ΑΞΙΟΛΟΓΗΣΗ ΤΗΣ ΑΟΡΤΙΚΗΣ ΣΤΕΝΩΣΗΣ

Κ. ΑΓΓΕΛΗ
Α. ΠΑΝΕΠΙΣΤΗΜΙΑΚΗ ΚΑΡΔΙΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ
AORTIC STENOSIS

Aortic stenosis is the most common valvular disease and the third most prevalent form of cardiovascular disease in the Western world. Its prevalence increases with population aging and is present in 3% to 7% of patients over 65 years of age up to 10% in that of >75 years.
Age distribution in severe aortic stenosis: male vs. female
Association Between Cardiovascular Risk Factors and Aortic Stenosis
The CANHEART Aortic Stenosis Study

Andrew T. Yan, MD, Maria Koh, MSc, Kelvin K. Chan, MD, MSc, Helen Guo, MSc, David A. Alter, MD, PhD, Peter C. Austin, PhD, Jack V. Tu, MD, PhD, Harindra C. Wijeyasurya, MD, PhD, Dennis T. Ko, MD, MSc.

**CENTRAL ILLUSTRATION** The Relationship Between Cardiac Risk Factors and Aortic Stenosis

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>1.71 (1.66-1.76)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.49 (1.44-1.54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1.17 (1.14-1.21)</td>
<td>&lt;0.001</td>
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Since the first successful surgical aortic valve replacement occurred more than a half-century ago, our focus has been on fixing the severely calcified valve, a mechanical problem that has been viewed as requiring a mechanical solution. There has been a steady reduction in the risk of this procedure and the introduction of less invasive transcatheter options, which together have allowed us to treat more patients earlier and with better outcomes. However, as we have shifted from thinking of the disease as a passive degenerative process to one characterized by an active biology, we still have yet to identify interventions that are effective at preventing the initiation or progression of CAVD. This study provides a helpful stimulus to turn our attention to the preven-
CARDIOVASCULAR IMAGING MODALITIES

Approaches to quantify stenosis

“Aortic stenosis”
Valvular Stenosis
Supravalvular Aortic Stenosis

Level of obstruction: Aorta
- Single discrete narrowing
- Long tubular hypoplasia

Physical exam
- Thrill in suprasternal notch or R carotid
- Loud A2

Associated with elfin facies, high Ca, PS – elastin gene
Bicuspid Aortic Valve – Associated Problems

Bicuspid aortic valve

Aortic medial changes

Bicuspid Aortic Valve – New Insights

Screen first degree relatives

Scan entire aorta (MRA or CT)
ECHO PARAMETERS….

- Pressure gradient (HG vs LG was defined as a mean transaortic pressure gradient 40 mm Hg).
- LV flow state (NF vs LF as an indexed LV stroke volume 35 ml/m²)
- AVA
- LV myocardium

**IMPLICATION**

“IF WE DON’T CALCULATE AVA, WE WILL MISS 15-35% OF CASES OF CRITICAL AS, MORE IMPORTANTLY WE WILL DEPRIVE THESE PATIENTS OF THE POTENTIAL BENEFIT OF AVR ON THEIR SYMPTOMS/SURVIVAL”

- Myocardial fibrosis
- Restrictive physiology
- Small LV cavity
- Resembles heart failure with preserved EF (Diastolic Heart failure)
- Pseudo-normalization of blood pressure
- Impaired LV function yet normal EF (around 50-60%)
We must remember...

• "composite" parameters like valve area by continuity or stroke volume suffer from the compounded risks of measurement error.

• The first reflex in the presence of a surprising, "paradoxic" set of echo data should be critical review of the raw data...

• If confirmed, these patients should perhaps be further evaluated with regard to LV longitudinal function and BNP.
In 2007, Hachicha et al. first described a group of patients with paradoxical low-flow, low-gradient severe AS. These patients are characterized by
1. an indexed aortic valve area < 0.6 cm²/m²,
2. Stroke volume index < 35 mL/m²,
3. mean transvalvular gradient < 40 mm Hg, and EF > 50%
SEVERE AORTIC STENOSIS

Paradoxical low flow AS

(20-30%)
Differences in Natural History of Low- and High-Gradient Aortic Stenosis from Nonsevere to Severe Stage of the Disease

Sebastian Herrmann, MD, Bastian Fries, MD, Dan Liu, MD, Kai Hu, MD, Stefan Stoerk, MD, PhD, Wolfram Voelker, MD, Catharina Ruppert, PhD, Kristina Lorenz, PhD, Georg Ertl, MD, and Frank Weidemann, MD, Würzburg and Ums, Germany

Clinical deterioration

<table>
<thead>
<tr>
<th></th>
<th>HG/AS</th>
<th>NF/LG</th>
<th>LF/LG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Follow-Up</td>
<td>Baseline</td>
</tr>
<tr>
<td>AVA [cm²]</td>
<td>1.4±0.4</td>
<td>0.8±0.1*</td>
<td>1.3±0.2</td>
</tr>
<tr>
<td>PGmean [mm Hg]</td>
<td>30.5±10.6</td>
<td>18.6±6*</td>
<td>33.0±5.6*†</td>
</tr>
</tbody>
</table>
Aortic Valve Area

Hydraulic formula
Flow = Area x Flow velocity

The continuity equation uses the law of conservation of mass, stating that "what goes in must come out"
- Reliably estimate valve area
CARDIOVASCULAR IMAGING

Aortic Stenosis

Hemodynamic Catheterization

Clinical Exam Symptoms ≠ Mean Gradient = Aortic Valve Area

Further Evaluation

Clinical Exam Symptoms = Mean Gradient ≠ Aortic Valve Area
Potential factors that may contribute to errors include:

- Image quality
- Annular calcification (which obscures the true dimension)
- Noncircular anulus (which invalidates the formula)
- Failure to measure the true diameter
Differential Left Ventricular Outflow Tract Remodeling and Dynamics in Aortic Stenosis

Praveen Mehrotra, MD, Aidan W. Flynn, MD, PhD, Katrina Jansen, MD, Timothy C. Tan, MBBS, PhD, Gay Mak, MD, Howard M. Julian, MD, Xin Zeng, MD, Michael H. Picard, MD, Jonathan J. Pasceri, MD, and Judy Hung, MD, Boston, Massachusetts; and Philadelphia, Pennsylvania

Journal of the American Society of Echocardiography
November 2015

Normal LVOT Anatomy and Dynamics

The LVOT is a complex tunnel that is formed posteriorly by the inter-
valvular fibrosa, which is in continuity with the anterior leaflet of the
mitral valve, and anteriorly by the muscular and membranous inter-
ventricular septum. In patients not exposed to the pressure load
of AS, we have observed that the LVOT is a very dynamic structure
with considerable variation in size and shape from end-diastole to
peak systole, with the degree of distensibility greater than twice
that observed in patients with AS. Whereas at end-diastole, the LVOT
is very elliptical, at peak systole, it expands because of deformation of
the intervalvular fibrosa (posterior LVOT wall) during isovolumic
contraction and ventricular systole. This change in area occurs pre-
dominantly, therefore, because of the significant increase in the

Aortic Stenosis

End-diastole
CSA: 3.36 cm²
Minor Axis: 17.3 mm
Major Axis: 26.5 mm
Ellipticity Index: 1.53

LA
LVOT
IVS

End-diastole
CSA: 3.96 cm²
Minor Axis: 19.0 mm
Major Axis: 27.1 mm
Ellipticity Index: 1.43

Peak systole
CSA: 3.59 cm²
Minor Axis: 19.8 mm
Major Axis: 25.7 mm
Ellipticity Index: 1.36
\( \Delta \) CSA: +7%
\( \Delta \) Minor Axis: +14%
\( \Delta \) Major Axis: 25%

Peak systole
CSA: 4.49 cm²
Minor Axis: 23.0 mm
Major Axis: 24.2 mm
Ellipticity Index: 1.65
\( \Delta \) CSA: +13%
\( \Delta \) Minor Axis: +21%
\( \Delta \) Major Axis: 31%

\( \Delta \) Ellipticity Index: -13%
DC: 4.6 x 10^4 mmHg

\( \Delta \) Ellipticity Index: -26%
DC: 12.3 x 10^4 mmHg
Aortic stenosis: flow matters

Philippe Pibarot

Effect of interrogation angle on frequency shift

\[
\Delta F = \frac{V \times 2F_o \times \cos \theta}{c}
\]

\[
V = \frac{\Delta F \times c}{2 \times F_o \times \cos \theta}
\]
APICAL VIEWS LEAD TO ~20% PARADOXICAL LOW-FLOW SEVERE AORTIC STENOSIS

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

Jeremy J. Thades, MD, Vojislav T. Nikolic, MD, MPH, Kwang Je Lee, MD, PhD, and Jae K. Oh, MD, Rochester, Minnesota; and Seoul, Korea

Journal of the American Society of Echocardiography
July 2013
Aortic valve area
Continuity equation

- LVOT diameter and velocity should be measured at the same distance from the aortic valve.

- When the PW sample volume is optimally positioned, the recording shows a smooth velocity curve with a well-defined peak.
Continuity equation in paradoxical low flow severe aortic stenosis: can we trust LVOT measurements only?

Aggeli C et al. ESC 2016
Dimensionless Index (LVOT and Aortic Valve Velocity Time Integral Ratio)

- Always preferable
- Because VTI or peak velocity ratio is inversely proportional to the area ratio of the LVOT and aortic valve
- Also useful in determining the severity of aortic stenosis
Pressure recovery

- The conversion of potential energy to kinetic energy across a narrowed valve results in a high velocity and a drop in pressure.

- Distal to the orifice, flow decelerates again. Kinetic energy will be reconverted into potential energy with a corresponding increase in pressure, the so-called PR

Pressure recovery

- Pressure recovery is greatest in stenosis with gradual distal widening

- Aortic stenosis with its abrupt widening from the small orifice to the larger aorta has an unfavorable geometry for pressure recovery

\[ PR = 4v^2 \times 2EOA/AoA \times (1-EOA/AoA) \]
Concept of Global LV Afterload in AS

- **Valvular** component (gradient, severity of stenosis)
- **Arterial** resistance ↑: atherosclerotic continuum
  - **Hypertension** >50% of pts, *measure RR at echo*

**Valvulo-arterial Impedance Zva**

\[
Z_{va} = \frac{RR_{systol.} + MG}{SVI}
\]

**Mortality** ↑ in Asympt AS >3.5, Paradox >5.5 mmHg/ml/m²

*Dumesnil J, Pibarot P, Carabello B. Eur Heart 2009 Sept 8*

*Hachicha Z, Dumesnil, Pibarot. JACC 2009; 54*

*Barasch E et al. J Heart Valve Dis 2008; 17*
Tissue Velocities and Myocardial Deformation in Asymptomatic and Symptomatic Aortic Stenosis

Helle Gervig Carstensen, MD, PhD, Linnea Hornbech Larsen, MD, PhD, Christian Hassager, MD, DMSc, Klaus Fuglsang Kofod, MD, DMSc, Morten Dalsgaard, MD, PhD, Charlotte Barup Kristensen, MD, Jan Skov Jensen, Prof, MD, PhD, DMSc, and Rasmus Mogelvang, MD, PhD, Copenhagen, Denmark

ASYMPTOMATIC

<table>
<thead>
<tr>
<th>RLS &gt; 15%</th>
<th>RLS 33-15%</th>
<th>RLS &lt; 33%</th>
</tr>
</thead>
</table>

Moderate Aortic stenosis

Severe Aortic stenosis

SYMPTOMATIC

<table>
<thead>
<tr>
<th>RLS &gt; 15%</th>
<th>RLS 23-15%</th>
<th>RLS &lt; 13%</th>
</tr>
</thead>
</table>

Severe Aortic stenosis LVEF ≥ 50%

Severe Aortic stenosis LVEF < 50%

Basal Longitudinal Strain: The Strongest Longitudinal Parameter of Symptomatic Status
Paradoxical Low-Flow, Low-Gradient Aortic Stenosis
New Evidence, More Questions

Philippe Pibarot, DVM, PhD, FAHA; Jean G. Dumesnil, MD, FRCP(C)

- Pronounced Concentric Remodeling
- Impaired Diastolic Filling
- Impaired Longitudinal systolic function
- Atrial Fibrillation
- Mitral Regurgitation
- Mitral Stenosis
- Tricuspid Regurgitation

↑ LV ejection time

Reduced Forward Stroke Volume

Reduced Transvalvular flow rate

Low-Flow, Low-gradient AS with Preserved LVEF
Impact of stroke volume on cardiovascular risk during progression of aortic valve stenosis

Mai Tone Lønnebakken, Giovanni De Simone, Sahrai Saeed, Kurt Boman, Anne B Rossebø, Edda Bahlmann, Christa Gohlke-Bärwolf, Eva Gerdts

Lønnebakken MT, et al. Heart 2017;0:1–6. doi:10.1136/heartjnl-2016-310917

asymptomatic patients with mild-to-moderate AS
- The AVA values obtained by the hybrid methods are systematically larger than those obtained by standard TTE.
- The best cut point of AVA by TTE to predict outcomes was close to 1cm², which is consistent with the guideline criteria. However, the cut point of AVA by hybrid CT-TTE for predicting mortality was larger: 1.2cm².
- The LVOT area measured by CT was larger than that measured by CMR.
Low gradient severe aortic stenosis with preserved ejection fraction: reclassification of severity by fusion of Doppler and computed tomographic data

Vasileios Kamperidis1,2, Philippe J. van Rosendaël1, Spyridon Kassanos1, Frank van der Kley1, Madelien Regeer1, Ibtihal Al Amri1, Georgios Sianos2, Nina Ajmone Marsan1, Victoria Delgado1, and Jeroen J. Bax1*

<table>
<thead>
<tr>
<th>Aortic Stenosis</th>
<th>Normal Flow – High Gradient</th>
<th>Low Flow – High Gradient</th>
<th>Normal Flow – Low Gradient</th>
<th>Low Flow – Low Gradient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe, n (%)</td>
<td>72 (100)</td>
<td>70 (97)</td>
<td>31 (100)</td>
<td>46 (100)</td>
</tr>
<tr>
<td></td>
<td>2 (3)</td>
<td>0 (0)</td>
<td>24 (52)</td>
<td>5 (12)</td>
</tr>
<tr>
<td>Moderate, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Patients with paradoxical low-flow, low-gradient AS have abnormal myocardial structure and systolic function

Low-Flow, Low-Gradient, Preserved LVEF

Hermann et al. JACC 2011;58;402-412
Stress Echocardiography to Assess Stenosis Severity and Predict Outcome in Patients With Paradoxical Low-Flow, Low-Gradient Aortic Stenosis and Preserved LVEF

Marie-Annick Clavel, DVM, PhD,* Pierre Vladimir Ennezat, MD,† Sylvestre Marechéaux, MD,‡ Jean G. Dumesnil, MD,* Romain Capoulade, MS,* Zeineb Hachicha, MD,* Patrick Mathieu, MD,* Annalik Bellouin, MD,† Sébastien Bergeron, MD,* Patrick Mcmoun, MD,‡ Marie Arsenault, MD,* Thierry Le Tourneau, MD,§ Agnès Pasquet, MD,‖ Christian Couture, MD,* Philippe Pibarot, DVM, PhD*" Quebec, Quebec, Canada; Lille, Compiègne, and Nantes, France; and Brussels, Belgium

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

Figure 3. Event-Free Survival According to AVA_{\text{proj}}

Event-free survival according to (A) projected aortic valve area (AVA_{\text{proj}}) at normal flow rate and (B) indexed AVA_{\text{proj}} during stress echocardiography. *Hazard ratio 0.99 adjusted for age and sex.
Adverse features on treadmill testing were defined as **low exercise capacity** (5 metabolic equivalents METS on treadmill exercise), an **abnormal blood pressure response to exercise** (<20 mmHg rise with exercise), **exercise-induced pulmonary hypertension** (PAP>60mmHg post exercise) and **poor contractile reserve** (<4% increase in EF post exercise).
The role of stress testing in evaluation of asymptomatic patients with aortic stenosis

Patrizio Lancellotti, Julien Magne, and Luc A. Piérard

KEY POINTS

- Risk stratification is essential in severe asymptomatic aortic stenosis.
- A normal exercise test predicts good 1-year outcome (<70 years old, physically active).
- Exercise echo may provide incremental prognostic information over resting echo and exercise test.
- Beyond symptoms, exercise echocardiography provides useful information on the valve, the left ventricle and the haemodynamics.
- An increase in mean transaortic pressure gradient by at least 18–20 mmHg or a limited contractile reserve predicts a worse outcome, even in truly asymptomatic patients.

72 years old male

Asymptomatic

Severe aortic stenosis: AVA 0.65 cm²

No symptoms during test

Workload 75 W, duration: 7 min

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<thead>
<tr>
<th></th>
<th>Heart rate (bpm)</th>
<th>Systolic blood pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>94</td>
<td>131</td>
</tr>
<tr>
<td>Exercise</td>
<td>137</td>
<td>154</td>
</tr>
</tbody>
</table>
Exercise PHT is a frequent condition (55%) in patients with asymptomatic severe aortic stenosis and preserved EF.
Cardiac event-free survival according to the presence or absence of exercise pulmonary hypertension
Prognostic Value of LV Deformation Parameters Using 2D and 3D Speckle-Tracking Echocardiography in Asymptomatic Patients With Severe Aortic Stenosis and Preserved LV Ejection Fraction

Yasufumi Nagata, MD,* Masaaki Takenaka, MD,* Victor Chen-Chia Wu, MD,* Masaki Iturou, MD,† Kengo Suzuki, MD, Kiyo Sato, MD,‡ Yoshihito Sato, MD,§ Yosihiko Akanhi, MD,¶ Kazuhiko Asouma, MD,‖ Yoshina Otsuji, MD,*
Receiver-Operating Characteristic Curve Analysis for the Prediction of Major Adverse Cardiac Events
Stress Echocardiography to Assess Stenosis Severity and Predict Outcome in Patients With Paradoxical Low-Flow, Low-Gradient Aortic Stenosis and Preserved LVEF

Marie-Annick Clavel, DVM, PhD,* Pierre Vladimir Ennezat, MD,† Sylvère Maréchaux, MD,‡ Jean G. Dumesnil, MD,* Romain Capoulade, MS,* Zeinab Hachicha, MD,* Patrick Mathieu, MD,* Annark Belloutin, MD,† Sébastien Bergeron, MD,* Patrick Melmoun, MD,‡ Marie Arsenault, MD,* Thierry Le Tourneau, MD,§ Agnès Pasquet, MD,∥ Christian Couture, MD,* Philippe Pibarot, DVM, PhD* Quebec, Quebec, Canada; Lille, Compiègne, and Nanterre, France; and Brussels, Belgium

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

**Diagram A**

- AVA (cm²) vs. Q (mL/s)
- Rest, Peak DSE, Projected

**Diagram B**

- **MEASUREMENTS**
  - LVOT VTI = 17 cm
  - LVET = 0.31 s
  - Ao VTI = 68 cm
  - ΔP = 20 mmHg
  - LVOT VTI = 22 cm
  - LVET = 0.28 s
  - Ao VTI = 81 cm
  - ΔP = 37 mmHg

**CALCULATIONS**

- $SV = 48 \text{ mL}$
  - AVA = 0.71 cm²
  - $Q = 165 \text{ mL/s}$
- $SV = 62 \text{ mL}$
  - AVA = 0.77 cm²
  - $Q = 220 \text{ mL/s}$

AVA_{proj} = AVA_{rest}(\DeltaAVA/\DeltaQ)(250-Q_{rest})

$= 0.71 + (0.06/55)(250-165) = 0.8 \text{ cm²}$
Resting Aortic Valve Area at Normal Transaortic Flow Rate Reflects True Valve Area in Suspected Low-Gradient Severe Aortic Stenosis

Narej S. Chahal, MBBS,* Maria Eleftheropoulou, MD,† Ana M. Gonzalez-Gonzalez, MD,* Ramsamy Manivannan, MBBS,* Rajdeep Khatter, MBBS,† Ivery Senior, MD**

(J Am Coll Cardiol Img 2015;8:1133-9)

Assessment of Patients With Suspected LFLGAS Using SE
Central Illustration: Impact of Flow and Ejection Fraction After Aortic Valve Replacement

Prevalence of Ejection Fraction/Flow Groups
- Normal Flow: 54%
- Paradoxical Low Flow: 28%
- Low Ejection Fraction: 18%

Expected Operative Mortality According to Ejection Fraction/Flow Groups

Observed Operative Mortality According to Ejection Fraction/Flow Groups
- Normal Flow: 6.3%
- Paradoxical Low Flow: 3.8%
- Low Ejection Fraction: 8.7%

Adjusted Cox Survival Curves

Overall Survival (%)
- Normal Flow
- Paradoxical Low Flow
- Low Ejection Fraction

Follow-up Time (Years)

Tricuspid Regurgitation Is Associated With Increased Risk of Mortality in Patients With Low-Flow Low-Gradient Aortic Stenosis and Reduced Ejection Fraction

Results of the Multicenter TOPAS Study (True or Pseudo-Severe Aortic Stenosis)

Abdelaziz Dahou, MD, MS,* Julien Magne, MD, PhD,† Marie-Annick Clavel, DVM, PhD,‡ Bertrand Capoulade, PhD,§ Philipp Emmanuel Berko, MD, PhD,∥ Jutta Bergler-Bright, MD, Paolo Marco Senechal, MD,⊥ Gerald Muntzligler, MD,∥ Ian Burwash, MD,∥ Henrique B. Ribeiro, MD,∥ Kim O’Connor, MD,* Patrick Mathieu, MD,* Helmut Baumgartner, MD, Andrea G. Dumoulin, MD,* Raphaël Rosenblat, MD,* Eric Lasser, MD,* Josep Rodés-Cabau, MD,* Philippe Pibarot, DVM, PhD*
Key Messages

• 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) or velocity (<4m/sec) 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 10-20% of AS patients and is often associated with more advanced stage of the disease and worse prognosis.
THE END

• Paradoxical LF/LG aortic stenosis is a challenging, heterogeneous clinical entity that requires special attention and further studies.

• AVR improves outcome in patients with low-flow, low-gradient severe AS and preserved LVEF.

• It is important to recognize this entity so we do not deny surgery to a symptomatic patient with small AVA and low gradient.

• Consider clinical status, BNP level, comorbidity, and operative risk before considering surgery.