Technical Challenges in Percutaneous Repair of Functional Mitral Regurgitation

Steven Burstein, MD

Director, Cardiovascular and Cardiac Catheterization Laboratories
PIH Health Good Samaritan Hospital
Los Angeles, CA
Diclosures

- Edwards Lifescience - speaker and proctor
- Boston Scientific – speaker, research participant, SAB
- Abbott – proctor, research participant
Challenges

- Is repair clinically indicated?
- What type of repair is appropriate?
- What does the data suggest?
- Intraprocedural technical challenges
- High risk situations and bailout options
- How is it different from surgical repair?
Classification of Mitral Regurgitation

Type I: Normal leaflet motion
Type II: Increased leaflet motion
Type IIIA: Restricted leaflet motion (systole and diastole)
Type IIIB: Restricted leaflet motion (systole)

(Notes: The middle scallop of the posterior leaflet is designated as P2 and the adjacent lateral and medial segments are P1 and P3. The opposing segments of the anterior leaflet are designated as A1, A2, and A3. AC and PC represent the anterior and posterior cardiac commissures. Dilation leaflet dysfunction (Carpenter type I, type A, type III) is classified on the basis of motion of the free margin of the leaflet in relation to the annular plane.)
The Mitral Apparatus
Mitral regurgitation may be due to disruption of a number of elements:

1. Annular dilation
2. Chordal retraction
3. Papillary muscle separation
4. Annular calcification
5. Leaflet fibrosis and calcification
Percutaneous Techniques

- Leaflet edge to edge apposition
- Annular reduction strategies
- Neo-chord insertion
- Papillary muscle apposition
Cardioband
Cardioband
Neochord Insertion
Papillary Muscle Approximation

Aorta

Left atrium

Mitral valve

Anterior leaflet

Posterior leaflet

Tethering force

Left ventricle

Anterior papillary muscle

Posterominal papillary muscle

Complete PMA

Incomplete PMA
Procedural Challenges

- Transseptal puncture
- Access and IVC hostility
- LA size and shape
- Leaflet morphology
Transseptal Puncture

(a) (b) (c) (d) (e)
Lipomatous septal hypertrophy
IVC tortuosity
IVC Filters
Heart Failure and Secondary Mitral Regurgitation: Echocardiographic Outcomes

- from the COAPT trial
- Federico M. Asch, MD
  - Director, Echocardiographic Core Lab
  - MedStar Health Research Institute
- On behalf of Gregg W. Stone, Michael Mack, Neil J Weissman and the COAPT Investigators

INDICATION FOR USE
- The MitraClip™ NTR/XTR Clip Delivery System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus (degenerative MR) in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation.
- The MitraClip™ NTR/XTR Clip Delivery System, when used with maximally tolerated guideline-directed medical therapy (GDMT), is indicated for the treatment of symptomatic, moderate-to-severe or severe secondary (or functional) mitral regurgitation (MR; MR ≥ Grade III per American Society of Echocardiography criteria) in patients with a left ventricular ejection fraction (LVEF) ≥ 20% and ≤ 50%, and a left ventricular end systolic dimension (LVESD) ≤ 70 mm whose symptoms and MR severity persist despite maximally tolerated GDMT as determined by a multidisciplinary heart team experienced in the evaluation and treatment of heart failure and mitral valve disease.

COAPT (NCT01626079)
COAPT

610 patients enrolled
Significant FMR (≥3 by core lab)
LVEF ≤50%

OPTIMAL HF MEDICAL THERAPY
Randomize 1:1

MitraClip  Control group
Standard of care

Primary endpoint: HF hospitalization at 1 year
<table>
<thead>
<tr>
<th></th>
<th>MITRA FR</th>
<th>COAPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>304</td>
<td>614</td>
</tr>
<tr>
<td>MR severity</td>
<td>ERA &gt; 20 mm² RV &gt; 30 mI/beat</td>
<td>ERA &gt; 30 mm² RV &gt; 45 mI/beat</td>
</tr>
<tr>
<td>GDMT</td>
<td>Patients receive medical treatment that can be adjusted during follow-up according to “real life” criteria</td>
<td>Patients receive maximally tolerated medical treatment minimally adjusted after randomization</td>
</tr>
<tr>
<td>Acute results +3 /at 12 months</td>
<td>9%—17%</td>
<td>5%—5%</td>
</tr>
<tr>
<td>Complications</td>
<td>14.6%</td>
<td>8.5%</td>
</tr>
<tr>
<td>LVEF</td>
<td>≥15%—&lt;40%</td>
<td>≥20%—&lt;50%</td>
</tr>
<tr>
<td>LV volume</td>
<td>No limit</td>
<td>LVESD ≤70 mm</td>
</tr>
<tr>
<td>1 or 2 Clip/patient</td>
<td>54.5%</td>
<td>98%</td>
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</table>
Background (i)

• Secondary or functional mitral regurgitation (SMR) is present in >50% of patients with heart failure (HF), and is severe in ~10-15%.

• Prognosis is poor when SMR is severe.

• COAPT: Randomized, open-label, multicenter trial in patients with HF and moderate-to-severe (3+) or severe (4+) SMR who remained symptomatic despite maximally-tolerated GDMT.
Death or HF admit

All-cause Mortality or HF Hospitalization (%)

Time After Randomization (Months)

MitraClip + GDMT

GDMT alone

HR [95% CI] =
0.57 [0.45-0.71]

P<0.001

NNT (24 mo) =
4.5 [95% CI 3.3, 7.2]
Change in LV Volumes Over Time

Left Ventricular End Systolic Volume (LVESV)

Paired measures, follow-up minus baseline
Mean ± SE

Adjusted Change in LVESV (mL) from Baseline

Months Post Procedure

Subjects with HF death prior to a follow-up visit were assigned the worst observed change from baseline at that visit. For all other subjects who had missing echo values, multiple imputation was used.

*p<0.05 (ANCOVA)
Change in Ejection Fraction Over Time

Left Ventricular Ejection Fraction (LVEF)

Paired measures, follow-up minus baseline
Mean ± SE

* p<0.05 (ANCOVA)

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Background (ii)

- SMR is a consequence of leaflet tethering and incomplete leaflet coaptation.

- Evaluation of SMR is challenging, due to asymmetric leaflet anatomy and regurgitant orifice, eccentric jets and enlarged left cardiac chambers.

- Expert panels have disagreed on how to define the severity of SMR, resulting in conflicting European and American guidelines.
Change in LV Volumes Over Time

Left Ventricular End Diastolic Volume (LVEDV)

Paired measures, follow-up minus baseline
Mean ± SE

Subjects with HF death prior to a follow-up visit were assigned the worst observed change from baseline at that visit. For all other subjects who had missing echo values, multiple imputation was used.
### Predictors of 24-Month Mortality or First HF Hospitalization

Multivariable Cox regression

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard Ratio [95% CI]</th>
<th>P-Value</th>
<th>Hazard Ratio [95% CI]</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVSP (mmHg)</td>
<td>1.02 [1.01, 1.04]</td>
<td>0.005</td>
<td>TR Grade (≥ 2+ vs ≤ 1+)</td>
<td>1.60 [1.07, 2.39]</td>
</tr>
<tr>
<td>STS Repl Score</td>
<td>1.12 [1.02, 1.23]</td>
<td>0.020</td>
<td>LVEF (%)</td>
<td>0.98 [0.96, 1.00]</td>
</tr>
<tr>
<td>LVEDV (mL)</td>
<td>1.00 [1.00, 1.01]</td>
<td>0.07</td>
<td>RVSP (mmHg)</td>
<td>1.01 [1.00, 1.02]</td>
</tr>
<tr>
<td>Sex (Female vs Male)</td>
<td>0.64 [0.37, 1.08]</td>
<td>0.09</td>
<td>EROA, PISA (cm²)</td>
<td>3.15 [1.08, 9.21]</td>
</tr>
<tr>
<td>EROA, PISA (cm²)</td>
<td>2.56 [0.79, 8.26]</td>
<td>0.12</td>
<td>STS Repl Score</td>
<td>1.07 [0.98, 1.18]</td>
</tr>
<tr>
<td>Isch vs Non-Isch CM</td>
<td>0.70 [0.43, 1.13]</td>
<td>0.15</td>
<td>Age (years)</td>
<td>0.99 [0.97, 1.01]</td>
</tr>
<tr>
<td>STS Repair Score</td>
<td>0.95 [0.88, 1.04]</td>
<td>0.26</td>
<td>STS Repair Score</td>
<td>0.96 [0.87, 1.07]</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>1.01 [0.98, 1.03]</td>
<td>0.56</td>
<td>Isch vs Non-Isch CM</td>
<td>0.92 [0.62, 1.36]</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.01 [0.98, 1.03]</td>
<td>0.57</td>
<td>LVEDV (mL)</td>
<td>1.00 [1.00, 1.00]</td>
</tr>
<tr>
<td>TR Grade (≥ 2+ vs ≤ 1+)</td>
<td>0.90 [0.51, 1.61]</td>
<td>0.73</td>
<td>Sex (Female vs Male)</td>
<td>0.97 [0.64, 1.46]</td>
</tr>
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</table>
Conclusions (i)

COAPT Echo Sub-study

- To duplicate the COAPT results, specific COAPT screening echo criteria and expert echo analysis should be applied to identify proper candidates for MitraClip.

- In patients with HF and 3+ or 4+ secondary MR, TMVr with MitraClip provided substantial death and HFH benefits in all echocardiographic subgroups, regardless of degree of LV dysfunction, LV dimensions, pulmonary hypertension, severity of TR or individual MR parameters (all responders).
Proportionate MR
Conclusions (ii)
COAPT Echo Sub-study

- Baseline MR severity predicts poor outcomes in patients with HF treated with GDMT alone, but not after MR has been corrected by MitraClip.
- RVSP was the only independent echocardiographic predictor of poor outcomes after MitraClip treatment.
Hemodynamic dilemma

- Low EF and dilated ventricles
- Continuous assessment of LAP and SBP
- Real time TEE assessment of LV performance
- The “RV” effect
Why is this different from SMVR?

- No cardiopulmonary bypass
- No surgical insult
- Realtime assessment of LV function
- Ability to titrate therapy – leave a little MR
- Bailout options exist – clip extraction, circulatory support
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