Αορτική στένωση με χαμηλή κλίση πίεσης: ποιες οι διαφορετικές οψεις του συνδρόμου και ποια η διαχείριση του ασθενούς;

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No conflicts of interest
Aortic stenosis

• Most frequent VHD and most frequent cause of valve procedure

• No pharmacological treatment – SAVR or TAVR the only treatment option

• Therapy is determined by:

  Severity of AS  Symptoms  LV systolic function
The problem...

“Ideal”
Mean G > 40 mmHg and AVA < 1 cm^2

“Problematic”
Mean G < 40 mmHg and AVA < 1 cm^2

Up to 50%
Why do we care about LG AS?

Valve disease problem?

Myocardial disease problem or increased arterial afterload problem?

Is it truly severely stenotic?
Gradient is dependent on:
- Flow (squared)
- AVA
- Arterial Compliance
- AV calcium

Flow ≠ SV
Flow rate = SV/SET

Low Flow
• SVi ≤ 35 ml/m²
• Flow < 200 – 250 ml/s

Subtypes of LG AS

LOW GRADIENT AS
AVA≤1.0cm² and MG<40mmHg

< 50%
LVEF ≥ 50%

≤ 35 ml/m²
SVi > 35 ml/m²

«CLASSICAL» LOW-FLOW LOW-GRADIENT

«PARADOXICAL» LOW-FLOW LOW-GRADIENT

NORMAL-FLOW LOW-GRADIENT

Accurate measurements are important

LVOTdiam = (5.7 x BSA) + 12.1

SV = LVEDV (Teichholz) x EF (BipSimp)

Classical LF (LEF) – LG AS

5-10% of AS population

LOW GRADIENT AS
AVA ≤ 1.0 cm² and MG ≤ 40 mmHg

≤ 50% LV EF
≥ 50%

+ SVi ≤ 35 ml/m²

«CLASSICAL» LOW-FLOW LOW-GRADIENT
«PARADOXICAL» LOW-FLOW LOW-GRADIENT
NORMAL-FLOW LOW-GRADIENT

≤ 35 ml/m²
SVi > 35 ml/m²
Why is it important?

Mortality with SAVR (8-33% at 30 d) and MM is high (40-60% at 2 y)

Low dose dobutamine challenge

Starting dobutamine dose of 2.5 to 5 mcg/kg/min

- Increase dose 2.5 to 5 mcg/kg/min every 3-5 minutes
- Maximum dobutamine dose of 20 mcg/kg/min

Infusion stopped when:
1) Maximum dobutamine dose reached (20 mcg/kg/min)
2) Positive result obtained
3) Heart rate rises 10-20 bpm over baseline or exceeds 100 bpm
4) Symptoms, blood pressure fall, or significant arrhythmias

Positive Result:
- An increase in effective AVA to a final valve area >1.0 cm² suggests that stenosis is not severe [47].
- Severe stenosis is suggested by an AS jet velocity ≥4.0 m/s or a mean gradient > 30-40 mmHg provided that valve area does not exceed 1.0 cm² at any flow rate [50,51].
- Absence of contractile reserve (failure to increase SV by >20%) is a predictor of a high surgical mortality and poor long-term outcome although valve replacement may improve LV function and outcome even in this subgroup [52].

• <20% SV increase
• AVA 1 – 1,2 cm²
Dobutamine stress echo

Rest – 127 ml/s  
AVA_{proj} = 0.75 \text{ cm}^2  
10 \text{ mcg/kg/min} – 175 ml/s

SV=43 ml  
Peak vel = 3.6 m/s  
Mean G = 33 mmHg  
AVA = 0.5 cm\(^2\)

SV=56 ml  
Peak vel = 4.2 m/s  
Mean G = 43 mmHg  
AVA = 0.6 cm\(^2\)
Presence of “contractile reserve” influences perioperative mortality

~1/3 of pts have no flow reserve

Best treatment for pseudosevere AS patients?

AVA > 1.2 cm² and mean G < 40 mmHg after DSE

Fougères E et al. Eur Heart J. 2012;33:2426-33
Patients without “contractile reserve”

Visual estimation of the valve – TOE
Projected AVA (TOPAS study)

Flow must increase at least 15%

\[
EOA_{\text{Projected}} = EOA_{\text{Rest}} + \frac{\Delta EOA}{\Delta Q} \times (250 - Q_{\text{Rest}})
\]

\[
VC = \frac{\Delta EOA}{\Delta Q}
\]

\[
VC = 0.015 / 70 = 0.0021
\]

\[
AVA_{\text{proj}} = \frac{AVA_{\text{peak}} - AVA_{\text{rest}}}{Q_{\text{peak}} - Q_{\text{rest}}} \times (250 - Q_{\text{rest}}) + AVA_{\text{rest}}
\]

Percentage of Correct Classification

Projected AVA likely best distinguishes true from pseudo-severe AS

Annabi MS et al. J Am Coll Cardiol 2018;71:475–85
AV calcium score

<table>
<thead>
<tr>
<th>Sex</th>
<th>AUC</th>
<th>Threshold</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
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<tbody>
<tr>
<td>AVC</td>
<td>0.91</td>
<td>1,681*</td>
<td>69</td>
<td>95</td>
<td>95</td>
<td>65</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>1,274*</td>
<td>86</td>
<td>89</td>
<td>93</td>
<td>79</td>
</tr>
<tr>
<td></td>
<td></td>
<td>791*</td>
<td>95</td>
<td>63</td>
<td>81</td>
<td>88</td>
</tr>
<tr>
<td>Men</td>
<td>0.90</td>
<td>3,381*</td>
<td>59</td>
<td>95</td>
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<tr>
<td></td>
<td></td>
<td>2,065*</td>
<td>89</td>
<td>80</td>
<td>88</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1,661*</td>
<td>95</td>
<td>70</td>
<td>84</td>
<td>90</td>
</tr>
</tbody>
</table>

MDCT measures AV calcification but not the valvular fibrosis – be careful in younger patients with bicuspid AS

Treatment of classical LF LG AS

AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity ≥4.0 m/s (or mean pressure gradient ≥40 mm Hg) with a valve area ≤1.0 cm² at any dobutamine dose.


<table>
<thead>
<tr>
<th>A) Symptomatic aortic stenosis</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention is indicated in symptomatic patients with severe low-flow, low-gradient (&lt;40 mmHg) aortic stenosis with reduced ejection fraction and evidence of flow (contractile) reserve excluding pseudosevere aortic stenosis.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<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>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>


TOPAS TAVI Registry (TCT 2016)
- Death: 4.3% at 30 days
- Survival: 80.4% at 1 year
- Absence of flow reserve had no impact on mortality
- Transfemoral approach in most pts
Paradoxical LF (NEF) – LG AS

- 5-15% of AS population
- 25-35% of AS population with preserved EF
- Flow rate<200 ml/s
How to approach such a patient?

- Velocity ratio can also be useful (if >0.25 ?LVOT diam or velocity underestimation)
- High valvuloarterial impedance
- Small body size: indexing to BSA may be helpful – avoid indexing in obese pts (?height)
- Severe AS is unlikely even with low flow if peak vel<3 m/s or mean G<20 mmHg

Next steps...

Step #2: Assess Symptomatic Status

Exercise testing

Symptoms Present

Step #3: Check for Presence of Hypertension

Step #4: Confirm Stenosis Severity

MDCT AoV Calcium Scoring

AoV Calcium Score
- >1200 AU (Women)
- >2000 AU (Men)

Low Dose DSE if feasible

True-Severe AS

Pseudo-Severe AS

Treating HTN is important

Role of low dose DSE

![Graph showing the role of low dose DSE with data points and annotations]

- CC = 94%
- Pseudo-severe AS on the basis of AVA proj > 1 cm² (33%)
- True-severe AS on the basis of AVA proj ≤ 1 cm² (87%)

Legend:
- ▲ True-Severe AS at AVR
- ▼ Pseudo-Severe AS at AVR
- Patients who underwent AVR within 3 months after Stress echo
- ○ AS severity not verified by AVR

Criteria that increase the likelihood of severe AS in paradoxical LF LG AS

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical criteria</td>
<td>• Typical symptoms without other explanation</td>
</tr>
<tr>
<td></td>
<td>• Elderly patient (&gt;70 years)</td>
</tr>
<tr>
<td>Qualitative imaging data</td>
<td>• LV hypertrophy (additional history of hypertension to be considered)</td>
</tr>
<tr>
<td></td>
<td>• Reduced LV longitudinal function without other explanation</td>
</tr>
<tr>
<td>Quantitative imaging data</td>
<td>• Mean gradient 30–40 mmHg&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>• AVA ≤0.8 cm&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>• Low flow (SVi &lt;35 mL/m&lt;sup&gt;2&lt;/sup&gt;) confirmed by techniques other than standard Doppler technique</td>
</tr>
<tr>
<td></td>
<td>(LVOT measurement by 3D TOE or MSCT; CMR, invasive data)</td>
</tr>
<tr>
<td></td>
<td>• Calcium score by MSCT&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Severe aortic stenosis very likely: men ≥3000; women ≥1600</td>
</tr>
<tr>
<td></td>
<td>Severe aortic stenosis likely: men ≥2000; women ≥1200</td>
</tr>
<tr>
<td></td>
<td>Severe aortic stenosis unlikely: men &lt;1600; women &lt;800</td>
</tr>
</tbody>
</table>

Does AVR improve survival in paradoxical LF LG AS patients?

Treatment of “paradoxical” LF LG AS

AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF $\geq 50\%$ if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms.


Intervention should be considered in symptomatic patients with low-flow, low-gradient (<40 mmHg) aortic stenosis with normal ejection fraction after careful confirmation of severe aortic stenosis (see Figure 2 and Table 6).

PPM should be avoided

Normal flow NF (NEF) – LG AS

Up to 25% of AS population
Inconsistent grading?

Reducing the AVA threshold is likely not helpful

Prognosis of NF LG AS pts

Prognosis of NF LG AS pts

Staged approach of pts with NF LG AS

• Measurement errors

• Symptoms? If no just follow up

• Hypertension? If yes treat HTN and then reassess

• Assess stenosis severity with calcium score

• (?Severely) symptomatic pts with evidence of severe AS (high calcium score or other imaging modality) and no other explanation of their symptoms may be referred for AVR

Take home messages

• LG AS is challenging

• Three types based on EF and flow (SVi):
  1. Classical: reduced EF, low flow, low gradient
  2. Paradoxical: normal EF, normal flow, low gradient
  3. Normal EF, normal flow, low gradient

• Aim is to separate true AS pts (AVR) from pseudosevere AS pts (conservative treatment)
Take home messages

• **Classical type:** use DSE to assess for flow reserve and pseudosevere AS (AVA > 1.2 cm² and mean G < 40 mmHg)

• Difficult cases: projected AVA ± CT AV Ca

• If true severe AS and presence of flow reserve – AVR

• Absence of flow reserve does not preclude symptomatic and LVEF improvement with AVR - ?TAVR better option
Take home messages

• **Paradoxical LF LG AS**: Integrated approach (body size and measurement errors – cause for low flow – symptoms – treat HTN)

• Confirm AS severity with CT AV Ca (2000 men and 1200 women) and/or other imaging techniques

• If true LF LG AS diagnosis is established – AVR (?TAVR) is likely beneficial

• **NF LG AS pts** have better prognosis than LF LG AS and likely represent a heterogeneous group

• Treat with AVR if only (?severely) symptomatic, no other explanation of their symptoms exist and confirmation of severe AS with other modality (CT AV Ca) is made – otherwise watchful waiting
Algorithm for classical LF LG AS

Classical Low-Flow, Low-Gradient AS
AVA ≤ 1.0 cm², MG < 40 mmHg, LVEF < 50%

Low dose Dobutamine Stress Echocardiography
(Stages: 5; 10; 15; 20 μg/kg/min)

Peak vel > 4 m/s or MG > 30-40 mmHg and AVA < 1.0 cm²

MG < 40 mmHg and AVA < 1.0 cm²

Projected AVA < 1.0 cm²
AND/OR
MDCT AoV Calcium Score > 1200 AU (Women) > 2000 AU (Men)

True-Severe AS

NO

Pseudo-Severe AS

ASSESSMENT OF LIFE EXPECTANCY AND SURGICAL RISK BY HEART TEAM

- TRUE-SEVERE AS
  - LIFE EXPECTANCY >1Yr
    - INTERMEDIATE SURGICAL RISK
      - SAVR OR TAVR
    - HIGH OR PROHIBITIVE SURGICAL RISK
      - TAVR

- PSEUDO-SEVERE AS
  - HEART FAILURE THERAPY WITH CLOSE CLINICAL AND ECHO FOLLOW-UP
  - LIFE EXPECTANCY <1Yr
    - CONSERVATIVE MANAGEMENT WITH BAV FOR RELIEF OF SYMPTOMS

SAVR vs TAVR

- Patients should have >1 year life expectancy

<table>
<thead>
<tr>
<th></th>
<th>Low Risk (Must Meet ALL Criteria in This Column)</th>
<th>Intermediate Risk (Any 1 Criterion in This Column)</th>
<th>High Risk (Any 1 Criterion in This Column)</th>
<th>Prohibitive Risk (Any 1 Criterion in This Column)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS PROM*</td>
<td>&lt;4% AND</td>
<td>4%-8% OR</td>
<td>&gt;8% OR</td>
<td>Predicted risk with surgery of death or major morbidity (all-cause) &gt;50% at 1 y OR</td>
</tr>
<tr>
<td>Frailty†</td>
<td>None AND</td>
<td>1 Index (mild) OR</td>
<td>≥2 Indices (moderate to severe) OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 Organ system OR</td>
<td></td>
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<tr>
<td></td>
<td>No more than 2 organ systems OR</td>
<td></td>
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<tr>
<td></td>
<td>≥3 Organ systems OR</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Procedure-specific impediment‡</td>
<td>None Possible procedure-specific impediment</td>
<td>Possible procedure-specific impediment</td>
<td>Severe procedure-specific impediment</td>
<td></td>
</tr>
</tbody>
</table>

- Also remember – increased risk of perioperative mortality with AVR:
  - mean G < 20 mmHg
  - absence of “flow” reserve
  - GLS < 9%
LV Dyssynchrony in classical LF LG AS

Fusion AVA

$\text{AVA}_{\text{CT}}$ is no better than $\text{AVA}_{\text{echo}}$

STEP #5: ASSESSMENT OF SURGICAL RISK BY HEART TEAM

- Low
  - SAVR

- Intermediate
  - SAVR or TAVR

- High or Prohibitive
  - TAVR

  - Pseudo-Severe AS
    - Medical Therapy and Close Clinical/Echo Follow-up

  - True-Severe AS

*BAV*
Treatment futility?

- Increased risk of poor outcome and lack of functional improvement following AVR:
  - very low baseline mean gradient (<20 mm Hg)
  - moderate/severe mitral regurgitation
  - severe right ventricular dysfunction
  - severe tricuspid regurgitation
  - extensive myocardial fibrosis by CMR