When Do You Worry About Mitral Regurgitation?

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Outline

• Mitral Valve Anatomy

• Etiology of Mitral Regurgitation
  – Degenerative (primary)
  – Functional (secondary)

• Guidelines for treatment of MR
  – Surgical Repair/Replacement
  – Transcatheter Repair/Replacement
Mitral Valve Anatomy

Figure 4. The mitral valve is nonplanar, although the original mitral valve rings were flat and planer. The mitral valve has a saddle shape, with the highest point (toward the left atrium, away from the left ventricle) at the middle of the anterior leaflet.
Moderate or Severe Valvular Disease Is Common and 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<.0001).

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Recognizing Chronic Mitral Regurgitation

• History:
  – May remain asymptomatic for years
  – Fatigue, decreased exercise tolerance, dyspnea
  – Congestion, orthopnea, LE edema, abd bloating, weight gain
  – Palpitations from atrial fibrillation

• Physical exam:
  – Blowing, holosystolic murmur heard best at apex, radiates to axilla
  – Splitting S2 due to early closure of A2
  – Loud P2 if significant pulmonary hypertension
  – S3 if heart failure with associated LV dysfunction
  – No correlation between murmur intensity and MR severity
Chronic Mitral Regurgitation Etiologies

**CAUSES**

- **Degenerative MR** (also known as primary or organic MR) is usually due to an anatomic abnormality of the mitral valve itself, including the leaflets, and/or the subvalvular apparatus, such as the chordae or papillary muscles.

- **Functional MR** (also known as secondary MR) is the result of left ventricular dilation. Left ventricular dysfunction leads to annular dilation and incomplete coaptation of the mitral valve resulting in MR.

- Retrograde blood flow into the LA leads to increased LA pressure, pulmonary hypertension, LV enlargement, LV dysfunction and atrial fibrillation.

Normal Mitral Valve

Degenerative MR: Prolapse

Degenerative MR: Flail

Functional MR
Degenerative Mitral Regurgitation

- Pathology of leaflets, annulus, chordae tendinae, papillary muscles
- Etiology: most common mitral valve prolapse
  - Young pts have severe myxomatous degeneration with gross redundancy of both leaflets and chordae (Barlow’s valve)
  - Older pts have fibroelastic deficiency leading to chordal rupture
  - Other IE, connective tissue disorders, rheumatic heart, cleft mitral valve, radiation heart disease
- Severe MR causes LV and LA volume overload and if prolonged leads to myocardial damage, heart failure and death
- MR is the disease and correction is curative
Degenerative MR (Primary)

Posterior

Anterior

Flail

Bi-Leaflet
Functional (secondary) Mitral Regurgitation

- Functional MR is a problem with LV function (dilation, WMA) not with the mitral apparatus
- Chronic functional MR worsens the prognosis of patients with LV systolic dysfunction and symptoms of HF (unless focal ischemic MR)
- GDMT for HF is the mainstay of therapy (diuretics, BB, ACEi or ARB, aldosterone antagonists)
When should I worry about MR?
Excess Mortality with LV dysfunction and worse symptoms (primary MR)

EF and Surgical Outcome

Symptoms and Surgery

EF <60% is Abnormal in MR

Enriquez-Sarano M, et al., Circulation 1994;90:830-837
Tribouilly CM et al., Circulation 1999;99:400-5
Mitral Valve Surgery Guidelines
Surgical Repair vs Replacement

- MV apparatus aides in LV contracts and maintains efficient prolate ellipsoid shape of LV
- Destruction of apparatus results in immediate decline in LV function
- Guidelines recommend repair over MVR
- Repair has lower operative mortality than replacement and LV function better preserved
- Repair avoids risk of bioprosthetic valves: thromboembolism, structural deterioration, IE, hemolytic anemia

- Posterior leaflet and annuloplasty repair only
  - Operative mortality <1%
  - 95% freedom from reoperation, 80% freedom from 3+/4+ MR at 15 to 20 years

- Anterior or both leaflets repaired
  - 80% freedom from reoperation and 60% freedom from 3+/4+ MR at 15-20 years
Functional (secondary) Mitral Regurgitation

- Chronic functional MR worsens the prognosis of patients with LV systolic dysfunction and symptoms of HF (unless focal ischemic MR)
- Functional MR is a problem with LV (dilations, WMA) not with the mitral apparatus
- GDMT for HF is the mainstay of therapy (diuretics, BB, ACEi or ARB, aldosterone antagonists)
- Cardiac resynchronization is recommended per usual indications and may lead to reduction in functional MR
- Surgery may be considered but outcomes not as good as with degenerative MR. Class IIb indication
# 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Table 18. Summary of Recommendations for Chronic Severe Secondary MR

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
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<tbody>
<tr>
<td>MV surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>MV surgery may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe secondary MR (stage D)</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>MV repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery</td>
<td>IIb</td>
<td>C</td>
</tr>
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</table>
When should I worry about MR?

• Mildly Concerned
  – When you hear a murmur on exam
  – Obtain TTE

• Worried
  – MR is moderate to severe
  – Refer to cardiology for further evaluation, imaging and monitoring

• Panic/Hysteria
  – CHF symptoms, LV dysfunction, pulmonary HTN, AF
Percutaneous Mitral Repair/Replacement
A Largely Untreated Patient Population

Mitral Regurgitation 2009 U.S. Prevalence

Total MR Patients\(^1,2\) 4,100,000

Eligible for Treatment\(^3,4\) (MR Grade ≥3+)
1,670,000

Annual Incidence\(^3\) (MR Grade ≥3+)
30,000

Annual MV Surgery\(^5\)

Untreated Large and Growing Clinical Unmet Need
14% Newly Diagnosed Each Year

MitraClip – FDA approved for primary MR

- Class IIB Transcatheter mitral valve repair may be considered for severely symptomatic patients with chronic severe primary MR who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain symptomatic despite optimal medical therapy.
Edge to Edge Repair

Degenerative MR (Primary)

Human s/p surgical Alfieri

Circulation. 2002;106:e173

Evalve clip repair in porcine heart (6 mos post repair)

Circulation 2003;108(Supp IV):493
Outcomes of the Initial Experience with Commercial Transcatheter Mitral Valve Repair in the US – TVT registry

### Study Population

**564 Patients**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
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<tbody>
<tr>
<td>Median age (% men)</td>
<td>83 yrs (56%)</td>
</tr>
<tr>
<td>NYHA III/IV</td>
<td>83.9%</td>
</tr>
<tr>
<td>HF hospitalization prior yr</td>
<td>51.8%</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>62.6%</td>
</tr>
<tr>
<td>Prior CVA</td>
<td>8.7%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25.0%</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>32.4%</td>
</tr>
<tr>
<td>Prior MI</td>
<td>24.6%</td>
</tr>
<tr>
<td>Creatinine $\geq$ 2 g/dl</td>
<td>16.7%</td>
</tr>
<tr>
<td>O2-dependency</td>
<td>14.7%</td>
</tr>
<tr>
<td>Median STS-PROM MV repair</td>
<td>7.9% (4.7, 12.2)</td>
</tr>
<tr>
<td>Median STS-PROM MV replacement</td>
<td>10.0% (6.3, 14.5)</td>
</tr>
</tbody>
</table>
Degenerative MR (Primary)

Change in Mitral Regurgitation
Clip implantation occurred in 94%

Mitral Regurgitation

Baseline

- Grade 4: 100%
- Grade 3: 60%

Post-Implant

- Grade 2: 30%
- Grade 1: 20%

93% MR ≤ 2
63.7% MR ≤ 1
p < 0.001
Commercial TMVR with MitraClip

Data Summary

- Prohibitive risk population with 86% DMR
- 91.8% procedure success
- Device-related adverse events: 2.7%
- Mortality: 2.3% in-hospital, 5.8% at 30-days
- Procedure complications: 7.8%
- EDD, MR, volume, clip site related to success
Intermountain MitraClip

- 84 commercial cases
- 3rd highest enroller in COAPT
- 1.5 clips per case
- >95% implant rate
- Avg MR reduction: -2.3 grades
- Fastest device time: 19 mins
- Avg device time: 65 mins
The COAPT Trial is designed to evaluate the safety and effectiveness of the MitraClip device in treating functional mitral regurgitation (MR) in patients with NYHA class II, III, or IV symptoms, hospitalization in the last year, or BNP > 300. Key inclusion criteria include functional MR (malcoaptation of A2/P2), NYHA class II, III, or ambulatory IV, hospitalization in the last year or BNP > 300, too high risk for surgery (STS > 8 or other), and LVEF > 20%.

Subjects treated with optimal medical therapy (OMT) by HF service include ACEi/ARB, BB, aldactone, and CRT.

Primary endpoints include recurrent heart failure (HF) hospitalizations.

Secondary endpoints include:
- Mitral regurgitation severity at 12 months
- Change in 6-minute walk test at 12 months
- Change in quality of life at 12 months
- Change in Left Ventricular end-diastolic volume at 12 months
- NYHA functional class I/II at 12 months
- Hierarchical composite of death and recurrent HF hospitalization
- Recurrent hospitalizations — all-cause

Safety endpoints include the composite of all-cause death, stroke, MI, or non-elective cardiovascular surgery for device-related complications at 30 days post-procedure within the MitraClip group.

The trial enrolled approximately 430 patients at up to 75 U.S. sites. The device group had 7/10 alive, while the control group had 2/8 alive. The trial is actively enrolling at IMC.
# Transcatheter Mitral Valve Repair/Replacement

(all off label or investigational except MitraClip)

## Repair
- MitraClip
- Annuloplasty (Accucinch)
- Chordal implantation

## Replacement
- S3 Valve-in-valve (Off label)
- S3 Valve in MAC (Off label)
- CardiAQ valve
- Tiara valve
- Tendyne valve
- Medtronic TMV
- Fortis valve
- EndoValve
- Gorman TMV
Conclusion

- Delay in mitral valve repair/replacement leads to excess morbidity and mortality
- Any patient with moderate or severe mitral regurgitation should be referred to cardiology for evaluation and close monitoring
- Severe degenerative MR requires surgical repair/replacement
- Severe functional MR requires intensive GDMT for heart failure, cardiac resynchronization and may benefit from surgery (IIB)
- Percutaneous options may address unmet need; mitraclip FDA approved for severe degenerative MR; other devices actively studied
Supplemental Material
Case 1 – Degenerative MR

• CC: Evaluation of MR

• HPI:
  – 45M with hx HTN, HLD was found to have murmur on exam by PCP
  – OSH TTE revealed normal LV size & function (EF 62%), mild MVP, severe MR (no HTN at time of study), nl LA size, no pulm HTN
  – Pt denies symptoms and reports that he is in better shape than many of his college students

• Problem List
  – Hypertension
  – Hyperlipidemia
  – Mitral valve prolapse
  – Mitral regurgitation

• Medications
  – Atorvastatin
  – Losartan

• Allergies
  – NKDA
Case 1 OSH TTE Report

- EF 62%, LVIDd 4.7cm
- Normal RV size and function
- LA and RA normal size
- Mitral valve appears thickened with mild prolapse. No evidence of mitral valve stenosis is present. Mitral valve area by pressure half-time is 4.6cm². Mean transmitral gradient 2.0 mmHg. Severe mitral valve regurgitation with ERO 0.51cm, MR volume 80ml

- Does the patient have severe MR?
- Does the patient require mitral valve repair or replacement?
# Echo Evaluation of MR

<table>
<thead>
<tr>
<th>Severity</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vena contracta</td>
<td>&lt;0.3</td>
<td>&gt;0.7</td>
</tr>
<tr>
<td>PISA radius</td>
<td>&lt;0.4</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Pulmonary venous flow</td>
<td>systolic dominant</td>
<td>systolic flow reversal</td>
</tr>
<tr>
<td>Mitral inflow</td>
<td>can be A wave dominant</td>
<td>E wave dominant ≥1.2m/s</td>
</tr>
<tr>
<td>Continuous wave doppler</td>
<td>soft and parabolic</td>
<td>dense and triangular</td>
</tr>
<tr>
<td>LV and LA</td>
<td>normal size</td>
<td>enlarged (in chronic MR)</td>
</tr>
<tr>
<td>duration</td>
<td>can be short</td>
<td>holosystolic</td>
</tr>
<tr>
<td>Regurgitant volume</td>
<td>&lt;30 ml</td>
<td>&gt;60 ml</td>
</tr>
<tr>
<td>EROA</td>
<td>0-0.20 cm²</td>
<td>&gt;0.40 cm²</td>
</tr>
</tbody>
</table>
Case 1 - TTE Images

EROA = 0.168
Reg Vol = EROA x VTI = 26.4
Case 1 - TTE Images

- MR VTI
  - Vmax: 612 cm/s
  - Vmean: 443 cm/s
  - Max PG: 150 mmHg
  - Mean PG: 91 mmHg
  - VTI: 157 cm

- Tricuspid Valve
  - TR Vmax: 229 cm/s
  - Max PG: 21 mmHg

- PW
  - 50%
  - 1.6 MHz
  - SF: 25 Hz
  - SV: 4 mm
  - 7.6 cm

- LA Area: 16.0 cm²
- RA Area: 14.6 cm²

Missing: PV Doppler
\[ \text{2pi} \times r^2 \times \text{aliasing velocity} \]

Peak MR velocity

\[ \text{EROA} = 0.168 \]

\[ \text{Reg Vol} = \text{EROA} \times \text{VTI} = 26.4 \]
Case 1 - conclusion

• Moderate MR
• Normal LV size & function
• No pulmonary hypertension
• No palpitations or LA enlargement
• Asymptomatic

Moderate Mitral regurgitation – recommend follow-up q6-12 months