MAKING SENSE OF “MODERATE” GRADIENTS IN PATIENTS WITH SYMPTOMATIC AORTIC STENOSIS

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DISCLOSURES

INSTITUTIONAL RESEARCH SUPPORT

MEDTRONIC
ABBOTT
BOSTON SCIENTIFIC
MAKING SENSE OF “MODERATE” GRADIENTS IN PATIENTS WITH SYMPTOMATIC “SEVERE” AORTIC STENOSIS

OR

“WHAT DO I DO WHEN THE NUMBERS DON’T MAKE SENSE?”
ASSESSING AS SEVERITY

- “Easy” when the data is concordant
- 83 y/o man with moderate DOE and fatigue

Exam:
- BP 130/78; P 60
- NO JVD; Carotid upstroke delayed, low volume, thrill
- IV / VI SEM TO Carotids, absent A2
- III / VI diastolic murmur
- Clear lungs
- No edema

ECHO: NL EF, AVA 0.6 cm sq, MEAN GRAD 81 mm Hg

ACC / AHA Stage D1
ASSESSING AS SEVERITY:
Not so easy with discordant data

- ~40% of AS patients have discordant data
- High gradient with AVA > 1 cm²
  - High flow states (e.g. AR, fever, anemia, AV fistula, hyperthyroid)
- Small AVA (≤ 1 cm²) with gradient < 40 mm Hg or Vmax <4 M/sec
- ~30% of patients with an Echo AVA ≤ 1 cm² have a low gradient
- Patients may have a low EF (< 50%) or a normal EF (≥ 50%) with a low SVI (< 35cc/m²)
- Patients with a normal EF, normal SVI (> 35cc/m²) and small AVA??

<table>
<thead>
<tr>
<th>STAGE</th>
<th>EF</th>
<th>AVA</th>
<th>MEAN GRADIENT</th>
<th>FLOW (SVI)</th>
<th>SEVERE</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>Any</td>
<td>≤ 1</td>
<td>≥ 40</td>
<td>NL/LOW</td>
<td>YES</td>
</tr>
<tr>
<td>D2</td>
<td>&lt; 50%</td>
<td>≤ 1</td>
<td>&lt; 40</td>
<td>LOW</td>
<td>+/-</td>
</tr>
<tr>
<td>D3</td>
<td>≥ 50%</td>
<td>≤ 1</td>
<td>&lt; 40</td>
<td>LOW</td>
<td>+/-</td>
</tr>
<tr>
<td>D?</td>
<td>≥ 50%</td>
<td>≤ 1</td>
<td>&lt; 40</td>
<td>NL</td>
<td>???</td>
</tr>
</tbody>
</table>
LOW FLOW LOW GRADIENT AORTIC STENOSIS: ACC/AHA STAGE D2 / D3 /D??

- “CLASSICAL” LF-LG AS (D2)
  - AVA ≤1.0 cm², MEAN GRADIENT < 40 mm Hg, LVEF < 50%, SVI < 35 cc / m²
  - 5-10% of all AS patients
  - Males > females
  - Often with CAD, significant MR

- “PARADOXICAL” LF-LG AS (D3)
  - AVA ≤1.0 cm², MEAN GRADIENT < 40 mm Hg, LVEF > 50%, SVI < 35 cc / m²
  - 5-15% of all AS patients
  - Females > males, elderly, HTN

- NORMAL FLOW LOW GRADIENT AS (D??)
  - AVA ≤1.0 cm², MEAN GRADIENT < 40 mm Hg, LVEF ≥ 50%, SVI ≥ 35 cc / m²
  - Seen in up to 25% of AS patients
  - Management not addressed in current guidelines
    - Consider stress echo, AV calcium score
ASSESSING AORTIC STENOSIS WHEN THE DATA DOES NOT MATCH

GOAL:

Differentiate True Severe Aortic Stenosis (TSAS) from Pseudo Severe Aortic Stenosis (PSAP) or Moderate AS

Determine which patients will benefit from AVR

SYSTEMATIC APPROACH TO THE PATIENT and THE DATA
HOW TO APPROACH LOW GRADIENT SEVERE AORTIC STENOSIS

- Symptom Status
  - Valve vs Non-valve etiology
- Reassess the primary hemodynamic data (usually echo)
  - Technical quality of the measurements
- Exercise or Pharmacologic Stress Testing
  - Stage D2 Severe AS (DSE)
  - ? Role in Stage D3 AS (? SE or DSE)
- Calcium scoring of the AV (MDCT)
- ? Role of invasive testing / hemodynamics
ASSESSING AS SEVERITY: THE CONTINUITY EQUATION

SV = \( \pi (\text{LVOTd}/2)^2 \times \text{LVOTvti} \)

SVI = \( \frac{SV}{\text{BSA}} \)

Valve flow rate (Q) = \( \frac{SV}{\text{LVET}} \)

Q is the flow rate across the valve during ejection and accounts for changes in LVET.
ASSESSING AS SEVERITY

- ALWAYS REVIEW THE PRIMARY (ECHO) DATA
- ATTENTION TO DETAIL IN THE MEASUREMENTS

ACC/AHA Guidelines: Meticulous attention to detail is required when assessing aortic valve hemodynamics, either with Doppler echocardiography or cardiac catheterization, and the inherent variability of the measurements and calculations should always be considered in clinical-decision making.

- EXAMINE THE PATIENT !!

- REVIEW PRIOR ECHO DATA IF AVAILABLE
ASSESSING THE ECHO DATA: POTENTIAL PITFALLS IN THE ECHO DATA

- LVOTd / Velocity
  - Careful review of LVOTd measurement
  - LVOT PW sample volume at location of LVOTd measurement

- Technical issues (underestimate severity by underestimating gradient)
  - CW Doppler from multiple windows
    - Max Velocity from RPS in up to 50% of pts

- Technical issues (overestimate severity, AVA too small)
  - LOVTd too small
  - **LVOTd = (5.7 x BSA) + 12.1 mm**
    - Differences of > 2mm(+/−) suggest measurement error
    - May not hold for obese, BAV
    - “Contamination” of the AS jet with MR
OBTAIN ADDITIONAL DATA BEYOND THE AVA AND GRADIENT

- Calculate the DVI (<0.25 severe AS, > 0.3 moderate AS)
- Use 2D / 3D volumes to calculate SV to corroborate the Doppler data
- 2D/3D Planimetry (if < 1 cm², severe AS)
  - Anatomic area > EOA derived from continuity equation
- Determine degree of AV calcification with CT
PHYSIOLOGIC CAUSES of LOW FLOW (low SVI, < 35cc/m$^2$)

- Low EF
- Normal EF
  - Impaired longitudinal function (low GLS)
  - Concentric LV remodeling / LVH with small cavity
  - Diastolic dysfn / poor LV filling
  - HTN / increased afterload
  - Significant MR / MS / TR
  - Afib
  - RV failure
  - Pericardial constriction

Figure. Factors contributing to low-flow state in patients with aortic stenosis (AS) and preserved left ventricle ejection fraction (LVEF).

Pibarot Circ 2013;128:1729
ADDITIONAL CONSIDERATIONS IN ASSESSING AS SEVERITY in LOW GRADIENT STATES

- Assess valve flow rate (as opposed to SVI)
  - \( Q = \frac{SV}{LVET} \)
  - < 200 cc/sec

- Small body size
  - Index AVA to BSA \( \leq 0.6 \text{ cm}^2/\text{m}^2 \)
  - May overestimate severity in obese

- HTN / reduced arterial compliance
  - Additional afterload and early wave reflection may blunt gradient
  - Reassess with BP controlled
GUIDELINE CRITERIA ARE INCONSISTENT

- AVA \( \leq 1 \text{ cm}^2 \) and MEAN GRADIENT \( \geq 40 \text{ mm Hg} \)
- With normal flow, AVA of 1 cm\(^2\) correlates with a mean gradient of 30 mm Hg and Vm of 3.5 m/s

CURRENT GUIDELINES SEEM TO WORK CLINICALLY

- AVA \( \leq 1.0 \text{ cm}^2 \) IS SENSITIVE but HAS LOW SPECIFICITY if \( V_m < 4.0 \text{ m/s} \) and/or mean gradient < 40 mm Hg
- MEAN GRADIENT \( \geq 40 \text{ mm Hg} \) IS SPECIFIC

For patients with discordant data, multi-step assessment is needed
LOW FLOW LOW GRADIENT AORTIC STENOSIS (D2)

- 53 Y/O MAN WITH A HEART MURMUR PRESENTED WITH DOE
- EXAM CONSISTENT WITH CHF, GR II/VI SEM
- ECHO WITH SEVERE LV DYSFUNCTION
- CALCIFIED AV WITH MEAN GRADIENT OF 22 mm Hg, AVA 0.6 cm², DI 0.16
- CATH WITH NO CAD
- DSE ORDERED TO ASSESS TRUE vs PSEUDO AS

CASE ADAPTED FROM ORSINELLI ed.
COLOR ATLAS AND SYNOPSIS OF ECHOCARDIOGRAPHY
MCGRAW HILL 2015
## DSE RESULTS

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>5 mcg/kg</th>
<th>10 mcg/kg</th>
<th>20 mcg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean AV gradient</strong> (mm Hg)</td>
<td>21</td>
<td>26</td>
<td>34</td>
<td>36</td>
</tr>
<tr>
<td><strong>AV peak gradient</strong> (mm Hg)</td>
<td>31</td>
<td>33</td>
<td>54</td>
<td>65</td>
</tr>
<tr>
<td><strong>LVOT TVI (cm)</strong></td>
<td>9</td>
<td>10</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td><strong>AV TVI (cm)</strong></td>
<td>57</td>
<td>62</td>
<td>64</td>
<td>75</td>
</tr>
<tr>
<td><strong>AV area (cm sq)</strong></td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.7</td>
</tr>
</tbody>
</table>

PRE OP and POST OP ECHO

ADAPTED FROM ORSINELLI ed. COLOR ATLAS AND SYNOPSIS OF ECHOCARDIOGRAPHY MCGRAW HILL 2015
DOBUTAMINE STRESS ECHO IN CLASSICAL LF - LG AORTIC STENOSIS (D2) 
Class IIa

Figure 17 Interpretation of the dobutamine SE results in patients with low-flow, low-gradient AS, and reduced LVEF. The first step is to determine the presence of flow reserve, which is generally defined as a relative increase in stroke volume (SV) >20%. If there is flow reserve, the peak effective aortic valve area (AVA) remains <1 cm² and the mean pressure gradient (MPG) exceeds 40 mmHg, the stenosis is considered severe. If there is no flow reserve, it is difficult to get a definitive answer with regard to stenosis severity. In this case, the use of projected AVA or the evaluation of calcium score by computed tomography (MDCT) should be considered. The estimation of the projected AVA may not be reliable when the ΔQ is <20%. If the projected AVA is <1 cm², the stenosis is severe. 

\[
\text{AVA}_{	ext{proj}} = \frac{Q}{\text{MPG}}
\]

\[
\text{AVA}_{\text{proj}} \geq 1.0 \text{ cm}^2, \text{AVA}_{\text{proj}} \leq 1.0 \text{ cm}^2
\]

\[
\Delta \text{AVA}_{\text{proj}} \text{ not measurable}
\]

\[
\text{AVA}_{\text{proj}} \geq 1.0 \text{ cm}^2, \text{AVA}_{\text{proj}} \leq 1.0 \text{ cm}^2
\]

\[
\text{MDCT AoV Calcium}
\]

\[
\text{Indeterminate AS}
\]

\[
\text{True-Severe AS}
\]

\[
\text{Pseudo-Severe AS}
\]

\[
\text{True-Severe AS}
\]
DOBUTAMINE STRESS ECHO (D2)
SEVERE AS vs “PSUEDO-AS”

- ASSESS “CONTRACTILE RESERVE” (aka “FLOW RESERVE”)
  - IMPROVEMENT IN EF (or GLS)
  - EVIDENCE OF FLOW RESERVE (INCREASE IN SV by 20%)
    - TRUE SEVERE AS
      - INCREASE IN MEAN GRADIENT (≥ 40 mm Hg)
      - MINIMAL CHANGE IN AVA (≤ 1.0 cm²), increase < 0.3 cm²
      - AVR (Class IIa)
    - “PSEUDO” SEVERE AS
      - MEAN GRADIENT < 40 mm Hg, AVA > 1.0 cm², increase > 0.3 cm²
      - Medical management

- INCREASE IN SV < 20%  DIAGNOSIS / SEVERITY OF AS ??
  - POOR PROGNOSIS
  - ASSESS VALVE FLOW RATE (Q) and AVA_{projected} which calculates the AVA at a standardized flow rate (250 cc / sec)
    - Projected AVA = AVA_{rest} + (Δ AVA / Δ Q) x (250 - Q_{rest})
  - AV CALCIUM SCORE with MDCT
  - IF SEVERE AS, CONSIDER AVR
“PARADOXICAL” LF/LG AS (D3)

- AVA < 1.0 cm², MEAN GRADIENT < 40 mm Hg, LVEF ≥ 50%, SVI < 35cc/m²
- IF FLOW RATE (SV/LVET) IS NORMAL (≥ 200 - 250 cc/sec), TSAS
- REVIEW PRIMARY DATA (especially the LVOTd)

CAUSES OF LOW FLOW

- CLASSICALLY SMALL HYPERTROPHIED LV (small SV)
- SIGNIFICANT MS / MR / TR
- RV DYSFUNCTION

KEY ROLE OF BP

PHYSICAL EXAM

UNCERTAIN ROLE OF STRESS TESTING

AVR (CLASS IIa)
Table 5 Criteria that increase the likelihood of severe AS in patients with AVA < 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
- AVA ≤ 0.8 cm²
- Low flow (SVI < 35 mL/m²) confirmed by other techniques than standard
- Doppler technique (LVOT measurement by 3D TEE or MSCT; CMR, invasive data)

Calcium score by MSCT

<table>
<thead>
<tr>
<th>Severe AS likely:</th>
<th>men ≥ 2000</th>
<th>women ≥ 1200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe AS very likely:</td>
<td>men ≥ 3000</td>
<td>women ≥ 1600</td>
</tr>
<tr>
<td>Severe AS unlikely:</td>
<td>men &lt; 1600</td>
<td>women &lt; 800</td>
</tr>
</tbody>
</table>
NORMAL FLOW LOW GRADIENT AS WITH NORMAL EF (STAGE D??)

- AVA ≤1.0 cm², MEAN GRADIENT < 40 mm Hg, LVEF ≥ 50%, SVI ≥ 35cc/m²
- NOT CONSISTENT WITH FLUID DYNAMICS
- INDEX TO BSA
- POSSIBLY DUE TO INCONSISTENT CUT POINTS or MEASUREMENT ERRORS
- SIMILAR OUTCOMES TO MODERATE AS
  - AVR NOT INDICATED
  - FOLLOW CLOSELY
AN INTEGRATED / STEP WISE APPROACH TO THE MANAGEMENT OF LOW GRADIENT SEVERE AORTIC STENOSIS

Assess accuracy of data

Determine type LG AS
Assess gradient
Assess flow (SVI)
Assess EF

Confirm Severe AS
Stress / DSE
Valve morphology
Valve Calcium Score

Select type of AVR
Valve morphology by echocardiography suspicious of aortic stenosis

Step 1: Assess velocity/gradient

LOW GRADIENT AS
V_{max} < 4m/s, ΔP_{max} < 40mmHg

HIGH GRADIENT AS
V_{max} ≥ 4m/s, ΔP_{max} ≥ 40mmHg

“Easy” Track

High flow status excluded

Step 2: Assess AVA

AVA ≤ 1.0 cm²
AVA > 1.0 cm²

Severe high gradient AS
(normal flow / low flow)
(normal EF / low EF)

Define whether high flow status is reversible

NO

Step 3: Exclude measurement errors that may cause gradient / flow / AVA underestimation!!

AVA > 1.0 cm²

→ moderate AS

Yes

Define flow status (SV index)

Low flow (SVI ≤ 35ml/m²)
Normal flow (SVI > 35ml/m²)

→ severe AS unlikely

Not reversible

→ severe AS

Reversible

→ re-assess at restored normal flow

Step 4: Define flow status (SV index)

→ severe AS unlikely

Step 5: Assess LVEF

LVEF < 50%
LVEF ≥ 50%

Step 6: Dobutamine echo

Flow reserve
No flow reserve

pseudosevere AS
true severe AS

Step 7: Calcium Score by CT (see table 5)

Integrated approach (table 5)

Figure 8 Integrated, stepwise approach to grading AS severity.
ASSESSING AS SEVERITY BASED ON FLOW and GRADIENT  
AVA $\leq 1 \text{ cm}^2$

<table>
<thead>
<tr>
<th></th>
<th>$\geq 35 \text{ cc/m}^2$</th>
<th>$&lt; 35 \text{ cc/m}^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\geq 40 \text{ mm Hg}$</td>
<td><strong>NF/HG SEVERE AS (D1)</strong></td>
<td><strong>LF / HG SEVERE AS (D1)</strong></td>
</tr>
<tr>
<td>$&lt; 40 \text{ mm Hg}$</td>
<td><strong>NF /LG ?? Moderate AS</strong></td>
<td><strong>LF/LG ? SEVERE AS (D2/D3)</strong></td>
</tr>
</tbody>
</table>
CONCLUSIONS

- DETERMINING AS SEVERITY IN PATIENTS WITH DISCORDANT DATA IS CHALLENGING but CRITICAL IN CLINICAL DECISION MAKING
  - ESSENTIAL to confirm severe AS
  - ~30-50% of patients with a small AVA and LG have non-severe AS

- WITH DISCORDANT DATA
  - VERIFY THE DATA QUALITY / ACCURACY
  - DSE IN STAGE D2 PATIENTS
  - CALCULATE SVI IN D3 PATIENTS
  - CONSIDER STRESS ECHO or AV CALCIUM SCORING IN D3 PATIENTS
  - NORMAL FLOW LOW GRADIENT PATIENTS (D??) PRESENT A CHALLENGE
  - CALCULATE RESTING FLOW RATE (Q) AND AVA projected IN SELECTED PATIENTS
THANK YOU
AVA PROJECTED AT NORMAL FLOW

Requires measuring LVET in addition to usual measurements

Projects AVA at a “normal” flow rate of 250cc/sec

VC derived from $\Delta$ AVA/ $\Delta$ Q rather than from regression analysis of the slope

Clavel JASE 2010:23:380
142 pts with Stage D2 AS (EF < 40%)

AVA$_{\text{Projected}}$ predicted severe AS better than conventional DSE parameters (AVA$_{\text{peak}}$, MG$_{\text{peak}}$ or Δ AVA)
## ASSESSING AS SEVERITY

### AVA Projected (Simplified)

<table>
<thead>
<tr>
<th>REST</th>
<th>PEAK</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVOTd = 2.0 cm; LVOT VTI 18 cm</td>
<td>LVOTd = 2.0 cm; LVOT VTI 33 cm</td>
</tr>
<tr>
<td>AV VTI 72; LVET 0.31s</td>
<td>AV VTI 85; LVET 0.28s</td>
</tr>
<tr>
<td>Mean gradient 21 mm Hg</td>
<td>Mean gradient 39 mm Hg</td>
</tr>
<tr>
<td>SV = ( \pi \times (2.0/2)^2 \times 18 = 57 \text{ cc} )</td>
<td>SV = ( \pi \times (2.0/2)^2 \times 33 = 104 \text{ cc} )</td>
</tr>
<tr>
<td>Q = 57/0.31 = 182 cc/s</td>
<td>Q = 104/0.28 = 370 cc/s</td>
</tr>
<tr>
<td>AVA 0.79</td>
<td>AVA 1.22</td>
</tr>
</tbody>
</table>

\( \Delta Q = 187; \Delta \text{AVA} 0.43 \)

Projected AVA = \( 0.79 + \frac{(0.43/188) \times (250 - 182)}{182} = 0.94 \)

**TRUE SEVERE AS**
ASSESSING AS SEVERITY
AVA Projected (Simplified)

REST
LVOT\(d\) = 1.96 cm; LVOT VTI 17 cm
AV VTI 60; LVET 0.31s
Mean gradient 20 mm Hg
SV = \(\pi (1.96/2)^2 \times 17 = 51\) cc
Q = 51/0.31 = 165 cc/s
AVA 0.85

PEAK
LVOT\(d\) = 1.96 cm LVOT VTI 20cm
AV VTI 62; LVET 0.30s
Mean gradient 31 mm Hg
SV = \(\pi (1.96/2)^2 \times 20 = 60\) cc
Q = 60/0.30 = 201 cc/s
AVA 0.97
\(\Delta Q = 36; \Delta A VA = 0.12\)

Projected AVA = 0.85 + (0.12/36) \times (250 - 165) = 0.85 + (0.003 \times 85) = 1.11

PSEUDO SEVERE AS