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Disclosures

• Core Lab Director for multiple tricuspid device trials for which I receive no direct compensation:
  – SCOUT Trial
  – Triluminate Trial
  – Tri-Repair Trial
• Speaker: Abbott Structural, GE, Philips, Boston Scientific
• Consultant: Gore&Associates, NaviGATE, Abbott Structural, GE, Philips
Natural History of Aortic Stenosis

“Surgical intervention should be performed promptly once even minor symptoms occur”

from Ross and Braunwald, Circulation 1968

Outcomes Unchanged!

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Circulation, published online March 3, 2014; Copyright © 2014 American Heart Association

Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88
### Stages of Valvular AS

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Valve Anatomy</th>
<th>Valve Hemodynamics</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At risk</td>
<td>Bicuspid aortic valve (or other congenital valve anomaly)</td>
<td>Aortic Vmax &lt; 2 m/s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aortic valve sclerosis</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Progressive</td>
<td>Mild-to-moderate leaflet calcification of a bicuspid or trileaflet valve with some reduction in systolic motion or Rheumatic valve changes with commissural fusion</td>
<td>Mild AS: Aortic Vmax 2.0–2.9 m/s or mean ΔP &lt; 20 mm Hg Moderate AS: Aortic Vmax 3.0–3.9 m/s or mean ΔP 20–39 mm Hg (Typically AVA &gt; 1.0 cm²)</td>
</tr>
</tbody>
</table>

**2014 ACC/AHA Valve Guidelines**  
**Concept of Valve Disease Stages**

- **Normal leaflets**
- **At risk**
- **Disease initiation**
- **Progressive Disease**
- **Valve obstruction**

<table>
<thead>
<tr>
<th>Inflammation</th>
<th>Age</th>
<th>Leaflet calcification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal leaflets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>At risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Disease initiation</strong></td>
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</tr>
<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Valve obstruction</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Current Imaging Window**

*Nishimura, RA et al. JAmCollCardiol 2014 Jun 10;63(22):2438-88*
Proposed TAVR-specific Classification

Tricommissural (1 commissure completely fused between 2 cusps, often referred to as “functional” or “acquired” [functional/acquired] BAV by the surgical and interventional community) in this morphology, fusion is not seen in the basal third of the sinus

Bicommissural raphe type (in which 2 cusps fused by a fibrous or calcified ridge of various heights, does not reach the height of the commissure) [in this morphology, fusion of cusps occurs at or proximal to the basal third of the sinus]

Bicommissural non-raphe type (2 cusps completely fused from their basal origin by no visible seam) [in this morphology, there are only 2 commissures with no raphe or third commissure]

Trileaflet vs Bileaflet Valve

- Submitted for review: bicuspid valve suspected on CT scan
- Color Doppler: clear imaging of flow into 3 commissures

Increased risk (up to 50%) of death from cardiovascular causes and risk of myocardial infarction even in the absence of a significant hemodynamic load.

Otto CM et al. NEJM 1999;341:142-7

The extent of aortic valve calcification was a strong predictor of subsequent events (p<0.001) and event-free survival.

Calcification Score
- 1 = no calcification
- 2 = mildly calcified (small isolated spots)
- 3 = moderately calcified (multiple larger spots)
- 4 = heavily calcified (extensive thickening and calcification of all cusps)

### Stages of Valvular AS

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</thead>
</table>
| **C1** | Asymptomatic severe | Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening | - Aortic $V_{\text{max}} \geq 4$ m/s or mean $\Delta P \geq 40$ mm Hg  
- AVA typically is $\leq 1.0$ cm$^2$ (or AVAi $\leq 0.6$ cm$^2$/m$^2$)  
- Very severe AS is an aortic $V_{\text{max}} \geq 5$ m/s or mean $\Delta P \geq 60$ mm Hg |
| **C2** | Asymptomatic Severe with LV dysfunction | Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening | - Aortic $V_{\text{max}} \geq 4$ m/s or mean $\Delta P \geq 40$ mm Hg  
- AVA typically is $\leq 1.0$ cm$^2$ (or AVAi $\leq 0.6$ cm$^2$/m$^2$) |

*Nishimura, RA et al JAmCollCardiol 2014 Jun 10;63(22):2438-88*
### Severity of AS: Criteria

<table>
<thead>
<tr>
<th>Severity</th>
<th>Peak Velocity (m/s)</th>
<th>Mean gradient (mm Hg)</th>
<th>AV area (cm²)</th>
<th>AVA Index (cm²/m²)</th>
<th>LVOT:AV VTI Index (DVI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&lt; 3.0 (2.6-2.9)*</td>
<td>&lt;20 (&lt;30)†</td>
<td>&gt;1.5</td>
<td>&gt;0.85* (&lt;1.2)‡</td>
<td>&gt;0.5</td>
</tr>
<tr>
<td>Moderate</td>
<td>3.0-4.0</td>
<td>20-40* (30-50)†</td>
<td>1.0-1.5</td>
<td>0.6-0.85*</td>
<td>0.25-0.50*</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;4.0</td>
<td>&gt;40 * or 50†</td>
<td>&lt;1.0</td>
<td>&lt;0.6</td>
<td>&lt;0.25</td>
</tr>
<tr>
<td>Critical</td>
<td>&gt; 5.0</td>
<td>&gt;60</td>
<td>&lt;0.6</td>
<td>&lt;0.6</td>
<td>&lt;0.4*</td>
</tr>
</tbody>
</table>

* EAE/ASE Recommendations
† ESC Guidelines
‡ Non ACC/ESC guidelines

Note: Aortic valve sclerosis velocity ≤ 2.5 m/s

Nishimura, RA et al. JAmCollCardiol 2014 Jun 10;63(22):2438-88

### New ASE Guidelines

EACVI/ASE CLINICAL RECOMMENDATIONS

Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography

Helmut Baumgartner, MD, FESC; (Chair), Judy Hung, MD, FASE, (Co-Chair), Javier Iberroeta, MD, PhD, John J. Chambers, MB BChir, FESC, Thor Edvardsen, MD, PhD, FESC; Steven Goldstein, MD, FASE, Pancrazio Lanedelli, MD, PhD, FESC; Melissa LeFevre, RDCS, Fletcher Miller Jr., MD, FASE, and Catherine M. Otto, MD, FESC, Mannheim, Germany; Boston, Massachusetts; Madrid, Spain; London, United Kingdom; Oslo, Norway; Washington, District of Columbia; Liège, Belgium; Bari, Italy; Durham, North Carolina; Rochester, Minnesota; and Seattle, Washington.

New ASE Guidelines

1. Appropriate in all patients with AS (yellow);
2. Reasonable when additional information is needed in selected patients (green);
3. Not recommended for clinical use (blue).

Appropriate in All Patients

Prognosis of Velocity

- High rate of clinical events, defined as death or aortic valve surgery for "asymptomatic" aortic stenosis
- On multivariate analysis, only baseline aortic jet velocity, functional status score, and the rate of change in aortic jet velocity were predictive of clinical outcome.

Of the patients with moderately or severely calcified aortic valves whose aortic jet velocity increased by 0.3 m/s or more within one year, 79% underwent surgery or died within two years.

Transaortic Velocity or VTI
1. Image peak velocity from at least two different windows
   - Use of a non-imaging CW probe, particularly for the right parasternal view
2. Use the highest velocity profile
   - Consider use of contrast to enhance Doppler signals

Technical Pearl: Peak Velocity

- Apical View
- Right Parasternal View

Doppler Imaging in Aortic Stenosis: The Importance of the Nonapical Imaging Windows to Determine Severity in a Contemporary Cohort

- $V_{\text{max}}$
  - RPS window in 50%,
  - apex in 39%,
  - suprasternal notch in 6%,
  - right supraclavicular in 5%

J Am Soc Echocardiogr
**Optimal Doppler Velocity Location Depends on Aortic Root Angulation**

- Overall, the highest AV velocity comes from RPS in 50%
- If the angle < 115 degree, it is from RPS in 67%
- AS is underestimated in 15% if only apex is used


**Right Parasternal Window**

- Use color Doppler to help determine if right parasternal view is most appropriate
Subcostal Window

- In patients with aortic stenosis (AS) and eccentric transaortic flow, greater pressure loss occurs as the jet collides with the aortic wall together with delayed and diminished pressure recovery. This leads to the elevated transaortic valve pressure gradients noted on both Doppler and cardiac catheterization.

A 23-years-old with known bicuspid aortic valve disease and elevated gradients (mean 57 mmHg, peak 92 mmHg, EOA 1.0 cm²) underwent TEE for further evaluation. TEE imaging confirmed the presence of a bicuspid aortic valve; however, despite single leaflet calcification there was no significant overall valve restriction.


Velocity and Gradient ignore the influence of cardiac output

- High cardiac output (stroke volume index >58 cc/m²) → high gradient
  - Aortic regurgitation
  - Hyperdynamic function
- Low cardiac output (stroke volume index < 35 cc/m²) → low gradient
  - Low flow/reduced EF
  - Low flow/normal EF
    - Small ventricular cavity
    - Significant MR
    - High BP
    - Abnormal contractile function (EF poor measure)

Continuity Equation

Continuity Equation utilizes the conservation of mass theory

“Mass can be neither created nor destroyed”

- Stroke Volume₁ = Stroke Volume₂
- \((\text{Area} \times \text{TVI})₁ = (\text{Area} \times \text{TVI})₂\)

NOTE: use of VTI is preferred over Velocity in the Continuity Equation
Conservation of Mass: Continuity Equation

\[ \text{Aortic Valve Area} \times \text{LVOT Area} = \text{LVOT Stroke Volume} \]

The Continuity Equation Normalizes for Flow!

\[ \text{Area}_{AV} = \frac{\text{Area}_{LVOT} \times \text{VTI}_{LVOT}}{\text{VTI}_{AV}} \]
Prognosis of AVA

- Cardiac symptoms were frequent (59%) and unassociated with the AS severity (all P > .13)
- 67% had low gradient/severe AS

- Excess mortality (vs expected) with AVA < 1.0 cm²
  - Symptomatic AS
    - Risk ratio, 1.78; [CI 1.33–2.35]; P < .001
  - Asymptomatic AS
    - Risk ratio, 1.65; [CI, 1.05–2.47]; P = .02

Severe AS < 1 cm² is likely highly sensitive but non-specific

Mean AVA of patients with < 1.0 cm² = 0.79 ± 0.14


Aortic Stenosis: Pitfalls of the Continuity Equation

- Accuracy of the LVOT diameter
  - error is squared
- LVOT velocity
  - angle θ
  - Use laminar flow before pre-stenotic acceleration
- CW aortic velocity inaccuracy
  - measure signal at multiple windows
  - Distinguishing AS from MR
- Nonsimultaneous measurement of LVOT and peak velocities
  - Varying cycle lengths
• Left ventricular outflow tract diameter (LVOTd) is measured in a zoomed parasternal long-axis view in midsystole from the white-black interface (inner-to-inner) of the septal endocardium to the anterior mitral leaflet, parallel to the aortic valve plane.
• Some experts prefer to measure within 0.3–1.0 cm of the valve orifice whereas others prefer the measurement at the annulus level.


Editorial Comment on measuring at the Annulus for CE (ALL PATIENTS):
1. Associated with strong outcomes data
2. Less variability with cardiac cycle
3. More reproducible and accurate

Michelena HI et al. Heart 2013 Jul;99(13):921-31

• Methods:
• With appropriate gain and processing adjustments, the LVOTd was measured in the parasternal long-axis view using a zoomed freeze-frame at early to mid-systole, inner edge to inner edge, from where the anterior cusp meets the ventricular anteroseptum, to the point where the posterior cusp meets the anterior mitral leaflet.

Michelena HI et al. Heart 2013 Jul;99(13):921-31
Editorial Comment

- The maximum diameter of the annulus bisects a trigone on one side, and a cusp on the other side (Yellow arrow).

- When equal cusps are imaged in LAX view the LVOT and annular diameters may be underestimated (Blue arrow).

Aortic Valve Anatomy

- The scalloped configuration of the hingelines of the leaflets leave fibrous interleaflet triangles or trigones between the sinuses.

- The virtual annulus marks the hingepoints of the cusps (Blue Line).

- The maximum diameter of the annulus bisects a trigone on one side, and a cusp on the other side (Yellow arrow).

  - When equal cusps are imaged in LAX view the LVOT and annular diameters may be underestimated (Red arrow)
LVOT and Annular Measurement Pearls

- Short-axis (SAX) views may thus be helpful in characterizing the appearance of the valve and aligning the LAX view perpendicular to the largest LVOT diameter

1. **Use the pattern of calcification and valve opening**
2. **Color Doppler jets (systolic and diastolic) may help align the LAX view**

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**Table 1** Checklist for verification of the accuracy of the measurement of LVOT area for the calculation of AVA for the assessment of aortic stenosis severity

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure LVOT (on the annulus) using the formula:</td>
<td>$\text{LVOT} = \sqrt{\frac{V_{LAX} \times \text{AVA}_{\text{max}}}{\pi}}$</td>
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**Notes:**
- Use the pattern of calcification and valve opening
- Color Doppler jets (systolic and diastolic) may help align the LAX view

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**Hahn and Pibarot JASE 2017**
Assuming that LVOT area is circular with TTE results in constant underestimation of the AVA with the continuity equation compared with MDCT planimetry.

The elliptical not circular shape of LVOT largely explains these discrepancies.


- 269 patients with isolated calcific AS
- Doppler and MDCT at same episode of care
- AVA was calculated by echocardiography (AVAEcho) and by MDCT (AVACT) using each technique measurement of LVOT area.
- And measured by planimetry (AVAPlani).
**Head-to-head Comparison**

- AVACT was larger than AVAEcho (difference 0.12 ± 0.16 cm²; p < 0.0001) but did not improve outcome prediction.

- Correlation gradient-AVA was slightly better with AVAEcho than AVACT (r = 0.65 with AVAEcho vs. 0.61 with AVACT; p = 0.01), and discordant gradient-AVA was not reduced.

- For long-term survival, after multivariable adjustment, AVAEcho or AVACT were independently predictive (hazard ratio [HR]: 1.26, 95% confidence interval [CI]: 1.13 to 1.42; p < 0.0001 or HR: 1.18, 95% CI: 1.09 to 1.29 per 0.10 cm² decrease; p < 0.0001) with a similar prognostic value (p ≥ 0.80).

- Thresholds for excess mortality differed between methods: AVAEcho ≤1.0 cm² (HR: 4.67, 95% CI: 2.22 to 10.50; p < 0.0001) versus AVACT ≤1.2 cm² (HR: 3.16, 95% CI: 1.64 to 6.43; p = 0.005).

(Clavel et al. J Am Coll Cardiol Img 2015;8:248–57)

**Doppler Index (Dimensionless Index)**

- Criteria for severe is a DI < 0.25.
- For TAVR patients, DI < 0.2
Aortic Stenosis: Pitfalls of the Continuity Equation

- Accuracy of the LVOT diameter
  - Error is squared
- LVOT velocity
  - Angle $\theta$
  - Use laminar flow before pre-stenotic acceleration
- CW aortic velocity inaccuracy
  - Measure signal at multiple windows
  - Distinguishing AS from MR
- Nonsimultaneous measurement of LVOT and peak velocities
  - Varying cycle lengths

Key: Image Correct LVOT Velocity Profile

- Use laminar flow before pre-stenotic acceleration

$\text{LVOT VTI} = 14.5 \text{ cm}$
MODAL velocity
- Not the maximum velocities of a few blood cells
- Rather the most frequent value in a distribution
  ▶ Lower gain and/or increase reject

Planimetry of AVA: When Doppler not available

- Transthoracic echo
  - Limitations of transthoracic resolution
    - Feasible in 76% of patients (range in literature 13-85%)
    - Highly calcified (more severe stenosis), more difficult
    - Lower window for short-axis views
    - Small range of mild to severe stenosis (0.25 cm²) makes small errors unacceptable
Aortic annulus moves cranially during early systole and caudally during the remainder of systole and isovolumic relaxation. 

* This motion affects the 2D TEE measurement of area 

* Although AVA correlated well between 2DTEE and 3DTEE methods (r = 0.95), 2DTEE showed a significantly larger AVA compared with 3DTEE method


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<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Valve Anatomy</th>
<th>Valve Hemodynamics</th>
</tr>
</thead>
</table>
| **D1** | Symptomatic severe high-gradient AS | Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening | • Aortic Vmax 2.4 m/s or mean ΔP ≥40 mm Hg  
• AVA typically is ≤1.0 cm² (or AVAi ≤0.6 cm²/m²) but may be larger with mixed AS/AR |
| **D2** | Symptomatic severe low-flow/low-gradient AS with reduced LV EF | Severe leaflet calcification with severely reduced leaflet opening | • AVA ≤1.0 cm² with Aortic Vmax <4 m/s or mean ΔP <40 mm Hg  
• Dobutamine stress echocardiography shows AVA ≤1.0 cm² with Vmax ≥4 m/s at any flow rate |
| **D3** | Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS | Severe leaflet calcification with severely reduced leaflet opening | • AVA ≤1.0 cm² with Aortic Vmax <4 m/s or mean ΔP <40 mm Hg  
• AVAi ≤0.6 cm²/m² and  
• Stroke volume index <35 mL/m²  
• Measured when patient is normotensive (systolic BP <140 mm Hg) |

Nishimura, RA et al./AmCollCardiol 2014 Jun 10;63(22):2438-88
LVEF < 50%
\[\Delta P < 40\text{mmHg}\]
AVA \[\leq 1.0\ \text{cm}^2\]

\[\uparrow SV \geq 20\%\]
\[\uparrow SV < 20\%\]

Dobutamine Stress Echo

True Severe AS
Pseudo-Severe AS
Medical Therapy

\[\Delta P \geq 40\text{mmHg} \& \text{EOA} < 1.2\ \text{cm}^2\]
(AVA_{proj} \leq 1.0-1.2\ \text{cm}^2)
(CT Ca \geq 1274\text{AU} \♀/2065\text{AU} \♂)

True Severe AS

No Contractile Reserve

Medical Therapy

AVR±CABG (?TAVR±PCI)

Contractile Flow Reserve

\[\Delta P < 40\text{mmHg} \& \text{EOA} \geq 1.2\ \text{cm}^2\]
(AVA_{proj} > 1.0-1.2\ \text{cm}^2)
(CT Ca \geq 1274\text{AU} \♀/2065\text{AU} \♂)

Pseudo-Severe AS

\[\Delta P < 40\text{mmHg} \& \text{EOA} \geq 1.2\ \text{cm}^2\]
(AVA_{proj} \geq 1.0-1.2\ \text{cm}^2)
(CT Ca \geq 1274\text{AU} \♀/2065\text{AU} \♂)

True Severe AS

\[\Delta P < 40\text{mmHg} \& \text{EOA} \geq 1.2\ \text{cm}^2\]
(AVA_{proj} \leq 1.0-1.2\ \text{cm}^2)
(CT Ca \geq 1274\text{AU} \♀/2065\text{AU} \♂)

True Severe AS

(CT Ca \geq 1274\text{AU} \♀/2065\text{AU} \♂)

Pseudo-Severe AS

Medical Therapy

AVR±CABG (?TAVR±PCI)

Distribution of Aortic Valve Calcification by Sex in the Various AS Groups

1. Range of AVC load in patients with “Discordant Gradient” is wide, suggesting that this group is heterogeneous.
2. Half of these patients had evidence of severe calcified aortic valve disease on the basis of AVC load measured by MDCT

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVC density</td>
<td>292 AU/cm²</td>
<td>476 AU/cm²</td>
</tr>
<tr>
<td>AVC</td>
<td>1,274 AU</td>
<td>2,065 AU</td>
</tr>
</tbody>
</table>

(Note: AVC density = AVC indexed to annulus cross-sectional LVOT area)
D3 Patients

Table 5: Criteria that increase the likelihood of severe AS in patients with AVE <1.0 cm² and mean gradient <40 mmHg in the presence of preserved EF.

1. Clinical criteria:
   - Physical examination consistent with severe aortic stenosis
   - Typical symptoms without other explanation
   - Elderly patient (>70 years)
2. Qualitative imaging data:
   - LVH (additional history of hypertension to be considered)
   - Reduced LV longitudinal function without other explanation
3. Quantitative imaging data:
   - Mean gradient 30-40 mmHg
   - AVE < 0.8 cm²
   - Low flow (SVI < 35 ml/m²) confirmed by other techniques than standard
   - Doppler technique (LVOT measurement by 3D TEE or MSOT, CMR, invasive data)
   - Stress score by MSOT:
     - Severe AS likely: men > 2000 women > 1200
     - Severe AS very likely: men > 3000 women > 1600
     - Severe AS unlikely: men < 1600 women < 800

AS: Aortic stenosis; AVE: aortic valve area; CMR: cardiac magnetic resonance imaging; EF: ejection fraction; LVOT: left ventricular outflow tract; MSOT: multislice computed tomography; SVI: stroke volume index; TEE: transesophageal echocardiography.

*Normal dynamics measured when the patient is normotensive.

**Values are given in arbitrary units using Agatston method for quantification of valve calcification.

Don’t forget the appearance of the valve on Echo

Classification of AS

- In patients with a valve area <1.0 cm², further classification based on the combination of velocity (gradient), transvalvular SV, and LV ejection fraction is recommended as follows:
  - high gradient (velocity ≥ 4 m/s or mean gradient ≥ 40 mmHg) vs. low gradient (mean gradient < 40 mmHg);
  - normal flow (SVi ≥ 35 mL/m²) vs. low flow (SVi < 35 mL/m²);
  - preserved ejection fraction (≥ 50%) vs. reduced ejection fraction (<50%).


Flow and Gradient

- LF/HG and NF/HG AS patterns raise less controversy and are encountered in up to 70% of patients. In these categories, AVR improves outcomes.

- | Flow Gradient | Normal  | Low   |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>NF/HG</td>
<td>LF/HG</td>
</tr>
<tr>
<td>Low</td>
<td>NF/LG</td>
<td>LF/LG</td>
</tr>
</tbody>
</table>

Hemodynamic profile and pattern of myocardial adaptation to pressure load similar to moderate AS however are outcomes similar to HG AS?

Associated with the reduced SVi, worse NYHA class, and poor survival at 3 years, improved survival with AVR.

Dayan V et al, J Am Coll Cardiol. 2015;66::2594-603
Patients with LF-LG AS have increased mortality compared with
- Moderate AS (hazard ratio [HR]: 1.68; 95% confidence interval [CI]: 1.31 to 2.17)
- NF-LG (HR: 1.80; 95% CI: 1.29 to 2.51),
- High-gradient (HR: 1.67; 95% CI: 1.16 to 2.39) AS.

AVR was associated with
- Reduced mortality in patients with LF-LG (HR: 0.44; 95% CI: 0.25 to 0.77).
- Similar benefit in patients with NF-LG (HR: 0.48; 95% CI: 0.28 to 0.83).

Compared with patients with high-gradient AS, those with LF-LG were less likely to be referred to AVR (odds ratio: 0.32; 95% CI: 0.21 to 0.49).


Not Recommended for Clinical Use (?)
Pressure Recovery in Aortic Stenosis

- Catheterization AVA by Gorlin formula is derived from recovered pressures.
- In these patients EOA by Doppler may lead to an overestimation of the severity of AS
  - Pressure recovery depends on the ratio of $EOA_{Dop}$ and $AO_A$
  - The smaller the $EOA_{Dop}$ relative to the $A_A$, the more flow turbulence will occur and the less pressure recovery


Pressure Recovery

- Pressure recovery becomes most relevant
  - Moderate to severe AS (Doppler EOA between 0.8 cm² and 1.2 cm²)
  - Small aortas (diameter at the sinotubular junction < 30 mm)

\[ P_{distal} - P_{VC} = 4v^2x \frac{2}{x} \times \left( \frac{EOA}{AO_A} \right) \times (1 - \left[ \frac{EOA}{AO_A} \right]) \]

Eccentric jets have less pressure recovery since reconvertable energy is lost when an eccentric jet hits the aortic wall.

- The Geometric Orifice Area (GOA) is determined by aortic valve planimetry using echocardiography, CTA, or MRI imaging with good correlation.

- The planimetered GOA was significantly larger (1.19 ± 0.35 cm²) than EOA (0.89 ± 0.29 cm²) in the bicuspid AS group (r = 0.71, P < .001, Δ = 0.29 ± 0.25 cm²). This difference is not seen with trileaflet valves.

Abbas A et al Echocardiography 2015;32:372–382
**Pressure Recovery in AS**

- **AVA = 0.85 cm², DI = 0.26**
- **Energy Loss Index**
  \[
  \text{Energy Loss Index} = \frac{\left( EOA \times A_A \right)}{A_A - EOA} \times \text{BSA}
  \]
  \[
  = \frac{(0.85 \text{ cm}^2 \times 6.15 \text{ cm}^2)}{(6.15 \text{ cm}^2 - 0.85 \text{ cm}^2)} \times \text{BSA}
  \]
  \[
  = \frac{5.23 \text{ cm}^4}{5.30 \text{ cm}^2} \times \text{BSA}
  \]
  \[
  = 0.99 \text{ cm}^2 / \text{m}^2
  \]
  \[
  = 0.63 \text{ cm}^2 / \text{m}^2
  \]
- **MODERATE AS**

---

**Planimetered AVA = 1.02 cm²**

\[ \text{AVA} = 1.02 \text{ cm}^2 \]

\[ = 0.65 \text{ cm}^2 / \text{m}^2 \]

**Note:** Patient exercised on Bruce Protocol for 14 min without symptoms.
**Energy Loss Index**

- The energy loss coefficient (ELCo) provides an accurate estimation of the energy loss (EL) due to aortic stenosis using the calculated EOA_{Dop} and the cross-sectional area of the ascending aorta in systole (AOA).

- Energy loss index Advantages:
  - Takes into account the effects of both pressure recovery and body size.
  - In a substudy of the SEAS (Simvastatin Ezetimibe in Aortic Stenosis) trial 47.5% of patients classified as having severe AS by indexed EOA were reclassified to nonsevere AS when using energy loss index.

\[
\text{Energy loss index} = \frac{(EOA \times A_O)(A_O - EOA)}{BSA} \leq 0.5-0.6 \text{ cm}^2/\text{m}^2 \text{ suggests severe}
\]

_Bahlmann E et al J Am Coll Cardiol Img 2010;3:555–62_

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**Global Load: Zva**

- Valvuloarterial impedance (Zva)
  - \( Zva = SBP + \Delta P_{\text{Mean}} / SVI \)
  - \( > 4.5 \text{ mmHg}^{-1} \cdot \text{m}^{-2} \) suggests severe

- \( \Delta P_{\text{mean}} = \Delta P_{\text{NET}} \) in the absence of significant pressure recovery

- \( \Delta P_{\text{NET}} + SBP = \text{Global Load} \)
Paradoxical Low-Flow, Low-Gradient Severe Aortic Stenosis Despite Preserved Ejection Fraction Is Associated With Higher Afterload and Reduced Survival

Zineb Hachicha, MD; Jean G. Dumont, MD; Peter Bogaty, MD; Philippe Pitariou, DVM, PhD

Paradoxical Low Flow patient:
1. Lower transvalvular gradient
2. Lower LV diastolic volume index
3. Lower LV ejection fraction (62.8% versus 68.7%; P<0.001)
4. Higher level of LV global afterload reflected by a higher valvulo-arterial impedance (5.3±1.3 versus 4.1±0.7 mm Hg · mL⁻¹ · m²; P<0.001)


Prognostic Importance of Impedance

PLF: Lower overall 3-year survival (76% versus 86%; P=0.006).

Hachicha Z et al. J. Am. Coll. Cardiol. 2009;54;1003-1011
Valvular Heart Disease

Projected Valve Area at Normal Flow Rate Improves the Assessment of Stenosis Severity in Patients With Low-Flow, Low-Gradient Aortic Stenosis

The Multicenter TOPAS (Truly or Pseudo-Severe Aortic Stenosis) Study

Claudia Blais, MSc; Ian G. Burwash, MD; Gerald Mundigler, MD; Jean G. Duménil, MD; Nicole Lobo, MD; Florian Rader, MD; Helmut Baumgartner, MD; Rob S. Beanlands, MD; Boris Chayer, Eng; Lyes Kadem, Eng, PhD; Domen Garcia, Eng, PhD; Louis-Gilles Durand, Eng, PhD; Philippe Pibarot, DVM, PhD

Multicenter Canadian-European study of patients with low flow AS

Blais et al, Circulation 2006;113:711-721

Concept of the Projected AVA (250 mL/s)

Slide courtesy of Philippe Pibarot

Use a simple mathematical formulation to project what would be the AVA at a standardized flow rate

Blais et al, Circulation 2006;113:711-721
### Calculation of the Projected AVA

**Graph:**
- **Axes:**
  - X-axis: Mean Transvalvular Flow Rate (ml/s)
  - Y-axis: AVA (cm²)
- **Points:**
  - Baseline AVA and Q
  - Slope = valve compliance (VC)
  - Formula:
    \[
    \text{AVA}_{\text{projected}} = 0.70 + 0.0021 \times (250 - 130) = 0.96 \text{ cm}^2
    \]
- **References:**
  - Blais et al., Circulation 2006;113:711-721
  - Clavel et al., JASE; 23:380-6, 2010

### Measurements

**DSE Rest**
- LVOTd = 2.00 cm
- LVOT VTI = 18 cm
- LVET = 0.31 s
- Ao VTI = 72 cm
- ΔP = 21 mmHg

**DSE Peak**
- LVOT VTI = 33 cm
- Ao VTI = 85 cm
- ΔP = 39 mmHg
- LVET = 0.28 s

**Calculation**
- SV = 57 ml
- AVA = 0.79 cm²
- \( Q_{\text{mean}} = 183 \text{ ml/s}^{-1} \)

**Simplified method:**
- \( \text{AVA}_{\text{proj}} = \text{AVA}_{\text{rest}} \times \text{slope} (250 - Q_{\text{rest}}) = 0.79 \times 0.0023 (250 - 183) = 0.94 \text{ cm}^2 \)

**References:**
- Clavel et al., JASE; 23:380-6, 2010
Predictors of Mortality in Patients with Low-EF, Low-Flow, Low-Gradient AS Treated Medically – TOPAS Study

- Simplified AVA proj ≤ 1.2 cm²
- Peak DSE
- LVEF ≤ 35%
- DASI ≤ 20
- Gender (female)
- Age ≥ 70 years

- HR: 2.7 [1.6-5.2], p < 0.0001
- HR: 1.7 [1.1-2.5], p = 0.01
- HR: 1.6 [1.1-2.4], p = 0.02
- HR: 1.3 [0.5-3.5], p = 0.6
- HR: 1.5 [0.6-3.9], p = 0.4

What is moderate AS for a good ventricle may be severe for a depressed ventricle

Other Measures of Aortic Stenosis Severity

- SWL = 100 x (ΔP_{Mean}/SBP + ΔP_{Mean})
  - Flow and AVA dependent
  - May lead to underestimation of AS severity
  - >25% suggests severe
- Systemic arterial compliance
  - SAC = SVI/SBP-DBP
  - ≤ 0.6 ml·mmHg⁻¹·m⁻² suggests severe
- Systemic vascular resistance
  - SVR = 80 xMBP/CO
  - > 2,000 dyne·s·cm⁻⁵ suggests severe
Other Prognostic Tools

Myocardial Mechanics: Strain

- Strain (ε) = deformation
- Strain Rate = rate at which deformation occurs
- Longitudinal systolic strain of the left ventricle is shortening, normalized for diastolic length
Longitudinal Left Ventricular Mechanics in Asymptomatic Severe Aortic Stenosis


Reduced global strain = 12%.

Marker of LVH and fibrosis?

Original Article

Two-Dimensional Strain for the Assessment of Left Ventricular Function in Low Flow–Low Gradient Aortic Stenosis, Relationship to Hemodynamics, and Outcome

A Substudy of the Multicenter TOPAS Study

Philipp Emanuel Bartko, MD; Georg Heizne, PhD; Senta Graf, MD; Marie-Annick Clavel, DVM, PhD;
Aliasghar Khorsand, PhD; Jutta Bergler-Klein, MD; Ian Gordon Burwash, MD;
Jean Gaston Dumensnil, MD; Mario Széchelt, MD; Helmut Baumgartner, MD; Raphael Rosenhek, MD;
Philipp Pibarot, DVM, PhD; Gerald Mundigler, MD


1. In patients (N = 47) with low flow–low gradient aortic stenosis, 2-dimensional strain parameters are strong predictors of outcome.

2. Peak stress SR may add incremental prognostic value beyond what is obtained from N-terminal pro–B-type natriuretic peptide and peak stress left ventricular ejection fraction.
In low-gradient groups, more interstitial fibrosis in biopsy samples and more late enhancement MRI segments were observed.

A close inverse correlation was found between interstitial fibrosis and mitral ring displacement ($r = 0.79, p < 0.0001$).

In patients with AS, lower average longitudinal strain is related to higher LV mass, concentric geometry and more severe AS.

Intrinsic myocardial dysfunction is common in patients with elevated LV afterload, especially in low-flow AS.

1. In patients ($N = 47$) with low flow–low gradient aortic stenosis, 2-dimensional strain parameters are strong predictors of outcome.
2. Peak stress PLSR may add incremental prognostic value.
LGE for histologic fibrosis but is poor at determining interstitial fibrosis (which is potentially reversible).
Extracellular Volume: Diffuse Myocardial Fibrosis

Native T1 mapping provides a noninvasive estimation of diffuse myocardial fibrosis and correlates with subclinical myocardial dysfunction in asymptomatic patients with AS [1].

Symptomatic patients were more likely to demonstrate increased T1 values compared to asymptomatic patients [2].

Patients with severe fibrosis were less likely to show improvement in symptoms, LV function and LVH after surgery compared with those patients with mild to moderate fibrosis [3].

Differing patterns of remodeling, with both native T1 and ECV correlate with prognostic markers such as NT-pro-BNP [4].

BNP and Outcomes in AS

- BNP ratio (measured BNP/maximal normal BNP value specific to age and sex) >1 defined BNP clinical activation
- BNP ratio >1 independently predicted mortality after diagnosis (p < 0.0001; hazard ratio [HR]: 1.91; 95% CI: 1.55 to 2.35) and provided incremental power to the survival predictive model
- Link to survival was confirmed in asymptomatic patients with normal EF
  - BNP ratio >1: adjusted HR: 2.35 [95% CI: 1.57 to 3.56]
  - BNP ratio 1-2.0: adjusted HR = 2.10 [95% CI: 1.32 to 3.36]
  - BNP ratio 2.0-3.0: adjusted HR = 2.25 [95% CI: 1.31 to 3.87]
  - BNP ratio of ≥3: adjusted HR = 3.93 [95% CI: 2.40 to 6.43]

N = 1953


BNP and Outcomes in AS

- AVR is independently associated with markedly improved prognosis in patients with clinically activated BNP

Patients with significant AS and preserved LVEF, a combination of BNP and LV-GLS provides synergistic risk stratification, independent of symptoms, risk factors, and echocardiographic variables.

Asymptomatic patients had significantly worse survival, in the setting of abnormal LV-GLS and/or BNP.

LV-GLS and BNP become abnormal earlier in the disease cascade, as compared to flow-dependent markers such as LV-SVI.

Thank you