Cardiovascular Surgical Pathology
Case 1

(No Disclosures; No Conflicts of Interest)

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Case 1  
Clinical History (73,M)

- Referral to Mayo Clinic  
  Worsening chest pain and SOB
- Past medical history  
  Exertional chest discomfort (2 yr)
- History of present illness  
  Exertional chest pain (2 wk)  
    More frequent than previously  
    More intense than previously  
    Now radiates to left shoulder  
  Nocturnal chest pain (2 wk)
Case 1
Clinical History (73, M)

- Coronary angiography
  100% occlusion of prox RCA
  99% stenosis of prox LAD
  80% stenosis of LAD-D1
  80% stenosis of LCX-OM1

- Echocardiography
  Severe aortic stenosis (0.6 cm²)
  Moderate mitral regurgitation
  LV EF 34% (normal, 50-70%)
  Moderate LV and LA dilatation
Case 1
Clinical History (73, M)

- Clinical diagnoses
  Severe coronary artery disease
  Unstable angina pectoris
  Severe aortic stenosis
  Moderate systolic dysfunction
- Surgical procedures
  Coronary artery bypass surgery
  Aortic valve replacement, with
    23-mm Carpentier-Edwards bovine pericardial bioprosthesis
Case 1
Aortic Valve

Fibrocalcific Cusps (Gross & Micro)
Case 1
Aortic Valve

Microscopy – None!
Case 1
Diagnosis

Heart, aortic valve, excision:
Degenerative fibrocalcific aortic valve disease,
associated with clinically severe aortic stenosis and no aortic regurgitation
Aortic Stenosis
Lecture Outline

- Mechanisms
- Causes
  Degenerative
  Bicuspid
  Rheumatic
- Myectomy
- Trends
- Summary
Aortic Stenosis
Mechanisms

What processes interfere with valve opening?

- Calcification
  Any region
- Fibrosis
  Cusps
- Fusion
  Commissures

Normal AV
Aortic Stenosis
Lecture Outline

• Mechanisms
• Causes
  Degenerative
  Bicuspid
  Rheumatic
• Myectomy
• Trends
• Summary
Aortic Stenosis
Causes and Demographics

<table>
<thead>
<tr>
<th>Causes</th>
<th>%</th>
<th>Age*</th>
<th>M:F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degenerative</td>
<td>60</td>
<td>70-90</td>
<td>1:1</td>
</tr>
<tr>
<td>Bicuspid</td>
<td>30</td>
<td>50-70</td>
<td>2:1</td>
</tr>
<tr>
<td>Rheumatic</td>
<td>5</td>
<td>50-70</td>
<td>1:1</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>&lt;70</td>
<td>1:1</td>
</tr>
</tbody>
</table>

* Age at time of surgery (in years)
Aortic Stenosis
Lecture Outline

- Mechanisms
- Causes
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Aortic Stenosis
Degenerative Type

Calcium in Valve Pockets (Autopsy)
Aortic Stenosis
Degenerative Type

3 Cusps (Surgical)
Calcium (X-Ray)
Aortic Stenosis
Degenerative Type

Mild Commissural Fusion (Surgical)
Aortic Stenosis
Degenerative Type

Unequal Sized Cusps (Surgical)
Aortic Stenosis
Degenerative Type

Fenestrations and Strands (Surgical)
Aortic Stenosis
Degenerative Type

• Age-related abnormalities
  In U.S. population >65 yr old *
  Aortic valve sclerosis: 25%
  Aortic valve stenosis: 5%

• Pathogenesis of aortic stenosis
  Not by random wear-and-tear
  Interplay of numerous factors

* Assessed by echocardiography
Aortic Stenosis
Degenerative Type

• Atherosclerotic risk factors
  Hyperlipidemia (esp apolipoprotein B, 2, & E), with Ox-LDL in valve; hypertension, ↑ age, & diabetes
• Inflammation and proliferation
  T cells, macrophages, monocytes, plasma cells, B cells, mast cells
  CAM’s, TGF-β, TNF-α, MMP, BMP
  Myofibroblasts (GF, angio II, ↓NO)
  Neoangiogenesis (VEG-F, PDGF)
Aortic Stenosis
Degenerative Type

- Calcification and ossification
  - Cellular osteoblast-like phenotype
  - Alkaline phosphatase, osteopontin, osteocalcin, osteonectin, bone sialoprotein, & tenascin-C
  - Microfocal → gross mass (CaPO$_4$)

- Genetic and metabolic factors
  - Osteoporosis and aortic stenosis
  - Vitamin D receptor polymorphism
  - Apolipoprotein E4 allele
Aortic Stenosis
Degenerative Type

Diagram (Circulation 2005;111:3316)
Aortic Stenosis
Degenerative Type

Calcium and Inflammation (H&E)
Aortic Stenosis
Degenerative Type

Chronic Inflammation (H&E, High Power)
Aortic Stenosis
Degenerative Type

T Cells (CD3)

B Cells (CD20)

Mac’s (CD68)

Mast Cells (SAB)

Inflammation (Special Stains)
Aortic Stenosis
Lecture Outline

• Mechanisms
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Aortic Stenosis
Congenitally Bicuspid Valve

Two Cusps (Autopsy)
Aortic Stenosis
Congenitally Bicuspid Valve

2 Cusps (Surgical)  Calcium (X-Ray)
Aortic Stenosis
Congenitally Bicuspid Valve

Location of Raphe (n = 567; 7 Studies)

Aortic Stenosis
Congenitally Bicuspid Valve

Relative Size of Cusps (n = 524)

- Equal: 27 (5%)
- Unequal: 484 (92%)
- Thirds: 13 (2%)

Aortic Stenosis
Congenitally Bicuspid Valve

Relative Cusp Size (Surgicals)

Equal (5%)
Unequal (90%)
Thirds (5%)
Aortic Stenosis
Congenitally Bicuspid Valve

Commissural Fusion (Surgical)
Aortic Stenosis
Congenitally Bicuspid Valve

Commissural Fusion (Surgical)
Aortic Stenosis
Congenitally Bicuspid Valve

Atypical BAV

Fenestrated Raphe (Surgical)
Aortic Stenosis
Congenitally Bicuspid Valve

• Occurrence
  Incidence (%): 1-2
  Sex (M:F ratio): 2-3:1

• Fate (by age 75) %
  Stenosis 85
  Regurgitation 10
  Infection 3
  Dissection 2
  Normal 0
Aortic Stenosis
Congenitally Bicuspid Valve

• Etiology

Inheritance: autosomal dominant trait, with incomplete penetrance
Mutation: Notch-1 gene encoding for membrane receptor important for normal cardiac development
Association: defective microfibrils in aortic valve & ascending aorta
Result: weak mechanical support (fibrocalcific valve, dilated aorta)
Aortic Stenosis
Congenitally Unicommissural Valve

Opened and Closed (Autopsy)
Aortic Stenosis
Congenitally Unicommissural Valve

Fibrosis (Surgical)
Aortic Stenosis
Congenitally Unicommissural Valve

Calcification (Surgical)
Aortic Stenosis
Congenitally Unicommissural Valve

1 Cusp (Surgical)
Calcium (X-Ray)
Aortic Stenosis
Lecture Outline

- Mechanisms
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  - Rheumatic
- Myectomy
- Trends
- Summary
Aortic Stenosis
Rheumatic Type

Fibrocalcific (Autopsy)
Candlewax
Aortic Stenosis
Rheumatic Type

Fibrosis (Surgical)
Calcium (X-Ray)
Aortic Stenosis
Rheumatic Type

Three Fused Commissures (Surgical)
Aortic Stenosis
Rheumatic Type

Two Fused Commissures (Surgical)
Aortic Stenosis
What Type Is It?

Rheumatic, Bicuspid, or Degenerative?

One Fused Commissure (Surgical)
Aortic Stenosis
What Type Is It?

Rheumatic Type

What if no history of rheumatic fever?
Postinflammatory (probably rheumatic)

One Fused Commissure (Surgical)
Aortic Stenosis
Lecture Outline

- Mechanisms
- Causes
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  - Bicuspid
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- Trends
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Aortic Stenosis
Subaortic Septal Myectomy

Angled Septum in Elderly (Autopsy)
Aortic Stenosis
Subaortic Septal Myectomy

• Gross
  Usually <10 g
  Multiple pieces

• Microscopy
  Hypertrophy & focal fibrosis
  H&E stain only
  Amyloid stain if >65 years old (CR or SAB)
Aortic Stenosis
Lecture Outline

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Aortic Stenosis
Past Trends

1159 Surgically Excised Valves

Cases (%)

Year

Degenerative
Bicuspid
Rheumatic
Aortic Stenosis
Past and Future Trends

Changes (1900-1990) & Projections (1990-2050)

U.S. Census Bureau (1993)
Aortic Stenosis
Future Trends

• Prevalence of various causes
  Degenerative: steady increase
  Bicuspid valve: stable rate (1-2%)
  Rheumatic: steady decrease

• Natural history of symptomatic AS
  High risk for sudden death (↓ CPR)
  5-yr survival: 50% (worse than CA)

• Effective therapy for aortic stenosis
  Aortic valve replacement (surgery)
  Major impact on health care costs
Aortic Stenosis
Lecture Outline

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Aortic Stenosis
Summary

- Handling surgical specimens
  Diagnostic versus research purposes
- Routine diagnostic evaluation
  Gross examination (no microscopy)
- Raphe vs commissural fusion
  Raphe: shallow, single ridge, obtuse
  Fusion: high, two cusps, acute angle
  Calcium: difficult distinction if marked
Aortic Stenosis

Summary

Comparison of Surgical Specimens
Case 1
Surgical Pathology of Aortic Valve Stenosis

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Aortic Stenosis
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Textbooks


Aortic Stenosis
References

Surgical Pathology


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Aortic Stenosis

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Surgical Pathology


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Bicuspid Aortic Valve


Aortic Stenosis

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Temporal Changes in Etiology


Aortic Stenosis

References

Histopathology


Aortic Stenosis

References

Subaortic Septal Myectomy