Mitral Regurgitation: Evaluation and Treatment

2020 CHI Cardiology Symposium
8 February, 2020
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Disclosures

None

Objectives:
1. Understand functional vs. degenerative MR
2. Understand MR severity grading
3. Understand indications for surgery/intervention
Outline

Epidemiology/Anatomy
Regurgitation Classification
Myxomatous Degeneration
MR Severity Grading
Guidelines for Management
MitraClip evaluation
COAPT Trial and Secondary MR (sMR)
Epidemiology

Mitral regurgitation
prevalence (any) 70% by TTE

Significant MR (Moderate-Severe)
2-3% of general population
≈ 7-8 million U.S. adults
≈ 150-200 million worldwide
Mitral valve anatomy

Pathophysiology

Chronic MR = Volume ↑↑

Insidious process:
Structural Δ’s PRECEDE sx’s

Symptoms:

“Heart Failure”
- Exertional SOB
- Activity Intolerance
- Fatigue
- Edema
- Orthopnea
- Cough

Palpitations (Atrial Fibrillation)

https://emedicine.medscape.com/article/890315-overview#a6
MR Etiology

Degenerative (pMR)
- Primary/Organic
- Structural Δ’s (prolapse, flail, perforation, etc.)

Functional/Secondary (sMR)
- LV dysfunction/enlargement
- LA/annular dilatation (“Atrial Functional”)
- Ca^{++}/Rheumatic degeneration
Carpentier Classification
MR Etiology

> 30,000 pts from 463 centers, Abott 2015

- FMR, 65%
- DMR, 22%
- Mixed, 13%
Myxomatous Degeneration: Fibroelastic Deficiency (FED)

VEC: Valvular Endothelial Cells
VIC: Valvular Interstitial Cells

Francesca N. Delling, and Ramachandran S. Vasan
Circulation. 2014;129:2158-2170
Myxomatous Degeneration: Spectrum of Disease

Myxomatous Degeneration: Progression of Disease

Proposed temporal spectrum of mitral valve (MV) prolapse (MVP) progression with potential interventions/nonsurgical therapies depending on progression stage (bottom).

Francesca N. Delling, and Ramachandran S. Vasan
Circulation. 2014;129:2158-2170
MR Severity - Echo

Regurgitation has four hallmarks:
- Flow convergence
- Flow acceleration
- Turbulence
- Downstream
### MR Severity - Echo

<table>
<thead>
<tr>
<th>Mitral Regurgitation</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Qualitative</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiographic grade</td>
<td>1+</td>
<td>2+</td>
<td>3-4+</td>
</tr>
<tr>
<td>Color Doppler jet area</td>
<td>Small, central jet (less than 4 cm² or less than 20% LA area)</td>
<td>Signs of MR greater than mild present, but no criteria for severe MR</td>
<td>Vena contracta width greater than 0.7 cm with large central MR jet (area greater than 40% of LA area) or with a wall-impinging jet of any size, swirling in LA</td>
</tr>
<tr>
<td>Doppler vena contracta width (cm)</td>
<td>Less than 0.3</td>
<td>0.3 – 0.69</td>
<td>Greater than or equal to 0.70</td>
</tr>
<tr>
<td><strong>Quantitative (cath or echo)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regurgitant volume (ml/beat)</td>
<td>Less than 30</td>
<td>30-59</td>
<td>Greater than or equal to 60</td>
</tr>
<tr>
<td>Regurgitant fraction (%)</td>
<td>Less than 30</td>
<td>30-49</td>
<td>Greater than or equal to 50</td>
</tr>
<tr>
<td>Regurgitant orifice area (cm²)</td>
<td>Less than 0.20</td>
<td>0.2-0.39</td>
<td>Greater than or equal to 0.40</td>
</tr>
<tr>
<td><strong>Additional Essential Criteria</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left atrial size</td>
<td>Enlarged</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular size</td>
<td>Enlarged</td>
<td></td>
<td></td>
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</tbody>
</table>
Follow-up: ASE Guidelines

Mild MR
- Echo: q3-5 years

Moderate MR
- Echo: annual

Severe MR
- Referral (3D TEE +/- intervention)

* Echo for any Δ murmur or symptoms
Treatment- Med Rx

Primary MR
- BP mgmt. (ARB/ACE-I)
  * MR is dynamic
- diuretics

Secondary MR
- β-blocker
- Revascularization
- CRT
Treatment: ARB?

**CENTRAL ILLUSTRATION:** Losartan Reduces Post-MI Profibrotic Mitral Valve Changes Without Eliminating Adaptive Leaflet Growth

<table>
<thead>
<tr>
<th>MI No Therapy</th>
<th>MI with ARB</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC Undergoing EMT</td>
<td>EC Undergoing EMT</td>
</tr>
<tr>
<td>VCAM-1⁺ EC</td>
<td>VCAM-1⁺ EC</td>
</tr>
<tr>
<td>Activated VIC</td>
<td>Activated VIC</td>
</tr>
<tr>
<td>Quiescent VIC</td>
<td>Quiescent VIC</td>
</tr>
<tr>
<td>Collagen Bundles</td>
<td>Collagen Bundles</td>
</tr>
<tr>
<td>CD45⁺</td>
<td>CD45⁺</td>
</tr>
</tbody>
</table>


Animal study with ARB = protective antifibrotic/anti-inflammatory effect. EMT- endothelial to mesenchymal transition.
1095 patients with Severe MR and HF

FMR 74%, DMR 21%, Other 5%
53% Medical Therapy and 47% Surgery

Journal of the American College of Cardiology Jan 2014, 63 (2) 185-186; DOI: 10.1016/j.jacc.2013.08.723
Treatment

Surgical

- Valve replacement
  - Mechanical (warfarin)
  - Bioprosthetic (90%, warfarin 3-6mo. then ASA)
- Valve repair
  - Ring +/- resection
  - Alfieri stitch

* DMR- prohibitive surgical risk
- Transcatheter repair (MitraClip)
ACC Guidelines: Surgery

LV Dysfxn:
- EF < 60%
- ESd > 4cm
- EF < 30% or ESd > 5.5 cm = Med Rx

IIb - Left Atrial Enlargement

Table 1: Guideline Recommendations for Surgery for Degenerative Mitral Regurgitation

<table>
<thead>
<tr>
<th>Indication</th>
<th>ACC/AHA</th>
<th>ESC/EACTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic patients</td>
<td>Class I</td>
<td>Class I</td>
</tr>
<tr>
<td>Asymptomatic patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV systolic dysfunction*</td>
<td>Class I</td>
<td>Class I</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PASP &gt; 50 mm Hg at rest</td>
<td>Class IIa</td>
<td>Class IIa</td>
</tr>
<tr>
<td>PASP &gt; 60 mm Hg with exercise</td>
<td>Class IIa</td>
<td>Class IIb</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Class IIa</td>
<td>Class IIa</td>
</tr>
<tr>
<td>Normal LV function, repair feasible</td>
<td>Class IIa</td>
<td>Class IIa†</td>
</tr>
</tbody>
</table>

This is a simplified table. See full guidelines (1,2) for complete recommendations. *Defined as ejection fraction ≤60% or elevated end-systolic diameter (≥40 mm in ACC/AHA guidelines; >45 mm in ESC/EACTS guidelines). †Specifically for patients with flail leaflet aortic regurgitation and end-systolic dimension ≥40 mm; there is a separate class IIb recommendation for such patients with left atrial volume index ≥60 ml/m².
109 Pts with Asymptomatic MR: Quantified by cMRI
Early Surgery: Asymptomatic Severe MR

![Graph showing event-free survival (%)]

- **OP**: 7-yr event-free survival 99 ± 1%
- **CONV**: 7-yr event-free survival 85 ± 4%

<table>
<thead>
<tr>
<th>Years</th>
<th>OP at Risk</th>
<th>CONV at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>127</td>
<td>127</td>
</tr>
<tr>
<td>3</td>
<td>125</td>
<td>125</td>
</tr>
<tr>
<td>5</td>
<td>106</td>
<td>105</td>
</tr>
<tr>
<td>7</td>
<td>72</td>
<td>78</td>
</tr>
</tbody>
</table>

*p = 0.001*
Surgical Risk

High/prohibitive risk patients

- advanced age
- frail
- multiple medical comorbidities:
  - ↓ EF, CKD/ESRD, PHTN, TR
- prior chest/cardiac surgery
- STS and EuroSCORE II risk calculation
Options?

Transcatheter “edge-edge” MV repair
- MitraClip
  - High/prohibitive risk patients
  - Mod-Severe/Severe (3-4+) MR
  - Degenerative etiology (currently…)

COAPT Trial for functional MR
Evaluation

CHI Mitral Valve Clinic
- Coordinator screening and education
- MD H&P, TTE review
- TEE + 3D
- R/L heart catheterization
- Carotid duplex
- 6 min walk test
Evalutation

CT Surgery H&P (Dr. Clements)
Multidisciplinary Team Case Review

If appropriate for MitraClip:
Interventional MD H&P (Drs. Ledford and Thel)
Procedure scheduled

≈ 6-8 week process
The third generation of MitraClip allows you to treat your everyday cases and more complex cases with greater ease.*

MitraClip NTR  ---  MitraClip XTR
+5 mm†
Procedure

Cardiac cath lab vs. hybrid OR
General anesthesia
1.5-4 hours (typical 2-2.5 hours)
Femoral venous access (24 fr device)
PACU recovery
CSSU overnight obs.
LoS 24-36 hours
Post MitraClip
Post MitraClip
Follow-Up

TTE post-op day 1
Plavix + ASA for 3-6 months
  - OAC + Plavix if afib or other indication
Diuretics + GDMT as indicated
Procedural antibiotic prophylaxis 1 year

F/U 30 day and 1 year
  - TTE + Mitral Clinic office visit
Transcatheter Mitral-Valve Repair in Patients with Heart Failure


Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation - COAPT

COAPT Trial

N = 614 with 3-4+ functional MR and HF
On maximally tolerated GDMT (by HF MD)
  - 91% βb, 66% ACE/ARB/ARNI, 50% MRA, 36% CRT
302 Clip + GDMT vs. 312 GDMT alone
LVEF 20-50% (31%)
LVESd < 7cm (6.2cm)

Excluded: life exp < 1 year, NYHA Class IV/Stage D, COPD + O² or chronic steroids, severe PHTN, Mod-Severe RV dysfxn, Severe AR or TR
COAPT Trial - Outcomes

Primary Outcome

Secondary Outcome

Freedom from device related complications: 96.6% @ 1 year

3+ sMR (Moderate-Severe?)

CENTRAL ILLUSTRATION: A Unifying Concept for the Quantitative Assessment of sMR

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Intermediate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>EROA &lt;20mm², RegVol &lt;30ml</td>
<td>EROA 20-29mm², RegVol 30-44ml</td>
<td>EROA ≥30mm², RegVol ≥45ml</td>
</tr>
</tbody>
</table>

Low Risk | RegFrac ≤50% | RegFrac ≥50% | High Risk


423 HFrEF pts on GDMT: “Moderate MR” stratified by EROA, RegVol, and RegFrac
3+ sMR COAPT Subgroup

Impact of EROA and LVEDV: $\text{EROA} > 30-40 \text{ mm}^2$

All-cause mortality or HF hospitalization through 12 months

<table>
<thead>
<tr>
<th>LVEDVI $&gt;96 \text{ ml/m}^2$ (N=88; 16.1%)</th>
<th>LVEDVI $\leq 96 \text{ ml/m}^2$ (N=131; 23.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MitraClip + GDMT (n=48)</td>
<td>MitraClip + GDMT (n=64)</td>
</tr>
<tr>
<td>GDMT alone (n=40)</td>
<td>GDMT alone (n=67)</td>
</tr>
</tbody>
</table>

HR [95% CI] = 0.49 [0.25, 0.97]  
P=0.04

HR [95% CI] = 0.37 [0.20, 0.67]  
P<0.001

### TMVR- Still Evolving

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<table>
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<tbody>
<tr>
<td><strong>A</strong></td>
<td><strong>B</strong></td>
<td><strong>C</strong></td>
</tr>
<tr>
<td><strong>D</strong></td>
<td><strong>E</strong></td>
<td></td>
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</tbody>
</table>

B. Tiara (Neovasc Inc, Canada) - TIARA I and II Trials  
D. Tendyne (Abbott Inc.) - SUMMIT Trial  
E. Intrepid (Medtronic Inc.) - APOLLO Trial

B, D, and E all transapical  
All others terminated, withdrawn, or still feasibility/early

Testa L. JAHA. Vol. 8, No. 22. DOI: (10.1161/JAHA.119.013352)
TMVR - Still Evolving

Device malfunction/migration
LVOT obstruction
Thrombosis
CVA
AKI/ARF
Access site/bleeding
Perivalvular regurgitation
Endocarditis
Mortality ≈ 25-30% at 1 year

Conclusions

Degenerative MR - primary valve disease

Functional MR - “secondary” (NICM, ICM, Afib, etc.)

Chronic MR is insidious
  - structural Δ’s typically precede HF signs/symptoms

Medical Therapy - limited in pMR, GDMT in sMR

Early Surgical Intervention!
  - severe MR +/- LVEF < 60% or LVSd > 4.0cm

High risk patients with DMR - MitraClip

COAPT Trial - FDA approved MitraClip (Medicare pending)

TMVR - Still evolving
References


INDICATIONS:
Clip Delivery System: The MitraClip 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.

Steerable Guide Catheter: The Steerable Guide Catheter is used for introducing various cardiovascular catheters into the left side of the heart through the interatrial septum.