Aortic regurgitation
Pathophysiology, clinical presentation and management

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A 55 year old female who immigrated from India 20 years ago referred to your clinic for the evaluation of an incidentally found murmur on physical examination by PCP. She has no complaints. Auscultation of her chest reveals a harsh 3/6 systolic ejection murmur at 2\textsuperscript{nd} right ICS with radiation up the carotids and high pitched holodiastolic decrescendo murmur heard at 4\textsuperscript{th} left ICS and. Brisk carotid upstroke noticed. Apical impulse is diffuse, hyperdynamic and displaced laterally and inferiorly. Echocardiogram showed LVEF of 55\%, aortic regurgitation with RV 75 ml, LVEDD 60 mm and LVESD 45 mm, aortic root measures 4.2 cm.

What is the next step in diagnosis?

a) Refer the patient for aortic valve replacement
b) Refer the patient for aortic valve replacement + Aortic root repair
c) Repeat echocardiogram in 6 months
d) Physical exam findings do not correlate with echo findings. Repeat echo.
Identify the incorrect statement?

a) Rapid increase in LV diastolic pressure leads to premature closure of mitral valve

b) IV inotropes with or without IV nitroprusside indicated

c) Tachycardia can have deleterious effect on hemodynamic profile of this patient

d) Early diastolic murmur, low pitched and short duration

e) Balloon pump is contraindicated
Conflicts of interest

• None
Learning objectives

- Pathophysiology and presentation of aortic regurgitation
- Select appropriate testing
- Interpretation of the tests to determine the severity
- Timing and type of intervention
Etiology

Valvular causes

Root causes
Etiology - valvular causes

Congenital Leaflet abnormalities
- Bicuspid, Unicuspid or quadricuspid aortic valve
- Ventricular septal defect

Acquired Leaflet abnormalities
- Senile calcification
- Infective endocarditis
- Rheumatic disease - Fibrous tissue infiltrated leaflets get retracted
- Radiation induced valvulopathy
- Structural deterioration of bioprosthetic valves
- Toxin induced - anorectic drugs *fenfluramine*, *dexfenfluramine* and *phenteramine*
Etiology- aortic root causes

**Congenital/genetic aortic root abnormalities**
- Connective tissue disease: Loeyz Deitz, Ehlers-Danlos, Marfan syndrome, osteogenesis imperfecta
- Annuloaortic ectasia

**Acquired aortic root abnormalities**
- Systemic hypertension
- Autoimmune disease: systemic lupus erythematosus, ankylosing spondylitis, Reiter’s syndrome
- Aortitis: syphilitic, Takayasu’s arteritis
- Aortic dissection
- Trauma
Type Ia - Sinotubular junction enlargement and dilation of ascending aorta

Type Ib - Due to dilated sinus of vasa and sinotubuljunction

Type Ic - Dilated annulus

Type Id - Perforated leaflet
• Type II is associated with excessive leaflet motion from leaflet prolapse as a result of either excessive leaflet tissue or commissural disruption.

• Type III is associated with restricted leaflet motion seen with congenitally abnormal valves, degenerative calcification, or any other cause of thickening/fibrosis or calcification of the valve leaflets.
Combined and root and leaflet causes

- Aortic root dilatation
- Tension and bowing of individual leaflets
- Intensification of AR
- Thicken and retract
Pathophysiology of chronic aortic regurgitation

- Chronic aortic regurgitation- volume overload for the left ventricle.
- **Preload**: degree of myocardial stretch before contraction = LVEDV
- **Afterload**: force opposing LV contraction = wall stress that exists during systole (can also be expressed as aortic impedance)
- Larger heart volume -> diastolic stretch of LV (increased sarcomere length) -> Increases the force of contraction; *Frank-Starling law*
**Pathophysiology: LV and AR**

- Wall stress is tension applied across a cross sectional area

  \[
  \text{wall stress} = \frac{\text{pressure} \times \text{radius}}{2(\text{wall thickness})}
  \]

- Larger the LV cavity size and/or higher the pressure in LV cavity greater the wall stress

- As wall stress goes high, myocardial oxygen demand goes high as more ATP is required for the myofibrils to develop tension
LV remodeling in Chronic AR

Wall stress = \( \frac{p \times r}{2t} \)

Wall stress = \( \frac{p \times R}{2T} \)
LV function in chronic AR

• LV systolic function/stroke volume is maintained through a combination of chamber dilatation and eccentric hypertrophy (elongated myofibers replicate in series)

• LV functions as an effective high-compliance pump, handling a large stroke volume, often with little increase in filling pressure.

• During exercise, peripheral vascular resistance declines and, with an increase in heart rate, diastole shortens and the regurgitation per beat decreases, facilitating an increment in effective (forward) cardiac output without substantial increases in end-diastolic volume and pressure
LV remodeling in Chronic AR

Wall stress = \( \frac{p \times r}{2t} \)

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Decrease LV function

• As the left ventricle decompensates, interstitial fibrosis increases, compliance declines, and LV end-diastolic pressure and volume rise.

• In advanced stages of decompensation, wedge pressure, right ventricular (RV), and right atrial pressures rise, and the effective (forward) cardiac output falls, at first during exercise and then at rest.

• The normal decline in LV end-systolic volume or the rise in EF fails to occur during exercise.

• Symptoms of HF develop, particularly those secondary to pulmonary congestion.
Symptoms

Chronic severe aortic regurgitation

Progressive LV dilation, eccentric hypertrophy

Reduction in coronary flow reserve and chronic ischemia

LV dysfunction

Symptoms

- Exertional dyspnea
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Angina pectoris
- Nocturnal angina
- Uncomfortable awareness of the heartbeat
- Do not tolerate tachycardia
- Do not tolerate bradycardia
- PVC could be devastating due to large stroke volume
- Large stroke volume they sense as pounding in the head
Physical examination - murmur

- High frequency murmur begins early in diastole immediately after A2
- Best heard with diaphragm; patient leaning forward
- Severity correlates with duration
- Left sternal border 3rd / 4th ICS vs right sternal border
- Can also have systolic flow murmur due to increased flow across aortic valve
- S3 in LV failure
- Mid to late diastolic apical rumble
<table>
<thead>
<tr>
<th>Sign</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Musset sign</td>
<td>Head bob with each heartbeat</td>
</tr>
<tr>
<td>Corrigan and Water hammer pulse</td>
<td>Bounding carotid pulse and radial/ulnar/brachial artery pulse respectively</td>
</tr>
<tr>
<td>Traube sign</td>
<td>Pistol shot systolic and diastolic sounds over femoral artery</td>
</tr>
<tr>
<td>Muller sign</td>
<td>Systolic pulsations of the Uvula</td>
</tr>
<tr>
<td>Quincke sign</td>
<td>Repeated flushing and blanching of the capillaries in the nail beds and lips</td>
</tr>
<tr>
<td>Duroziez sign</td>
<td>Systolic murmur heard over the femoral artery when it is compressed proximally and a diastolic murmur when it is compressed distally</td>
</tr>
</tbody>
</table>
Assessment of severity of echo

• Color flow doppler
  • Jet width
  • Vena Contracta
  • Flow convergence- effective regurgitant orifice area

• PW doppler, flow reversal in descending aorta

• CW doppler- Density of regurgitant jet, Pressure half time

• Quantitative stroke volume method
Jet width/LVOT width

- Parasternal long axis view, apical to the aortic valve.
- <25%, 25 to 64% and ≥65%
- Not useful in eccentric jets or multiple regurgitant jets.
Vena contracta

- VC is the narrowest area of the jet, surrogate for ERO
- Zoomed in parasternal long axis view.
- VC <0.3 cm – mild
- VC >0.6 cm - severe
Proximal flow convergence

Regurgitant volume = ERO x VTI

\[ ERO = \frac{2\pi r^2 \times V_a}{V_{max}} \]

RV < 30 ml – mild
RV > 60 ml - severe
Diastolic flow reversal in descending aorta

• Proximal descending aorta or abdominal aorta. More specific when seen in abdominal aorta.
Pressure half time

- PHT is affected by compliance of Left ventricle
  Patients with severe AR with well compensated left ventricles, PHT can be in the moderate range
- On the other hand, patients with severe diastolic dysfunction may have short PHT even with mild Aortic regurgitation

- PHT > 500 msec - Mild AR
- PHT < 200 msec - Severe AR
Stroke volume method

\[ \text{CSA}_{\text{LVOT}} \times \text{VTI}_{\text{LVOT}} - \text{CSA}_{\text{MV}} \times \text{VTI}_{\text{MV}} = \text{RV} \]
## Summary - severity of aortic regurgitation

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mild aortic regurgitation</th>
<th>Severe aortic regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venacontract width (cm)</td>
<td>&lt;0.3</td>
<td>≥0.6</td>
</tr>
<tr>
<td>Jet width/LVOT width*</td>
<td>&lt;25</td>
<td>≥65</td>
</tr>
<tr>
<td>Jet CSA/LVOT CSA*</td>
<td>&lt;5</td>
<td>≥60</td>
</tr>
<tr>
<td>ERO (cm²)</td>
<td>&lt;0.1</td>
<td>≥0.3</td>
</tr>
<tr>
<td>Rvol (ml/beat)</td>
<td>&lt;30</td>
<td>≥60</td>
</tr>
<tr>
<td>RF (%)</td>
<td>30</td>
<td>≥50</td>
</tr>
</tbody>
</table>

*Central jets only*
Other imaging modalities-
Cardiac MRI

• If echocardiographic evaluation is suboptimal can consider CMR.

• Most accurate non-invasive technique for assessing LV end systolic volume, diastolic volume and mass.

• Accurately quantifies the severity of AR based on antegrade and retrograde flow volumes in the ascending aorta.
Management

Asymptomatic patients with mild to moderate AR and normal LV size (ACC stage B), periodic follow up and echo every 12 to 24 months.

Asymptomatic severe AR patients with normal LV size and function (ACC stage C1)- echo every 6 months.
Antihypertensive therapy

• No specific therapy to prevent disease progression in chronic AR.
• Short term studies spanning 6 to 24 months have shown benefit with hydralazine, felodipine, nifedipine and ACEI; however prospective RCT have not shown any benefit in preventing LV dysfunction or progression of AR.

Antihypertensive therapy

• Treatment of hypertension is recommended with patients with chronic AR (stages B&C) preferably with dihydropyridine calcium channel blockers or ACE/ARBs. (COR I; LE B)

Timing of intervention

- **Stage B**: Progressive aortic regurgitation
- **Stage C1**: Progressive LV dilation, eccentric hypertrophy
- **Stage C2**: Decrease in LVEF
- **Stage D**: Symptoms
  - Death
Survival in severe symptomatic aortic regurgitation without intervention

Onset of symptoms

- LV function may deteriorate even during the asymptomatic period
- Small group of patients may incur significant impairment in LVEF
- Biomarkers such as BNP and echo parameters such as myocardial strain may play a role in identifying high risk patients but more data is needed at this time


Severity of symptoms and prognosis after surgery

LVEF and prognosis after successful AVR

What does it mean for our patients?

LV dysfunction is more likely reversible after AVR

| If detected early | Before left ventricle is markedly dilated | Before significant symptoms develop |

Send patients for surgery even with mild symptoms and/or even with mild LV dysfunction/cavity dilation.
Indications for AVR in chronic AR

Severe AR (Stage C&D)

Symptomatic Stage D

Asymptomatic Stage C

AVR Class I

...
Asymptomatic (Stage C)

- LVEF <50%
  - Stage C2
  - AVR (Class I)

- Other cardiac surgery
  - AVR (Class I)

- LVEF 50%
  - LVESD >50 mm
  - Stage C2
  - AVR (Class IIa)

- LVEF >50%
  - LVESD <50 mm
  - LVEDD <65 mm
  - Low Surgical risk
  - AVR (Class IIb)

- LVEF >50%
  - LVESD <50 mm
  - LVEDD <65 mm
  - Periodic monitoring
Stage B aortic regurgitation

Progressive AR (Stage B; moderate) → Other Cardiac surgery

- Yes: AVR (Class IIa)
- No: Periodic monitoring
AVR vs. replacement of aorta vs. Both

- Indications for surgery are same regardless of the etiology
- Concomitant surgery to repair aortic sinuses or replace the ascending aorta when aortic dilation is greater than 45 mm
Operative procedures

• Standard approach is AVR. Concurrent aortic root replacement when indicated.

• Leaflet repair may be an option in select group of patients
  • Torn leaflet from trauma
  • Prolapsed leaflet
  • Leaflet perforation from IE- pericardial patch

• Primary aortic root disease- replacement with a graft that has prosthetic valve and reimplantation of coronaries.

• In a select group of patients, native valve can be spared, and aortic root can be repaired or replaced.
Bicuspid aortic valve - Ascending aorta

Repair aortic sinuses or replace AA

- >5.5 cm
- >5 cm with family history of dissection
- ≥0.5 cm/ year
- When undergoing AVR + >4.5 cm
TAVR and AR

• Valve-in-valve THV for failing bioprosthesis
• Challenges for native pure aortic regurgitation
  • Absence of annular or leaflet calcifications
  • Large stroke volume
  • Aortic root dilation – predisposes to embolization or malposition
• This can be addressed to some extent by oversizing the valve
• Few case reports and small case series of non dedicated THV (both balloon and self expandable)
• Dedicated valves- Jena Valve, J valve- currently under investigation in high risk patients with native aortic valve regurgitation.

• Infective endocarditis
• Aortic dissection
• Trauma
• Large regurgitant volume floods noncompliant LV
• Rapidly rising LV diastolic pressures exceeding that of LA
• Premature closure of MV
• Profound hypotension
• Shock

• Physical examination is not very impressive.
• Most of the signs of severe aortic regurgitation are absent.
• Early closure of the mitral valve may be audible in some cases.
• Even a normal LV can not sustain the burden of acute AR
• Prompt surgical intervention
• While waiting for surgery IV inotropic agent ± vasodilator
• **Beta blocker and IABP contraindicated.**
• Hemodynamically stable patients with IE, can defer surgery for 5 to 7 days
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