Assessing Function by Echocardiography in Valvular Heart Disease

Asymptomatic Severe Aortic Stenosis

Catherine Szymanski
No Disclosure
Asymptomatic period (increasing obstruction, myocardial overload)

Onset of severe symptoms

Average death age (male)

Average survival (yr)

Symptomatic severe AS: indication of AVR (class I)
Indication for AVR in AS

SEVERE STENOSIS

- Peak velocity ≥ 4 m/s
- Mean gradient: ≥ 40 mmHg
- Aortic valve area (AVA): ≤ 1.0 cm²
- Indexed AVA: ≤ 0.6 cm²/m²

+ SYMPTOMS and/or LVEF<50%

= AVR (Class I)
Should Early Elective Surgery be performed in Severe Asymptomatic AS?

- Good Prognosis
- Sudden death: 0.3% to 1% per year
- Operative risk: < 2%
- Valve prosthesis complications: 1 to 3% per year

Medical Management

- Risk of rapid progression
- Risk of irreversible myocardial damage
- ↑ operative mortality in severely symptomatic pts
- Mortality on the waiting list up to 15%
- Risk related to delayed symptom reporting
- Event at 2 years: varying: 21 to 67%

or

Aortic Valve Replacement
Effects of AS on Myocardial Function and Structure

LV Concentric Remodeling

- Diastolic dysfunction:
  - LA pressure ↑
  - LA dilatation

- Systolic dysfunction:
  - Subendocardial fibrosis

Integrated Approach: Consider valve, ventricle, ventricular-vascular coupling
Left Ventricular Afterload in Aortic Stenosis = Valvular Load + Arterial Load

\[ Z_{va} = \frac{LVSP}{SV_{i}} = \frac{MG + SAP}{SV_{i}} \]

>3.5: Moderate
>4.5: Severe

Hachicha Z. Circulation 2007; 115: 2856-2864
Prognostic Impact of Global Afterload

Retrospective analysis of 544 asymptomatic pts
≥ moderate AS (≥ 2.5 m/s), LVEF ≥ 50%; Follow-up 2.5±1.8 years

Overall Survival, (%) vs. Follow-up (years)

- $Z_{va} < 3.5$
- $3.5 \leq Z_{va} < 4.5$
- $Z_{va} \geq 4.5$

Age-Gender matched general population

- 3 years
  - $Z_{va} < 3.5$
    - 88 ± 3%
  - $3.5 \leq Z_{va} < 4.5$
    - 80 ± 3%
  - $Z_{va} \geq 4.5$
    - 70 ± 5%

Multivariate Analysis
- $3.5 \leq Z_{va} < 4.5$: 2.3; p=0.03
- $Z_{va} \geq 4.5$: 2.8; p=0.01

Hachicha Z. JACC 2009; 54: 1003-1011
Alterations in multidirectional myocardial functions in patients with aortic stenosis and preserved ejection fraction: a two-dimensional speckle tracking analysis

Arnold C.T. Ng¹,²†, Victoria Delgado¹†, Matteo Bertini¹, Marie Louisa Antoni¹, Rutger J. van Bommel¹, Eva P.M. van Rijnsoever¹, Frank van der Kley¹, See Hooi Ewe¹, Tomasz Witkowski¹, Dominique Auger¹, Gaetano Nucifora¹, Joanne D. Schuijf¹, Don Poldermans³, Dominic Y. Leung⁴, Martin J. Schalij¹, and Jeroen J. Bax¹"
<table>
<thead>
<tr>
<th>Variable</th>
<th>Total population (n = 420)</th>
<th>Aortic sclerosis (n = 118)</th>
<th>Mild aortic stenosis (n = 81)</th>
<th>Moderate aortic stenosis (n = 109)</th>
<th>Severe aortic stenosis (n = 112)</th>
<th>P-value*</th>
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</thead>
<tbody>
<tr>
<td>Demographic characteristics</td>
<td></td>
<td></td>
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<tr>
<td>Age, (years)</td>
<td>66.1 ± 14.5</td>
<td>60.8 ± 14.9</td>
<td>67.6 ± 14.2</td>
<td>66.5 ± 15.0</td>
<td>70.2 ± 12.0</td>
<td>&lt;0.001</td>
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<tr>
<td>Male gender, (%)</td>
<td>60.7</td>
<td>59.3</td>
<td>69.1</td>
<td>61.5</td>
<td>55.4</td>
<td>0.28</td>
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<tr>
<td>Body mass index, (kg/m²)</td>
<td>26.0 ± 4.3</td>
<td>26.0 ± 3.7</td>
<td>25.9 ± 3.8</td>
<td>26.8 ± 5.5</td>
<td>25.3 ± 3.9</td>
<td>0.10</td>
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<tr>
<td>Body surface area, (m²)</td>
<td>1.90 ± 0.21</td>
<td>1.90 ± 0.21</td>
<td>1.92 ± 0.21</td>
<td>1.92 ± 0.21</td>
<td>1.85 ± 0.19</td>
<td>0.065</td>
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<td>Medical history</td>
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<td></td>
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<tr>
<td>New York Heart Association class (%)</td>
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<td></td>
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<tr>
<td>I</td>
<td>71.1</td>
<td>94.1</td>
<td>81.0</td>
<td>59.6</td>
<td>50.5</td>
<td>&lt;0.001</td>
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<tr>
<td>II</td>
<td>18.1</td>
<td>5.1</td>
<td>10.1</td>
<td>26.6</td>
<td>29.4</td>
<td></td>
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<tr>
<td>III</td>
<td>10.8</td>
<td>0.8</td>
<td>8.9</td>
<td>13.8</td>
<td>20.1</td>
<td></td>
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<tr>
<td>IV</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Hypertension, (%)</td>
<td>51.1</td>
<td>50.8</td>
<td>44.3</td>
<td>56.0</td>
<td>51.4</td>
<td>0.48</td>
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<td>Diabetes, (%)</td>
<td>16.4</td>
<td>17.8</td>
<td>13.9</td>
<td>17.4</td>
<td>15.6</td>
<td>0.88</td>
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<td>Hyperlipidaemia, (%)</td>
<td>29.0</td>
<td>28.8</td>
<td>20.3</td>
<td>27.5</td>
<td>37.0</td>
<td>0.092</td>
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<td>Current smoker, (%)</td>
<td>16.2</td>
<td>16.9</td>
<td>12.8</td>
<td>20.2</td>
<td>13.9</td>
<td>0.44</td>
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<tr>
<td>Systolic blood pressure, (mmHg)</td>
<td>147 ± 26</td>
<td>145 ± 24</td>
<td>146 ± 26</td>
<td>150 ± 28</td>
<td>146 ± 27</td>
<td>0.51</td>
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<tr>
<td>Diastolic blood pressure, (mmHg)</td>
<td>81 ± 12</td>
<td>80 ± 11</td>
<td>81 ± 12</td>
<td>82 ± 12</td>
<td>79 ± 14</td>
<td>0.59</td>
</tr>
</tbody>
</table>
N=70, Age 73±10, AVA 0.56±0.20

LV longitudinal myocardial strain is reduced in patients with LV concentric hypertrophy

LV EF markedly underestimates the extent of myocardial systolic impairment in the presence of LV concentric hypertrophy in AS patients

Cramariuc D. Heart 2010; 96: 106-112
Impaired myocardial deformations, exercise tolerance and prognosis in asymptomatic AS

Compared with controls, severe AS patients (n=65) has significantly lower global longitudinal strain (-18% vs. -21%, p<0.05) despite similar LVEF, more pronounced in the basal segments.

Prognostic value of basal longitudinal strain in patients with severe asymptomatic AS (48 pts)

Longitudinal strain in the basal segments stratified patients according to the composite endpoint: hospitalization for cardiac cause, aortic valve replacement, cardiovascular death within 12 months

Strain analysis in patients with severe aortic stenosis and preserved left ventricular ejection fraction undergoing surgical valve replacement

Victoria Delgado, Laurens F. Tops, Rutger J. van Bommel, Frank van der Kley, Nina Ajmone Marsan, Robert J. Klautz, Michel I.M. Versteegh, Eduard R. Holman, Martin J. Schalij, and Jeroen J. Bax*

• 73 severe AS patients (65 ± 13 years; AVA 0.8 cm\(^2\)) with preserved LVEF (61 ± 11%), before and 17 months after AVR

Delgado V. Eur Heart J 2009; 30: 3037-3047
Prognostic markers in Asymptomatic AS

• 163 patients with severe asymptomatic AS
• Mean AVA: 0.45 ± 0.09 cm²/m² [0.2-0.6]
• Mean pressure gradient: 46 ± 14 mmHg [25-86]
• Mean LVEF: 67 ± 17 [55-84]
• Mean follow-up: 20 ± 19 months [4-102]
• Predefined endpoints: 74 patients
  – 6 deaths
  – AVR required in 57 patients
  – Symptoms without AVR in 11 patients

Lancellotti, Donal, Magne et al. Heart 2010; 96: 1364-1371
Risk stratification in asymptomatic moderate to severe AS: the importance of the valvular, arterial, and ventricular interplay

Multivariate Analysis

Adjustment for gender, systemic arterial compliance, E-wave, E/A ratio and response to exercise (abnormal vs. normal)

- Peak aortic velocity ≥ 4.4 m.s⁻¹
- Zva ≥ 4.9 mmHg.ml⁻¹.m⁻²
- Longitudinal strain ≤ 15.9%
- Ind. LA area ≥ 12.2 cm²/m²

Hazard ratio

HR = 1.7, p = 0.027
HR = 1.9, p = 0.013
HR = 2.2, p = 0.003
HR = 2.8, p = 0.001

Lancellotti, Donal, Magne et al. Heart 2010; 96: 1364-1371
Predictors in Asymptomatic AS

A  AV velocity

B  Valvulo-arterial impedance

C  2D longitudinal strain

D  LA size

Lancellotti, Donal, Magne et al. Heart 2010; 96: 1364-1371
Impact of Cumulative Number of Predictive Variable

Event-free Survival, %

Follow-up, years

Risk Factor =0, (n=20)
Risk Factor =1, (n=56)
Risk Factors =2, (n=57)
Risk Factors ≥3, (n=30)

76±6%
73±10%
73±10%
70±8%
40±8%
35±8%
15±8%
10±6%
p<0.001
Brain Natriuretic Peptide in Asymptomatic AS

Severity of AS
LV mass
Symptomatic status
NYHA Class
Systolic dysfunction
Symptom free survival

2D strain and BNP reflect Afterload and Early Myocardial Dysfunction

- Highest BNP and low systolic strain in increased afterload
- N=173 asymptomatic severe AS, EF ≥55%, 22% low SVi<35ml/m^2

Lancellotti P. Eur J Echocardiogr 2010; 11:537-543
Risk Score for predicting outcome in asymptomatic AS

Risk Score for Predicting Outcome in Patients With Asymptomatic Aortic Stenosis

Jean-Luc Monin, MD, PhD; Patrizio Lancellotti, MD, PhD; Mehran Monchi, MD; Pascal Lim, MD; Emmanuel Weiss, MD; Luc Piérad, MD, PhD; Pascal Guéret, MD

- 107 pts followed in Créteil
- Risk score according to independent variables
- Validation in Liège (107 pts)

Score = (Peak velocity × 2) + (nat log BNP × 1.5) + 1.5 (if female)

Monin, Lancellotti et al. Circulation 2009; 120: 69-75
Outcome according to Score quartiles

Development cohort (%)
Créteil, N=104

Validation cohort (%)
Liege, N=107

Monin, Lancellotti et al. Circulation 2009; 120: 69-75
Observed 2-year Event Rate in the Combined Cohort

Monin, Lancellotti et al. Circulation 2009; 120: 69-75
Exercise Echo in Asymptomatic AS

N = 69 patients, AS<1.0 cm², Follow-up 15 ± 7 months

Incremental prognostic value of Exercise Doppler Echo

AVA + Test

MPG

Lancellotti P. Circulation 2005;112:I-377–I-382
PROGNOSTIC VALUE OF EXERCISE ECHO IN AS Pts WITH NORMAL EXERCISE TEST

186 pts with <1.5 cm² AS (53% <1 cm²), semi-supine test

Maréchaux S. Eur Heart J 2010; 31,1390-1397
Parameters during exercise Doppler echo

Symptoms (BP)

Exercise-induced changes
- mean P gradient
- AVA
- LV EF
- LV filling P
- functional MR
- pulmonary P

Contractile reserve
- TDI
- 2D strain

Inducible ischemia
ASYMPTOMATIC AS (IN WHOM?)
(<1 cm² [<1.5 cm²] + EF > 50%)

Careful history taking

EXERCISE TESTING

Severe Dyspnea
Dizziness, Angina
Drop in SBP
Arrhythmias

ST Changes
∆SBP < 20 mmHg
Moderate dyspnea (COPD)
Fatigue

BNP

AV SURGERY

> 70 years
Comorbidities

MPG

BNP

EXERCISE ECHO

LV dysfunction
LOW FLOW AORTIC STENOSIS

AVA < 1 cm² (<0.6 cm²/m²)
with LV Dysfunction (EF ≤ 40%)
And Mean Gr ≤ 30 (AHA) 40 (ESC) mm Hg

Approximatively 5-10% of AS population
High risk pts : 5y survival 50 %
If operated (AVR): operative mortality : 8-30%

Monin et al. JACC 2001  Nishimura et al. Circulation 2002
**STRESS ECHO in Aortic Stenosis with low gradient**

Dobutamine infusion

1. Dosage
   a. Rate: start at 5 + increase by 2.5/5 min
   b. Max: 20 µg/kg/min
   c. More (40 µg/kg/min)?
   d. Atropine?

2. Increase HR ≥ 10 bpm
Dobutamine Stress Echo (class IIa)

↑ SV ≥ 20%

Contractile Reserve

ΔP_{mean} > 30
AVA ≤ 1.0

True Severe AS

AVR±CABG

ΔP_{mean} ≤ 30
AVA > 1.0

Pseudo Severe AS

Medical treatment

↑ SV < 20%

No Contractile Reserve

ΔP_{mean} > 30
AVA ≤ 1.0

Indeterminate AS

Medical ? AVR ?
Concept of the Projected AVA (250 mL/s)

Projected AVA

Aortic Valve Area (cm²)

Mean Transvalvular Flow Rate (ml/s)

* Peak AVA during DSE

Blais C. Circulation 2006; 113: 711-721
Outcomes

- 136 patients
- Mean AVA: 0.7cm² [0.6-0.8]
- Mean pressure gradient: 29 mmHg [23-34]
- Cardiac Index: 2.11 l/min/m² [1.75-2.55]
- Group 1, n=92, contractile reserve
- Group 2, n=44, no contractile reserve

Operative mortality:
- 5% (3 of 64 pts) if CR +
- 32% (10 of 35 pts) if CR-

Long term survival:
- 79% if CR +
- 38% if CR-

Monin JL. Circulation 2003; 102: 218-224
AS without CR

- 81 patients without CR (SV↑<20%), AVA 0.75±0.16, EF 29±7%, age 71±10 year
- Better longterm survival with AVR, but high OP mortality

![Survival curve](image)

OP mortality 22%

5 year survival
AVR 54%±7%
Medical 13±7%

*Tribouilloy C. JACC 2009; 53; 1865-1873*
Postoperative LVEF is NOT related to LV contractile function

Quere JP. Circulation 2006; 113: 1738-1744
Dyssynchrony

TVI 20.6 cm
MPG 26 mmHg
AVA 0.93 cm²

TVI 16.5 cm
MPG 20 mmHg
AVA 0.91 cm²

Dyssynchrony
Other risk factors

- MPG < 20 mmHg and CAD
- BNP > 550 pg/mL
- 6MWT < 320 m

- Prior AF
- Euroscore > 10
- Older age
- Comorbidities

Bergler-Klein et al., Circ 2007, Clavet et al., Circ 2008
Dobu stress echo

CR +, SV > 20% ?

Yes

AVA ≤ 1 cm²
AVA < 0.3 cm²
MPG > 30 mmHg

AVA > 1 cm²
AVA > 0.3 cm²
MPG < 30 mmHg

No

Dyssynchrony?

Measure projected EOA or EOAi

EOA < 1 cm² or EOAi < 0.55 cm²/m²
Non available

Other risk factors: BNP > 550 pg/ml
6MWT functionnal capacity, AF, Euroscore, CAD, MPG < 20 mmHg at rest, comordities, older age

Yes

Medical treatment. Transplant? CRT+/-CDI?

No

Aortic valve replacement
Paradoxical Low Flow, Low Gradient AS Despite Normal LV Ejection Fraction

Hachicha Z, Circulation 2007; 115:2856-2864
Normal Flow AS

LVEDV: 115 ml
LVEF: 60%
SV: 70 ml
AVA: 0.7 cm²
ΔP: 45 mmHg

Paradoxical Low Flow AS

LVEDV: 85 ml
LVEF: 60%
SV: 50 ml
AVA: 0.7 cm²
ΔP: 25 mmHg

Pibarot P, Dumesnil J. JACC Img 2009;2:400-403
Aortic Stenosis Severity

512 Patients

SEVERE AS
(Indexed AVA ≤ 0.6 cm²/m²)
&
PRESERVED LV FUNCTION
(LVEF ≥ 50%)

331 patients (65%)
SVI > 35ml/m²
Normal Flow (NF) Group

181 patients (35%)
SVI ≤ 35ml/m²
Paradoxical Low Flow (PLF) Group

Hachicha Z. Circulation 2007; 115:2856-2864
Low Transvalvular Gradients Despite Severe AS and Normal LVEF

Hachicha Z. Circulation 2007; 115:2856-2864
Global LV Hemodynamic Load: Valvulo-Arterial Impedance ($Z_{va}$)

$$Z_{VA} = \frac{SAP + MG}{SVi} \text{ (mmHg/ml/m}^2\text{)}$$

$P<0.001$

Hachicha Z. Circulation 2007; 115:2856-2864

Take Home Messages

✓ In asymptomatic severe AS, clinical outcome can be predicted by measurements that integrate the « 3-V » components:

Valvular, Vascular and Ventricular

Cramariuc D. JACC Img 2009;2:390-399

Lancellotti P. Eur J Echocardiogr 2010;11:537-543

Hachicha Z. Circulation 2007;115:2856-2864
An integrated approach to evaluate asymptomatic AS patients should systematically be used:

- **Aortic jet velocity** (measure of stenosis severity)
- **Valvular-arterial impedance** (estimate of global LV afterload)
- **LA area** (marker of LV diastolic dysfunction)
- **Long-axis function** (indicator of LV systolic dysfunction)
- **Abnormal Stress Echo response**
  - Symptoms at early stage
  - Limited contractile reserve
  - Larger increase in MPG