Severe Aortic Stenosis: Definition, prevalence and outcome in 2011

My Declaration of interest:
No conflicts of interest to declare

Catherine M. Otto, MD
J. Ward Kennedy-Hamilton Endowed Chair in Cardiology
University of Washington, Seattle
Development versus progression of calcific aortic valve disease.

Progressive Risk Factors to Disease
- Metabolic Syndrome
- Obesity
- Hypertension
- Smoking
- Renal Failure
- Hyperlipidemia
- Male Gender
- Oxidative Stress
- Age

Normal Aortic Valve → Aortic Valve Sclerosis → Calcific Aortic Valve Disease

Clinical Factors Associated with Aortic Valve Ca++ (MESA)

Katz R et al, Circulation 2006; 113: 2113-2119
Progression from Sclerosis to Stenosis

Age 67
Aortic sclerosis

Age 77
Severe valve Ca++

About 10% of patients per 5 years

\[ V_{\text{max}} 2.1 \text{ m/s} \]

\[ V_{\text{max}} 4.7 \text{ m/s} \]
### Initiation of Disease

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>RR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>2.19 (1.84–2.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men</td>
<td>1.87 (1.31–2.69)</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>1.26 (1.08–1.46)</td>
<td>0.004</td>
</tr>
<tr>
<td>BP meds.</td>
<td>1.40 (1.02–1.92)</td>
<td>0.04</td>
</tr>
<tr>
<td>Smoking</td>
<td>2.49 (1.49–4.15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lipid meds.</td>
<td>1.76 (1.25–2.49)</td>
<td>0.001</td>
</tr>
<tr>
<td>Crt ≥ 1.1</td>
<td>0.62 (0.40–0.96)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

### Disease Progression

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>β (95% CI)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>18.3 (-0.1, 36.8)</td>
<td>0.05</td>
</tr>
<tr>
<td>Men</td>
<td>37.5 (6.6, 68.5)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Mean follow-up 2.4 ± 0.9 yrs

Owens DS et al. Am J Cardiol 2010
Aortic stenosis
STAGES OF DISEASE

Disease initiation

Clinical risk factors

Sclerosis to stenosis

Age
Valve anatomy
Lipids

Progressive valve obstruction

???

Oxidized LDL accumulation
Inflammation
Cytokine release
Phenotypic transformation
Calcification
Osteogenesis

Owens DS and Otto CM, JACC CV Imaging 2009
Aortic Stenosis:
Prevalence of valvular heart disease by age

Aortic Stenosis: Prevalence

![Graph showing prevalence of aortic stenosis procedures from 1985 to 2005. The graph compares MV repair, All MV surgery, AV replacement, and All valve replacement procedures. The number of procedures is expressed in thousands.]
Aortic Stenosis: Prevalence

Age categories in isolated AVR

Isolated AVR: Age categories (n=31,200)

<table>
<thead>
<tr>
<th>Year</th>
<th>&lt;61 years</th>
<th>61-65 years</th>
<th>66-70 years</th>
<th>71-75 years</th>
<th>76-80 years</th>
<th>81-85 years</th>
<th>&gt;85 years</th>
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<tr>
<td>1999</td>
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<td>2008</td>
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d'Arcy J L et al. Heart 2011;97:91-93

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Aortic Stenosis Severity

**Echocardiography**

Jet velocity

\[ V_{\text{max}} \]

Pressure gradient

\[ \Delta P = 4v^2 \]

Valve Area

**Continuity equation**

\[ SV_{\text{LVOT}} = SV_{\text{AS-Jet}} \]

\[ CSA_{\text{LVOT}} \times VT_{\text{LVOT}} = AVA \times VT_{\text{AS-Jet}} \]

\[ AVA = (VT_{\text{LVOT}} \times CSA_{\text{LVOT}})/VT_{\text{AS-Jet}} \]
What is severe aortic stenosis?

60M Bicuspid aortic valve: New onset dyspnea

La imagen muestra una válvula aórtica bicúspide con un diagrama de ecocardiografía y una media de velocidad de 5.4 m/s.
Definitions of Disease Severity
Aortic Stenosis with normal LV function

<table>
<thead>
<tr>
<th>Severity</th>
<th>AS-Jet (m/s)</th>
<th>Mean $\Delta P$ (mmHg)</th>
<th>AVA ($cm^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&lt; 3</td>
<td>&lt; 20*</td>
<td>&gt; 1.5</td>
</tr>
<tr>
<td>Moderate</td>
<td>3-4</td>
<td>20-40*</td>
<td>1.0 -1.5</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt; 4</td>
<td>&gt; 40*</td>
<td>&lt; 1.0</td>
</tr>
</tbody>
</table>

<0.6 cm²/m²

*ESC +10 mm Hg
Outcome in asymptomatic aortic stenosis: Predictive value of aortic velocity


Outcome in asymptomatic aortic stenosis: Predictive value of aortic velocity

Rosenhek R et al, Eur Heart J 2004

Stewart R et al, Euro Heart J 2010

Lancellotti et al, Heart 2010
Why Measure Aortic Stenosis Severity?

Ensure AS is the cause of symptoms.
Aortic Stenosis:
My definition of severe aortic stenosis

Symptoms due to aortic valve obstruction

Valve obstruction

causing

due to

Symptoms
## Aortic Stenosis Severity
Is AS severe enough to be the cause of symptoms?

<table>
<thead>
<tr>
<th>$V_{\text{max}}$</th>
<th>Symptoms</th>
<th>AVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 m/s</td>
<td>Not due to AS</td>
<td>4.0 cm$^2$</td>
</tr>
<tr>
<td>2 m/s</td>
<td>Not due to AS</td>
<td>2.0 cm$^2$</td>
</tr>
<tr>
<td>3 m/s</td>
<td>Maybe due to AS?</td>
<td>1.0 cm$^2$</td>
</tr>
<tr>
<td>4 m/s</td>
<td>Likely due to AS</td>
<td>0.5 cm$^2$</td>
</tr>
</tbody>
</table>
AS Severity versus Clinical Symptoms

Aortic jet velocity (cm/s)
700
600
500
400
300
200
100
0

Aortic jet velocity
Baseline
Final
Asymptomatic
AVR/Died

Otto, Burwash, Legget, Munt et al, Circulation 1997
Grading AS severity in your patient

<table>
<thead>
<tr>
<th>$V_{\text{max}}$</th>
<th>$\Delta P$</th>
<th>AVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3.0 m/s</td>
<td>&lt; 20 mmHg</td>
<td>&gt; 1.5 cm²</td>
</tr>
<tr>
<td>3 - 4 m/s</td>
<td>20-40 mmHg</td>
<td>1 - 1.5 cm²</td>
</tr>
<tr>
<td>&gt; 4.0 m/s</td>
<td>&gt; 40 mmHg</td>
<td>&lt; 1.0 cm²</td>
</tr>
</tbody>
</table>

- **MILD**
- **MODERATE**
- **SEVERE**
Severe Aortic Stenosis
LISTEN TO THE PATIENT

Symptom (simp’tum):
Any subjective evidence of disease or a patient’s condition, i.e. such evidence as perceived by the patient. *

Normal body sensation or “aches and pains” of daily life

A possible indicator of a serious problem that should be reported.

* Dorland’s Medical Dictionary
Aortic Stenosis
LISTEN TO THE PATIENT

Late Symptoms
- HEART FAILURE
- SYNGOPE
- ANGINA

Early Symptoms
- ↓ Exercise tolerance
- Dyspnea
- Exertional dizziness
Evaluation of AS Severity

Detection of symptom onset

Cumulative proportion of symptom-free survival

- No symptoms
- Limiting symptoms

Time (months)

At risk  | 79  | 46  
         | 77  | 41  
         | 73  | 33  
         | 71  | 28  
         | 70  | 25  

No symptoms
Limiting symptoms

Symptoms provoked on exercise testing

Das, Rimington, Chambers. Eur Heart J 2005
Aortic Stenosis: My definition of severe aortic stenosis

Symptoms due to aortic valve obstruction

Valve obstruction causing Symptoms due to

Asymptomatic AS with a degree of valve obstruction highly likely to cause symptoms in the near future?
Outcomes in Asymptomatic AS
Retrospective study

Sudden death without known symptoms
11 (4.1%) or < 1%/year

N = 622
Age 72 ± 11 yrs
F/U 5.4 ± 4 yrs
Vmax ≥ 4 m/s
0.9±0.2 cm²

Pellikka PA et al, Circulation 2005
Severe Asymptomatic AS
Predictors of Symptom Onset

Rosenhek et al, NEJM 2000; 343: 611-7
Evaluating Aortic Valve Calcification
Role of Imaging

TTE  TEE  CT
Imaging of the Aortic Valve Using Fluorodeoxyglucose Positron Emission Tomography

Retrospective study from database, PET and CT imaging 84 patients (42 aortic stenosis, 42 age-matched controls)

Marincheva-Savcheva G. et al. JACC 2011
Aortic Stenosis: Outcomes with asymptomatic VERY severe AS

Rosenhek R, Circulation 2010
Aortic Stenosis: Outcomes with severe and VERY severe AS

Kitai T et al. Heart 2011
92F severe AS, CHF, high surgical risk

STS score 12.6, EuroSCORE 18.7
**TAVI: Transcatheter Aortic Valve Implantation**

**Partner Cohort B (TAVI vs Medical Rx)**

Leon MB et al. NEJM, Online First Sept 22, 2010

<table>
<thead>
<tr>
<th></th>
<th>TAVI</th>
<th>Medical Rx (37% with BAV, 10% AVR)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (1 yr)</td>
<td>31%</td>
<td>50%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>22%</td>
<td>44%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>10.6%</td>
<td>4.5%</td>
<td>0.04</td>
</tr>
<tr>
<td>Major Vasc Comp.</td>
<td>16.8%</td>
<td>2.2%</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
Paradoxical low-flow low-gradient severe AS with normal EF

N=512
Severe AS
AVA ≤ 0.6 cm²/m²
Normal LV output in 65%
SV > 35 mL/m²
Low Flow in 35%

Low-gradient “severe” AS with normal EF

Jander N, Minners J, Holme I et al. (SEAS investigators) Circulation 2011; 123: 887-895
Severe Asymptomatic Aortic Stenosis
Which patients benefit from early AVR?

Once AS is severe, what predicts

- Hemodynamic progression?
- Symptom onset?

What is the risk of early intervention versus watchful waiting –

Why not replace the valve now?
Valve Durability and Complications

Prosthetic valve choices

**Tissue Valve**
No anticoagulation but limited durability

**Mechanical Valve**
Durable but Requires anticoagulation

**TAVI**
For high risk pts Durability not known

Benefit depends on a prosthetic valve that functions better than the diseased native valve
AVR for Severe Asymptomatic AS?
Markov Decision Analysis Model

Reference Case:
- 65 year old man
- Severe AS
- Pre-AVR mortality 1%/year
- Post-AVR utility 0.9
- Post-AVR CHF 11.3%

Watchful waiting >>> AVR
- QALY 7.4 vs 5.3
- Cost < AVR

Gada, Scuffam, Griffin & Marwick. Circ CV Qual Outcomes 2011
AVR for Severe Asymptomatic AS?
Markov Decision Analysis Model

Sensitivity analysis

- Early AVR favored only if pre-op annual risk >13%
- Watchful waiting preferred regardless of probability of post-op CHF

Gada, Scuffam, Griffin & Marwick. Circ CV Qual Outcomes 2011
### Definitions of AS severity

#### Otto Classification

<table>
<thead>
<tr>
<th>Clinical outcome</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aortic sclerosis</strong></td>
<td>▪ Evaluation and treatment of conventional cardiac risk factors.</td>
</tr>
<tr>
<td>Marker of atherosclerotic CAD</td>
<td></td>
</tr>
<tr>
<td>with a 50% increased risk of myocardial infarction and CV</td>
<td></td>
</tr>
<tr>
<td>death over 5 years.</td>
<td></td>
</tr>
<tr>
<td><strong>Mild AS</strong></td>
<td>▪ Continue cardiac risk factor modification.</td>
</tr>
<tr>
<td>Low rate of symptom onset</td>
<td>▪ Echocardiography every 3-5 years.</td>
</tr>
<tr>
<td><strong>Moderate AS</strong></td>
<td>▪ Continue cardiac risk factor modification.</td>
</tr>
<tr>
<td>Intermediate rate of symptom onset.</td>
<td>▪ Echocardiography every 1-2 years.</td>
</tr>
<tr>
<td></td>
<td>▪ Educate patient about disease progression and typical early symptoms of severe AS.</td>
</tr>
<tr>
<td></td>
<td>▪ Evaluate for other causes of symptoms if present (unlikely to be due to AS).</td>
</tr>
</tbody>
</table>
### Definitions of AS severity

#### Otto Classification

<table>
<thead>
<tr>
<th>Clinical outcome</th>
<th>Management</th>
</tr>
</thead>
</table>
| **Asymptomatic severe AS** | Low risk of sudden death but rate of symptom onset is directly related to aortic velocity. | - Continue cardiac risk factor modification.  
- Echocardiography annually.  
- Clinical evaluation every 6 months with monitoring for symptom onset.  
- Exercise testing and/or BNP levels if symptom status is unclear. |
| **Symptomatic severe AS** | Mortality is 50% at one year with a high risk of sudden death and recurrent hospitalizations for CHF. | - Prompt aortic valve replacement.  
- Symptoms must be considered to be due to AS when severe valve obstruction is present. |
| **Decompensated severe AS with LV dysfunction** | Mortality is high with any treatment but outcomes are improved in those who survive AVR. | - Hospitalization with optimization of loading conditions.  
- AVR if risk and other clinical parameters allow. |