Low-Flow Low Gradient Aortic Stenosis: New Challenges, New Solutions

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I, Philippe Pibarot, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
Two Different Patterns of Low-Flow, Low-Gradient AS

NORMAL-LVEF
NORMAL-FLOW
HIGH-GRADIENT

50-70%"/>50-70%

NORMAL-LVEF
"PARADOXICAL"
LOW-FLOW
LOW-GRADIENT

10-25%"/>10-25%

LOW-LVEF
"CLASSICAL"
LOW-FLOW
LOW-GRADIENT

5-10%"/>5-10%

Pibarot & Dumesnil
JACC, in press
“Classical” Low-Flow, Low-Gradient AS with Reduced LVEF
Low-Flow, Low-Gradient “Severe” AS

True-Severe AS

Low Flow → Normal Flow

Pseudo-Severe AS

Low Flow → Normal Flow

AVA

ΔP

Gradient = \frac{Q^2}{K \times AVA^2}
LVEF ≤ 40%

ΔP < 40

AVA ≤ 1.0

Dobutamine-Stress Echo

↑ SV ≥ 20%

Contractile Reserve

ΔP ≥ 40
AVA < 1.2

True-Severe AS
SAVR ± CABG

ΔP < 40
AVA ≥ 1.2

Pseudo-Severe AS
MEDICAL Rx TRIAL

↑ SV < 20%

No Contractile Reserve

AS Severity: Indeterminate

MSCT: Ca Score ≥ 1650?

No

Yes

True-Severe AS
SAVR (High Op. Risk)
TAVR?
Case Study #1

Resting Echo

Dobutamine Stress Echo
Case Study #1

Resting Echo

SV = 53 ml
LVEF = 40%
Peak ∆P = 49 mmHg
Mean ∆P = 29 mmHg
AVA = 0.77 cm²

Dobutamine Stress Echo

SV = 73 ml
LVEF = 50%
Peak ∆P = 92 mmHg
Mean ∆P = 52 mmHg
AVA = 0.75 cm²
Case Study #1:

- **Contractile reserve:** Yes
- **Stenosis severity:** True-severe
**Case Study #2**

**Resting Echo**

- SV = 34 ml
- LVEF = 15%
- Peak ΔP = 18 mmHg
- Mean ΔP = 12 mmHg
- AVA = 0.85 cm²

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**Dobutamine Stress Echo**

- SV = 46 ml
- LVEF = 25%
- Peak ΔP = 21 mmHg
- Mean ΔP = 13 mmHg
- AVA = 1.2 cm²
Case Study #2:

- **Contractile reserve:** Yes
- **Stenosis severity:** Pseudo-severe
Outcome of Pseudo-Severe AS Under Conservative Treatment

Pseudo Severe AS:
\[ \Delta P < 40 \& \text{AVA} \geq 1.2 \text{ at DSE} \]

Fougères et al.
Eur Heart J. 2012
Case Study #3

- 76 y.o. woman
- Risk factors:
  - Obese, Hyperchol.
  - Hypertension, COPD
  - 3-vessel CAD
- CABG × 3: Aug 95
- MI: Jan 96
- CHF: LVEDD: 64 mm, LVEF 25%, BNP: 832 pg/ml
- Aortic stenosis, mild mitral regurgitation
- Current medication: ASA, ARBs, Statin, Digoxin, Brochodil.
Resting Echo

LVEF = 25%  
SV = 51 ml  
AVA = 0.8 cm²  
ΔP = 46 / 27 mmHg

Dobutamine Stress Echo

LVEF = 30%  
SV = 57 ml  
AVA = 0.8 cm²  
ΔP = 52 / 30 mmHg
Case Study #3:

- **Contractile reserve:** No
- **Stenosis severity:** Indeterminate
Measurement of aortic valve calcification using multislice computed tomography: correlation with haemodynamic severity of aortic stenosis and clinical implication for patients with low ejection fraction

Caroline Cueff, Jean-Michel Serfaty, Claire Cimadevilla, Jean-Pierre Laissy, Dominique Himbert, Florence Tubach, Xavier Duval, Bernard Lung, Maurice Enriquez-Sarano, Alec Vahanian, David Messika-Zeitoun

Performance of MSCT Calcium score > 1651 AU to correctly differentiate severe from non-severe AS

Case study #3
Score: 2010

Cueff et al. Heart 97:721-6, 2011
LVEF ≤ 40%
ΔP < 40
AVA ≤ 1.0

Dobutamine-Stress Echo

↑ SV ≥ 20 %

Contractile Reserve

ΔP ≥ 40 & AVA < 1.2

True-Severe AS
SAVR ± CABG

ΔP < 40 & AVA ≥ 1.2

Pseudo-Severe AS
MEDICAL Rx TRIAL

↑ SV < 20 %

No Contractile Reserve

AS Severity: Indeterminate

MSCT: Ca Score ≥ 1650?

No

True-Severe AS
SAVR (High Op. Risk)

Yes

TAVR?
**Risk Stratification using Contractile Reserve**

**Group I** = contractile reserve $\Delta SV \geq 20\%$ under DSE

**Group II** = no contractile reserve

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Monin et al, Circulation 2003;108:319-324

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- **Group I, Valve Replacement**: $p = 0.001$ vs medical
- **Group II, Valve Replacement**: $p = 0.07$ vs medical
- **Group I, Medical Treatment**
- **Group II, Medical Treatment**

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126 Patients
Outcome After Aortic Valve Replacement for Low-Flow/Low-Gradient Aortic Stenosis Without Contractile Reserve on Dobutamine Stress Echocardiography

Christophe Tribouilloy, MD, PhD,* Franck Lévy, MD,† Dan Rusinaru, MD,† Pascal Guéret, MD,‡ Hélène Petit-Eisenmann, MD,§ Serge Baleynda, MD,|| Yannick Jobic, MD,¶ Catherine Adams, MD,# Bernard Lelong, MD,** Agnès Pasquet, MD,†† Christophe Chauvel, MD,‡‡ Damien Metz, MD,§§ Jean-Paul Quéré, MD,* Jean-Luc Monin, MD, PhD‡

A
Total Population

B
Matched Patients

Tribouilloy et al. JACC, 53;1865-1873, 2009
PATIENT'S CARDIAC OUTPUT REQUIREMENTS

PROSTHESIS-PATIENT MISMATCH!

BSA

AVR

EOA

PROSTHETIC VALVE EOA
Combined Impact of PPM and LV Dysfunction on Operative Mortality

1200 patients undergoing AVR

Operative Mortality (%)

Prosthesis-Patient Mismatch

Non significant

Moderate

Severe

3% P=0.05

5% P=0.08

16% P<0.001

23% P<0.001

67% P<0.001

LVEF ≤ 40% (n = 123)

LVEF ≥ 40% (n = 1027)

Prosthesis-Patient Mismatch: TAVR vs. SAVR

Clavel et al., JACC, 53:1883–91, 2009
PARTNER-A 2-Year Outcomes: Prosthetic Valve Hemodynamic Performance

Kodali et al.; NEJM 2012
Recovery of LVEF in Patients with Low-LVEF, Low-Flow, Low-Gradient AS: TAVR versus SAVR

Low-Flow, Low-Gradient AS

LV Ejection Fraction, (%)

Baseline Discharge 1 year

Visits

*: different from SAVR
†: different from baseline
‡: different from discharge

Clavel Circulation, 122:1928-36., 2010
Key Messages: Classical Low-Flow AS

- Dobutamine stress echocardiography is essential for risk stratification and clinical decision making
- Assessment of stenosis severity remains a major challenge in patients with no contractile reserve: usefulness of MSCT
- Particularly important to avoid patient-prosthesis mismatch when operating on these patients
- Transcatheter aortic valve replacement: a new promising therapeutic avenue?
“Paradoxical” Low-Flow, Low-Gradient AS with Preserved LVEF
Case Study #4

- 78 y.o. female with history of calcific AS
- NYHA class III
- Mild hypertension
- No evidence of obstructive CAD
- LVEF: 60%
- AS severity on echo:
  - AVA: 0.7 cm²
  - BSA: 1.7 m², indexed AVA: 0.4 cm²/m²
  - Peak/mean gradient: 51/29 mmHg
Case Study: Discrepancy between AVA and Gradient

LVEF: 60%
Small LV cavity: LVEDD: 39 mm  LVEDV: 79 ml
LVOT-D: 2.0 cm
LVOT-A: 3.1 cm²
LVOT-VTI: 15 cm
LVOT-SV: 46 mL
(SVi=27 mL/m²)

Peak ΔP: 51 mmHg
Mean ΔP: 29 mmHg
Ao-VTI: 65 cm
AVA: 0.7 cm²

2D Volumetric method to corroborate SV measure:
LVEDV (79 mL) × LVEF (60%) = 48 mL
Dobutamine Stress Echocardiography

15 µg/kg/min

Peak ΔP: 94 mmHg
Mean ΔP: 57 mmHg
AVA: 0.77 cm²

Multislice CT

Valve Calcium score: 1900 AU

Coronary Artery Calcification

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

Zeineb Hachicha, MD; Jean G. Dumesnil, MD; Peter Bogaty, MD; Philippe Pibarot, DVM, PhD

↑Age
Women
Hypertension
MetS - Diabetes

Hachicha Z et al., Circulation, 2007
Dumesnil et al. Eur Heart J, 2009
Pibarot & Dumesnil JACC, in press, 2012
Features of Paradoxical Low-Flow, Low-Gradient AS

The Aortic Valve:
- AVA < 1.0 cm²  AVAi < 0.6 cm²/m²  DVI < 0.25
- Severely thickened/calcified valve
- Mean gradient < 40 mmHg
- Valvulo-arterial impedance > 4.5 mmHg.ml⁻¹.m⁻²

The Left Ventricle
- EDD < 47 mm  EDV < 55 mL/m²
- RWT ratio > 0.50
- Myocardial fibrosis
- Impaired LV filling
- LVEF > 50%
- GLS < 15%
- SVi < 35 mL/m²

Pibarot & Dumesnil, JACC 58;413-415, 2011
Case Study #5

- 75 y.o. female
- Calcific AS
- NYHA class III
- No CAD at angio
- LVEF: 73%
- LVEDV: 38 mL/m²
- AS severity at catheter:
  - AVA: 0.85 cm²
  - Indexed AVA: 0.5 cm²/m²
  - Mean gradient: 32 mmHg

Courtesy of Dr G Dreyfus, Monaco Hospital
Prevalence of Paradoxical Low-Flow, Low-Gradient AS

- Hachicha 2006 Echo (512 pts)
- Barasch 2006 Echo (215 pts)
- Cramariuc 2009 Echo (1591 pts)
- Minners 2010 Echo (333 pts)
- Minners 2010 Cath (333 pts)
- Hermann 2011 Echo & Cath (86 pts)
- Adda 2011 Echo (150 pts)
- Lancellotti 2012 Echo (150 pts)
- Mohty 2012 Cath (780 pts)

Paradoxical Low-Flow
AVA<1.0 cm²
LVEF>50%; SVi<35 mL/m²

Paradoxical Low-Flow, Low-Gradient
AVA<1.0 cm²: MG<40 mmHg
LVEF>50%; SVi<35 mL/m²
Do Patients with Paradoxical Low-Flow, Low-Gradient AS have worse outcomes?
Paradoxical Low-Flow, Low-Gradient Severe Aortic Stenosis Despite Preserved Ejection Fraction Is Associated With Higher Afterload and Reduced Survival

Zeineb Hachicha, MD; Jean G. Dumesnil, MD; Peter Bogaty, MD; Philippe Pibarot, DVM, PhD

Hachicha Z et al., Circulation. 115:2856-2864, 2007
150 Pts with asymptomatic severe (AVA<1.0 cm$^2$) AS LVEF>50%

Outcome of AS Patients with Paradoxical Low-Flow vs. Normal Flow
A Substudy of the SEAS trial

Jander et al.
Circulation.
2011;123:887-895.
Outcome of Patients with Paradoxical Low-Flow, Low-Gradient AS

Case Match Study: $3 \times 187$ patients

Clavel et al.
JACC 2012
2- Does AVR improve outcome in patients with Paradoxical Low-Flow, Low-Gradient AS???
Impact of AVR on Survival in Patients with Low-Gradient Severe AS and Preserved LVEF

102 patients, AVA<1.0 cm²
$\Delta P_{\text{Mean}} < 40$ mmHg
LVEF ≥ 50%

Whole Cohorts

Propensity Score-Matched Cohorts

Impact of AVR on Survival in Patients with Paradoxical Low-Flow, Low-Gradient AS

Clavel et al. JACC 2012
Key Messages: Paradoxical Low-Flow AS

- A preserved LVEF (≥ 50%) does not exclude the presence of myocardial systolic dysfunction and low transvalvular flow in AS patients.

- A low transvalvular gradient (<40 mmHg) does not exclude the presence of a severe stenosis in patients with small AVA and preserved LVEF.

- Paradoxical low-flow, low-gradient is found in 10-25% of AS patients and is often associated with more advanced stage of the disease and worse prognosis.
Key Messages: Paradoxical Low-Flow, Low-Gradient AS

- AVR improves outcome in patients with paradoxical low-flow, low-gradient severe AS

- TAVR may provide an alternative to SAVR in these patients?
Thank You!