Low Flow Low Gradient Aortic Stenosis with preserved LVEF

An elusive concept

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Low Flow Low Gradient Aortic Stenosis with preserved LVEF

Does it exist?

Does AVR help?

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1704 severe AS with normal LVEF

1704 severe AS with normal LVEF

1704 severe AS with normal LVEF

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

Hachicha Z, Pibarot P. Circulation 2007; 115: 2856-64

Background—Recent studies and current clinical observations suggest that some patients with severe aortic stenosis on the basis of aortic valve area may paradoxically have a relatively low gradient despite the presence of a preserved left ventricular (LV) ejection fraction (≥50%). Of these patients, 331 (65%) had normal LV flow output defined as stroke volume index ≥35 mL·m⁻², and 181 (35%) had paradoxically low-flow output defined as stroke volume index ≤35 mL·m⁻². When compared with normal flow patients, low-flow patients had a higher prevalence of female gender (P<0.05), a lower transvalvular gradient (32±17 versus 41±15 mm Hg; P<0.0001), a lower LV diastolic volume index (52±12 versus 59±13 mL·m⁻³; P<0.001), lower LV ejection fraction (62±8% versus 68±7%; P<0.0001), a 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·m⁻²; P<0.001), and a lower overall 3-year survival (76% versus 85%; P=0.006). Only age (hazard ratio, 1.04; 95% CI, 1.01 to 1.06; P=0.025), valvulo-arterial impedance >3.3 mm Hg·mL⁻¹·m⁻² (hazard ratio, 2.6; 95% CI, 1.2 to 5.7; P=0.017), and medical treatment (hazard ratio, 3.3; 95% CI, 1.8 to 6.7; P=0.0003) were independently associated with increased mortality.

Conclusion—Patients with severe aortic stenosis may have low transvalvular flow and low gradients despite normal LV ejection fraction. A comprehensive evaluation shows that this pattern is in fact consistent with a more advanced stage of the disease and has a poorer prognosis. Such findings are clinically relevant because this condition may often be misdiagnosed, which leads to a neglect and/or an underestimation of symptoms and an inappropriate delay of aortic valve replacement surgery. (Circulation. 2007;115:2856-2864.)
Low Flow Low Gradient AS
Does it exist?
Low Flow Low Gradient AS
Does it exist?

Yes, but unfrequent
Patient 1: recent pulmonary edema

79 year-old woman, BSA 1.45 m², no CAD

LVEF = 68%, LVH

Calcified aortic valve

LVOT VTI 11 cm
LVOT 19.5 mm
SVI 23 ml/m²

Low cardiac output

Vmax = 3.5 m/s
Mean Gradient 30 mmHg
AVA 0.42 cm², AVAi 0.29 cm²/m²

Severe AS, Low Gradient
Patient 1: recent pulmonary edema

Normal LVEF
Patient 1: recent pulmonary edema

Normal LVEF

Low gradient

Vmax = 3.5 m/s
Mean Gradient 30 mmHg
AVA 0.42 cm²,  AVAi 0.29 cm²/m²
Patient 1: recent pulmonary edema

Normal LVEF

Low gradient

Low flow

LVOT VTI 11 cm
LVOT 19.5 mm
SVI 23 ml/m²

Vmax = 3.5 m/s
Mean Gradient 30 mmHg
AVA 0.42 cm², AVAi 0.29 cm²/m²
Patient 1: recent pulmonary edema

Normal LVEF  Low gradient  Low flow

Severe aortic stenosis

Paradoxical low flow
Patient 1: recent pulmonary edema

Severe aortic stenosis

Paradoxical low flow

LV longitudinal dysfunction

Adda J, Habib G – Circulation CV Imaging 2012
Patient 2: dyspnea on exertion

61 year-old woman, BSA 1.64 m², no CAD

LVEF = 63%, moderate LVH

Calcified aortic valve

Normal cardiac output

Severe AS, Low Gradient

LVOT VTI 22 cm
LVOT 21 mm
SVI 45 ml/m²

Vmax = 3.5 m/s
MG 30 mmHg
AVA 0.9 cm² - AVAi 0.55 cm²/m²
Patient 2: dyspnea on exertion

Normal LVEF
Patient 2: dyspnea on exertion

Normal LVEF

Low gradient

Vmax = 3.5 m/s
MG 30 mmHg
AVA 0.9 cm² - AVAi 0.55 cm²/m²
Patient 2: dyspnea on exertion

Normal LVEF

Low gradient

Normal Flow

Vmax = 3.5 m/s
MG 30 mmHg
AVA 0.9 cm² - AVAi 0.55 cm²/m²

LVOT VTI 22 cm
LVOT 21 mm
SVI 45 ml/m²
Patient 2: dyspnea on exertion

Normal LVEF

Low gradient

Normal Flow

Less severe aortic stenosis

Less severe LV longitudinal dysfunction

Adda J, Habib G – Circulation CV Imaging 2012
2 questions for Philippe

1. *Are you sure that both have severe AS?*
2. *Will you send both patients to surgeon?*
LF LG AS: 3 important questions

1. Was LVOT correctly measured?

2. Does the patient have both low gradient and low flow?

3. Are the proposed cut-off values consistent?
Critical issue: LVOT measurement

- Underestimation of LVOT diameter leads to underestimation of AVA
- Underestimation of stroke volume leads to false diagnosis of LFLG AS
Critical issue: LVOT measurement

- Underestimation of LVOT diameter leads to underestimation of AVA
- Underestimation of stroke volume leads to false diagnosis of LFLG AS
Critical issue: LVOT measurement

- underestimation of LVOT diameter leads to underestimation of AVA

- underestimation of stroke volume leads to false diagnosis of LFLG AS
Critical issue: LVOT measurement

- underestimation of LVOT diameter leads to underestimation of AVA

- underestimation of stroke volume leads to false diagnosis of LFLG AS

- re-check LVOT measurement
- perform TEE (and look at the valve !!)
- use alternative techniques to assess AS severity (CT scan, catheterization)
LF LG AS: 3 important questions

1. Was LVOT correctly measured?

2. Does the patient have both low gradient *and* low flow?

3. Are the proposed cut-off values consistent?
Low gradient aortic stenosis

340 patients severe AS - $\text{AVA}_i \leq 0.6 \text{ cm}^2/\text{m}^2$, LVEF $> 50%$

5 centers: Marseille, Liège, Rennes, Bordeaux, Montpellier
Low gradient aortic stenosis

Adda J, Habib G – Circulation CV Imaging 2012

340 patients severe AS - $\text{AVA}_i \leq 0.6 \text{ cm}^2/\text{m}^2$, LVEF > 50%

258 patients (76 %) High gradient

82 patients (24 %) Low gradient
Low gradient aortic stenosis

340 patients severe AS - AVA_i ≤ 0.6 cm^2/m^2, LVEF > 50%

258 patients (76 %) High gradient

9 % Low Flow Low Gradient

15 % Normal Flow Low Gradient
Low gradient aortic stenosis

Adda J, Habib G – Circulation CV Imaging 2012

340 patients severe AS - $\text{AVA}_i \leq 0.6 \text{ cm}^2/\text{m}^2$, LVEF > 50%

- 9% of severe AS
- Very severe AS
- High global afterload
- Reduced longitudinal LV systolic function

9% Low Flow Low Gradient

15% Normal Flow Low Gradient
Low gradient aortic stenosis

Adda J, Habib G – Circulation CV Imaging 2012

340 patients severe AS - $AV_A \leq 0.6 \text{ cm}^2/\text{m}^2$, LVEF > 50%

- 9% of severe AS
- Very severe AS
- High global afterload
- Reduced longitudinal LV systolic function

- 15% of severe AS
- Less severe AS
- Normal global afterload
- Less severe LV longitudinal dysfunction

9% Low Flow Low Gradient

15% Normal Flow Low Gradient
Clinical Outcome in Asymptomatic Severe Aortic Stenosis

Insights From the New Proposed Aortic Stenosis Grading Classification

Patrizio Lancellotti, MD, PhD,* Julien Magne, PhD,* Erwan Donal, MD, PhD,† Laurent Davin, MD,* Kim O’Connor, MD,‡ Monica Rosca, MD,* Catherine Szymanski, MD,* Bernard Cosyns, MD, PhD,§ Luc A. Piérard, MD, PhD*

Liège, and Brussels, Belgium; Rennes, France; and Quebec, Canada
150 consecutive patients with asymptomatic severe AS and normal exercise test.
New classification of AS

Lancellotti P, JACC 2012

- 150 consecutive patients with asymptomatic severe AS and normal exercise test.
LF LG AS: 3 important questions

1. Was LVOT correctly measured?

2. Does the patient have both low gradient and low flow?

3. Are the proposed cut-off values consistent?
1. « When one combines the current prospective clinical data with earlier hemodynamic echo and invasive data that relate maximal velocity and gradients across the valve for severe AS, a good argument can be made for bringing the cut-off valve area for severe AS closer to 0.8 cm² (index 0.45 cm²/m²).

2. A refinement of the guidelines in this respect would help harmonize the definition of severe AS....

3. ...and would appropriately reclassify some patients with “severe” AS into moderate severity”
Patient 1: recent pulmonary edema

Severe aortic stenosis
Paradoxical low flow
Patient 2: dyspnea on exertion

Normal LVEF

Low gradient

Normal Flow

Moderate aortic stenosis

Vmax = 3.5 m/s
MG 30 mmHg
AVA 0.9 cm² - AVAi 0.55 cm²/m²
LVOT VTI 22 cm
LVOT 21 mm
SVI 45 ml/m²
LFLG aortic stenosis

1. **Does it really exist?**

2. **Does AVR help?**
Are patients with severe AS and low gradient improved by surgery?

I don’t know !!!
### Studies on the role of surgery in LFLG AS

<table>
<thead>
<tr>
<th>Author</th>
<th>LF / LG AS (n)</th>
<th>AVR (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Barasch E, J Heart Valve Dis 2008</td>
<td>47 LG AS</td>
<td>(15 AVR)</td>
</tr>
<tr>
<td>4. Dumesnil JG, Eur Heart J 2009</td>
<td>123 LFLG AS</td>
<td>(44 AVR)</td>
</tr>
<tr>
<td>7. Clavel AM, JACC 2012</td>
<td>187 LFLG AS</td>
<td>(83 AVR)</td>
</tr>
</tbody>
</table>
Limitations of previous studies

1. Retrospective, non randomized
2. Few studies, few patients, few events
3. Symptomatic status unknown in the majority
4. Various definitions of AS severity and of LF and/or LG AS
5. Reasons for surgery / no surgery unknown in the majority
6. Influence of associated CABG
7. Comorbidities not taken into account
Effect of surgery on LF AS

Hachicha Z - Circulation 2007 ; 115 : 2856-64

493 severe AS
and LVEF > 50%

322 patients

171 patients

37 (11%) PLF group

32 (19%) NF group

P = 0.006 (0.045*; NS**)

Follow-up (years)

Number of patients at risk

322
171
232
112
139
58
92
39
52
23
52
7
36
5
4
3
2
1
0

Survival (%)
Effect of surgery on LF AS

Hachicha Z - Circulation 2007 ; 115 : 2856-64

493 severe AS and LVEF > 50%

171 patients with Low-Flow AS

80 pts LF

AVR 6 (7.5%)

91 pts LF

no AVR 26 (29%)

Survival (%)

Follow-up (years)

P = 0.006 (0.045*; NS**)
Surgery does not improve outcome

1. prospective study (SEAS study)
2. 1525 asymptomatic AS
3. 435 LG severe AS  (MG < 40 mmHg, AVA < 1 cm$^2$)
4. 184 moderate AS  (MG 25-40 mmHg, AVA < 1.5-1 cm$^2$)
5. 45 +/-14 months follow-up
6. Significant CAD excluded

Jander N – Circulation 2011; 123: 887-95
LG AS is no more than a moderate AS

- 435 LG - SAS
- 35 HG – SAS
- 184 moderate AS

- No significant difference in major cardiovascular events or death
- No beneficial effect of surgery
Surgery is beneficial?

- **187 PLG - SAS**
- **187 HG – SAS**
- **187 moderate AS**

Clavel MA - J Am Coll Cardiol 2012

Overall Survival (%)

<table>
<thead>
<tr>
<th>Follow-up Time, (years)</th>
<th>PLG-SAS group*</th>
<th>HG-SAS group</th>
<th>MAS group</th>
</tr>
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<tbody>
<tr>
<td>8</td>
<td>0</td>
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<td>70</td>
</tr>
<tr>
<td>0</td>
<td>80</td>
<td>80</td>
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</tr>
</tbody>
</table>

*N patients at risk:
- 187
- 178
- 163
- 141
- 101
- 75
- 56
- 35
- 22
- 187
- 163
- 143
- 119
- 80
- 53
- 31
- 18
- 11
- 187
- 175
- 149
- 115
- 86
- 63
- 46
- 36
- 18

p<0.0001
(p=0.04)
Surgery is beneficial?

Clavel MA - J Am Coll Cardiol 2012

Overall Survival, (%)

Follow-up Time, (years)

HG-SAS group AVR
MAS group AVR
PLG-SAS group AVR
MAS group Cons.
PLG-SAS group Cons.
HG-SAS group Cons.

p<0.0001
(p<0.0001)
Surgery is beneficial?

Clavel MA - J Am Coll Cardiol 2012

At least moderate AS and LVEF ≥50%
1589 patients

AVA≤1cm²

AVA≤0.6cm²/m²

805 patients

AVA≤0.6cm²/m²

AVA>1cm²

743 patients

AVA>0.6cm²/m²

41 patients

MG≥40mmHg

396 patients

MG<40mmHg

409 patients

Svi>35ml/m²

186 patients

Svi<35ml/m²

223 patients

Patients excluded

Reason for therapeutic management during follow-up

AVR, nb (%)

187 patients

Matched according to AMA

150 (80%)

187 patients

Matched according to MG

187 patients

83 (44%)

74 (40%)
Survival is worse in LFLG

Adda J, Habib G – Euroecho 2011

Survival in Low Flow Low Gradient vs other groups

LFLG AS  P=0.02
Survival is worse in LFLG

Adda J, Habib G – Euroecho 2011

Survival in Low Flow Low Gradient vs other groups

LFLG AS  P=0.02

Group 4 : Low Flow - Low Gradient

AVR  P=0.57

no AVR
Take-home messages

1. LF LG aortic stenosis is a real entity observed in 10% cases of severe AS with normal LVEF
2. These patients present with high global afterload and reduced longitudinal systolic function, as assessed by 2D strain
3. They are associated with worse prognosis
4. **They must be differentiated from patients with NFLG aortic stenosis**
5. Benefit of surgery is not proven in LG aortic stenosis but it is probably beneficial in selected symptomatic patients with both low flow and low gradient AS
Paradoxical Low-Flow, Low-Gradient Aortic Stenosis
Adding New Pieces to the Puzzle

“Additional outcome studies are needed to determine the most appropriate modality and timing of treatment in patients with low-flow, low-gradient AS……..”
Additional outcome studies are needed to determine the most appropriate modality and timing of treatment in patients with low-flow, low-gradient AS.
Is surgery beneficial?

Ozkan A – Circulation 2013

- 260 PLG – SAS
- AVR in 123 (47%) patients
- 28 +/- 24 months FU
- 105 (40%) deaths during FU
- 73% deaths in medical group!

Medical therapy = 2-fold increase in mortality than AVR
Is surgery beneficial?

- Non randomized study
- Patients without AVR
  - Higher prevalence of diabetes
  - Lower SVI
  - Higher sPAP
  - Higher creatinin level

Medical therapy = 2-fold increase in mortality than AVR
Since the healthier group of patients underwent surgery, it is not surprising that AVR was associated with lower mortality.

So it must be cautioned that the finding that AVR substantially reduces mortality may be an overestimate of the true benefit.
Is surgery beneficial?


- 1704 severe AS with normal LVEF
- 352 (21%) NFLG AS
- 53 (3%) LFLG AS

Good outcome under medical therapy in NFLG AS

Reduced survival in LFLG AS
Is surgery beneficial?


- 1704 severe AS with normal LVEF
- 352 (21%) NFLG AS
- 53 (3%) LFLG AS

Better outcome after surgery in LFLG AS

No survival benefit after surgery in NFLG AS
Take-home messages

1. Verify that AS is really severe
2. Verify that the symptoms of the patients are related to AS
3. Verify that the patient has both LF and LG AS
4. Consider comorbidity and operative risk
5. Propose surgery in selected symptomatic patients with both low flow and low gradient AS and acceptable operative risk
Conclusion

Don’t send to surgery patients with moderate AS!!