Mitral Regurgitation in the MitraClip Era

Patient selection for MitraClip Therapy

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La Timone Hospital
Marseille - France

Nice, March 28th, 2015
In patients with an indication for valve repair but judged inoperable or at unacceptably high surgical risk, percutaneous edge-to-edge repair may be considered in order or improve symptoms

Indication for primary MR: Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a ‘heart team’, and have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).  

Indication for secondary MR: The percutaneous mitral clip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a team of cardiologists and cardiac surgeons, and who have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).
A patient with ischemic MR

History of the disease
- 74 year-old man,
- diabetic ischemic cardiomyopathy
- multiple coronary stentings, 3-vessel disease
- previous inferior MI
- severe chronic renal failure
- paroxysmal AF
- repeat episodes of CHF

Clinical examination
- NYHA IV
- mitral systolic murmur 2/6
- arterial pressure: 90 / 60 mmHg
LVEF = 24%
TTE: mitral regurgitation
TTE: mitral regurgitation

Tenting distance = 10 mm
TTE: severe MR
TTE: severe MR

- mitral ERO = 40 mm²
- regurgitant volume = 60 ml
LVEF = 24%

LVEDD = 78 mm

LVESD = 60 mm

LVEDV = 273 ml (148 ml/m²)

LVESV = 207 ml (112 ml/m²)

severe mitral regurgitation: ERO = 40 mm²

regurgitant volume = 60 ml
Assessment of Mitral Regurgitation

1. Mechanism

2. Quantification

3. Suitability for MitraClip
Assessment of Mitral Regurgitation

1. Mechanism
2. Quantification
3. Suitability for MitraClip
Carpentier’s classification

Normal Leaflet Motion

Excessive Leaflet Motion

Restricted Leaflet Motion

Systolo-Diastolic

Systolic
Carpentier’s classification

- **Normal Leaflet Motion**
- **Excessive Leaflet Motion**
- **Restricted Leaflet Motion**

- **Systolo-Diastolic**
- **Systolic**
### Chronic mitral regurgitation

<table>
<thead>
<tr>
<th>Organic MR (primary) type II</th>
<th>Functional MR (secondary) type IIIb</th>
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- **Organic MR (primary) type II**
- **Functional MR (secondary) type IIIb**
Chronic mitral regurgitation

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![Echocardiogram image](image-url)
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<th>Organic MR (primary) type II</th>
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<tbody>
<tr>
<td></td>
<td>ischemic CM</td>
</tr>
<tr>
<td></td>
<td>non ischemic CM</td>
</tr>
<tr>
<td>Chronic mitral regurgitation</td>
<td></td>
</tr>
<tr>
<td>-----------------------------</td>
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<td><strong>Organic MR</strong> (primary) type II</td>
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![Image of echocardiogram](image-url)
**Chronic mitral regurgitation**

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![Image of ultrasound scan]
Chronic mitral regurgitation

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![Echocardiogram image](image)
Mechanism of ischemic MR

1. apical displacement of PLPM
   - tethering of mitral leaflets
   - tenting of the mitral valve
   - restriction of leaflet closure
   - mitral regurgitation

2. other mechanisms
   - annular dilatation / loss of contractility
   - LV asynchrony
Mechanism of functional MR
Symmetric vs Asymmetric functional MR

Normal Valve

Asymmetric Tethering

Symmetric Tethering

Inferior and/or posterior MI
Regional remodeling
Predominant posterior leaflet restriction

Anterior MI
Regional remodeling
Both leaflet restriction

Agricola et al. EJE, 2004

Asymmetric functional MR

- inferior MI
- local remodelling
- posterior leaflet tethering
- tenting MV
- eccentric jet
Symmetric functional MR

- anterior MI
- non ischemic CM
- local and global remodeling
- apical leaflet tethering
- tenting MV
- central jet
- annular dilatation and flattening
Role of intra LV asynchrony
Role of intra LV asynchrony
Cardiac resynchronization therapy

Courtesy of Stéphane Lafitte
Evaluation of Mitral Regurgitation

1. Mechanism

2. Quantification

3. Suitability for MitraClip
## EAE guidelines 2010

### Table 3  Grading the severity of organic mitral regurgitation

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
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<tbody>
<tr>
<td>Qualitative</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MV morphology</td>
<td>Normal/Abnormal</td>
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<td>Flail leaflet/Ruptured PMs</td>
</tr>
<tr>
<td>Colour flow MR jet</td>
<td>Small, central</td>
<td>Intermediate</td>
<td>Very large central jet or eccentric jet adhering, swirling and reaching the posterior wall of the LA</td>
</tr>
<tr>
<td>Flow convergence zone(^{a})</td>
<td>No or small</td>
<td>Intermediate</td>
<td>Large</td>
</tr>
<tr>
<td>CWV signal of MR jet</td>
<td>Faint/Parabolic</td>
<td>Dense/Parabolic</td>
<td>Dense/Triangular</td>
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<tr>
<td>Semi-quantitative</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>VC width (mm)</td>
<td>3</td>
<td>Intermediate</td>
<td>(\geq 7) ((\geq 8) for biplane)(^{b})</td>
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<tr>
<td>Pulmonary vein flow</td>
<td>Systolic dominance</td>
<td>Systolic blunting</td>
<td>Systolic flow reversal(^{c})</td>
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<tr>
<td>Mitral inflow</td>
<td>A wave dominant(^{d})</td>
<td>Variable</td>
<td>E wave dominant ((&gt; 1.5\ \text{cm/s}))(^{e})</td>
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<tr>
<td>TVI mit /TVI Ao</td>
<td>1</td>
<td>Intermediate</td>
<td>(&gt; 1.4)</td>
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<td></td>
<td></td>
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<tr>
<td>EROA (mm(^{2}))</td>
<td>(&lt; 20)</td>
<td>20–29; 30–39(^{f})</td>
<td>(\geq 40)</td>
</tr>
<tr>
<td>R Vol (mL)</td>
<td>30</td>
<td>30–44; 45–59(^{f})</td>
<td>(\geq 60)</td>
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\(^{a}\) Flow convergence zone: the zone of flow convergence of the MR jet may be normal, or may be reduced in size. \(^{b}\) For biplane (bicuspid) mitral valve. \(^{c}\) Systolic flow reversal indicates that the MR jet begins and ends within the left atrium. \(^{d}\) A wave dominant indicates that the A wave of the mitral valve closure is dominant over the E wave. \(^{e}\) E wave dominant indicates that the E wave of the mitral valve closure is dominant over the A wave. \(^{f}\) If the MR jet is predominantly central, then the size of the jet should be assessed at the level of the mitral valve. \(^{g}\) LV and LA size and the systolic pulmonary pressure.
### Table 3  Grading the severity of organic mitral regurgitation

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LV and LA size and the systolic pulmonary pressureg

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a: Flow convergence zone
b: ≥7 (>8 for biplane)
c: Systolic flow reversal
d: A wave dominant
f: 20–29; 30–39
f: 30–44; 45–59

g: LV and LA size and the systolic pulmonary pressure
What is a severe MR?

RV (ml) \geq 60

RO (mm^2) \geq 40
Prognosis of asymptomatic MR

Sarano – NEJM 2005
What is a severe ischemic MR?

- Reg Vol > 30 ml
- ERO > 20 mm²

Grigioni F – Circulation 2001
Prognostic value of exercise echo


ERO at rest

Increase in ERO during exercise
Limitations of PISA method

- PISA shape affected
  - by the aliasing velocity
  - in case of non-circular orifice
  - by systolic changes in regurgitant flow
  - by adjacent structures (flow constrainment)
- PISA is more a hemi-ellipse
- Errors in PISA radius measurement are squared
- Inter-observer variability
- Not valid for multiple jets

**FUNCTIONAL MR**

Hemielliptic EROA

**ORGANIC MR**

Hemispheric EROA
Hemielliptic ERO in functional MR
3d quantification of MR

Khanna Echocardiography 2004
Lange Int J Cardiol 2002
Valocik Eur J Echo 2005
Breburda JACC 1998
Stiges JASE 2003
Matsumura AHJ 2008
Quantitative 2D echocardiography
Evaluation of Mitral Regurgitation

1. Mechanism

2. Quantification

3. **Suitability for MitraClip**
P2 / A2 localization

Anterolateral commissure

Anterior leaflet

A2

P2

Posteromedial commissure

Posterior leaflet
Carpentier’s nomenclature

Type I: normal valvular motion
Annular dilatation, valve perforation

Type II: excessive leaflet motion
Mitral prolapse

Type IIIa: restricted leaflet motion both in systole and diastole
Leaflet thickening/shortened chordae

Type IIIb: restricted leaflet motion in systole
Ischaemic, functional MR
Ideal valve morphology for Mitraclip

Recommended criteria

**Functional MR**

- moderate to severe MR
- pathology in the A2-P2 area
- coaptation length > 2 mm
- coaptation depth < 11 mm
- mitral valve orifice > 4 cm²
- posterior leaflet length > 10 mm
Ideal valve morphology for Mitraclip

Recommended criteria

- Moderate to severe MR (Grade 3 or more out of 4 grades)
- Pathology in A2-P2 area
- Coaptation length $> 2$ mm (depending on leaflet mobility)
- Coaptation depth $< 11$ mm
- Flail gap $< 10$ mm
- Flail width $< 15$ mm
- Mitral valve orifice area $> 4$ cm$^2$ (depending on leaflet mobility)
- Mobile leaflet length $> 1$ cm
Ideal cases for Mitraclip

Ideal morphologies for a MitraClip implantation.

Wunderlich NC, Siegel RJ EHJCVI 2013
Ideal cases for Mitraclip

Wunderlich NC, Siegel RJ EHJCVI 2013

Coaptation length > 2 mm
Ideal cases for Mitraclip

Wunderlich NC, Siegel RJ EHJCVI 2013

Coaptation depth < 11 mm
Ideal cases for Mitraclip

Wunderlich NC, Siegel RJ EHJCVI 2013

Posterior leaflet tissue > 10 mm
Difficult cases for Mitraclip
Difficult cases for Mitraclip
Good candidate for Mitraclip
Typical Mitraclip procedure for functional MR
Per-procedural assessment
Atrial septal puncture
1st clip positionning
Residual MR after 1st clip
2nd clip placement
Final Result after 2 clips
6-months Follow-up
6-months Follow-up

January 2014

September 2014
Evaluation of Mitral Regurgitation

1. Pre-interventional assessment
   - mechanism
   - quantification
   - suitability for surgical or interventional repair

2. Per-interventional assessment
   - intra-operative echocardiography
   - monitoring of catheterization procedures
ACC/AHA 2014 Guidelines for the Management of Patients With Valvular Heart Disease

‘move the timing of intervention earlier in the disease course with the goal of preventing irreversible LV dysfunction, arrhythmias and pulmonary hypertension due to longstanding LV volume overload.’ *

Nishimura, RA et al.
2014 AHA/ACC Valvular Heart Disease Guideline

<table>
<thead>
<tr>
<th>Intervention Description</th>
<th>Grade</th>
<th>Level</th>
<th>Range</th>
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<tbody>
<tr>
<td>MV repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF &gt;60% and LVEDD &lt;40 mm) in whom the likelihood of a successful and durable repair without residual MR is &gt;90% with an expected mortality rate of &lt;1% when performed at a Heart Valve Center of Excellence.</td>
<td>IIA</td>
<td>B</td>
<td>(149, 203, 205-209)</td>
</tr>
<tr>
<td>MV repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function in whom there is a high likelihood of a successful and durable repair with 1) new onset of AF or 2) resting pulmonary hypertension (PA systolic arterial pressure &gt;50 mm Hg)</td>
<td>IIA</td>
<td>B</td>
<td>(154, 205, 210-215)</td>
</tr>
<tr>
<td>Concomitant MV repair is reasonable in patients with chronic moderate primary MR (stage B) undergoing cardiac surgery for other indications.</td>
<td>IIA</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>MV surgery may be considered in asymptomatic patients with chronic severe primary MR and LVEF ≤50% (stage D)</td>
<td>IIB</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>MV repair may be considered in patients with rheumatic mitral valve disease when surgical treatment is indicated if a durable and successful repair is likely or if the reliability of long-term anticoagulation is questionable.</td>
<td>IIB</td>
<td>B</td>
<td>(194, 202, 203)</td>
</tr>
<tr>
<td>Transcatheter MV repair may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe primary MR (stage D) who have a reasonable life expectancy but a prohibitive surgical risk because of severe comorbidities.</td>
<td>IIB</td>
<td>B</td>
<td>(216)</td>
</tr>
<tr>
<td>MVR should not be performed for treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless MV repair has been attempted and was unsuccessful.</td>
<td>III, Harm</td>
<td>B</td>
<td>(195-198)</td>
</tr>
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Source: [http://circ.ahajournals.org/content/early/2014/02/27/CIR.0000000000000029.citation](http://circ.ahajournals.org/content/early/2014/02/27/CIR.0000000000000029.citation) / * Nishimura RA, et al. Heart June 2014 Vol 100 No 12; 905-7
## Indications for mitral valve surgery in secondary mitral regurgitation

<table>
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<tr>
<th>Indication</th>
<th>Class</th>
<th>Level</th>
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<tr>
<td>Surgery is indicated in patients with severe MR undergoing CABG, and LVEF &gt; 30%</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Surgery should be considered in patients with moderate MR undergoing CABG.</td>
<td>IIA</td>
<td>C</td>
</tr>
<tr>
<td>Surgery should be considered in symptomatic patients with severe MR, LVEF &lt; 30%, option for revascularization, and evidence of viability.</td>
<td>IIA</td>
<td>C</td>
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<tr>
<td>Surgery may be considered in patients with severe MR, LVEF &gt; 30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated.</td>
<td>IIb</td>
<td>C</td>
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European Association of Echocardiography Recommendations on Stress-echo

Degenerative MR

Key point
Exercise echocardiography is useful in asymptomatic patients with severe organic MR and borderline values of LV ejection fraction (60–65%) or LV end-systolic diameter (closed to 40 mm or 22 mm/m²). The absence of contractile reserve could identify patients at increased risk of cardiovascular events. Moreover, exercise echocardiography may also be helpful in patients with equivocal symptoms out of proportion of MR severity at rest.

![Degenerative MR Graph](image)


Functional MR

Key point
Exercise echocardiography is useful in patients with functional ischaemic MR and chronic LV systolic dysfunction to unmask the dynamic behaviour of MR. Patients with an increase in EROA by ≥ 13 mm² are patients at increased risk of cardiovascular events. In these patients, exercise echocardiography also helps to identify the presence and extent of viable myocardium at jeopardy.

![Functional MR Graph](image)
As ischaemic MR is a dynamic condition: stress testing may play a role in its evaluation. Echocardiographic quantification of MR during exercise is feasible, provides a good demonstration of dynamic characteristics and has prognostic importance. An exercise-induced increase of ≥13 mm² of the EROA has been shown to be associated with a large increase in the relative risk of death and hospitalization for cardiac decompensation. The

- Application of stress echo for measurement of dynamic MR as seen in IMR
- Increase in EROA associated with increase in mortality and hospitalization
ESC/EACTS 2012 GUIDELINES

- Asymptomatic patients
- Preserved LV function
- Surgical candidates
- LA dilation
- Pulmonary hypertension with exercise

Table 12: Indications for surgery in severe primary mitral regurgitation

<table>
<thead>
<tr>
<th>Class (^a)</th>
<th>Level (^b)</th>
<th>Ref (^c)</th>
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<tr>
<td>IIb</td>
<td>C</td>
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Surgery may be considered in asymptomatic patients with preserved LV function, high likelihood of durable repair, low surgical risk, and:
- left atrial dilatation (volume index ≥60 ml/m\(^2\) BSA) and sinus rhythm, or
- pulmonary hypertension on exercise (SPAP ≥60 mmHg at exercise).
MitraClip in Specific Patient Populations

Patient groups in which significant clinical benefits have been reported:

- Degenerative MR, declined for surgery\textsuperscript{1}
- Severe LV dysfunction refractory to medical therapy\textsuperscript{2}
- Severe Heart Failure, despite optimal medical therapy\textsuperscript{3}
- CRT non-responders\textsuperscript{4}
- Bivalvular Disease: Severe Aortic Stenosis and Mitral Regurgitation\textsuperscript{5}


The following parameters should be taken into consideration by the Heart Team\textsuperscript{6}:

- Moderate to severe or severe MR (Functional or Degenerative)
- Echocardiographic criteria for eligibility
- Level of surgical risk
- Greater than one year life expectancy
Step 1 Selection of the patient
The first basic step in patient selection is clinical and global echo evaluation

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<tr>
<th>Predicted surgical procedural mortality risk &gt;12% (STS calculated or Surgeon estimated based on pre-specified co-morbidities)</th>
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<tr>
<td>Symptomatic 3+ or 4+ MR</td>
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<td>Degenerative or Functional</td>
</tr>
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<td><strong>KEY exclusion criteria</strong></td>
</tr>
<tr>
<td>EF ≤ 20% and/or LVESD &gt;60mm</td>
</tr>
<tr>
<td>MVA &lt;4cm²</td>
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<td>Leaflet anatomy unsuitable for MitraClip Device</td>
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