Disease of the aorta: When to worry? When to refer?

DATE: SEPT 11, 2016 PRESENTED BY: ABIGAIL KHAN, MD

Typical case

• 32 year old female with palpitations, dyspnea
• Echocardiogram ordered
Outline

• Imaging the aorta: evaluation of aortic size
• Overview of chronic aortic disease
  – Focus on thoracic disease
• Management of the dilated aorta
  – Medical
  – Surgical referral
• Who to refer and when

Imaging and Sizing the Aorta
Imaging the aorta

- Chest x-ray
- Transthoracic echocardiogram
- Transesophageal echocardiogram
- CT
- MRA

### Choice of modality

<table>
<thead>
<tr>
<th>Echocardiography</th>
<th>CT</th>
<th>MRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>No radiation</td>
<td>Image coronaries</td>
<td>No radiation</td>
</tr>
<tr>
<td>Valve function</td>
<td>Good for dissections, stents</td>
<td>Valve function</td>
</tr>
<tr>
<td>Chamber size/function</td>
<td>Can measure max size</td>
<td>Chamber size/function</td>
</tr>
<tr>
<td>Bedside use</td>
<td></td>
<td>Can measure max size</td>
</tr>
<tr>
<td>Oblique imaging</td>
<td>Radiation risk</td>
<td>Time consuming</td>
</tr>
<tr>
<td>Limited windows</td>
<td>Less functional information</td>
<td>Access</td>
</tr>
<tr>
<td>Inferior aortic wall visualization</td>
<td></td>
<td>Coronaries not as well evaluated</td>
</tr>
<tr>
<td>Visualization</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NOTE: Measurements may not agree!
What is normal size?


What is normal size?

Devereux et al. Am J Cardiol 2012; 110(8): 1189-1194
What is normal size?

Etiology of Thoracic Aortic Disease
Thoracic aortic disease

- Inherited aortopathy
  - e.g. Marfan syndrome, BAV
- Acquired disease
  - Degenerative related to HTN, smoking, athero
- Inflammatory disease
  - Vasculitis, infection
- Congenital disease
  - Coarctation, vascular rings

Inherited aortopathy

- Bicuspid aortic valve
- Marfan syndrome
- Loeys-Dietz syndrome
- Ehlers-Danlos syndrome
- Familial aortopathy
Bicuspid aortic valve

- 1% of population
- Aortopathy affects 30-80% of patients with BAV
  - Tubular ascending aorta affected in 2/3
  - Descending aorta can be involved
  - Root phenotype also exists
- Dissection rare but can occur
  - 0.1% per patient year

Tzemos et al. JAMA 2008; 200: 1317-35

BAV management

- Yearly imaging even if valve function is relatively normal
  - Can screen every two years if aorta < 4 cm
- Screen first degree relatives
- No data regarding use of beta-blockers or ARBs
  - Ongoing trial
- Continued aortic dilation can occur after aortic valve replacement; need to continue surveillance

Michelena et al. Int J Card 2015; 201: 400-7
Marfan syndrome

• Most common connective tissue disorder
  – 2-3/1000 people
• Fibrillin gene mutation
  – Increased TGF-β signaling
  – >500 known mutations
• Autosomal dominant inheritance
  – 75% inherited
  – 25% sporadic

Revised Ghent criteria

<table>
<thead>
<tr>
<th>Family history</th>
<th>No family history</th>
</tr>
</thead>
<tbody>
<tr>
<td>One of any of the following:</td>
<td>One of any of the following:</td>
</tr>
<tr>
<td>1. Ectopia lentis</td>
<td>1. Aortic criterion + ectopia lentis</td>
</tr>
<tr>
<td>2. Systemic score ≥ 7</td>
<td>2. Aortic criterion + causal FBN1</td>
</tr>
<tr>
<td>3. Aortic criterion</td>
<td>3. Aortic criterion + systemic score ≥ 7</td>
</tr>
<tr>
<td>4. Ectopia lentis + causal FBN1</td>
<td></td>
</tr>
</tbody>
</table>

Aortic criterion= Aortic diameter Z-score≥2 or aortic root dissection
Calculate z-score at www.marfandx.org

Loeps BL J Med Genet 2010; 47:476e485
Systemic score

<table>
<thead>
<tr>
<th>Wrist/Thumb sign</th>
<th>Pectus deformities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hindfoot deformities</td>
<td>Flat foot</td>
</tr>
<tr>
<td>Spontaneous PTX</td>
<td>Dural ectasia</td>
</tr>
<tr>
<td>Protrusio acetabull</td>
<td>Scoliosis or Kyphosis</td>
</tr>
<tr>
<td>Reduced elbow extension</td>
<td>Facial features</td>
</tr>
<tr>
<td>Striae</td>
<td>Severe myopia</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>Reduced US/LS + Increased arm span/height</td>
</tr>
</tbody>
</table>

Photos and calculator at http://www.marfandx.org/dx/score
MFS: Medical management

• Strict BP control
• Beta-blocker in all patients
• ARB unless contraindicated
• Repeat imaging initially at 6 month interval, then annual unless root is growing in size

AT II blockade and MFS

• Initial enthusiasm: mouse data and a small trial
• COMPARE trial: Open label, losartan vs. no losartan. Rate of aortic growth 0.26 mm vs. 0.45 mm/year (p=0.01).
• 3 subsequent trials have failed to show an overall benefit
  – Marfan Sartan: 303 patients randomized to losartan vs. placebo; 86% on beta-blockers.
  – Apparent benefit in patients with FBN1 mutation
    – Lacro: 608 patients randomized to losartan vs. atenolol
    – Forteza: 140 patients randomized to losartan vs. atenolol

Brooke et al. NEJM 2000; 358:2787-95
Millet et al. EHJ 2015; 36: 2100-06
Groenink et al. EHJ 2013; 34:3491-50
Lacro et al. NEJM 2014; 371: 2061-71
Forteza et al. EHJ 2016; 37: 978-85
Case #1

- Diagnosed with MFS
  - FBN gene testing +
  - MRI confirmed aortic dimensions
- Repeat echo in 6 months showed stable aortic size
- Regular follow-up
  - Beta-blocker, losartan
  - Pregnancy counseling
  - Family screening

Case #2

- 29 year old male with no history of heart disease presents to PCP with 1 year of gradually progressive DOE, orthopnea, PND and exertional chest pressure

- Referral to cardiology with echo ordered
Case #2

8 cm ascending aorta, severe AI and LV dysfunction → emergent transfer and surgery

Genetic testing reveals TGF-β variant of unknown significance

Loeys-Dietz syndrome

- TGF-β mutations
- Autosomal dominant
- Manifestations:
  - Ocular hypertelorism, bifid uvula, cleft palate, club feet
  - Arterial tortuosity
  - Vascular dilation and dissection
- Can dissect at small diameters
- Need to image entire vasculature yearly
Ehlers-Danlos

A group of genetic connective tissue disorders

- Overall frequency 1 in 5000
  - Hypermobility type most common
  - Vascular type (Type IV EDS) is rare

Ehlers-Danlos, type IV

- ~1 in 100,000
- COL3A1 mutation
- Autosomal dominant
- Manifestations
  - Thin skin, easy bruising, hypermobility
  - Arterial aneurysms and rupture
  - Intestinal and uterine manifestations
- 80% have a major event by age 40
Turner syndrome

- 1/2000 women
- 50% monosomy X, 50% mosaic
- Aortic disease
  - ~30% of women have aortic dilation
  - 100x higher risk of aortic dissection
- Associated cardiovascular abnormalities
  - Diffuse vasculopathy, ↑ arterial stiffness, hypertension
  - BAV (30%), coarctation (12%)


Case #3

- 37 year old female
  - Diagnosed with TS in adolescence
    - Bicuspid aortic valve
    - Hypertension on atenolol
  - Prior echocardiogram: “Aorta not well visualized”
  - Self-referred to cardiology practice

- MRI: Aortic root and mid-ascending 37 mm
  - BSA 1.88 m²
**Turner syndrome**

*Imaging*

> Aortic Dilatation and Dissection in Turner Syndrome

Lex Ann Matura, PhD; Vincent B. Ho, MD; Douglas R. Rosing, MD; Carolyn A. Bendy, MD

Background: Thoracic aortic aneurysms and dissections in Turner syndrome (TS) are uncommon. Methods: Aortic diameters and thoracic computerized tomography (CT) computed tomography were prospectively measured in 35 TS women. Results: Aortic diameter of 3.7 cm or greater was significant for TS. Conclusion: The risk for aortic dissection is rarely increased in young women with TS. Because of their small stature, ascending aortic dimensions >5 cm may represent significant dilatation; thus, the use of aortic size index is preferred. Individuals with a dilated ascending aorta defined as aortic size index >2.5 cm²/m² require chronic cardiovascular surveillance. Those with aortic size index ≥3 cm²/m² are at highest risk for aortic dissection. (Circulation. 2007;116: 1663-70)

Key Words: aneurysm • aorta • magnetic resonance imaging • sex chromosomes

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**Familial thoracic aortic aneurysm**

- Arterial dilation and risk of dissection
- No systemic features of CTD
- Autosomal dominant, penetrance is variable
- Many associated mutations
- No data on benefits of medical management
Sporadic vs. genetically mediated?

<table>
<thead>
<tr>
<th>Sporadic</th>
<th>Genetically-mediated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older age</td>
<td>Younger patient</td>
</tr>
<tr>
<td>Smoking</td>
<td>Family history</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Characteristic imaging features</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>Syndromic</td>
</tr>
<tr>
<td>Descending aorta</td>
<td>• Multisystem involvement</td>
</tr>
</tbody>
</table>

Screening

• Screen 1st degree relatives of individuals with thoracic aneurysm or dissection with imaging
  – Genetic testing can also be useful
  – Screen “healthy at risk” individuals every 5 years since age of onset is variable
• Consider screening second degree relatives if multiple affected family members

Timing of Surgery

Recommendations on interventions on ascending aortic aneurysms

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery is indicated in patients who have aortic root aneurysm, with maximal aortic diameter ( \geq 50 ) mm for patients with Marfan syndrome.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Surgery should be considered in patients who have aortic root aneurysm, with maximal ascending aortic diameters:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ( \geq 45 ) mm for patients with Marfan syndrome with risk factors.</td>
<td>IIA</td>
<td>C</td>
</tr>
<tr>
<td>- ( \geq 50 ) mm for patients with bicuspid valve with risk factors.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ( \geq 55 ) mm for other patients with no elastopathy.</td>
<td>IIB</td>
<td>C</td>
</tr>
<tr>
<td>Lower thresholds for intervention may be considered according to body surface area in patients of small stature or in the case of rapid progression, aortic valve regurgitation, planned pregnancy, and patient’s preference.</td>
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</tr>
</tbody>
</table>

Risk factors for early surgery

- Marfan syndrome
  - Family history of dissection
  - Rapid expansion (>2-5 mm/year)
  - Progressive AR, severe AR or MR
  - Female contemplating pregnancy
  - CSA/height > 10

- Bicuspid aortic valve
  - Family history of dissection
  - Rapid expansion
  - Coarctation
  - Hypertension

2010 ESC Guidelines for the management of grown-up congenital heart disease. EHJ 2010; 31: 2815-57
2010 ACCF/AHA Guidelines and Management of Adults with Thoracic Aortic Disease. Circ 2010; 121: 1544-79
Additional Conditions

Aortitis

<table>
<thead>
<tr>
<th>Infectious</th>
<th>Inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus</td>
<td>Giant cell arteritis</td>
</tr>
<tr>
<td>Salmonella</td>
<td>Takayasu arteritis</td>
</tr>
<tr>
<td>Other rare causes</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>• Syphilis</td>
<td>Ankylosing spondylitis</td>
</tr>
<tr>
<td></td>
<td>Wegener’s granulomatosis</td>
</tr>
<tr>
<td></td>
<td>Reactive arthritis</td>
</tr>
<tr>
<td></td>
<td>Behcet syndrome</td>
</tr>
</tbody>
</table>

If imaging/history is suggestive, refer!
Case #4

- 61 year old male with aortic coarctation
- Childhood history
  - Diagnosed at age 14
  - Underwent end to end anastomosis (failed)
  - Subsequent interposition graft
  - Lifelong treatment for hypertension
- Recent history
  - Worsening BP control despite multiple agents
  - DOE, intermittent dizziness

Aortic Coarctation

![Image of Aortic Coarctation](image-url)
Coarctation repairs

- End to End
- Patch
- Interposition graft
- Subclavian flap
- “Jump” graft

Aortic coarctation

- 5-8% of congenital heart disease
  - BAV, VSD, intracranial aneurysms (3-5%), MV disease
- Long-term complications after repair
  - Hypertension
  - Increased aortic stiffness
  - Re-coarctation
  - Aortic aneurysm
  - Coronary artery disease
Case #4

- Referred as a new patient to ACHD clinic
  - MRI: Discrete coarctation with minimal diameter 6 mm. No aneurysm.
  - Cardiac catheterization: P2P gradient 24 mmHg
- Referred to surgery
  - Complex redo redo procedure
  - Ascending to descending extra-anatomic graft
  - Improved BP control at initial follow-up

Aortic coarctation

- Long-term follow-up:
  - Regular imaging (echo for gradients, CT or MRI for anatomy)
  - Hypertension management
  - Physical exam:
    • Upper and lower BPs
    • Radiofemoral delay
  - Consideration of screening for cerebral aneurysms
  - ACHD specialist care required
Summary: Questions to ask

- How old is the patient?
- Which portion is dilated (root, ascending?)
- Is the aortic valve bicuspid?
- Do they have risk factors for degenerative disease?
  - Smoking, HTN, hyperlipidemia
- Are there other findings to suggest a connective tissue disorder or syndrome?
- Is there a family history?
Who to refer

- Known conditions
  - Connective tissue disorder
  - Aortic coarctation (ACHD specialist)
  - Turner syndrome
- Suspicion for connective tissue disorder
  - Dilated aorta of unknown etiology in young patient
- Family history
  - Multiple affected family members or 1st degree relatives of patients with known inherited aortic disease
  - Consideration of genetics evaluation