Aortic Stenosis: Epidemiology and Natural History

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Disclosures
• Edwards LifeSciences

Alexander Fleming (1881-1955)
The Changing Face of Valve Disease

- Shift from rheumatic to “degenerative” etiologies
- Moderate to severe valve disease occurs in*:
  - 1.9% people 55 to 64 years-old
  - 8.5% people 65 to 74 years-old
  - 13.2% people 75 years and older
- Prevalence of valve disease increase as the elderly population continues to grow
- Elderly have an inherent increase in risks associated with surgery and complexity of medical management


Prevalence of Valve Disease by Age

![Graph showing the prevalence of valve disease by age](image)

Prevalence of Valve Disease by Age


Distribution of Native Heart Valve Disease

![Graph showing the distribution of native heart valve disease](image)

Iung et al. Nat. Rev. Cardiol. 2011; 8: 162-172
Aortic Valve Stenosis: Etiology

- Calcific aortic stenosis
  - With any underlying aortic valve morphology
- Congenital aortic stenosis
  - Typically bicuspid or unicuspid aortic valve
- Rheumatic heart disease
- Rare causes (e.g., radiation-induced)

Valve Morphology in Patients Undergoing Surgery for Aortic Stenosis by Age

<table>
<thead>
<tr>
<th>Aortic Valve Structure</th>
<th>Cases, n (%)</th>
<th>Age Groups of Patients by Decades at Time of Aortic Valve Replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
<td>21-30</td>
</tr>
<tr>
<td>Unicuspid</td>
<td>150 (47)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Bicuspid</td>
<td>126 (38)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>98 (30)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Unspecified</td>
<td>30 (9)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

Women:

<table>
<thead>
<tr>
<th>Aortic Valve Structure</th>
<th>Cases, n (%)</th>
<th>Age Groups of Patients by Decades at Time of Aortic Valve Replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unicuspid</td>
<td>50 (33)</td>
<td>7 (5)</td>
</tr>
<tr>
<td>Bicuspid</td>
<td>126 (87)</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>98 (68)</td>
<td>7 (5)</td>
</tr>
<tr>
<td>Unspecified</td>
<td>30 (21)</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

Subtotals, n (%) 340 (100)

Calcific Aortic Stenosis: Risk Factors

- Male gender
- Hypertension
- Elevated LDL cholesterol
- Cigarette smoking
- Underlying bicuspid or unicuspid aortic valve
- End-stage renal disease
- Paget’s disease

Calcific Aortic Stenosis: Genetics

- NOTCH1 (signaling and transcription regulator)
  - Associated with aggressive calcific aortic stenosis, bicuspid aortic valve, and thoracic aortic aneurysm
  - Promote calcification by decreasing RunX2 activity, which regulates osteoblasts
- vitamin D receptor gene
- apolipoprotein E2 allele

Calcific Aortic Stenosis: Mechanisms

- Calcific aortic stenosis is a biologically active process
- Lipid accumulation
  - LDL accumulation and oxidation
- Inflammation
  - T-cells, monocytes, inflammatory mediators, cytokines
- Calcification
  - Osteoblast expression, bone formation
**Oxidized LDL in Aortic Valve Remodeling**


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**Calcific Aortic Stenosis: Mechanisms**


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**PET-CT Imaging of Aortic Valve Inflammation and Calcification**

PET-CT Imaging of Aortic Valve Inflammation and Calcification


Hemodynamic Progression of Aortic Stenosis

Aortic jet velocity
↑ 0.32 ± 0.34 m/sec per year

Mean gradient
↑ 7 ± 7 mmHg per year

Aortic valve area
↓ 0.12 ± 0.19 sqcm per year


Hemodynamic Progression of Aortic Stenosis

Eveborn G W et al. Heart 2012 [epub ahead of print]
Pathophysiology Aortic Stenosis

- LV outflow obstruction
- LVSP
- LVET
- LVDP
- Aortic P
- LV Mass
- LV dysfunction
- Myocardial O2 consumption
- Myocardial ischemia
- Diastolic time
- Myocardial O2 supply
- LV failure

Natural History of Aortic Stenosis


Survival with Symptomatic Aortic Stenosis

Event-free survival without valve replacement for 123 subjects with initially asymptomatic aortic stenosis

Cox regression analysis showing event-free survival in groups defined by aortic jet velocity at entry

Aortic Jet Velocity and Aortic Valve Area in subjects who developed symptoms requiring aortic valve replacement or died (AVR/Died) compared with those who remained asymptomatic for the baseline and final studies.


Survival Free of Symptoms Censored at Aortic Valve Surgery

Survival of patients with AS compared with that of Minnesota white population (referent group) matched for age and sex.

Outcomes of Patients with Initially Asymptomatic Aortic Stenosis: Causes of Death


Sudden Death in Non-Surgical Patients

- 11 patients with sudden death not preceded by aortic valve replacement or known symptoms (4.1% overall or ~1%/year)
- No medical follow-up for >1 year in 5 of these patients
- Ages ranged from 55 to 92 years
- Aortic valve velocities ranging from 4.0 to 5.8 m/sec
- Aortic valve areas ranging from 0.53 to 1.28 sqcm


Kaplan–Meier Analysis of Overall Survival Among 126 Patients with Asymptomatic Severe Aortic Stenosis, as Compared with Age- and Sex-Matched Persons Controls

Mean Rate of Progression of Aortic-Jet Velocity among 41 Patients Who Had Cardiac Events and 29 Who Did Not.


Event-free Survival among Patients with Mild Aortic-Valve Calcification Compared with Moderate or Severe Calcification


Kaplan–Meier event-free survival rate for patients with asymptomatic very severe aortic stenosis stratified according to peak aortic jet velocity and aortic valve area

Summary

- Aortic stenosis is the most common acquired valve disease in developed nations
- Aortic stenosis is a hemodynamically progressive disease
- Uncorrected symptomatic severe aortic stenosis is associated with a dismal prognosis
- Aortic valve replacement stabilizes long term prognosis and improves symptoms

Summary: Asymptomatic Aortic Stenosis

- Patients with asymptomatic aortic stenosis have a generally favorable prognosis with “watchful waiting”
- Low incidence of sudden cardiac death
- Variable rates of progression
- Early valve replacement for asymptomatic patients remains controversial

THANK YOU!