Valvular Heart Disease

for the General Internist

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Objectives:

• Describe the Etiology and natural history of common valve disorders, including mitral valve stenosis and regurgitation, aortic valve stenosis and regurgitation

• Outline key aspects of pathophysiology for common valve disorders

• Assess a patient with suspected valve disease and manage subsequent surveillance after diagnosis

• Construct an evidence-based management plan for the patient with a valve disorder
Valvular Heart Disease

Topics

• Aortic valve (stenosis, regurgitation)

• Mitral valve (stenosis, regurgitation)

• Special (tricuspid, bicuspid, endocarditis, prosthetic)
Valvular Heart Disease

Goals

• Etiology, natural history
• Pathophysiology highlights
• Diagnosis, surveillance
• Treatment options
Case 1

• 74 year old male, 6 months of progressive dyspnea and intermittent lightheadedness with exertion

• HR 70, BP 140/92, 3/6 late-peaking crescendo-decrescendo murmur at right sternal border, single S2

• HCT 38 mg/dL and Cr 0.9
Case 1

A follow up echocardiogram is most likely to show:

A) Aortic sclerosis
B) Aortic stenosis
C) Mitral regurgitation
D) Mitral stenosis
Case 1

A follow up echocardiogram is most likely to show:

A) Aortic sclerosis
B) Aortic stenosis
C) Mitral regurgitation
D) Mitral stenosis
Aortic stenosis

Definition

• Most common form of LV outflow obstruction

• Involves leaflet thickening, calcification, reduction in valve area, and a pressure gradient across the valve

Clinical Pearl:
LVOT obstruction ~ HCM, LVH, sub-valvular and supra-valvular etiologies
Aortic stenosis

Etiology

- Degenerative calcific – most common > 70y
- Rheumatic – most common worldwide, + MV
- Calcified bicuspid – 2%, predominates < 70y

Clinical Pearl: When < 70y, think about bicuspid valve and concomitant aortopathy
Aortic stenosis

From Otto, *Practice of Clinical Echocardiography*, 2017
Aortic stenosis

Pathophysiology

• Health – effective AVA = LVOT ~3-4cm²

• When AVA ↓ 50%, pressure gradient develops

• ↑ LV impedance, wall stress → LVH, ↑ LVEDP
Aortic stenosis

AVA 3.5 cm$^2$

LV thickness 1 cm
Aortic stenosis

AVA 1 cm^2

LV thickness 1.5 cm

Fibrosis, ↑LVEDP, WMA
Aortic stenosis

Presentation

• Asymptomatic + systolic murmur

• Progressive dyspnea, angina, or (pre)syncope

• Symptoms can precede LV dysfunction

Clinical Pearl:
Patients may voluntary restrict activity at the onset of symptoms – ask!
Aortic stenosis

Natural history

• Prolonged asymptomatic period for years

• Asymptomatic severe – high 2/5 year event rates

• Onset of symptoms – rapid progression 1-2 years

Clinical Pearl: Risk ~ chest radiotherapy, ESRD, CVD risk factors
Aortic sclerosis

Mild-Moderate AS

None

Early

Late

At risk

Severe AS

Symptom severity

If AVR
Aortic stenosis

Evaluation

- **Echocardiography** – diagnosis and follow up
- **Catheterization** – hemodynamics, angiography
- **CT/CMR** – morphology, aorta, pre-procedure planning
Aortic stenosis

Physical Exam

Moderate or severe AS

• Delayed carotid upstroke (+LR 13.1)
• A2 reduced or absent (+LR 10.7)
• Late peaking murmur (+LR 29.5)
• Prolonged duration of the murmur (+LR 29.5)

McGee S, Evidence-Based Physical Diagnosis
Aortic stenosis

Echocardiography

Clinical Pearl:
Key parameters are calculated aortic valve area, peak velocity, and mean gradient.

AVA = 0.35 cm²
Peak velocity = 6.8 m/s
Mean gradient = 111 mmHg
Mild AR
# Aortic stenosis

## Criteria

<table>
<thead>
<tr>
<th>Class</th>
<th>Anatomic characteristics</th>
<th>Aortic valve area (AVA, cm(^2))</th>
<th>Peak velocity (m/s)</th>
<th>Mean gradient (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Mild calcification</td>
<td></td>
<td>2-2.9</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Moderate</td>
<td>Moderate calcification</td>
<td>-</td>
<td>3-3.9</td>
<td>&lt;20-39</td>
</tr>
<tr>
<td>Severe</td>
<td>Severe, restricted</td>
<td>(\leq 1.0)</td>
<td>(\geq 4)</td>
<td>(\geq 40)</td>
</tr>
<tr>
<td>Low-flow, low-gradient, low EF</td>
<td>Severe, restricted</td>
<td>(\leq 1.0)</td>
<td>&lt; 4 rest, augments with dobutamine</td>
<td>&lt; 40 rest, augments</td>
</tr>
<tr>
<td>Paradoxical low-flow, low-gradient (normal EF)</td>
<td>Severe, restricted</td>
<td>(\leq 1.0) Indexed &lt; 0.6 cm(^2)/m(^2) and SV&lt;sub&gt;i&lt;/sub&gt; &lt; 35 mL/m(^2)</td>
<td>&lt; 4</td>
<td>&lt; 40</td>
</tr>
</tbody>
</table>
Aortic stenosis
Monitoring (2014 ACC/AHA Guidelines)

Clinical Pearl:
Average annual progression is 0.1 cm$^2$, 7 mmHg, and 0.3 m/s.

• Moderate – repeat echo 1-2 years
• Severe – repeat echo 6-12 months
Aortic stenosis

Treatment

Valve replacement (2014 ACC/AHA Class I indications)

- Symptomatic severe AS
- Asymptomatic severe AS when LVEF < 50%
- Severe AS with other cardiac surgery
Aortic stenosis

Treatment

• Surgical (SAVR)

• Trans-catheter (TAVR or TAVI)

• Palliative

Key Questions:
1) What is their life expectancy?
2) Will QOL improve with AVR?
3) What is their surgical risk?
## TAVI

<table>
<thead>
<tr>
<th>Balloon expandable</th>
<th>Self-expanding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sapien</td>
<td>CoreValve</td>
</tr>
<tr>
<td>No sewing ring</td>
<td>No sewing ring</td>
</tr>
<tr>
<td>Bovine pericardial</td>
<td>Porcine pericardial</td>
</tr>
<tr>
<td>Pacemaker rate +</td>
<td>Pacemaker rate ++</td>
</tr>
<tr>
<td>Rapid pacing</td>
<td>No rapid pacing</td>
</tr>
</tbody>
</table>
Society of Thoracic Surgeons - Predicted Risk of Mortality (STS-PROM)

Factors

• Demographics
• Renal, lung disease
• Coronary Disease
• Valve disease
• Shock

Does not include

• Procedural impediments
• Major organ issues
• Comorbidities
• Frailty
Aortic stenosis

Frailty assessment

Frailty-AVR Study, JACC 2017
## Global surgical risk

<table>
<thead>
<tr>
<th>Factor</th>
<th>Low risk</th>
<th>Intermediate</th>
<th>High</th>
<th>Prohibitive</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS-PROM</td>
<td>&lt;4% AND</td>
<td>4-8% OR</td>
<td>&gt;8% OR</td>
<td>&gt;50% risk of death in one year OR</td>
</tr>
<tr>
<td>Frailty</td>
<td>None AND</td>
<td>1 index OR</td>
<td>≥ 2 indices OR</td>
<td></td>
</tr>
<tr>
<td>Organs affected</td>
<td>None AND</td>
<td>1 OR</td>
<td>≤ 2 OR</td>
<td>≥ 3 OR</td>
</tr>
<tr>
<td>Procedural impediments</td>
<td>None</td>
<td>Possible</td>
<td>Possible</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Frailty = ADLs, ambulation; Procedural (e.g. vascular calcium, radiation, etc.)

*2014 ACC/AHA Valve Guidelines*
# Aortic stenosis

## Treatment

<table>
<thead>
<tr>
<th>Aortic valve replacement type</th>
<th>Indications - Severe AS</th>
<th>Risks</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgical</strong></td>
<td>STS-PROM &lt; 4</td>
<td>↑ AKI, AF, bleeding</td>
<td>Durability (long-term experience)</td>
</tr>
<tr>
<td><strong>Trans-catheter</strong></td>
<td>STS-PROM &gt; 4 or SAVR prohibitive</td>
<td>↑ CVA, vascular, paravalvular leak, pacer</td>
<td>Women, +/- ↓ mortality with trans-femoral</td>
</tr>
<tr>
<td><strong>Medical</strong></td>
<td>Life expectancy ≤ 1 year or no QOL improvement</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Aortic regurgitation
Case 2

• 74 year old male presenting with 6 months of progressive dyspnea and intermittent lightheadedness with exertion

• Exam notable for HR 70, BP 130/43, and 2/6 mid-peaking crescendo/decrescendo murmur at the right sternal border with 2/4 diastolic murmur and prominent carotid upstroke

• HCT 38 mg/dL and Cr 0.9
Case 2

A follow up echocardiogram is most likely to show:

A) Aortic regurgitation
B) Aortic stenosis
C) Mitral regurgitation
D) Mitral stenosis
Case 2

A follow up echocardiogram is most likely to show:

A) **Aortic regurgitation**
B) Aortic stenosis
C) Mitral regurgitation
D) Mitral stenosis
Aortic regurgitation

Definition

- Disease of aortic valve leaflets or aortic root, resulting in inadequate closure of the aortic valve leaflets and retrograde flow of stroke volume from the aorta to the left ventricle.
Aortic regurgitation

Etiology

| Clinical Pearl: Systemic disease and family history can provide important historical clues |
|---|---|---|
| Acquired | VES | Connective tissue |
| *Calcification, IE, *rheumatic, radiation, toxins | Hypertension, autoimmune, aortitis, dissection, trauma |
Aortic regurgitation

Aortic regurgitation

Pathophysiology

Clinical Pearl:
Aortic regurgitation presents both a pressure and volume problem, thereby increasing wall stress.
Aortic regurgitation

Presentation

• Asymptomatic for years → ventricular remodeling

• Left sided heart failure symptoms

• Angina (↓ diastolic flow), palpitations (LV enlargement)
Aortic regurgitation

Physical Exam

Moderate-severe chronic AR

- Grade 3/4 early diastolic murmur L-PS (+LR 9.9, -LR 0.1)
- Diastolic pressure ≤ 50 mmHg (+LR 19.3); ≥ 70 mmHg (-LR 0.2)
- Pulse pressure ≥ 80 mmHg (+LR 10.9); ≤ 60 mmHg (-LR 0.3)
- Hill’s foot-arm ≥ 60 mmHg (+LR 17.3)
- Absence of sustained apical impulse (+LR 0.1)

McGee S, *Evidence-Based Physical Diagnosis*
Aortic regurgitation

Evaluation

• Echocardiography – diagnosis and follow up

• Catheterization – hemodynamics, angiography

• CT/CMR – morphology, aorta, pre-procedure planning
Aortic regurgitation
Aortic regurgitation

Monitoring (2014 ACC/AHA Guidelines)

- **Annual** history and physical
- **Mild** – repeat echo 3-5 years
- **Moderate** – repeat echo 1-2 years
- **Severe** – repeat echo 6-12 months
Aortic regurgitation

Treatment

Valve replacement (2014 ACC/AHA Class I indications)

• Symptomatic severe AR

• Asymptomatic severe AR with LVEF < 50%

• Severe AR if other cardiac surgery needed
Mitral stenosis
Case 3

• 70 year old woman presenting with 6 months of recurrent hospitalizations for heart failure with pulmonary edema.

• Exam notable for HR 96, BP 150/95, and 2/6 apical systolic murmur with 2/4 diastolic murmur with associated rumble and prominent P2 component at the apex. Lung crackles.
Case 3

A follow up echocardiogram is most likely to show:

A) Aortic sclerosis
B) Aortic stenosis
C) Mitral regurgitation
D) Mitral stenosis
Case 3

A follow up echocardiogram is most likely to show:

A) Aortic sclerosis
B) Aortic stenosis
C) Mitral regurgitation
D) Mitral stenosis
Mitral stenosis

Definition

• Obstruction across the MV between LA and LV

• High LA pressure – transmits to right side
Mitral stenosis

Etiology

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rheumatic</strong></td>
<td>Commissural fusion</td>
</tr>
<tr>
<td>Endemic – young</td>
<td>Thick mitral apparatus</td>
</tr>
<tr>
<td>Treated – 4\textsuperscript{th} decade</td>
<td></td>
</tr>
<tr>
<td><strong>Senile calcific</strong></td>
<td>Annular/leaflet calcification</td>
</tr>
<tr>
<td>Older, renal disease</td>
<td></td>
</tr>
<tr>
<td><strong>Radiation</strong></td>
<td>Aortic, coronary, pericardium, myocardium</td>
</tr>
<tr>
<td>Hodgkin’s, breast, lung (10-20y)</td>
<td></td>
</tr>
<tr>
<td><strong>Congenital</strong></td>
<td>Parachute, Shone’s</td>
</tr>
<tr>
<td>Young</td>
<td></td>
</tr>
</tbody>
</table>

Clinical Pearl: DDx obstruction ~ myxoma, cor triatriatum, prosthetic obstruction
Mitral stenosis

Rheumatic

Senile calcific

Normal
Mitral stenosis

Natural history

Rheumatic
  • slow progression in developed world, latency ~ 16 years
  • rapid progression in developing world (carditis)

Senile calcific
  • Sparse data; variable

Clinical Pearl:
Risk ~ chest radiotherapy, ESRD, CVD risk factors
Mitral stenosis

Pathophysiology

- **Healthy state** - MVA = ~ 4 cm$^2$

- **MS = MVA ↓ → LA pressure ↑, LA remodeling**

- **Complications = AF (LAA clot), pHTN, RV ↓**
Mitral stenosis

Physical Exam

• Loud S1 + OS = pliable

• S2-OS time = severity
  • >110 ms = mild
  • < 70 ms = severe
Mitral stenosis

Presentation

• Left-sided (dyspnea, orthopnea, PND), palpitations,

• Right-sided (edema, satiety), hemoptysis (bronchial)

• Atrial fibrillation (valvular), embolic phenomena

Clinical Pearl:
Valvular AF refers to MS; the CVA risk is much higher and requires warfarin (not DOACs).
Mitral stenosis

Evaluation

• **2D echocardiography** – anatomy, feasibility

• **Doppler** – hemodynamics, exercise

• **TEE** – assess for LAA clot, guide therapy
# Mitral stenosis

## Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>2D Anatomy</th>
<th>Valve &amp; Clinical Hemodynamics</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-D</td>
<td>Rheumatic changes?</td>
<td>MVA ≤ 1.5 cm² LA size pHTN</td>
<td>Dyspnea (rest/exercise)</td>
</tr>
</tbody>
</table>
Mitral stenosis

Monitoring (2014 ACC/AHA Guidelines)

• Evaluate MVA, RV size, and RVSP

• Progressive (MVA > 1.5 cm²) – 3-5 years

• Severe (MVA ≤ 1.5 cm²) – 1-2 years

• Very Severe (MVA < 1 cm²) – 12 months
Mitral stenosis

Management

• Balloon comissurotomy (PBMC)
• Surgical comissurotomy
• Surgical valve replacement
• Trans-catheter valve replacement ("valve in MAC")

Clinical Pearl:
Diuretics and heart rate control are key medical management strategies
Mitral stenosis

Treatment (rheumatic)

Valve intervention (2014 ACC/AHA Class I indications)

• PBMC – symptomatic, MVA ≤ 1.5 cm$^2$, favorable

• Surgery – severe + unfavorable anatomy for PBMC

• Surgery – severe + other cardiac surgery
Mitral stenosis
Mitral stenosis

Long-term outcomes

Untreated

• Progression $\sim 0.1 \text{ cm}^2 / \text{year}$, wide variability
• Asymptomatic $\sim 16$ years (N. America)
• If mild symptoms $\sim$ disability 7-9 years

Treated

• PBMC excellent short-term; @ 12y $\sim 40\%$ re-intervention
Mitral regurgitation
Case 4

• 74 year old male presenting with 6 months of progressive dyspnea and intermittent lightheadedness with exertion

• Exam notable for HR 70, BP 140/92, and 3/6 holo-systolic murmur at the apex with inaudible S2

• HCT 38 mg/dL and Cr 0.9
Case 4

A follow up echocardiogram is most likely to show:

A) Aortic sclerosis
B) Aortic stenosis
C) Mitral regurgitation
D) Mitral stenosis
Case 4

A follow up echocardiogram is most likely to show:

A) Aortic sclerosis
B) Aortic stenosis
C) Mitral regurgitation
D) Mitral stenosis
Mitral regurgitation

Definition

• Retrograde blood-flow from LV to LA in systole

• Disruption of the mitral apparatus or ventricle
# Mitral regurgitation

## Etiology

<table>
<thead>
<tr>
<th></th>
<th>Pathology</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organic (primary)</strong></td>
<td>Problems with valve apparatus (leaflets, chordae, papillary, annulus)</td>
<td>MV prolapse</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flail leaflet</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Perforation (endocarditis)</td>
</tr>
<tr>
<td><strong>Functional (secondary)</strong></td>
<td>Left ventricular remodeling</td>
<td>Post-infarct</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-ischemic CM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypertrophic CM</td>
</tr>
</tbody>
</table>
Mitral regurgitation

Images courtesy of Dr. Alina Nicoara, Duke University
Mitral regurgitation

Pathophysiology

• Results in volume load to LV $\rightarrow$ $\uparrow$ wall stress

• Eccentric LV remodeling (new sarcomeres)

• LV/LA dilation, $\downarrow$ contractility, $\uparrow$ LVESD, $\downarrow$ LVEF
Mitral regurgitation

Presentation

• Dyspnea on exertion - ↑ LAP, pulmonary edema/HTN

• Fatigue - ↓ cardiac output

• Palpitations – atrial fibrillation, tachyarrhythmia
Mitral regurgitation

Diagnosis

• Exam – Apical murmur, sequelae of disease

• Echocardiography – 2D, Doppler

• CMR or catheterization – ancillary data, clarification
Mitral regurgitation

Physical Exam

Moderate-severe chronic AR

- Grade 3/6 apical systolic murmur (+LR 4.4, -LR 0.1)
- Presence of an S3 (+LR 1.8)
Mitral regurgitation

Monitoring (2014 ACC/AHA Guidelines)

- Annual history and physical
- Mild – repeat echo 3-5 years
- Moderate – repeat echo 1-2 years
- Severe – repeat echo 6-12 months
Mitral regurgitation

Treatment

- Mitral valve repair (surgical, percutaneous)
- Mitral valve replacement
- Goal directed medical therapy (heart failure, cardiac resynchronization) for functional MR
Mitral regurgitation (severe)

Treatment (2014 ACC/AHA Class I indications)

• Surgery – D: LVEF > 30% or with other cardiac surgery

• Surgery – C2: LVEF 30-60% or LVESD ≥ 40 mm

• MV repair – posterior leaflet; other leaflets “if durable”
Special situations
Tricuspid regurgitation

Etiology

• **Functional** - 80%, annular dilation, leaflet tethering

• **Primary** – rheumatic, prolapse, Ebstein’s, endocarditis, carcinoid, RV biopsy, CIED
Infective endocarditis

Antibiotic prophylaxis (2007 AHA Guideline)

Prosthetic heart valves or repair material

History of infective endocarditis

Valve disease in a transplanted heart

Congenital heart disease

- Unrepaired cyanotic
- Catheter based repair (complete) first 6 months
- Prosthetic repair with residual defect
Bicuspid aortic valve

Key points

Clinical Pearl:
Listen for a mid-systolic click and feel for radial-femoral pulse delay as a bedside screen for bicuspid valve and coarctation of the aorta, respectively.

Among patients with CoA, 50% bicuspid

• Associated with TAA (screen), VSD, PDA, ICA
• Screen patients for TAA and 1st degree relatives

Siu, et al. JACC 2010
Prosthetic valve

Key points

• Annual thrombosis risk
  Mechanical 1-2%, bio-prosthetic 0.5-1%; TV > MV > AoV

• Pathologies – thrombus, IE +/- destruction, pannus

• Diagnostic – TEE, 4D cardiac CT, fluoroscopy
### Prosthetic Valve Thrombosis Prevention (2014 ACC/AHA Guidelines)

<table>
<thead>
<tr>
<th>Valve type</th>
<th>Warfarin (INR goal)</th>
<th>Antiplatelet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical</td>
<td>- 2.5 = AVR (no TE risk*)</td>
<td>ASA 81 mg</td>
</tr>
<tr>
<td></td>
<td>- 3 = AVR (TE), MVR</td>
<td></td>
</tr>
<tr>
<td>Bio-prosthetic</td>
<td><em>Optional first 3 months</em></td>
<td>ASA 81 mg</td>
</tr>
</tbody>
</table>

*TE risk factors – AF, CVA, prior thrombosis, EF < 30%

*Direct oral anticoagulants not established (do not use)*