**2014 AHA/ACC Guidelines: Stages of Progression of VHD**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At risk</td>
<td>Patients with risk factors for development of VHD</td>
</tr>
<tr>
<td>B</td>
<td>Progressive</td>
<td>Patients with progressive VHD (mild-to-moderate severity and asymptomatic)</td>
</tr>
<tr>
<td>C</td>
<td>Asymptomatic severe</td>
<td>Asymptomatic patients who have the criteria for severe VHD. C1: Asymptomatic patients with severe VHD in whom the left or right ventricle remains compensated. C2: Asymptomatic patients with severe VHD, with decompensation of the left or right ventricle</td>
</tr>
<tr>
<td>D</td>
<td>Symptomatic</td>
<td>Patients who have developed symptoms as a result of VHD</td>
</tr>
</tbody>
</table>

In patients with stenotic lesions, there is an additional category of **very severe** stenosis based on studies of the natural history showing that prognosis becomes poorer as the severity of stenosis increases.

**2014 ACC/AHA Valve Guidelines**

- **Medical therapy for aortic stenosis**
  - Guideline based medical therapy for hypertension, hyperlipidemia, diabetes, HF, CAD, etc.
  - Life style: exercise, diet, not smoking
  - Statin therapy is NOT indicated for prevention of AS progression
  - Periodic clinical and echo monitoring
### 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 commissur fusion</td>
<td>- Mild AS: Aortic Vmax 2.0-2.9 m/s or mean ΔP 20-39 mm Hg&lt;br&gt;- Moderate AS: Aortic Vmax 3.0-3.9 m/s or mean ΔP 40-59 mm Hg&lt;br&gt; (Typically AVA &gt; 1.0 cm²)</td>
</tr>
</tbody>
</table>

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

### Echocardiographic Parameters of Aortic Stenosis Severity

- **Morphology**
  - Tricuspid vs Bicuspid
  - Severity of calcification
  - Planimetry
- **Ventriculo-Arterial Load**
  - Systemic Arterial Compliance and Resistance
  - Systemic Arterial Impedance
- **Hemodynamic Assessment**
  - Resting
  - Velocity, Gradient, Area
  - Stress
  - Dobutamine
  - Treadmill

### Aortic Stenosis Etiology/Pathology: Congenital

- **Bicuspid aortic valve**:
  - ~2% of live births
  - ~30% of patients are functionally stenotic
  - <70 yrs old, 50% are bicuspid

### Proposed TAVR-specific Classification

- **Tricommissural (1 commissure completely fused between 3 cusps)**
  - Frequently referred to as “functional” or “acquired” BAV by the surgical and interventional community
  - This morphology, fusion is not seen in the basal third of the sinus

- **Bicommissural raphe type**
  - 2 cusps fused by a fibrous or calcified ridge of various heights, does not reach the height of the commissure
  - 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 seen in the morphology, fusion occurs at or proximal to the basal third of the sinus

Jilaihawi H et al JACC Img 2016

### Prognosis of Aortic Sclerosis

- 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

### Trileaflet vs Bileaflet Valve

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

Aortic Stenosis

**Prognosis of Calcification**

- 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).

**Severities of Aortic Stenosis (AS)**

- **Symptomatic** Stage: D1
- **Asymptomatic** Stage: C1

**Stage Definitions**

- **D1-Stages**
  - Severe
  - Moderate
  - Mild
  - No Calcification

**Stages of Valvular AS**

**Odds Ratios**

- AVA ≤1.0 cm² with Aortic Leaflet Calcification
- AVA ≤1.0 cm² with Aortic Leaflet Thickness

**Echocardiographic Criteria of AS**

- **Valve Area**
  - Severe
  - Moderate
  - Mild
  - No Calcification

**Stages of Valvular AS**

- **Symptomatic** Stage: D1
- **Asymptomatic** Stage: C1

**Adverse Events**

- **Low surgical risk**
- **High surgical risk**

**Risk Factors**

- **Symptomatic** Stage: D1
- **Asymptomatic** Stage: C1
Abnormal Aortic Valve with Reduced Systolic Opening

Symptomatic
- LVEF <50%
- DSE with AVA ≤ 1 cm² and Vₘₚ ≥ 4 m/s (Stage D3)
- AVA ≤ 0.6 cm²/m² AND SVI <35 mL/m²

Asymptomatic (Stage B)
- Other cardiac surgery
- AVR (IIa)

Severe AS
- Vₘₚ ≤ 3.9 m/s and ΔPₘ ≤ 40 mmHg

Moderate AS
- 3.0-4.0 m/s
- 20-40* (30-50)*
- 1.0-1.5
- 0.6-0.85*
- 0.25-0.50*

Severe AS
- >4.0
- >40* or 50*
- <1.0
- <0.6
- <0.25

Critical AS
- >5.0
- >60
- >0.6
- >0.4*

Note: Aortic valve sclerosis velocity ≤2.5 m/s

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

Severity of AS: Criteria

Class I Indication for Diagnostic Testing
1. TTE is indicated in patients with signs or symptoms of AS or a bicuspid aortic valve for accurate diagnosis of the cause of AS, hemodynamic severity, LV size and systolic function, and for determining prognosis and timing of valve intervention. (Level of Evidence: B)

ACC/AHA 2014 Risk Assessment
Combining STS Risk Estimate, Frailty, Major Organ System Dysfunction, and Procedure-Specific Impediments

2014 ACC/AHA VALVE GUIDELINES

Choice of Intervention for AS

Indication for AVR
- Low-intermediate surgical risk
- High surgical
- Prohibitive surgical

Heart Valve Team (I)
- Surgical AVR (I)
- TAVR (Ila)
- Palliative Care

Bridge to SAVR or TAVR for severe symptoms

Yes
- Predicted post-TAVR survival >1 yr

No

Planimetry of AVA

- 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
Planimetry of AVA

- Transesophageal echo
  - Correlation between TEE AVA planimetry (0.56 +/- 0.31 cm²) and the Gorlin formula (0.56 +/- 0.31 cm²) was excellent (r = 0.95)
  - Acute changes in stroke volume do not result in significant alterations in the AVA measured by multiplane TEE
  - Feasibility 93%
  - Pitfalls
    - Transducer/image must be at the tips of the leaflets
    - Simultaneous imaging of all cusps
    - Calcification may make planimetry difficult

R Hoffmann, FA Flachskampf, and P Hanrath J Am Coll Cardiol, 1993; 22:529-534

2D TEE vs 3D TEE for AVA

- 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


Prognosis of Velocity

- High rate of clinical events, defined as death or aortic valves 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.


Spectrum of Aortic Stenosis

Rosenhek R et al. Circulation 2010;121:151-156

Prognosis of Rate of Velocity Increase

- 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.


Peak Velocity and Mean Gradient


Mean Gradient (mmHg)

Peak Flow Velocity (m/s)

Apical View

Peak transaortic velocity of 4.0 m/s corresponds to a mean gradient of 40 mmHg
Pitfall of Velocity and Gradient

- 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
    - Smaller 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
  - (Area x TVI)₁ = (Area x TVI)₂

Conservation of Mass: Continuity Equation

- Continuity Equation Normalizes for Flow!
  - Areaₐᵥ = Areaₕᵥ x VTIV.downcase x VTIAV

Doppler Index (Dimensionless Index)

- Criteria for severe is a DI < 0.25.
  For TAVR patients, DI < 0.2

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 < 1.0 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
  - 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

*Variability ± 8%*

---

**ASE Guidelines**

- “Accurate SV calculations depend on precisely recording the LVOT diameter and velocity. It is essential that both measurements are made at the same distance from the aortic valve.”
- “Flows acceleration at the annulus level and even more proximally occur in many patients, particularly those with calcific AS, so that the sample volume needs to be moved apically from 0.5 to 1.0 cm to obtain a laminar flow curve without spectral dispersion. In this case, the diameter measurement should be made at this distance from the valve.”


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**LVOT measurement in Aortic Stenosis**

- Methods:
  - With appropriate gain and processing adjustments, the LVOT 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.


---

**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.

---

**Aortic Valve Annular Dimensions: Biplane TEE**

- The annulus is approximately perpendicular to the long-axis of the aorta.

*Because the trigone between the L and N coronary cusps is imaged, be careful NOT to measure the calcification of the trigone (red arrow).*

*Use of biplane imaging to align the annulus*
LVOT & Annular Measurement

- The largest systolic diameter LVOT measurement should be used in calculating the aortic valve area.
- Avoid measuring basal septal hypertrophy (yellow arrows).
- Measure LVOT (dashed arrow) just apical to the annulus (red arrow).
- In the setting of acoustic shadowing of the distal annulus, a lower or higher window can be better used to image the entire plane of the annulus.
- Avoid measuring the calcification of the MV as the border of the LVOT (blue arrow).

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.

Aortic Valve Area Calculation in Aortic Stenosis by CT and Doppler Echocardiography

- 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 (AVAPlan).

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 adjustments, 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 10.56; p = 0.0001) versus AVACT ≤ 1.2 cm² (HR: 3.16, 95% CI: 1.64 to 6.13; p = 0.005).

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

Key: Image Correct LVOT Velocity Profile

Use laminar flow before pre-stenotic acceleration
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

Aortic Stenosis:

Pitfalls of the Continuity Equation

- Accuracy of the LVOT diameter
  - Error is squared
- LVOT velocity
  - Angle 0
  - 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

Technical Pearl: Peak Velocity

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

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

- V_max
  - RPS window in 50%,
  - Apex in 39%,
  - Suprasternal notch in 6%
  - Right supraclavicular in 5%


Non-apical Imaging Windows

- Age >75 was associated with

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
**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

**Gorlin equation vs continuity equation**

\[ A = \frac{CO(DFP \text{ or } SEP)(HR)}{44.3C \sqrt{\Delta P}} \]

- Discharge coefficient corrects formula to measure true anatomic area while continuity equation measures physiological area
- Physiological area is smaller than anatomic area
- Peak instantaneous gradient as measured by TTE is higher than the peak-to-peak gradient measured by LHC
- Peak-to-peak gradient approximates mean gradient
- Mean gradients by both modalities correlate well

**Cath vs Echo: Pressure Recovery**

When the blood flow contracts through a stenotic orifice, potential energy (pressure) is converted into kinetic energy (velocity) resulting in a pressure drop and acceleration of flow. Downstream from the vena contracta, some kinetic energy is irreversibly dissipated as heat because of flow turbulence.

The remainder of the kinetic energy that is reconverted back to potential energy is called the “pressure recovery”

- 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 (A_{A}).
  - Pressure recovery depends on the ratio of EOA_{Dop} and A_{A}
  - The smaller the EOA_{Dop} relative to the A_{A}, the more flow turbulence will occur and the less pressure recovery.
  - Eccentric jets have less pressure recovery since reconvertable energy is lost when an eccentric jet hits the aortic wall.

**Pressure Recovery in Aortic Stenosis**

\[ ELCo = \frac{EOA_{Dop} \times A_{A}}{A_{A} - EOA_{Dop}} - \frac{Q}{50 \sqrt{EL}} \]
Cath vs Echo

- Catheterization AVA by Gorlin formula is derived from recovered pressures.
  - 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)
- In these patients EOA by Doppler may lead to an overestimation of the severity of AS

Energy loss index = (EOA x Aa)/(Aa - EOA))/BSA ≤ 0.5–0.6 cm²/m² suggests severe


Double Envelop Pitfalls

- AVA_DDE overestimates AVA_CE by 0.17±0.23 cm² (p < 0.002) which may be clinically-significant for pre-procedural as well as intra-procedural decision-making.

Teo E...Hahn RT et al (submitted)

Accuracy of the Single-Cycle Length Method for Calculating Aortic Valve Area in Non-sinus Rhythms

- Afib:
  - Single-cycle length method with long R-R cycles is comparable to standard methods
- Frequent Ectopy:
  - Post-ectopic beat results in a significantly larger AVA compared to sinus beats due to a ~23% increase in stroke

Kerry A. Donegan, MD, and Rebecca T. Hahn, MD

Stage of Valvar AS

<table>
<thead>
<tr>
<th>Definition</th>
<th>Valve Anatomy</th>
<th>Valve Hemodynamics</th>
<th>Hemody/ Consequence</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>D0</td>
<td>Symptomatic</td>
<td>Severe leaflet</td>
<td>AVA 2.4-3.2 cm² with Aortic Vmax &lt; 4 m/s or DSE shows AVA 2.0 cm² with Vmax 3.5 m/s at any flow rate</td>
<td>LVEF &lt;50%</td>
</tr>
<tr>
<td></td>
<td>severe low-</td>
<td>calcification with</td>
<td></td>
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<tr>
<td></td>
<td>flow/low-</td>
<td>severely reduced</td>
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<td></td>
<td>grade AS</td>
<td>leaflet opening</td>
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<td></td>
<td>with reduced</td>
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<td></td>
<td>LV EF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D1</td>
<td>Symptomatic</td>
<td>Severe leaflet</td>
<td>AVA 2.2-3.0 cm² with Aortic Vmax &lt; 4 m/s or DSE shows AVA 2.0 cm² with Vmax 3.5 m/s at any flow rate</td>
<td>LVEF &lt;50%</td>
</tr>
<tr>
<td></td>
<td>severe low-</td>
<td>calcification with</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>flow severe</td>
<td>severely reduced</td>
<td></td>
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<tr>
<td></td>
<td>AS</td>
<td>leaflet opening</td>
<td></td>
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<tr>
<td></td>
<td>or paradoxical flow/low severe AS</td>
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<td></td>
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<td></td>
<td>Increased WRT</td>
<td>Heart Failure</td>
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<td></td>
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<td></td>
<td>Small LV &amp; low SV Restrictive diastolic filling</td>
<td>Angina</td>
</tr>
</tbody>
</table>


Nishimura, RA et al, Circulation March 3, 2014
Pressure Gradient

\[ \Delta P = F \times R \]
\[ R \propto \frac{\eta \times L}{r^4} \]
\[ \Delta P \propto \frac{E}{r^4} \]

- The magnitude of the pressure gradient is determined by the severity of the stenosis and the flow rate across the valve.

Determinants of Flow Rate

- Ventricular stroke volume
  - Systolic function
  - Heart Rate
  - Ventricular volume
  - Diastolic filling
    - Atrial-ventricular interaction
- Arterial afterload

Cardiac and systemic compensatory mechanisms attempt to maintain cardiac output and arterial pressure:
1. Systemic vasoconstriction
2. Increased blood volume
3. Increased heart rate and inotropy

Low Gradient, Severe AS

Low Gradient (mean < 35-40 mmHg)
Severe AS (AVA < 0.8 cm² or 0.5 cm²/m²)

- Reduced EF (< 45%)
- Usefulness in setting of low “stroke volume” and low gradient (mean gradient <30 mmHg) in patients with calculated valve area <1.0 cm² given the potential flow dependence of valve opening

3.2. Diagnosis and Follow-Up

- **Class IIa**
  - Low-dose dobutamine stress testing using echocardiographic or invasive hemodynamic measurements is reasonable in patients with stage D2 AS with all of the following, (Level of Evidence: B):
    a. Calcified aortic valve with reduced systolic opening;
    b. LVEF less than 50%;
    c. Calculated valve area 1.0 cm² or less; and
    d. Aortic velocity <4.0 m/s or mean pressure gradient <40 mm Hg.

- **Mild to Moderate AS**, Dobutamine will increase valve area by \( \geq 0.3 \text{ cm}^2 \) with no significant change if severe AS
  - Goal is to increase **STROKE VOLUME** by 20%
  - Maximum dobutamine 30 μg/kg/min
    - Maximum inotropic effect of dobutamine at this dose
    - Less chronotropic effect/less ventricular tachycardia
  - Mild to Moderate AS, Dobutamine will increase valve area by \( \geq 0.3 \text{ cm}^2 \) with no significant change if severe AS

- **Useful in setting of low “stroke volume” and low gradient (mean gradient <30 mmHg)” in patients with calculated valve area <1.0 cm² given the potential flow dependence of valve opening**

Nishimura, RA et al, Circulation March 3, 2014

DiFilippi CR et al, AJC 1995;75:191
Lin SS et al Am Heart J 1998;136:1010-6
Siewertmann et al, CHEST 2001;119:1766-1777
Mare et al JACC 2003;41:27-31
The Complex Nature of Discordant Severe Calcified Aortic Valve Disease Grading

1) Define AVC load thresholds best segregating moderate and severe AS in the unadulterated AS form with normal LVEF, normal flow, and concordant grading (CG);
2) Assess, with these thresholds, the severity of calcified aortic valve disease in AS with discordant grading.


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.

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

Valvular Heart Disease

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

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

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

Low-Gradient Aortic Stenosis and Contractile Reserve

Many patients do not normalize flow rate under DSE. Can we further define the low contractile reserve patients?

Quere J et al. Circulation 2006;113:1738-1744
**Calculation of the Projected AVA**

Simplified method: 
AVA proj = 0.70 + 0.0021 \times (250 - 130) = 0.96 cm²

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

Clavel et al. JASE; 23:200-6, 2010

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**Predictors of Mortality in Patients with Low-EF, Low-Flow, Low-Gradient AS**

Treated Medically – TOPAS Study

*Slide courtesy of Philippe Pibarot*

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR &gt; 1.7</td>
<td>1.6-5.5</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Peak DSE</td>
<td>1.5-6.5</td>
<td>0.01</td>
</tr>
<tr>
<td>LVET &lt; 0.28</td>
<td>1.2-4.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Age &gt; 70 years</td>
<td>1.3 (1.2-3.5)</td>
<td>0.6</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>1.5 (0.6-3.9)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

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

Clavel et al. Circulation 2006;113:711-721

Clavel et al. JASE 23:200-6, 2010

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**Low Gradient, Severe AS**

- Low Gradient (mean < 35-40 mmHg)
- Severe AS (AVA < 0.8 cm² or 0.5 cm²/m²)

**D2: Reduced EF (< 50%)**

**D3: Normal EF (≥ 50%)**

**Flow-dependent AS**

- Paradoxic Low Flow (SVI < 35 ml/m²)

**Dobutamine Stress Echo**

- Small Ventricles
- High Zva
- Intrinsic Myocardial Dysfunction
- Severe MR/TR

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**Etiologies of Paradoxical Low Flow**

- Paradoxic Low Flow (SVI < 35 ml/m²)
  - Abnormal LV mechanics (Intrinsic myocardial dysfunction)
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 ($r = 0.79$, $p < 0.0001$).


Longitudinal Left Ventricular Mechanics in Asymptomatic Severe Aortic Stenosis

Reduced global strain = 12%.

Marker of LVH and fibrosis?

Etiologies of Paradoxical Low Flow

- Paradoxical Low Flow (SVI < 35 ml/m²)
  - Tachycardia

  The mean systolic aortic valve gradient averaged 64 mm Hg during sinus rhythm and fell to 52 mm Hg during pacing ($p < 0.001$).
  Stroke volume index fell from 37 ml/m² to 24 ml/m² ($p < 0.01$).

Etiologies of Paradoxical Low Flow

- Paradoxical Low Flow (SVI < 35 ml/m²)
  - Hypertension (Valvulo-arterial impedance)

  AS created in 24 pigs to test the effect of HTN on gradients
  - Marked reduction in peak/mean gradients with progressive systolic hypertension
  - Increase in LV afterload with ↑ systemic arterial resistance and ↓ in systemic arterial compliance leads to a reduced mean flow rate

Etiologies of Paradoxical Low Flow

- Paradoxical Low Flow (SVI < 35 ml/m²)
  - Small LV cavity/thick walls
  - Severe diastolic dysfunction

Effect of Afterload Reduction in AS

Normal EF

86 year old female
- Class III/IV CHF
- Echo
  - EF: 60%
  - Moderate to Severe MR
  - Moderate to Severe AS
  - Velocity 3.3 m/s, Mean Gradient – 30 mmHg
  - AR 0.5 cm², AVA – 0.9 cm²/m²
- Cath
  - Mean gradient – 25 mmHg
  - Peak gradient – 30mmHg
  - AVA – 0.6 cm²
Effect of Afterload Reduction in AS

- In cath lab, nitropride titrated up to final dose 125 mcg/min
- Echo
  - Peak velocity = 4.2 m/s
  - Mean gradient = 36 mmHg
  - A/V A = 0.7 cm²
  - A'VA = 0.4 cm²/m²
- Cath
  - Mean gradient = 35 mmHg
  - Peak gradient = 45 mmHg

Other Measures of Aortic Stenosis Severity

- Valvuloarterial impedance (Zva)
  - Zva = SBP + ΔPmean/SVI
  - > 4.5 mmHg⁻¹·m⁻² suggests severe

Prognostic Importance of Impedance

Overall Survival Versus Zva

Overall Survival Versus Zva and Type of Treatment

Paradoxical Low-Flow, Low-Gradient Severe Aortic Stenosis Despite Preserved Ejection Fraction Is Associated With Higher Afterload and Reduced Survival

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)

Etiologies of Paradoxical Low Flow: “Other”

- Paradoxical Low Flow (SVI < 35 ml/m²)
  - Reduced RV Stroke volume
    - RV dysfunction
    - Severe TR
  - Severe mitral valve disease (MR and MS)

More Complicated than D2 and D3

Outcome and Impact of Aortic Valve Replacement in Patients With Preserved LVEF and Low-Gradient Aortic Stenosis

Eighteen studies were included in the analysis.
**Symptoms**

- **Symptomatic patients with NF-LG should also receive particular attention and that additional diagnostic tests should be considered in these patients to corroborate the stenosis severity and determine the indication for AVR.**

**Conclusions:**

- Symptomatic patients with NF-LG should also receive particular attention and that additional diagnostic tests should be considered in these patients to corroborate the stenosis severity and determine the indication for AVR.