Mixed aortic valve disease

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• No conflict of interest
2017 ESC/EACTS Guidelines for the management of valvular heart disease


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Key points

- In combined VHD, pathology is considered severe even if both stenosis and regurgitation are only of moderate severity and pressure gradients become of major importance for assessment.

- Management of multiple valve disease is dictated by the predominant VHD.
Aortic stenosis

- Progresses faster in patients with degenerative disease than in those with a rheumatic or congenital aetiology.


- A higher degree of valvular calcification is independently associated with faster stenosis progression and worse outcome.

- Among symptomatic patients with medically treated moderate-to-severe aortic stenosis, mortality from the onset of symptoms is approximately 25% at 1 year and 50% at 2 years.

Aortic regurgitation

- Slow progression. Risk of developing symptoms or LV dysfunction <6.0% per year

Mixed aortic valve disease
Clinical assessment

What are the differentiating features of predominant lesions?

Differentiating dominant lesion clinically:

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Predominant aortic stenosis</th>
<th>Predominant aortic regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse</td>
<td>Low volume slow-rising</td>
<td>Large volume collapsing</td>
</tr>
<tr>
<td>Apex beat</td>
<td>No or minimally displaced, heaving</td>
<td>Displaced, thrusting</td>
</tr>
<tr>
<td>Systolic thrill</td>
<td>Present</td>
<td>Not present</td>
</tr>
<tr>
<td>Systolic murmur</td>
<td>Long murmur, with late systolic peaking</td>
<td>Short, peaking early in systole</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Low systolic BP, normal diastolic and narrow pulse pressure</td>
<td>High systolic, low diastolic and wide pulse pressure</td>
</tr>
</tbody>
</table>
Stepwise integrated approach for the assessment of aortic stenosis severity (Modified from Baumgartner et al.)

Valve morphology by echocardiography suspicious of AS

- Assess velocity/gradient

**LOW-GRADIENT AS**
- $V_{\text{max}} < 4 \text{ m/s, } \Delta P_m < 40 \text{ mmHg}$

  - Assess AVA
    - $\text{AVA} \leq 1.0 \text{ cm}^2$
      - Moderate AS
      - Exclude measurement errors that may cause underestimation of gradient/flow/AVA
    - $\text{AVA} > 1.0 \text{ cm}^2$
      - Define flow status (SVi)
        - Low flow ($SV_i \leq 35 \text{ mL/m}^2$)
          - Severe AS Unlikely
        - Normal flow ($SV_i > 35 \text{ mL/m}^2$)
          - Severe AS Unlikely

  - Define whether high flow status is reversible
    - Not reversible
    - Reversible
      - Re-assess at restored normal flow

**HIGH-GRADIENT AS**
- $V_{\text{max}} \geq 4 \text{ m/s, } \Delta P_m \geq 40 \text{ mmHg}$

  - High flow status excluded
    - Yes
      - Severe high-gradient AS (normal flow/low flow) (normal EF/low EF)

  - Assess LVEF
    - LVEF $\leq 50\%$
      - Dobutamine echo
        - Flow reserve present
          - Pseudosevere AS or true severe AS
        - No flow reserve
          - Integrated approach
    - LVEF $\geq 50\%$
      - Calcium score by CT

VHD (MR, MS, AS, AR) severity not matching with symptoms

- Δ 18-20 mmHg MPG in AS
- MPG ≥15-18 mmHg in MS
- Δ > 10-13 mm² EROA in MR

Asymptomatic moderate-severe VHD (MR, MS, AS, AR)

Symptoms, Δ blood pressure, exercise tolerance

Valve

- Δ E/e’ (LV filling pressure)
- PH (SPAP ≥60 mmHg)

Ventricle

- Δ < 4-5% LVEF (lack of CR)
- Δ < 2% GLS (lack of CR)
- Δ SV < 20% (lack of FR)
- Δ WMSI (Ischemia)
- LV dyssynchrony
- RV dysfunction (TAPSE < 19 mm)

Match symptoms with the cardiac involvement

Risk stratification

Guide decision making and help define the optimal timing for surgery
What is new in the 2017 Valvular Heart Disease Guidelines?

<table>
<thead>
<tr>
<th>Changes in recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2012</strong></td>
</tr>
<tr>
<td>Indications for surgery in asymptomatic aortic stenosis</td>
</tr>
<tr>
<td>IIb C</td>
</tr>
<tr>
<td>IIb C</td>
</tr>
<tr>
<td>Increase of mean pressure gradient with exercise by &gt;20 mmHg.</td>
</tr>
</tbody>
</table>

**IIa C**
Markedly elevated BNP levels (>threefold age- and sex-corrected normal range) confirmed by repeated measurements without other explanations.

**New IIa C recommendation:**
Severe pulmonary hypertension (systolic pulmonary artery pressure at rest >60 mmHg confirmed by invasive measurement) without other explanation.
## What is new in the 2017 Valvular Heart Disease Guidelines?

### Changes in recommendations

<table>
<thead>
<tr>
<th></th>
<th>2012</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications for intervention in symptomatic aortic stenosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIb C</td>
<td>Intervention may be considered in symptomatic patients with low-flow, low-gradient aortic stenosis and reduced ejection fraction without flow (contractile) reserve.</td>
<td>Intervention should be considered in symptomatic patients with low-flow, low-gradient aortic stenosis and reduced ejection fraction without flow (contractile) reserve, particularly when CT calcium scoring confirms severe aortic stenosis.</td>
</tr>
</tbody>
</table>

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See: [www.escardio.org/guidelines](http://www.escardio.org/guidelines)
Deterioration ≥2NYHA classes 3%  28%  32% (p=0.006)

Follow-up 3.3±1.7 years

Figure 3 Progression of AVA and \( PG_{\text{mean}} \) from baseline to follow-up. *\( P < .05 \), HG/AS versus NF/LG and LF/LG. †\( P < .05 \), follow-up versus baseline values, compared using Wilcoxon signed rank test.
Low-Flow, Low-Gradient Aortic Stenosis With Normal and Depressed Left Ventricular Ejection Fraction  Philippe Pibarot and Jean G. Dumesnil, JACC 60:19; 2012.

Figure: Overall survival under medical management according to dobutamine stress echocardiographic parameters

*Adjusted for age, sex, coronary artery disease and chronic kidney failure
Identification of Aortic Stenosis Severity by Dobutamine Stress Echocardiographic Criteria

B
Prediction of Mortality Under Medical Management

Conclusion: Among the many echocardiographic measures of longitudinal velocity and deformation, BLS has the strongest association with symptomatic status in aortic stenosis, and BLS < 13% is related to adverse outcomes in severe asymptomatic aortic stenosis.
Mechanisms of AR

Table 11: Grading the severity of chronic AR with echocardiography

<table>
<thead>
<tr>
<th>AR severity</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic leaflets</td>
<td>Normal or abnormal</td>
<td>Normal or abnormal</td>
<td>Abnormal/flail, or wide coaptation defect</td>
</tr>
<tr>
<td>LV size</td>
<td>Normal*</td>
<td>Normal or dilated</td>
<td>Usually dilated†</td>
</tr>
<tr>
<td>Qualitative Doppler</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jet width in LVOT, color flow</td>
<td>Small in central jets</td>
<td>Intermediate</td>
<td>Large in central jets; variable in eccentric jets</td>
</tr>
<tr>
<td>Flow convergence, color flow</td>
<td>None or very small</td>
<td>Intermediate</td>
<td>Large</td>
</tr>
<tr>
<td>Jet density, CW</td>
<td>Incomplete or faint</td>
<td>Dense</td>
<td>Dense</td>
</tr>
<tr>
<td>Jet deceleration rate, CW (PHT, msec)</td>
<td>Incomplete or faint, Slow, &gt;500</td>
<td>Medium, 500-200</td>
<td>Steep, &lt;200</td>
</tr>
<tr>
<td>Diastolic flow reversal in descending aorta, PW</td>
<td>Brief, early diastolic reversal</td>
<td>Intermediate</td>
<td>Prominent holodiastolic reversal</td>
</tr>
<tr>
<td>Semiquantitative parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VCW (cm)</td>
<td>&lt;0.3</td>
<td>0.3-0.6</td>
<td>&gt;0.6</td>
</tr>
<tr>
<td>Jet width/LVOT width, central jets (%)</td>
<td>&lt;25</td>
<td>25-45</td>
<td>46-64</td>
</tr>
<tr>
<td>Jet CSA/LVOT CSA, central jets (%)</td>
<td>&lt;5</td>
<td>5-20</td>
<td>21-59</td>
</tr>
<tr>
<td>Quantitative parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVol (mL/beat)</td>
<td>&lt;30</td>
<td>30-44</td>
<td>45-59</td>
</tr>
<tr>
<td>RF (%)</td>
<td>&lt;30</td>
<td>30-39</td>
<td>40-49</td>
</tr>
<tr>
<td>EROA (cm²)</td>
<td>&lt;0.10</td>
<td>0.10-0.19</td>
<td>0.20-0.29</td>
</tr>
</tbody>
</table>

* Assume normal unless otherwise specified
† Assume dilated unless otherwise specified
Density of regurgitant jet

- Perfectly central jets may appear denser than eccentric jets of higher severity
Jet deceleration rate (pressure halftime)

- Poor alignment of Doppler beam may result in lower pressure half-time
- Affected by changes that modify LV-aorta pressure gradient (if short, implies significant AR or high LV filling pressure - If long, excludes severe AR)
Flow reversal in the proximal descending aorta

- Depends on compliance of the aorta; less reliable in older patients
- Brief velocity reversal is normal
- Can be present in arteriovenous fistula in upper extremity, ruptured sinus of Valsalva
- May not be holodiastolic in acute AR
<table>
<thead>
<tr>
<th>Modality</th>
<th>Optimization</th>
<th>Example</th>
<th>Advantages</th>
<th>Pitfalls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color flow Doppler 2D</td>
<td>Jet width/ LVOT diameter</td>
<td>• Long-axis view</td>
<td>• Simple sensitive screen for AR</td>
<td>• Underestimates AR in eccentric jets</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Zoomed view</td>
<td>• Rapid qualitative assessment</td>
<td>• May overestimate AR in central jets as AR jet may expand unpredictably below the orifice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Imaging plane for optimal VC measurement may be different from PISA</td>
<td></td>
<td>• Is affected by the size of the LVOT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Measure in LVOT within 1 cm of the VC</td>
<td></td>
<td></td>
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<td></td>
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</table>
| Jet width/LVOT diameter | • Long-axis view  
• Zoomed view  
• Imaging plane for optimal VC measurement may be different from PISA  
• Measure in LVOT within 1 cm of the VC | ![Example Image](image1.png) | • Simple sensitive screen for AR  
• Rapid qualitative assessment | • Underestimates AR in eccentric jets  
• May overestimate AR in central jets as AR jet may expand unpredictably below the orifice  
• Is affected by the size of the LVOT |
| Jet area/LVOT area | • Short-axis view  
• Zoom view  
• Measure within 1 cm of the VC | ![Example Image](image2.png) | • Estimate of regurgitant orifice area | • Direction and shape of jet may overestimate or underestimate jet area |
<table>
<thead>
<tr>
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<th>Optimization</th>
<th>Example</th>
<th>Advantages</th>
<th>Pitfalls</th>
</tr>
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</table>
| Color flow Doppler 2D    | Jet width/LVOT diameter                                                      | ![Example](image1.png)                      | • Simple sensitive screen for AR  
• Rapid qualitative assessment  
• Underestimates AR in eccentric jets  
• May overestimate AR in central jets as AR jet may expand unpredictably below the orifice  
• Is affected by the size of the LVOT |                                                                                |
|                          | Jet area/LVOT area                                                           | ![Example](image2.png)                      | • Estimate of regurgitant orifice area  
• Direction and shape of jet may overestimate or underestimate jet area |                                                                                |
| VC                       | Parasternal long-axis view                                                   | ![Example](image3.png)                      | • Surrogate for regurgitant orifice size  
• May be used in eccentric jets  
• Independent of flow rate and driving pressure  
• Less dependent on technical factors  
• Good at identifying mild or severe AR  
• Problematic in the presence of multiple jets or bicuspid valves  
• Convergence zone needs to be visualized  
• The direction of the jet (in relation to the insonation beam) will influence the appearance of the jet |                                                                                |
Figure 20  Color flow Doppler of AR in the parasternal long- and short-axis views. The three components of the jet are shown with arrows: flow convergence (FC), VC, and jet height (or width) in the LV outflow.
Neither exercise nor dobutamine SE can be used to regrade AR severity in a patient with symptoms, because the test-induced increase in heart rate shortens diastole, limiting quantification of AR severity.

\(^a\) See table of recommendations for definitions of aortic diameter

\(^b\) Surgery should also be considered if significant changes in LV and aortic size occur during FU (see table)
Additional testing with TEE or CMR is indicated when:

- TTE is suboptimal in patients with suspected AR,
- the mechanism for significant AR is not identified,
- the echo/Doppler parameters are discordant or inconclusive regarding the AR severity,
- the aortic root and ascending aorta need better assessment, or
- a discrepancy is present between the TTE findings and the clinical setting.

**Image Description:***

- **MRI Image:** Shows a cross-sectional view of the heart with visible chambers and structures.
- **Flow Curve:** Graph displaying flow dynamics with peak values and time intervals.
- **Flow Calculations:**
  - Total flow: 140 ml
  - Regurgitant flow: 44 ml
  - Effective flow: 140 - 44 = 96 ml
  - Regurgitant fraction: \( \frac{44}{140} = 31\% \)
Surgery-free survival by aortic regurgitant fraction.

Main questions

• What is the fate of asymptomatic MAVD patients with preserved LV function?
• What is the optimal timing of surgical intervention in this population?
Event-Free Survival Stratified by Peak Aortic Jet Velocity

Kaplan-Meier event-free survival for patients with a combination of moderate aortic stenosis and moderate aortic regurgitation (red line), severe aortic stenosis and moderate aortic regurgitation (green line), moderate aortic stenosis and severe aortic regurgitation (blue line), and severe aortic stenosis and severe aortic regurgitation (orange line).
Outcomes of Asymptomatic Adults with Combined Aortic Stenosis and Regurgitation

Nina Rashidi, MD, Zoran B. Popovic, MD, William J. Stewart, MD, and Thomas Marwick, MD, PhD, MPH, Cleveland, Ohio

Figure 4 Main indication for AVR according to the operative report. Patients are divided into four categories: severe AR and moderate or less AS, (3) severe AS and moderate or less AR, and (4) moderate or less AS and groups (P = NS). CABG, Coronary artery bypass grafting; Gr, grade.

Figure 5 Valve etiologies in those who underwent AVR in each category. Calcified valves predominated in the stenotic categories, and bicuspid valves predominated when the main lesion was AR. Grp, Group.

Figure 6 Preoperative symptom status in each group. Symptoms developed before AVR in each category, with heart failure symptoms dominating overall. CHF, Congestive heart failure; Grp, group.
Outcomes in Moderate Mixed Aortic Valve Disease
Is it Time for a Paradigm Shift?

Alexander C. Egbe, MD, MPH, Sushil A. Luis, MBBS, Ratnasari Padang, MBBS, PhD, Carole A. Warness, MD

CENTRAL ILLUSTRATION

Moderate Mixed Aortic Valve Disease: AE Rates

<table>
<thead>
<tr>
<th>Time (Years)</th>
<th>Cardiac Death</th>
<th>Cardiac Death + AVR</th>
<th>Cardiac Death + AVR + Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>251</td>
<td>251</td>
<td>251</td>
</tr>
<tr>
<td>5</td>
<td>117</td>
<td>138</td>
<td>218</td>
</tr>
<tr>
<td>10</td>
<td>53</td>
<td>71</td>
<td>159</td>
</tr>
<tr>
<td>15</td>
<td>26</td>
<td>31</td>
<td>94</td>
</tr>
</tbody>
</table>
➢ Asymptomatic patients with moderate MAVD behaved similarly to asymptomatic patients with severe AS with regard to the development of symptoms and need for AVR, hence the need for vigilance in follow-up.
Ventricular mechanics in patients with aortic valve disease: longitudinal, radial, and circumferential components

Benedetta Leonardi,1 Renee Margossian,2 Stephen P. Sanders,2 Marcello Chinali,1 Steven D. Colan2

1Department of Cardiology, Bambino Gesù Children's Hospital, IRCCS Rome, Italy; 2Department of Cardiology, Children's Hospital Boston, the Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, United States of America

Figure 1.
Comparison of LV ESSm in patients with AS, AR, ASR, and HS. Myocardial afterload (ESSm) was significantly lower (p = 0.01) in both the AS and ASR groups. LV = left ventricle; ESS = end-systolic wall stress; AS = aortic stenosis; AR = aortic regurgitation; ASR = aortic stenosis/regurgitation or mixed aortic valve disease; HS = healthy subjects.

Figure 2.
Comparison of the ratio of strainL with strainC and torsion in patients with AS, AR, ASR, and HS. The strain ratio was significantly lower (p = 0.05) in both the AS and ASR groups. AS = aortic stenosis; AR = aortic regurgitation.

Figure 3.
Comparison of LV torsion in patients with AS, AR, ASR, and HS. Torsion was significantly elevated (p = 0.01) in both the AS and ASR groups. LV = left ventricle; AS = aortic stenosis; AR = aortic regurgitation.
Relative wall thickness (RWT = 2PWd / LVEDD) allows further classification of LV mass increase as either concentric hypertrophy (RWT > 0.42) or eccentric hypertrophy (RWT ≤ 0.42).
Cardiovascular Adverse Events After Aortic Valve Replacement in Mixed Aortic Valve Disease: Beyond Ejection Fraction.

Egbe AC, Warnes CA.

Cardiovascular adverse event (CAE) rates in (A) the entire cohort; (B) patients with relative wall thickness (RWT) >0.46 (blue) versus RWT ≤0.46 (orange); (C) patients with left ventricular mass index (LVMI) >180 g/m² (gray) versus RWT ≤180 g/m² (red); and (D) patients with left ventricular ejection fraction (LVEF) <50% (purple) versus RWT ≥50% (yellow).

Fig. 1. Descriptive flow-chart of population groups and subgroups in our study. Descriptive flow-chart of the study population divided in patients with MAS and PAS who underwent TAVI. Each group was then subdivided according to PPAR

![Graph showing survival curves](image)

**Fig. 3.** Survival curves in PAS and MAS patients. Kaplan-Meier survival curves from all-cause (A) and cardiovascular (B) mortality in patients with PAS and MAS who underwent TAVI. Blue line: PAS; Red line: MAS. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
CASE No 1

• 75 year old man
• 1.62m, 62Kg (BSA 1.66m²)
• CABG 10 years ago
  (LIMA-LAD, SVG-RCA)
• ICD 7 years ago
• Follow-up echocardiogram (3/2016)
AVA: 1.40 cm²,
AVAi: 0.85 cm²/m²
DVI: 0.40
AVA: 0.72 cm²  
AVA_i: 0.44 cm²/m²  
DVI: 0.21
Baseline: AV: \( V_{\text{max}} = 3.2 \text{m/sec}, \) PG=41mmHg, 
MG=24.7mmHg, VTI=85.8 cm
LVOT: \( V_{\text{max}} = 0.7 \text{m/sec}, \) VTI=15cm
DVI=0.17, \( \text{AVA} = 0.61 \text{cm}^2, \text{AVA}_i=0.36 \text{ cm}^2/\text{m}^2, \) 
Stroke Volume=52ml

Peak: AV: \( V_{\text{max}} = 3.3 \text{m/sec}, \) PG=43mmHg, 
MG=26.6mmHg, VTI=48.4 cm
LVOT: \( V_{\text{max}} = 1.0 \text{m/sec}, \) VTI=19m
DVI=0.39, \( \text{AVA} = 1.36 \text{cm}^2, \text{AVA}_i=0.82 \text{ cm}^2/\text{m}^2, \) 
Stroke Volume=66ml

\[
\text{AVA}_{\text{proj}} = \text{AVA}_{\text{rest}} + \left( \frac{\text{DAVA}}{DQ} \right) \times (250 - Q_{\text{rest}}) = 1.03 \text{ cm}^2
\]
Coronary Angiogram

- PCI SVG to RCA
- Patent LIMA to LAD.

**Learning Point:**
When a patient with HFrEF has a deterioration of symptoms and a decrease of AVA, pseudosevere AS (with AVAproj measurement) need to be excluded.
CASE No 2

• 27 year old woman
• 1.70 m, 72 Kg
• Her GP requested a TTE due to palpitations + systolic murmur-aortic position (2/2014)
VC=0.6 cm
Jet width/LVOT diameter=45%
Exercise ECG test

Endpoint Details
Fatigue/Patient request

Exercise ECG
Appropriate HR response to exercise. No arrhythmias noted. No significant ST changes. Patient reported feeling light-headed 4/10 during exercise which did not change throughout exercise. It went away in recovery. Resting hypertension noted. Patients BP was taken every min during exercise and recovery. It appeared to drop during exercise but remained stable. BP readings were 128/85, 136/95, 133/93, 126/95, 135/91 and then rose to 150/93 at peak exercise. The BP then dropped to 136/88 in immediate recovery. Patient had no symptoms with BP drop in immediate recovery. Otherwise uneventful recovery.
MDT Meeting 24/1/18

- CTCA and potential candidate for Minimally Invasive Aortic Valve Replacement (mini-AVR)

**Learning Point:**
Patients with moderate MAVD need to be followed every 6 to 12 months and monitored closely for rapid progression of valve disease or development of symptoms.
TAKE HOME MESSAGES

➢ The combination of pressure and volume load in MAVD poses a unique haemodynamic stress on the LV different from that of isolated AS or AR.

➢ Asymptomatic patients with moderate MAVD behaved similarly to asymptomatic patients with severe AS with regard to the development of symptoms and need for AVR.

➢ Almost 40% of the asymptomatic patients with moderate MAVD will become symptomatic and require AVR within 3 years from the time of diagnosis, similar to the patients with severe AS.
Thank you

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dr.ntalas@gmail.com

@DrNtalas
<table>
<thead>
<tr>
<th></th>
<th>MAVD (n = 117)</th>
<th>Moderate AR (n = 117)</th>
<th>Moderate AS (n = 117)</th>
<th>Severe AS (n = 117)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>79 (68)</td>
<td>79 (68)</td>
<td>79 (68)</td>
<td>79 (68)</td>
<td></td>
</tr>
<tr>
<td>Age, yrs</td>
<td>64 ± 8</td>
<td>63 ± 8</td>
<td>63 ± 5</td>
<td>64 ± 6</td>
<td>0.853</td>
</tr>
<tr>
<td>Follow-up, yrs</td>
<td>8.1 ± 4</td>
<td>7.8 ± 9</td>
<td>9.6 ± 5</td>
<td>7.1 ± 3</td>
<td>0.061</td>
</tr>
<tr>
<td>Echocardiography data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic peak velocity, m/s</td>
<td>3.5 ± 0.2</td>
<td>1.7 ± 0.6</td>
<td>3.4 ± 0.3</td>
<td>4.5 ± 0.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Aortic mean gradient, mm Hg</td>
<td>36 ± 2</td>
<td>16 ± 7</td>
<td>35 ± 4</td>
<td>48 ± 6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Aortic valve area, cm²</td>
<td>1.38 ± 0.06</td>
<td>1.81 ± 0.08</td>
<td>1.22 ± 0.07</td>
<td>0.8 ± 0.02</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Aortic valve area index, cm²/m²</td>
<td>0.69 ± 0.03</td>
<td>0.98 ± 0.04</td>
<td>0.55 ± 0.04</td>
<td>0.41 ± 0.03</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pressure half time, ms</td>
<td>361 ± 92</td>
<td>391 ± 109</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>61 ± 5</td>
<td>65 ± 7</td>
<td>58 ± 6</td>
<td>56 ± 4</td>
<td>0.19</td>
</tr>
<tr>
<td>LV end-diastolic dimension, mm</td>
<td>53 ± 7</td>
<td>58 ± 6</td>
<td>50 ± 6</td>
<td>48 ± 5</td>
<td>0.042</td>
</tr>
<tr>
<td>LV end-systolic dimension, mm</td>
<td>33 ± 8</td>
<td>36 ± 6</td>
<td>31 ± 7</td>
<td>28 ± 6</td>
<td>0.051</td>
</tr>
<tr>
<td>LV mass index, g/m²</td>
<td>138 ± 56</td>
<td>94 ± 14</td>
<td>103 ± 31</td>
<td>123 ± 31</td>
<td>0.016</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.40 ± 0.07</td>
<td>0.32 ± 0.04</td>
<td>0.38 ± 0.03</td>
<td>0.42 ± 0.04</td>
<td>0.064</td>
</tr>
<tr>
<td>LV diastolic dysfunction</td>
<td>38 (32)</td>
<td>6 (5)</td>
<td>14 (12)</td>
<td>26 (22)</td>
<td>0.024</td>
</tr>
<tr>
<td>Left atrial volume index, ml/m²</td>
<td>31 ± 8</td>
<td>24 ± 5</td>
<td>26 ± 7</td>
<td>29 ± 3</td>
<td>0.17</td>
</tr>
<tr>
<td>RV systolic pressure, mm Hg</td>
<td>44 ± 3</td>
<td>33 ± 8</td>
<td>37 ± 8</td>
<td>41 ± 5</td>
<td>0.17</td>
</tr>
<tr>
<td>Aortic dimension 46-50 mm</td>
<td>21 (18)</td>
<td>18 (15)</td>
<td>11 (9)</td>
<td>17 (15)</td>
<td>0.096</td>
</tr>
<tr>
<td>Aortic dimension &gt;50 mm</td>
<td>3 (3)</td>
<td>0</td>
<td>0</td>
<td>1 (1%)</td>
<td>0.29</td>
</tr>
</tbody>
</table>
Conclusions:
Asymptomatic patients with combined aortic valve disease can be safely followed until surgical criteria defined for AS, AR, or the aorta are reached. Good surgical and postoperative outcomes are achieved when following such a strategy. However, high event rates can be expected despite a relatively young age of the population and even in patients with moderate disease severity. AV-Vel, which reflects both stenosis and regurgitant severity, provides an objective and easily assessable parameter to risk stratify these patients.
Conclusions

- The AE outcomes in moderate MAVD appeared to be similar to those with asymptomatic isolated severe AS with preserved LV systolic function. This suggests that it would be inappropriate to apply guideline recommendations for isolated moderate AS or moderate AR to this population.

- 11% of moderate MAVD patients with concentric hypertrophy can become symptomatic even in the absence of severe aortic valve disease.

- Patients with moderate MAVD be followed every 6 to 12 months and monitored closely for rapid progression of valve disease or development of symptoms, similar to patients with isolated severe AS.

- Early valve replacement may be considered for MAVD patients without comorbidities in centers with low risk for such procedures.

Fig. 2. PPAR incidence according to baseline AR degree. Relative incidence of PPAR according to the baseline AR degree associated to severe AS. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
Outcome of Patients with Mixed Aortic Valve Disease Undergoing Transfemoral Aortic Valve Replacement  

J. Seeger et al. Structural Heart, 2017; 1:3-4, 162-167

Figure 1. Kaplan-Meier curves for event-free survival from death. The rate of mortality did not differ within 30 days, 12- and 24-months in patients undergoing TAVR for aortic stenosis (AS) or mixed aortic valve disease (MAVD). CI, confidence interval.
Conclusion
TAVR in patients with mixed aortic valve disease is associated with comparable 30 days, 12- and 24-month clinical outcome compared to patients undergoing TAVR for severe aortic stenosis.

<table>
<thead>
<tr>
<th>Table 5. Twelve months outcome.</th>
<th>AS</th>
<th>MAVD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality, n (%)</td>
<td>61 (14.7%)</td>
<td>9 (17.2%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Stroke disabling, n (%)</td>
<td>15 (3.6%)</td>
<td>1 (1.9%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Repeat procedure, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>-</td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>2 (0.5%)</td>
<td>0 (0%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Endocarditis, n (%)</td>
<td>1 (0.2%)</td>
<td>0 (0%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Rehospitalization for CHF, n (%)</td>
<td>51 (12.3%)</td>
<td>6 (11.5%)</td>
<td>0.77</td>
</tr>
<tr>
<td>All-cause mortality or disabling stroke, n (%)</td>
<td>76 (18.3%)</td>
<td>10 (19.9%)</td>
<td>0.87</td>
</tr>
</tbody>
</table>

Note. Values are mean ± standard deviation. Given are Kaplan-Meier estimates, p-values are for point-in-time comparison.
AS, aortic stenosis; CHF, congestive heart failure; MAVD, mixed aortic valve disease.

<table>
<thead>
<tr>
<th>Table 6. Twenty-four-months outcome.</th>
<th>AS</th>
<th>MAVD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality, n (%)</td>
<td>73 (22.1%)</td>
<td>9 (17.9%)</td>
<td>0.93</td>
</tr>
<tr>
<td>Stroke disabling, n (%)</td>
<td>16 (4.8%)</td>
<td>1 (2.0%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Repeat procedure, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>-</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2 (0.6%)</td>
<td>0 (0%)</td>
<td>0.56</td>
</tr>
<tr>
<td>All-cause mortality or disabling stroke</td>
<td>89 (26.9%)</td>
<td>10 (19.9%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Rehospitalization for CHF, n (%)</td>
<td>56 (16.9%)</td>
<td>9 (17.9%)</td>
<td>0.94</td>
</tr>
</tbody>
</table>

Note. Given are Kaplan-Meier estimates, p-values are for point-in-time comparison.
AS, aortic stenosis; CHF, congestive heart failure; MAVD, mixed aortic valve disease.
<table>
<thead>
<tr>
<th></th>
<th>AS</th>
<th>AR</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
<td></td>
<td>Prolonged PHT if left ventricular hypertrophy with impaired relaxation</td>
</tr>
<tr>
<td>AR</td>
<td>Gorlin formula using thremodilution 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></td>
</tr>
</tbody>
</table>
Modified Gorlin Equation for the Diagnosis of Mixed Aortic Valve Pathology

Lawrence N. Scotten¹, David K. Walker¹, James W. Dutton²

¹Vivitro Systems Inc., ²Royal Jubilee Hospital, Victoria, Canada

\[ AVA_G = \frac{Q}{C \cdot 44.5 \cdot \sqrt{\Delta P_{(SEP)}}} \]

The modified \((AVA_M)\) equation for aortic valve area that accounts for aortic valve regurgitation is then:

\[ AVA_M = \frac{Q \cdot (1 - RF)^{-1}}{C \cdot 44.5 \cdot \sqrt{\Delta P_{(SEP)}}} \]
Modified Gorlin Equation for the Diagnosis of Mixed Aortic Valve Pathology

Lawrence N. Scotten\(^1\), David K. Walker\(^1\), James W. Dutton\(^2\)

\(^1\)Vivitro Systems Inc., \(^2\)Royal Jubilee Hospital, Victoria, Canada

Figure 8: Left panel: Gorlin aortic valve area (AVAc); right panel: Modified aortic valve area (AVAm). Both panels compare calculated valve area to geometric orifice area using interpolated data from Figures 7. The dashed lines represent the line of identity. Gorlin and modified aortic valve area equations are shown in the respective graphs.

Fig. 5. Survival curves in patients who developed PPAR and those who have not, independently of baseline AR degree. Kaplan-Meier survival curves from all-cause (left panel) and cardiovascular (right panel) mortality in patients who developed PPAR and those who have not, independently of baseline AR grade. Blue line: PPAR < 1+/3+; Red line: PPAR ≥ 1+/3+. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
Conclusion:
MAS was associated with lower device success. However, despite these findings, it had no influence on long-term postoperative outcomes.

<table>
<thead>
<tr>
<th>VARC-2 composite endpoints</th>
<th>PAS + No PPAR (n = 467)</th>
<th>MAS + No PPAR (n = 238)</th>
<th>PAS + PPAR ≥ 1+/3+ (n = 169)</th>
<th>MAS + PPAR ≥ 1+/3+ (n = 178)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device success</td>
<td>454 (97.2)</td>
<td>225 (94.5)</td>
<td>146 (96.4)</td>
<td>146 (92)</td>
<td>0.265</td>
</tr>
<tr>
<td>Early safety (&lt; 30 days)</td>
<td>127 (27.2)</td>
<td>76 (31.9)</td>
<td>49 (29)</td>
<td>46 (25.8)</td>
<td>0.295</td>
</tr>
<tr>
<td>Clinical efficacy (1 yr)</td>
<td>101 (21.6)</td>
<td>52 (21.8)</td>
<td>66 (39.1)</td>
<td>59 (33.1)</td>
<td>0.252</td>
</tr>
<tr>
<td>Clinical efficacy (2 yr)</td>
<td>141 (30.2)</td>
<td>65 (27.3)</td>
<td>78 (46.2)</td>
<td>73 (41)</td>
<td>0.334</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-yr</td>
<td>64 (13.7)</td>
<td>29 (12.2)</td>
<td>42 (24.9)</td>
<td>43 (24.2)</td>
<td>0.785</td>
</tr>
<tr>
<td>2-yr</td>
<td>89 (19.1)</td>
<td>42 (17.6)</td>
<td>56 (33.1)</td>
<td>58 (32.6)</td>
<td>0.882</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-yr</td>
<td>33 (7.1)</td>
<td>23 (9.7)</td>
<td>25 (14.8)</td>
<td>35 (19.7)</td>
<td>0.325</td>
</tr>
<tr>
<td>2-yr</td>
<td>39 (8.4)</td>
<td>31 (13)</td>
<td>33 (19.5)</td>
<td>42 (23.6)</td>
<td>0.439</td>
</tr>
</tbody>
</table>
### Table 17  Impact of multivalvular disease on assessment of valvular regurgitation with Doppler echocardiography

<table>
<thead>
<tr>
<th>By this Valvular Lesion</th>
<th>Impact on this Regurgitant Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
<td>Little impact, although hemodynamically significant AR will increase AS gradient.</td>
</tr>
</tbody>
</table>
• End-systolic circumferential midwall stress (ESWS) was calculated from Mirsky's variation of the LaPlace relationship as it pertains to the left ventricle

• Stress = P * b * h * h * (1/2 * b) where P = pressure measured at the dicrotic notch of the aortic pressure tracing, h = wall thickness, a = midwall semi-major axis (L2 + h) at end-systole and b = midwall semi-minor axis (-D + -b-) at end-systole. The result obtained by this formula was converted to dyn X 10^3/cm^2 by multiplying by a conversion factor of 1332 dyn/cm^2/mm Hg. Wall thickness was obtained using the method of Hugenholtz et al.