Διαδικασία αξιολόγησης σε ασθενή με ανεπάρκεια της μιτροειδούς βαλβίδος

Ποιός ο κατάλληλος ασθενής για mitraclip και πότε τον παραπέμπουμε

Ε ΒΑΒΟΥΡΑΝΑΚΗΣ
Καθηγητής Καρδιολογίας ΕΚΠΑ
Δ/της Γ’ΠΚΚ
Structural Heart Disease

Increases with Age

Prevalence (%) of moderate to severe valve disease

- All valve disease
- Mitral valve disease
- Aortic valve disease

Age (years)

$> 9.3\%$ for $\geq 75$ year olds ($p < .0001$)
Mitral regurgitation (MR) progresses to Heart Failure

Cioffi G et al. European Journal of Heart Failure 2005
As mitral regurgitation becomes more severe, morbidity and mortality risk increases

- Poor quality of life
- Repeat hospitalisations

Untreated Mitral Valve Regurgitation

% of Patients

Mortality

Proportion of Surviving Patients Hospitalized for Heart Failure

Years

1 2 3 4 5

20 29 37 46 50

41 50 58 68 90

Goal 2014
MR is a serious disease
Mitral Regurgitation

- Functional MR
- Degenerative MR
- Mixed MR
Carpentier Classification of Mitral Regurgitation

**PRIMARY MR**
- **Type I**: Normal leaflet motion
- **Type II**: Increased leaflet motion
- **Type IIIa**: Restricted leaflet motion (systole and diastole)
- **Type IIIb**: Restricted leaflet motion (systole)

**SECONDARY MR**
- Leaflet perforation
- Cordal elongation or rupture
- Rheumatic disease
- Ischemic or nonischemic LV remodeling

Carpentier et al. / Thorac Cardiovasc Surgery 1980;79:338-348
Patho-Anatomy of Mitral Regurgitation

MR can have multiple lesions

Primary: Numerous etiologies from Barlow’s to FED
Secondary: Ischemic or non-ischemic DCM or atrial origin
Degenerative MR

- Disease process that structurally alters the valve apparatus.
- Primary disease of valve and chordae
- MR results from excessive valve leaflet motion
- Barlow’s disease: thickened leaflets
Pathophysiology of Secondary MR

**Normal Mitral Valve**
- LV
- Papillary Muscle
- Chordae
- Mitral Annulus
- AO
- LA

**Secondary Mitral Regurgitation**
- LV Distortion
- Papillary Muscle Displacement
- Tethered Chordae
- Restricted Leaflet Closure
- Anterior Leaflet "Bend"
- Annular dilation

**Imaging**
- Ultrasound imaging of mitral valve and regurgitation.
Mixed Mitral Regurgitation

- **Pathology**
  - An abnormality of the mitral valve that is described as a combination of two or more affected areas seen in FMR and DMR.
  - Findings include annulus dilatation, excessive tissue on the leaflets and elongated chordae tendineae.

- TTE and Doppler flow of mixed severe MR due to annulus dilatation, lengthening of the chordae tendineae and a redundancy of the leaflets, especially of the posterior one.
Functional Mitral Regurgitation: The Clinical Problem and Competitive Landscape

Relative Sizes of Clinical Need – Primary vs Functional MR
Expected Global Annual Worldwide Incidence

DMR
≈650,000

FMR
≈2,750,000

>4x
**MitraClip - Class IIB Recommendation**

Indications for transcatheter MV repair for primary MR:

- ≥ NYHA Class III HF symptoms
- ≥ 3+ chronic primary MR
- Prohibitive surgical risk
Bad ventricle what do we do here
Etiology of MR and Outcome

Cumulative incidences

- Death
- Death/HF hosp

- FMR
- DMR

No. at risk for Death
Follow-up (months)

- 49.0%
- 35.7%
- 31.2%
- 24.7%

p=0.002
p=0.028
Relationship between MR and mortality in secondary MR

(Grigioni, Circulation 2001;103:1759-63)
Medical Therapy
First line treatment, limited to symptom management

Mitral Valve Surgery
Reliable reduction of MR to be considered based on patient risk status

Transcatheter Mitral Valve Repair
Less invasive therapy to be considered in patients judged as inoperable or at high surgical risk

Other Interventions
CRT, Ventricular Assist Devices, Heart transplantation, Cardiac Restraint Devices
How are treated patients with isolated FMR?

Duke Databank: 1,538 pts not undergoing CABG with echocardiographic 3+ to 4+ FMR and LVEF $\geq 20\%$ between 200 and 2010.
Indications for mitral valve intervention in chronic secondary mitral regurgitation (continued)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>When revascularization is not indicated, surgery may be considered in patients</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>with severe secondary mitral regurgitation and LVEF &gt;30%, who remain</td>
<td></td>
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<tr>
<td>symptomatic despite optimal medical management (including CRT if indicated)</td>
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<td></td>
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<tr>
<td>and have a low surgical risk.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In patients with severe secondary mitral regurgitation and LVEF &lt;30% who</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>remain symptomatic despite optimal medical management (including CRT if</td>
<td></td>
<td></td>
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<tr>
<td>indicated) and who have no option for revascularization, the Heart Team may</td>
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<tr>
<td>consider percutaneous edge-to-edge procedure or valve surgery after careful</td>
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<td></td>
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<tr>
<td>evaluation for ventricular assist device or heart transplant according to</td>
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<tr>
<td>individual patient characteristics.</td>
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</tr>
</tbody>
</table>
Mitral Regurgitation

• Mitral regurgitation is the second most common type of heart valve disease needing surgery in Europe
• Intervention in asymptomatic patients with severe MR not well established (IIA).
• Consensus in symptomatic patients (Need to change for FMR?)
• Poor prognosis in absence of surgery, even with optimal medical therapy (OMT)
Filling a treatment gap

Less invasive than surgical intervention.
More definitive and durable reduction in MR than medical therapy.
Secondary MR and LV Remodelling

Myocardial Insult

Is FMR another variable associated with adverse outcomes or a risk factor which may potentially be treated?
Primary Effectiveness Endpoint
All Hospitalizations for HF within 24 months

- MitraClip + GDMT
- GDMT alone

Cumulative
HF Hospitalizations (n)

Time After Randomization (Months)

No. at Risk:
MitraClip: 302 285 263 253 236 191 178 161 124
GDMT: 312 294 271 245 219 176 145 121 88

HR (95% CI) = 0.53 [0.40-0.70]
P<0.001

Median [25%, 75%] FU = 19.1 [11.9, 24.0] mos
All-cause Mortality

HR [95% CI] = 0.62 [0.46-0.82]  
P<0.001

NNT (24 mo) = 5.9 [95% CI 3.9, 11.7]

Time After Randomization (Months)

No. at Risk:
MitraClip + GDMT  
GDMT alone
0 302 312
3 286 294
6 269 271
9 253 245
12 236 219
15 191 176
18 178 145
21 161 121
24 124 88

All-cause Mortality (%)
ΠΩΣ ΝΑ ΑΠΟΦΑΣΙΣΩ ΑΝ ΚΑΠΟΙΟΣ ΑΣΘΕΝΗΣ ΕΙΝΑΙ ΚΑΤΑΛΛΗΛΟΣ ΓΙΑ ΜΙΤΡΑΚΛΙΠ;
### Questions

- How severe is VHD?
- What is the aetiology of VHD?
- Does the patient have symptoms?
- Are symptoms related to valvular disease?
- Are any signs present in asymptomatic patients that indicate a worse outcome if the intervention is delayed?
- What are the patient’s life expectancy and expected quality of life?
Echocardiographic criteria for the definition of severe valve regurgitation: an integrative approach *(continued)*

(Adapted from Lancellotti et al.)

<table>
<thead>
<tr>
<th>Qualitative</th>
<th>Mitral regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve morphology</td>
<td>Flail leaflet/ruptured papillary muscle/large coaptation defect</td>
</tr>
<tr>
<td>Colour flow regurgitant jet</td>
<td>Very large central jet or eccentric jet adhering, swirling, and reaching the posterior wall of the LA</td>
</tr>
<tr>
<td>CW signal of regurgitant jet</td>
<td>Dense/triangular</td>
</tr>
<tr>
<td>Other</td>
<td>Large flow convergence zone</td>
</tr>
</tbody>
</table>
Transthoracic echocardiography
mild vs severe MR
Echocardiographic criteria for the definition of severe valve regurgitation: an integrative approach (continued)

(Adapted from Lancellotti et al.)

<table>
<thead>
<tr>
<th></th>
<th>Mitral regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Quantitative</strong></td>
<td><strong>Primary</strong></td>
</tr>
<tr>
<td>EROA (mm$^2$)</td>
<td>≥40</td>
</tr>
<tr>
<td>Regurgitant volume</td>
<td></td>
</tr>
<tr>
<td>(mL/beat)</td>
<td>≥60</td>
</tr>
<tr>
<td>+ enlargement of cardiac chambers/vessels</td>
<td>LV, LA</td>
</tr>
<tr>
<td></td>
<td><strong>Secondary</strong></td>
</tr>
<tr>
<td></td>
<td>≥20</td>
</tr>
<tr>
<td></td>
<td>≥30</td>
</tr>
</tbody>
</table>
Echocardiographic criteria for the definition of severe valve regurgitation: an integrative approach (continued)

(Adapted from Lancellotti et al.)

<table>
<thead>
<tr>
<th></th>
<th>Mitral regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Semiquantitative</strong></td>
<td></td>
</tr>
<tr>
<td>Vena contracta width (mm)</td>
<td>≥7 (&gt;8 for biplane)</td>
</tr>
<tr>
<td>Upstream vein flow</td>
<td>Systolic pulmonary vein flow reversal</td>
</tr>
<tr>
<td>Inflow</td>
<td>E-wave dominant ≥1.5 m/s</td>
</tr>
<tr>
<td>Other</td>
<td>TVI mitral/TVI aortic &gt;1.4</td>
</tr>
</tbody>
</table>
TTE Vena contracta measurement
Systolic blunting of left superior pulmonary vein (a)
Reversal of systolic flow due to severe MR (b)
TOE Estimation of MR severity by the PISA technique
TOE using X-plane imaging demonstrating moderate to severe eccentric MR
Use of 3D software to align planes of MR on 3D TEE Imaging
Planimetry of EROA
MitraClip Anatomic Eligibility - EVEREST II

- Coaptation length ≥ 2mm
- Coaptation depth < 11mm

Primary MR jet due to malcoaptation of A2-P2 scallops:
- MVOA > 4 cm²
- LVEF > 25%
- LVESD < 55 mm

- Flail gap < 10mm
- Flail width < 15mm
Key TTE Views
Parasternal Long Axis (PLAX)

Jet origin?

- Central anterior and posterior leaflet (A2/P2)
- Medial (A3/P3)
- Lateral (A1/P1)

Video c/o Asma Hussaini, MS PA-C
Key TTE Views
Parasternal Short Axis (PSAX)

- Jet origin?
- MVA < 4 cm² (planimetry)?
Key TTE Views

4-Chamber (4CH) and 2-Chamber (2CH)

4 CH
- Qualitative and quantitative assessment of MR?
- Transvalvular gradient?

2 CH
- Line of coaptation?
TOE assessment of MR
Measurement of the flail gap in 4Ch view and LVOT view.
Key TEE Evaluation
Flail Width

Flail width < 15 mm?

Flail width > 15 mm

Video c/o Asma Hussaini, MS PA-C
Key TEE Views
3D en face or Surgeon’s View

MV anatomy? MVA?

Aortic valve
Left atrial appendage
Atrial septum
Flail of P2

A1 A2 A3
P1 P2 P3

Video c/o Asma Hussaini, MS PA-C
Third-Generation MitraClip Systems

- Original MC size
- Improved delivery system

• Longer clip arms (+3mm)
• Longer grippers (2 additional rows of frictional elements)
• Improved delivery system
- Longer arms = more leaflet insertion
- Longer arms = more efficient in Barlow’s
- Longer arms = easier grasping
- Longer arms = reduced need for second clip
- Longer arms = risk of leaflet distortion (?)
- Longer arms = risk of leaflet perforation (?)
- Longer arms = higher risk of clip entanglement (?)

Clip Arms at 120 degrees
## MitraClip Anatomic Eligibility

### MitraClip XTR

**Predictions:**
- Similar patients (larger flails)
- Better results
- Faster cases

<table>
<thead>
<tr>
<th>Everest Era Exclusions</th>
<th>Current NT(_R) Exclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV orifice &lt; 4 cm(^2)</td>
<td>Relative (3.5 mm(^2) excluded)</td>
</tr>
<tr>
<td>Origin outside of P2</td>
<td>Relative</td>
</tr>
<tr>
<td>Rheumatic disease</td>
<td>Excluded</td>
</tr>
<tr>
<td>Repaired valve</td>
<td>Relative</td>
</tr>
<tr>
<td>Grasping area calcification</td>
<td>If severe or thick</td>
</tr>
<tr>
<td>Flail gap &gt; 10 mm</td>
<td>Strong Relative</td>
</tr>
<tr>
<td>Flail width &gt; 15 mm</td>
<td>Relative</td>
</tr>
<tr>
<td>Coaptation depth &gt; 11 mm Coaptation length &lt; 2 mm</td>
<td>Allowed</td>
</tr>
</tbody>
</table>
## MV Anatomic Considerations

- MV Disease (& Carpentier Type)
- Type of MR (Primary or Secondary)
- Jet location (A1/P1, A2/P2, A3/P3)
- Jet direction (M or L? A or P?)
- Number of jets
- Jet type (eccentric, central)
- Flail gap (< 10 mm)
- Flail width (< 15 mm)
- Coaptation length (> 2 mm)
- Coaptation depth (<15 mm)
- MVA (> 4.0 cm²)
- Transmitral gradient
- Calcium or cleft in grasping area

## Other Anatomic Considerations

- Right atrium
  - Pacemaker lead
- Interatrial septum
  - PFO
  - Prior cardiac surgery
- Lipomatous septum
- Left atrium
  - Enlarged or small
- LAA thrombus
- Left ventricle
  - Enlarged or small
**Contemporary Practice**

Consider impact of team decisions on patient and program outcomes

<table>
<thead>
<tr>
<th>Optimal Anatomy</th>
<th>Challenging Anatomy</th>
<th>Unsuitable (?) Anatomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central A2/P2</td>
<td>Lateral A1/P1; Medial A3/P3</td>
<td>Cleft or perforation</td>
</tr>
<tr>
<td>No calcification</td>
<td>No calcium in grasping zone</td>
<td>Calcium in grasping zone</td>
</tr>
<tr>
<td>PML &gt; 10 mm</td>
<td>PML 7-10 mm</td>
<td>PML &lt; 7 mm</td>
</tr>
<tr>
<td>MV orifice &gt; 4 cm²</td>
<td>MVA &gt; 3 cm²</td>
<td>MVA &lt; 3 cm² or MPG 5 mmHg</td>
</tr>
<tr>
<td>Flail gap &lt; 10 mm</td>
<td>Flail width &gt; 15 mm (with sufficient MVA for &gt; 1 clip)</td>
<td>Multiple segments, Barlows valve</td>
</tr>
<tr>
<td>Flail width &lt; 15 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal leaflets and mobility</td>
<td>Carpentier IIIB (restricted closure) or repaired valve</td>
<td>Carpentier IIIA (restricted opening)</td>
</tr>
</tbody>
</table>

Adapted with permission, B Whisenant. TVT 2018. Chicago, IL.
Why Do We Care About Anatomy?

Post-procedural MR > 2+ predicts mortality!

- **Anatomic parameters may predict procedural outcome and MR reduction**

Sorajja et al. 2017. MitraClip Outcomes STS/ACC TVT Registry. JACC.
Severity of TR and Clinical Events

STS/ACC TVT Registry

38.5%
23.5%
23.4%

Cumulative Incidence of Mortality

Follow-Up (Months)

No. at risk

Severe 298 198 141 83 47
Moderate 666 451 307 203 131
Mild/none 883 631 431 277 153

p < 0.0001

Sorajja P et al., J Am Coll Cardiol. 2017
Mitral regurgitation is a dynamic condition!!

- Symptoms despite non severe valve disease
  - Exertional breathlessness
  - Chest pain
  - Recurrent/Unexplained acute pulmonary edema
- Asymptomatic significant valve disease
  - Detect occult symptoms indication for surgery
  - May add diagnostic and prognostic benefit
- Intermediate severity of MR who are scheduled for CABG (to identify those who may benefit from combined revascularization and MVR).
Stress echocardiography in MR

Table 2  SE cut-off values associated with clinical significance, outcome or limited response to therapy

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cut-off values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraventricular obstruction</td>
<td>• LVOT gradient &gt;50 mmHg</td>
</tr>
<tr>
<td>Inadequate functional reserve</td>
<td>• ΔWMSI &lt;0.25 in dilated cardiomyopathy (ESE, DSE)</td>
</tr>
<tr>
<td>Inadequate flow reserve</td>
<td>• ΔLVEF &lt;7.5% in patients with biventricular pacing and heart failure (ESE, DSE)</td>
</tr>
<tr>
<td>Dynamic mitral regurgitation</td>
<td>• ΔLVEF&lt;4–5% in Primary MR, AR (ESE)</td>
</tr>
<tr>
<td>Systolic pulmonary hypertension</td>
<td>• Δ global longitudinal strain &lt;2% in Primary MR (ESE)</td>
</tr>
<tr>
<td>Limited valve compliance/fixed stenosis</td>
<td>• Δ stroke volume &lt;20% (DSE)</td>
</tr>
<tr>
<td>Prosthesis dysfunction or PPM</td>
<td>• ΔEROA ≥ 10–13 mm² in MR patients (ESE)</td>
</tr>
<tr>
<td>Functional MS after mitral valve repair</td>
<td>• Mean transmitral gradient in MS</td>
</tr>
<tr>
<td>RV dysfunction</td>
<td>• &gt;15 mmHg (ESE)</td>
</tr>
<tr>
<td>Increase in B-lines</td>
<td>• &gt;18 mmHg (DSE)</td>
</tr>
<tr>
<td>Reduced coronary flow reserve (CFR)</td>
<td>• Mean transaortic gradient in AS</td>
</tr>
<tr>
<td></td>
<td>• ΔMPG &gt; 18–20 mmHg (ESE)</td>
</tr>
<tr>
<td></td>
<td>• Mean transmitral gradient in MV Prosthesis</td>
</tr>
<tr>
<td></td>
<td>• &gt;10 mmHg (ESE or DSE)</td>
</tr>
<tr>
<td></td>
<td>• Mean transaortic gradient in AV Prosthesis</td>
</tr>
<tr>
<td></td>
<td>• &gt;20 mmHg (ESE or DSE)</td>
</tr>
<tr>
<td></td>
<td>• Δ mean transmitral gradient &gt;7 mmHg</td>
</tr>
<tr>
<td></td>
<td>• TAPSE &lt; 19 mm in Primary MR (ESE)</td>
</tr>
<tr>
<td></td>
<td>• &gt;5 (28-region chest scan) (ESE)</td>
</tr>
<tr>
<td></td>
<td>• CFR &lt; 2.0 (VSE)</td>
</tr>
</tbody>
</table>

P. Lancellotti et al., European Heart Journal  2016
Prognosis of dynamic SMR
Stress echocardiography in MR
Provides information about disease severity and individual outcome

• MR severity, SPAP, and left and right ventricular contractile reserve should be evaluated according to the clinical context.

• An increase by ≥1 grade in MR (from moderate-to-severe MR, (increase in ERO ≥13 mm2)), a SPAP ≥ 60 mmHg and a lack of contractile reserve (<5% increase in EF or <2% increase in global longitudinal strain) are markers of poor prognosis.

• Induce greater LV dyssynchrony with increased MR, indication for CRT.

P. Lancelloti et al., European Heart Journal 2016
75 year old man, mixed FMR, EF 35%

1st Department of Cardiology, University of Athens
1st Mitral Clip Implantation
### One More Clip?

<table>
<thead>
<tr>
<th></th>
<th>Additional Clip should be OK</th>
<th>Consider Additional Clip if necessary</th>
<th>Done</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean MV Gradient</td>
<td>(&lt; 3) mmHg</td>
<td>(4-5) mmHg</td>
<td>(\geq 6) mmHg</td>
</tr>
<tr>
<td>Planimetered Area</td>
<td>(&gt; 3) CM(^2)</td>
<td>(2-3) CM(^2)</td>
<td>(&lt; 2) CM(^2)</td>
</tr>
<tr>
<td>P1/2t*</td>
<td>(&lt; 80) msec</td>
<td>(80 – 110) msec</td>
<td>(&gt; 110) msec</td>
</tr>
</tbody>
</table>

*Pressure \(1/2\) time is not validated for MitraClip

### Consider Removing Depending on MR Severity

<p>| | |</p>
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Mean MV Gradient</td>
<td>(\geq 7) mmHg (\rightarrow) evaluate MVA</td>
</tr>
<tr>
<td>Planimetered Area</td>
<td>(&lt; 1.6) CM(^2)</td>
</tr>
<tr>
<td>P1/2t</td>
<td>(&gt; 130) msec</td>
</tr>
</tbody>
</table>
2\textsuperscript{nd} Mitral Clip Implantation
Conclusions on Diagnosis of MR

- Earlier diagnosis and treatment of severe MR is crucial!
- Poor prognosis on OMT
- Break the vicious circle - Avoiding extensive LV-remodeling / LV-dysfunction - Higher chance of LV reverse remodeling
- Low-threshold for extensive evaluation by Imaging
- SMR can be dynamic! • Consider stress echo - to identify/provoke dyspnea - increase in severity of MR and SPAP