secondary MR

• 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
Preference for Repair Over Replacement

Mitral Repair and Replacement with CABG

Years 2008-2012, The Adult Cardiac Surgery Database, The Society of Thoracic Surgeons
Treatment Choice is Controversial

• Lower periop morbidity and mortality with repair

• Better long-term correction with replacement
  – Gillinov et al, J Thorac Cardiovasc Surg 2001;122:1125-41

• Based on retrospective observational studies

• Need randomized evidence
SMR Trial Design

**Enrollment**
- Assessed for Eligibility (n=3458)
  - Excluded (n = 3207)
    - Did not meet inclusion criteria (n=3011)
    - Refused to participate (n=131)
    - Other (n=65)
  - Randomized (n = 251)

**Allocation**
- Allocated to Mitral Valve Repair (n=126)
  - Received MV Repair (n=115)
  - Received MV Replacement (n=11)
- Allocated to Mitral Valve Replacement (n=125)
  - Received MV Replacement (n=124)
  - Received MV Repair (n=1)

**Follow-Up**
- Withdrawal before month 12 (n=3)
  - Death before month 12 (n=18)
- Withdrawal before month 12 (n=1)
  - Death before month 12 (n=22)

**Analysis**
- Primary Endpoint Analysis (n=126)
  - Excluded from Analysis (n=0)
- Primary Endpoint Analysis (n=125)
  - Excluded from Analysis (n=0)
Primary Endpoint

- Degree of left ventricular reverse remodeling
  - Assessed by left ventricular end systolic volume index (LVESVI) using TTE at 12 months
  - Group difference based on Wilcoxon Rank-Sum test with deaths categorized as lowest LVESVI rank
- Powered (90%) to detect an improvement of 15mL/m² from repair or replacement in LVESVI at 12 months
Secondary Endpoints

• Mortality
• Recurrent MR
• MACCE
  – Mortality
  – Stroke
  – Subsequent MV surgery
  – HF hospitalization
  – Increase in NYHA class \( \geq 1 \)
• Serious adverse events
• Quality of life
Median change in LVESVI

Median with 95% CI for change in LVESVI from baseline to 1 yr

Z=1.33, p=0.18
(All pts)
Recurrent MR at 1 year

Moderate or Severe Recurrent MR

<table>
<thead>
<tr>
<th></th>
<th>Percent with moderate or severe recurrent MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repair</td>
<td>32.6</td>
</tr>
<tr>
<td>Replacement</td>
<td>2.3</td>
</tr>
</tbody>
</table>

*p < 0.001*
LVESVI with Recurrent MR

Mean LVESVI for Patients Undergoing Repair

- Repair with MR
- Repair without MR

- Baseline
- 12 Months

$p < 0.001$
Mortality

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

12 Month Mortality: 14.2% (repair) vs. 17.6% (replacement), \( p = 0.47 \)

Hazard Ratio, 0.79 (95% CI, 0.42, 1.47), \( P = 0.4542 \)
MACCE at 12 Months

Hazard Ratio, 0.91 (95% CI, 0.58, 1.42)
P = 0.6753

- MV Repair
- MV Replacement

<table>
<thead>
<tr>
<th>Months</th>
<th>MV Repair</th>
<th>MV Replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>126</td>
<td>125</td>
</tr>
<tr>
<td>3</td>
<td>105</td>
<td>96</td>
</tr>
<tr>
<td>6</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>9</td>
<td>90</td>
<td>88</td>
</tr>
<tr>
<td>12</td>
<td>87</td>
<td>86</td>
</tr>
</tbody>
</table>
Serious Adverse Events

Overall SAE Rate (100-pt years)
202.1 (repair) vs. 189.0 (replacement)
p=0.49

P=NS
Quality of Life at 1 year

- SF-12
  - Repair: Δ=16.6%
  - Replacement: Δ=18.4%

- MLHF
  - Repair: Δ=46.9%
  - Replacement: Δ=19.6%
NYHA Classification & Death

![Chart showing NYHA Classification & Death]
Limitations

• Trial does not include revascularization alone arm
  – Lack of equipoise with severe MR given current guidelines
  – Revascularization alone currently studied in ongoing CTSN trial (MMR)

• Primary end point measures LV remodeling not a clinical endpoint
  – Abundant evidence correlates LVESVI with clinical outcomes
  – Trial with mortality endpoint requires several thousand pts

• Only 1 year results reported
  – Pts will be followed for 2 yrs
Summary

• There was no difference in the degree of reverse remodeling and mortality

<table>
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<th>Mortality</th>
<th>Repair</th>
<th>Replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 day</td>
<td>1.6%</td>
<td>4.0%</td>
</tr>
<tr>
<td>1 year</td>
<td>14.3%</td>
<td>17.6%</td>
</tr>
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</table>

• Significantly more recurrent MR at 1 year (32.6% vs 2.3%) with MV repair compared to chordal sparing MV replacement

• No difference in MACCE, overall SAEs, NYHA Class and QOL
Conclusions

• Chordal-sparing MV Replacement provides a more durable correction of severe IMR with no differences seen in reversal of LV remodeling or clinical outcomes – MR recurrence may have an important effect on long-term outcomes

• Additional follow-up and subset analysis may provide insight about predictors and clinical impact of MR recurrence optimizing therapeutic decisions for individual patients
Investigators

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- Columbia University Medical Center
- University of Maryland
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- Duke University
- East Carolina Heart Inst
- Brigham and Women's Hospital
- Ohio State University Medical Center
- Sacre-Coeur de Montreal
- University of Southern California
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- Mission Hospital
- NIH Heart Center at Suburban Hospital
- Jewish Hospital
- Sunnybrook Health Sciences Centre
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