Σύμπλοκες βαλβιδοπάθειες
Στένωση αορτής & ανεπάρκεια μιτροειδούς

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Multivalve disease: prevalence

• According to the Society of Thoracic Surgeons Database, multivalve surgery accounted for **8.6%** of all 86,580 valvular surgical procedures performed between 1986 and 1995. 


• In the EuroHeart Survey, up to **15%** of the patients undergoing valve surgery had multiple valve disease.

Prevalence of MR in pts undergoing AV procedure

**Aortic valve replacement**

- Tunick, Am J Cardiol 1990
- Adams, Am J Cardiol 1990
- Tassan-Mangina, Clin Cardiol 2003
- Moazami, J Card Surg 2004
- Barreiro, Circulation 2005
- Kuel Circulation 2006
- Caballero-Borrego, Eur J Cardiothor Surg 2008
- Wan, J Thorac Cardiovasc Surg 2009
- Jeong, Am J Cardiol 2011

N = 7758

Variable inclusion/exclusion criteria

Mainly non-quantitative MR assessment

Mild 30-80%

Moderate – Severe 15%

**TAVI**

- Webb, Circulation 2007
- Tzikas, Cath Cardiovasc Interv 2010
- Durst, J Heart Valve Dis 2011
- Hekimian, JASE 2011
- De Chiara, Cath Cardiovasc Interv 2011
- Samimi, Int J Cardiol 2011
- Toggweiler, JACC 2012

N = 950

Organic 50-80%

Mainly non-quantitative MR assessment

Mild 70-80%

Moderate – Severe 25-45%
Multivalve disease: aetiology

- Rheumatic heart disease
- Degenerative
- Endocarditis
- End-stage renal disease on haemodialysis
- Connective disorders (Marfan and Ehlerse-Danlos syndromes)
- Thoracic and mediastinal radiation therapy
- Carcinoid disease
- Adverse drug effects (ergot-derived agonists, anorectic agents)
Multivalve disease – evaluation tips

Separate assessment of each valve lesion

Interaction between different valve lesions

Myocardial dysfunction assessment

Diagnosis
Multivalve disease – evaluation tips

- **Echocardiography** is the preferred method.

- **Haemodynamic interactions**, including changes in stroke volume and in intracardiac pressure, **may affect the diagnostic accuracy** of several non-invasive echo diagnostic methods (and also invasive methods).

- Doppler-echocardiographic measures that have been validated in single valve disease may not be valid in multivalve disease. **Measurements that are less dependent on loading conditions are preferred**, such as direct planimetry of the stenotic valve.
AS and MVR: pathophysiology

# Multivalve disease – diagnostic caveats

**Impact of the diagnosis of:**

<table>
<thead>
<tr>
<th>AS</th>
<th>AR</th>
<th>MR</th>
<th>MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA</td>
<td>Prolonged PHT if left ventricular hypertrophy with impaired relaxation</td>
<td>High intraventricular pressure may result in higher RV whereas EROA is less affected</td>
<td>Low-flow low-gradient MS. Prolonged PHT if impaired left ventricular relaxation</td>
</tr>
<tr>
<td>Gorlin formula using thermodilution technique invalid. Owing to high transaortic volume flow rate, maximum velocity, and pressure gradients may be higher than expected for a given valve area</td>
<td>NA</td>
<td>Not significantly affected</td>
<td>Owing to increased anterograde aortic flow, there is an overestimation of MVA by the continuity equation. Overestimation of MVA with PHT method. This approach is not valid</td>
</tr>
</tbody>
</table>

**The presence of:**

<table>
<thead>
<tr>
<th>MR</th>
<th>MS</th>
<th>TR</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR could favour a low-flow, low-gradient state. Aortic valve area calculation remains accurate. High-velocity MR jet may be mistaken for the AS jet (MR is longer in duration)</td>
<td>Low-flow low-gradient state. Aortic valve area calculation remains accurate</td>
<td>Gorlin formula invalid</td>
</tr>
<tr>
<td>Not significantly affected</td>
<td>Blunted hyperdynamic circulation</td>
<td>Not affected</td>
</tr>
<tr>
<td>NA</td>
<td>Not significantly affected</td>
<td>Not affected</td>
</tr>
<tr>
<td>Owing to increased anterograde mitral flow, there is an underestimation of MVA by the continuity equation. MVA may be underestimated with PHT method</td>
<td>Gorlin formula invalid</td>
<td></td>
</tr>
</tbody>
</table>

AR, aortic regurgitation; AS, aortic stenosis; EROA, effective regurgitant orifice; MR, mitral regurgitation; MS, mitral stenosis; MVA, mitral valve area; PHT, pressure half-time; RV, regurgitant volume; NA, not applicable.

*Aortic gradient should not be used as the sole measure of AS severity, since it may underestimate it.*

Philippe Unger et all. Heart 2011;97:272e277
Significant stenosis and regurgitation can be found on the same valve. Disease of multiple valves may be encountered in several conditions, particularly in rheumatic and congenital heart disease, but also less frequently in degenerative valve disease. There is a lack of data on combined or multiple-valve diseases. This does not allow for evidence-based recommendations.

2017 ESC/EACTS Guidelines for the management of valvular heart disease
Surgical decision-making process

Risks associated with multivalve surgery

- Perioperative risk of non correcting all significant lesions
  - Likelihood of the necessity and risk of a future reoperation
Multivalve disease – management

- Combined valve replacement tends to be associated with greater perioperative risk and poorer survival:
  - **Operative risk:** 0.9 - 3.9% for single valve interventions rose to 6.5% in cases of multiple valve disease. (EuroHeart Survey-2003)
  - **Mortality** increased from 4.3% and 6.4% for isolated aortic and mitral valve replacement, respectively, to 9.6% for combined valve replacement.

Society of Thoracic Surgeons National Database report-2005
Mitral valve repair should be preferred to replacement as it improves late survival

AV replacement indications if surgery is indicated for severe MR:

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>d) Concomitant aortic valve surgery at the time of other cardiac/ascending aorta surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAVR is indicated in patients with severe aortic stenosis undergoing CABG, or surgery of the ascending aorta or of another valve.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>SAVR should be considered in patients with moderate aortic stenosis* undergoing CABG, or surgery of the ascending aorta or of another valve after Heart Team decision.</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

*Moderate aortic stenosis is defined by a valve area of 1.0–1.5 cm² or a mean gradient of 25–40 mmHg in the presence of normal flow conditions. However, clinical judgement is required.
Severe organic MR undergoing surgery with low flow-low grad AOS

LVOT diam 2.2cm

Mean grad 20mmHg
AVA 0.75cm²
Svi 35ml

LVOT VTI 9.5cm

Philippe Unger et al. Heart 2011;97:272e277
Does SAVR/TAVI affect the MVR severity?
Multivalve disease – management

Impact of isolated aortic valve replacement on mitral regurgitation

<table>
<thead>
<tr>
<th>First author, Year</th>
<th>Aetiology of MR</th>
<th>Number of patients</th>
<th>Timing of the postop echo</th>
<th>Method of MR assessment</th>
<th>% of patients with improvement in MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timmeck 1990</td>
<td>Functional + Organic</td>
<td>N = 27 ≥ mild MR</td>
<td>58 days</td>
<td>CFM</td>
<td>67%</td>
</tr>
<tr>
<td>Adams 1990</td>
<td>Organic + Functional</td>
<td>N = 46 ≥ mild MR</td>
<td>6 months</td>
<td>PW mapping</td>
<td>27%</td>
</tr>
<tr>
<td>Harris 1997</td>
<td>Functional</td>
<td>N = 28 ≥ moderate MMR</td>
<td>2-3 months</td>
<td>CFM</td>
<td>44%</td>
</tr>
<tr>
<td>Brasch 2000</td>
<td>Organic + Functional</td>
<td>N = 16 ≥ moderate MMR</td>
<td>2-3 months</td>
<td>CFM</td>
<td>67%</td>
</tr>
<tr>
<td>Christenson 2000</td>
<td>Functional</td>
<td>N = 58 ≥ mild MR</td>
<td>1 week/5 months</td>
<td>CFM</td>
<td>67%</td>
</tr>
<tr>
<td>Tassan-Mangina 2003</td>
<td>Functional</td>
<td>N = 23 ≥ mild MR</td>
<td>1 week/5 months</td>
<td>CFM</td>
<td>67%</td>
</tr>
<tr>
<td>Moazami 2004</td>
<td>Functional</td>
<td>N = 80 ≥ mild MR</td>
<td>&gt;60 days</td>
<td>CFM</td>
<td>82%</td>
</tr>
<tr>
<td>Barreiro 2005</td>
<td>Organic + Functional</td>
<td>N = 70 ≥ moderate MMR</td>
<td>1 year</td>
<td>CFM</td>
<td>67%</td>
</tr>
<tr>
<td>Ruel 2006</td>
<td>Functional</td>
<td>N = 107 ≥ 2+ MR</td>
<td>1 year</td>
<td>CFM/PW Doppler mapping</td>
<td>82%</td>
</tr>
<tr>
<td>Vandlen Eyden 2007</td>
<td>Organic + Functional</td>
<td>N = 80 ≥ moderate MMR</td>
<td>1 year</td>
<td>CFM/PW Doppler mapping</td>
<td>82%</td>
</tr>
<tr>
<td>Caballero-Borrogo 2008</td>
<td>Functional</td>
<td>N = 153 non-severe MMR</td>
<td>Before discharge</td>
<td>CFM/PW Doppler mapping/ PV flow</td>
<td>72%</td>
</tr>
<tr>
<td>Waisbren 2008</td>
<td>Functional (No CABG)</td>
<td>N = 167 ≥ moderate MMR</td>
<td>Before discharge</td>
<td>CFM/PW Doppler mapping/ PV flow</td>
<td>72%</td>
</tr>
<tr>
<td>Wan 2009</td>
<td>Functional</td>
<td>N = 159 ≥ moderate MMR</td>
<td>1 year</td>
<td>ASE recommendations</td>
<td>56%</td>
</tr>
<tr>
<td>Unger 2008</td>
<td>Organic + Functional</td>
<td>N = 52 ≥ mild MR</td>
<td>1 year</td>
<td>PISA</td>
<td>69%</td>
</tr>
<tr>
<td>Matsumura 2010</td>
<td>Functional</td>
<td>N = 110 ≥ moderate MMR</td>
<td>Early postoperative</td>
<td>CFM</td>
<td>64%</td>
</tr>
<tr>
<td>Joo 2011</td>
<td>Functional</td>
<td>N = 118 &gt; mild MR</td>
<td>1 year</td>
<td>PISA</td>
<td>72%</td>
</tr>
</tbody>
</table>

16 studies
1294 patients with MR

Functional only (10) or
Functional + organic (6)

Mostly retrospective

Mainly qualitative or
½ quantitative
MR assessment

From OR
up to
18 months

Improvement
55-65%
(27-82%)

Deterioration
5-10%
Most patients present some decrease in MR severity after isolated AVR. Which are the *predictive factors* of this beneficial effect?
### Predictive factors of MR severity after AV intervention (SAVR/TAVI)

#### Factors related to **decrease** in MR severity

<table>
<thead>
<tr>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced LV systolic pressure (haemodynamic success of SAVR/TAVR)</td>
</tr>
<tr>
<td>Reversal of LV remodelling</td>
</tr>
<tr>
<td>Absence of mitral annular calcification</td>
</tr>
<tr>
<td>Secondary mitral regurgitation</td>
</tr>
<tr>
<td>LVEDD ≥50 mm</td>
</tr>
<tr>
<td>LVESD ≥36 mm</td>
</tr>
<tr>
<td>Absence of atrial fibrillation</td>
</tr>
<tr>
<td>Absence of pulmonary hypertension</td>
</tr>
<tr>
<td>Mean gradient ≥40 mm Hg</td>
</tr>
<tr>
<td>Valve type (balloon-expandable)</td>
</tr>
<tr>
<td>Previous coronary artery disease or myocardial infarction</td>
</tr>
</tbody>
</table>

#### Factors related to **increase** in MR severity

<table>
<thead>
<tr>
<th>Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-prosthesis mismatch (persistently high LV pressure)</td>
</tr>
<tr>
<td>Continued LV remodelling</td>
</tr>
<tr>
<td>Dilated mitral annulus</td>
</tr>
<tr>
<td>Primary mitral regurgitation</td>
</tr>
<tr>
<td>Dilated left atrium</td>
</tr>
<tr>
<td>Dilated mitral annulus</td>
</tr>
<tr>
<td>Self-expanding valve with deep implant</td>
</tr>
<tr>
<td>Moderate or greater aortic regurgitation</td>
</tr>
</tbody>
</table>

Sannino A, Grayburn PA. Heart 2018 (modified)
MV surgery indications
if surgery is indicated for severe AS:

- **Severe** MR associated with AS should be corrected at the time of AVR, particularly if the aetiology is **organic**.

≠

- The management of **less-than-severe** and particularly **secondary** MR remains debated.
Different MR aetiologies in pts with severe AS

A. Flail P2 scallop
B. Calcification
C. Prolapse
D. Secondary ischemic MR
Threshold of MR severity when exist severe AS?

- Frequent downgrading after AVR
- Rarely downgrading after AVR
  - Risk of future reoperation

Ischaemic (functional) MR
ERO > 20mm²

Organic MR
ERO > 40mm²

ERO ≈ 30 cm² ???

Proposed algorithm for the evaluation and management of patients with severe aortic stenosis (AS) and concomitant mitral regurgitation (MR).

Comprehensive Evaluation of the Mechanism and Severity of MR per ASE Guidelines
- If TTE findings uncertain or discordant, consider TEE, CMR or RLHC

Mild or Moderate MR

SAVR vs TAVR per guideline indications
- no current indication for surgical or transcatheter therapy for mild/moderate (Stage B) MR

EROA 0.2-0.29cm²
Rvol 30-44ml
RF<30-39%

Severe MR

Is there classic secondary MR due to LV dysfunction/leaflet tethering?
- yes
  - Optimize guideline-directed medical therapy, CRT, and revascularization, if indicated, then reassess MR severity
- no

Primary MR

No major anatomic lesion;
- MR could potentially improve with resolution of AS

Major anatomic lesion unlikely to improve with resolution of AS
(i.e. flail leaflet, absent coaptation)

1) Guideline-directed SAVR vs TAVR; reassess MR severity at one month; if still severe MR, minimally invasive surgical or transcatheter MVR/repair vs
2) Medical therapy/hospice (Cohort C)

1) Combined SAVR + MVR or repair (low/intermediate risk) vs
2) TAVR or SAVR followed by minimally invasive surgical or transcatheter MVR/repair (intermediate or high risk) vs
3) Medical therapy/hospice (Cohort C)

Anna Sannino, and Paul A Grayburn Heart 2018 (modified)
CASE 1

Severe AS undergoing surgery with concomitant moderate primary MR/MS
Severe AS and moderate MR/MS
Severe AS and moderate to severe MR/TVR
Severe AS
Moderate MR / Moderate MS
SEVERE SECONDARY TVR ELEVATED RV PRESSURES

TVR

PVR

IVC
Severe AS undergoing surgery with concomitant moderate MR/MS (rheumatic heart disease)

Clinical decision

AO & MV VALVE REPLACEMENT
TR VALVE REPAIR
CASE 2

Severe AS undergoing surgery
with concomitant secondary moderate MR
Severe AS / Low LVEF
Low LVEF – Moderate MR
Low LVEF – Moderate MR
Low flow-low gradient AS – moderate secondary MR
Severe AS undergoing surgery with concomitant secondary-ischemic MR high operative risk / comorbidities

Clinical decision

PCI to LAD + TAVI

Optimized medical therapy

Close f-up of MR, considering future Mitraclip
Key points - Combined AOS/MR

✓ Combined AOS/MR is a **highly prevalent condition**

✓ **Haemodynamic interactions** between valve lesions can promote, exacerbate, or, in contrast, blunt the clinical expression of each singular lesion

✓ Several diagnostic **echocardiography** tools used for single valve disease assessment, might not be so accurate for a multivalvulopathy evaluation and need much caution and deep **pathophysiology knowledge**

✓ Therapeutic decisions should be made by a **heart valve team**, considering the severity of MVD, the patient’s life expectancy and comorbidities, and the risks of multiple prostheses and eventual reoperation

✓ The introduction of **transcatheter valve therapies** is changing the therapeutic paradigm, but further studies are needed to guide therapeutic decision-making
Σας ευχαριστώ