Degenerative Mitral Regurgitation: Etiology and Natural History of Disease and Triggers for Intervention

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Primary Mitral Regurgitation
Definition

• Due to primary abnormality (organic) of one or more components of the valve apparatus

• Leaflets, chordae tendineae, papillary muscles and/or annulus
Etiologies of MR

• Degenerative-(MVP, partial flail and flail leaflet)
  – includes myxomatous(younger) and fibroelastic disease(older)

• Rheumatic Carditis-Inflammatory process impacting chordal structures and leaflets primarily in children and young adults

• Infective endocarditis- valve deformity, vegetation and/or chordal rupture
Etiologies of MR-con’t.

- Congenital- cleft mitral valve

- Drugs- Ergotamine, bromocriptine. Evidence linking to development of MR is weak

- Mitral annular calcification- older adults associated with mild to moderate MR
Etiologies of MR-con’t.

- Flail leaflet is defined as the loss of normal leaflet attachment to the LV so the leaflet tip points toward the roof of the atrium. Occurs when most of the anterior or posterior leaflet is detached from the papillary muscle.

- Partial Flail involves only one scallop or smaller segment of the leaflet.
Evaluate mitral valve morphology, LV size and function, LA size
- Trace or mild MR is common in normal subjects and does not need to be further classified if above are normal
- Dilated LV/abnormal LVEF or dilated LA could be cause or consequence of MR
- An isolated inferolateral or posterobasal wall motion abnormality (e.g., following an MI) with globally preserved LV function can result in secondary MR
- Dilated LV with normal LVEF suggests severe MR
- Flail leaflet is highly specific for severe MR

Define Leaflet Motion (Carpentier Classification)

Type I
- Normal

Type II
- Prolapse or Flail

Type IIIA
- Restricted in both systole and diastole

Type IIIB
- Restricted in systole only

Abnormal Leaflet Morphology

Normal Leaflet Morphology

Abnormal Leaflet Morphology by Definition

Abnormal Leaflet Morphology (minor age-related thickening allowed)

Secondary (atrial functional) MR

Primary MR

or

Mixed Etiology
- Example: known secondary MR due to ischemic cardiomyopathy with new torn chord and flail leaflet
- Common Pitfall: anterior leaflet override due to posterior leaflet restriction is pure secondary MR and NOT mixed etiology

or

Secondary MR

Abbreviations:
LA = left atrial; LV = left ventricular;
LVEF = left ventricular ejection fraction
MR = mitral regurgitation

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Natural History

• Chronic MR imposes a pure volume overload on the LV, resulting in eccentric hypertrophy and LV dilation.

• Increased preload, combined with low-to-normal afterload, augments left ventricular ejection fraction (LVEF), which is typically supranormal.

• As the LV dilates, LV wall stress increases. Incipient and irreversible myocardial dysfunction may occur due to the longstanding LV volume overload.

• Because ejection fraction is a load-dependent measure of LV function, it can be preserved even as myocardial contractile function becomes abnormal.
<table>
<thead>
<tr>
<th>Factor Type</th>
<th>Specific Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factors related to the LV or LA</td>
<td>• Systolic dysfunction (EF &lt;60%)</td>
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<tr>
<td></td>
<td>• LV enlargement (LVESD &gt;4 cm)</td>
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<td></td>
<td>• LA enlargement (LA systolic volume index ≥60 mL/m²)</td>
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<tr>
<td>Clinical factors</td>
<td>• Age</td>
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<tr>
<td></td>
<td>• Presence/absence of heart failure</td>
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<td></td>
<td>• Functional class</td>
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<td>• Presence/absence of CAD</td>
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<tr>
<td>Rhythm/Hemodynamic factors</td>
<td>• AF</td>
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<td></td>
<td>• Pulmonary hypertension</td>
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<tr>
<td>Factors related to MR, Timing of Intervention</td>
<td>• Severity of regurgitation</td>
</tr>
<tr>
<td></td>
<td>• Flail leaflet</td>
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<td>• Delay in MV intervention after onset of LV dysfunction</td>
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**Factors Affecting Prognosis in Primary MR**

- AF = atrial fibrillation; CAD = coronary artery disease; EF = ejection fraction; LA = left atrium; LV = left ventricle; LVESD = left ventricular end-systolic diameter; MR = mitral regurgitation; MV = mitral valve.

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### Recommendations for Chronic Primary MR Intervention

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
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<tbody>
<tr>
<td>I</td>
<td>B</td>
<td>Mitral valve surgery is recommended for symptomatic patients with chronic severe primary MR (stage D) and LVEF greater than 30% (73-75).</td>
<td>2014 recommendation remains current.</td>
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<tr>
<td>I</td>
<td>B</td>
<td>Mitral valve surgery is recommended for asymptomatic patients with chronic severe primary MR and LV dysfunction (LVEF 30% to 60% and/or left ventricular end-systolic diameter [LVESD] ≥40 mm, stage C2) (76-82).</td>
<td>2014 recommendation remains current.</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>Mitral valve repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior leaflet (83-99).</td>
<td>2014 recommendation remains current.</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>Mitral valve repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR involving the anterior leaflet or both leaflets when a successful and durable repair can be accomplished (84,89,95,100-104).</td>
<td>2014 recommendation remains current.</td>
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<tr>
<td>I</td>
<td>B</td>
<td>Concomitant mitral valve repair or MVR is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications (105).</td>
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Mitral valve repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF >60% and LVESD <40 mm) in whom the likelihood of a successful and durable repair without residual MR is greater than 95% with an expected mortality rate of less than 1% when performed at a Heart Valve Center of Excellence (101,106-112).

Mitral valve surgery is reasonable for asymptomatic patients with chronic severe primary MR (stage C1) and preserved LV function (LVEF >60% and LVESD <40 mm) with a progressive increase in LV size or decrease in ejection fraction (EF) on serial imaging studies (112-115). (Figure 2)

NEW: Patients with severe MR who reach an EF ≤60% or LVESD ≥40 have already developed LV systolic dysfunction, so operating before reaching these parameters, particularly with a progressive increase in LV size or decrease in EF on serial studies, is reasonable.

There is concern that the presence of MR leads to progressively more severe MR (“mitral regurgitation begets mitral regurgitation”). The concept is that the initial level of MR causes LV dilatation, which increases stress on the mitral apparatus, causing further damage to the valve apparatus, more severe MR and further LV dilatation, thus initiating a perpetual cycle of ever-increasing LV volumes and MR. Longstanding volume overload leads to irreversible LV dysfunction and a poorer prognosis. Patients with severe MR who develop an EF ≤60% or LVESD ≥40 have already developed LV systolic dysfunction (112-115). One study has suggested that for LV function and size to return to normal after mitral valve repair, the left ventricular ejection fraction (LVEF) should be >64% and LVESD <37 mm (112). Thus, when longitudinal follow-up demonstrates a progressive decrease of EF toward 60% or a progressive increase in LVESD approaching 40 mm, it is reasonable to consider intervention. Nonetheless, the asymptomatic patient with stable LV dimensions and excellent exercise capacity can be safely observed (116).
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<tr>
<td>IIa</td>
<td>B</td>
<td>Mitral valve repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function (LVEF &gt;60% and LVESD &lt;40 mm) in whom there is a high likelihood of a successful and durable repair with 1) new onset of AF or 2) resting pulmonary hypertension (pulmonary artery systolic arterial pressure &gt;50 mm Hg) (111,117–123).</td>
<td>2014 recommendation remains current.</td>
</tr>
<tr>
<td>IIa</td>
<td>C</td>
<td>Concomitant mitral valve repair is reasonable in patients with chronic moderate primary MR (stage B) when undergoing cardiac surgery for other indications.</td>
<td>2014 recommendation remains current.</td>
</tr>
<tr>
<td>IIb</td>
<td>C</td>
<td>Mitral valve surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF less than or equal to 30% (stage D).</td>
<td>2014 recommendation remains current.</td>
</tr>
<tr>
<td>IIb</td>
<td>B</td>
<td>Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe primary MR (stage D) 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 severely symptomatic despite optimal GDMT for heart failure (HF) (124).</td>
<td>2014 recommendation remains current.</td>
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<td>III: Harm</td>
<td>B</td>
<td>MVR should not be performed for the treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless mitral valve repair has been attempted and was unsuccessful (84,89,90,95).</td>
<td>2014 recommendation remains current.</td>
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**Figure 2. Indications for Surgery for MR (Updated Figure 4 From the 2014 VHD guideline)**

- **Mitral Regurgitation**
  - **Primary MR**
    - **Severe MR**
      - **Vena contracta ≥0.7 cm**
      - **RVol ≥60 mL**
      - **RF ≥50%**
      - **ERO ≥0.4 cm²**
      - **LV dilation**
    - **Symptomatic (stage D)**
      - **LVEF >30%**
        - No → **MV Repair** (IIa)
        - Yes → **MV Surgery*** (IIb)
    - **Asymptomatic (stage C)**
      - **LVEF 30% to ≤60% or LVESD ≥40 mm (stage C2)**
        - **Progressive increase in LVESD or decrease in EF**
          - Yes → **MV Surgery** (I)
          - No → **MV Surgery*** (IIb)
      - **LVEF >60% and LVESD <40 mm (stage C1)**
        - **Likelihood of successful repair >95% and expected mortality <1%**
          - Yes → **MV Repair** (IIa)
          - No → **Periodic Monitoring**
      - **New-onset AF or PASP >50 mm Hg (stage C1)**
        - **Periodic Monitoring**
  - **Secondary MR**
    - **CAD Rx**
    - **HF Rx**
    - **Consider CRT**
    - **Symptomatic severe MR (stage D)**
    - **Asymptomatic severe MR (stage C)**
    - **Progressive MR (stage B)**

*MV repair is preferred over MV replacement when possible.

AF indicates atrial fibrillation; CAD, coronary artery disease; CRT, cardiac resynchronization therapy; EF, ejection fraction; ERO, effective regurgitant orifice; HF, heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; RF, regurgitant fraction; RVol, regurgitant volume; and Rx, therapy.
**Figure 2** Indications for Surgery for MR (Updated Figure 4 From the 2014 VHD guideline)

- **Mitral Regurgitation**
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      - Vena contracta ≥0.7 cm
      - RVol ≥60 mL
      - RF ≥50%
      - ERO ≥0.4 cm²
      - LV dilation
        - **Symptomatic (stage D)**
          - LVEF >30%
          - MV Surgery* (IIb)
        - **Asymptomatic (stage C)**
          - LVEF 30% to ≤60% or LVESD ≥40 mm (stage C2)
          - MV Surgery* (IIa)
    - **Progressive MR** (stage B)
      - Vena contracta <0.7 cm
      - RVol <60 mL
      - RF <50%
      - ERO <0.4 cm²
      - New-onset AF or PASP >50 mm Hg (stage C1)
        - **Likelihood of successful repair >95% and expected mortality <1%**
          - Yes
            - MV Repair (IIa)
          - No
            - Periodic Monitoring
      - **Progressive increase in LVESD or decrease in EF**
      - MV Surgery* (IIb)
  - **Secondary MR**
    - CAD Rx
    - HF Rx
    - Consider CRT
      - **Symptomatic severe MR** (stage D)
      - Asymptomatic severe MR (stage C)
      - Progressive MR (stage B)
    - Persistent NYHA class III-IV symptoms
      - Periodic Monitoring

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# Clinical Pearls – Triggers for Intervention

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Symptoms Trump EVERYTHING!