Thoracic Aortic Aneurysms: Etiology, Diagnosis, and Management

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• No relationships to disclose
• Will discuss the off-label use of ARBs in thoracic aortic disease
Aortic Anatomy 101: Nomenclature

- Aortic arch
- Ascending thoracic aorta
- Sinotubular junction
- Aortic root (Sinuses of Valsalva)
- Annulus
- Descending thoracic aorta
- Abdominal aorta
Aortic Anatomy 101: Incorrect Nomenclature

- Aortic arch
- Descending aorta
- Aortic root
- Annulus
Be wary of poorly worded imaging reports

Aortic root?  Ascending aorta?
Background

- Actual prevalence of thoracic aortic aneurysms is unknown
- Diagnosis rate
  - 16.3 cases per 100,000 men per year
  - 9.1 cases per 100,000 women per year
- Diagnosis rate is increasing
  - Aging population
  - Improved diagnostic imaging techniques
  - More frequent use of imaging
- Overall mortality rates are poorly defined.

Background

- Involve different segments of thoracic aorta
  - 60% aortic root and/or ascending aorta
  - 10% arch
  - 40% descending aorta
  - 10% thoracoabdominal aorta

- The etiology, natural history, and treatment of thoracic aneurysms differ for each segment

- Common underlying histopathology is degeneration of the aortic media.
Medial Degeneration of the Aorta

Normal

Degradation of the extracellular matrix
Loss of elastic fibers
Smooth muscle cell necrosis/apoptosis
Acquired Medial Degeneration

- **Senile medial degeneration**
  - Occurs commonly with age
  - Process is accelerated by hypertension
  - Primarily affects descending thoracic aorta
- **Atherosclerosis as a risk factor?**
  - Weakly associated with descending aneurysms
  - Not associated with root or ascending aneurysms

Ascending vs. Descending Aneurysms

Congenital Aneurysms: Marfan Syndrome

- Autosomal dominant disorder of connective tissue
  - Due to mutations in the gene for fibrillin-1 (FBN1)
- Associated with aneurysms of the aortic root
  - *Annuloaortic ectasia.*
Congenital Aneurysms: Bicuspid Aortic Valve

- BAV associated with an increased risk of aortic dilatation, aneurysm, and dissection
- \( \approx 50\% \) have a dilated ascending aorta or root
- Originally considered to be “post-stenotic dilatation”
  - Rates similar for AS, AI, or normally functioning BAV
- Medial degeneration appears to be the culprit
- Several patterns of involvement:
  - 60% ascending aorta; 10% aortic root; 30% both.

Familial Thoracic Aortic Aneurysm and Dissection Syndrome

- Medial degeneration is seen in ascending aneurysms or dissection in the absence of known risk factors
- Cases may be sporadic, but are often familial
  - ≈ 20% of those with thoracic aortic aneurysms have a family history of a thoracic aneurysm
- Dominant inheritance
- Marked variability in the expression and penetrance
- Known mutations identified in ≈ 20% of families:
  - ACTA2 (14%), TGFBR2 (4%), MYH11 (1%).

Congenital Thoracic Aortic Aneurysms

- Whether due to MFS, BAV, or a familial thoracic aortic aneurysm syndrome, relatives may be affected

- Therefore first-degree relatives of affected patients should be screened with an imaging study!
Thoracic Aortic Aneurysms: Less Common Etiologies

- Other connective tissue disorders
  - Ehlers-Danlos syndrome, vascular type (type IV)
  - Loeys-Dietz syndrome
- Turner syndrome
- Vasculitis
  - Takayasu's arteritis
  - Giant cell arteritis
  - Non-specific aortitis
- Infectious aortitis (mycotic aneurysm)
- Syphilitic aortitis
- Trauma.
Thoracic Aortic Aneurysms: Presentation and Detection

- Symptoms are uncommon
- Few are detectable on physical exam
  - AI murmur may be present
- Large majority are discovered incidentally
  - on a routine CXR, CT, or echocardiogram
- Others go undetected until they dissect or rupture.
Thoracic Aortic Aneurysms: Diagnostic Modalities

- Contrast-enhanced CT scanning
- Magnetic resonance imaging (MRI and MRA)
- Echocardiography (TTE and TEE)
Contrast-enhanced CT Scanning: Standard Axial Imaging
A Limitation of Axial CT: The Risk of Mismeasurement
CTA with 3-D Reconstruction Better Defines True Aortic Anatomy
CTA with Planar Reformats

Coronal

LAO
MRA (MRI with gadolinium): Aortic Root Aneurysm

Coronal

LAO
MRI without Contrast: Black Blood and Bright Blood Imaging
Transthoracic Echocardiography:
Aortic root visualized, but not ascending aorta
Transthoracic Echo: Ascending aorta visualized, but ? underestimate
Transesophageal Echocardiography
## Which Modality to Choose: A General Guideline

<table>
<thead>
<tr>
<th>Routine TAA</th>
<th>Contrast-enhanced CT</th>
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<tbody>
<tr>
<td>Disease of the aortic root</td>
<td>Echocardiogram</td>
</tr>
<tr>
<td>Tortuous aorta or arch aneurysm</td>
<td>CTA (3-D reconstruction) or MRA</td>
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<tr>
<td>Allergy to iodinated contrast</td>
<td>MRA</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>Non-contrast MRI or Non-contrast CT</td>
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</table>
Thoracic Aortic Aneurysms: Natural History

Asymptomatic TAA

Growth
Rates of Growth

Thoracic Aortic Aneurysms: Natural History

Asymptomatic TAA

Growth

Rupture

Dissection
Medical Management of Thoracic Aortic Aneurysms
Beta Blockers

- Proven benefit in Marfan syndrome
- No demonstrable benefit in Marfan syndrome with small aneurysms
- No trials in TAAs of other etiologies
- Mainstay of therapy
New Therapeutic Strategy For Treating Marfan Syndrome

- Hal Dietz et al
  - Many consequences of Marfan syndrome result from excessive TGF-β signaling
- Previous studies had shown that losartan, an angiotensin II type 1 receptor (AT1) blocker, inhibits activity of TGF-β.
Efficacy of Losartan in Mouse Model of MFS: Aortic Growth by Echo Over 6 Months

Habashi J, et al. Science 2006;312:117--121
Efficacy of Losartan in Mouse Model of MFS: Aortic Wall Architecture
COMPARE (COzaar in Marfan PAAtients Reduces Aortic Enlargement) Trial

- Multicenter, open-label, randomized, controlled trial with blinded assessments in adults with MFS
- 233 subjects (not already on ACEI/ARB) were randomized to 50 mg losartan as add on Rx vs. no additional Rx
- Primary endpoint = rate of aortic dilatation by MRI after 3 years of follow-up
- Aortic root growth was significantly slower in losartan group (0.77 vs. 1.35 mm, P < 0.014)
  - No correlation between BP and aortic root growth

A randomized, open-label, controlled trial of BB alone or BB + losartan over 3 years

Taiwan, 28 subjects

Atenolol vs. losartan for MFS: A randomized double-blind placebo-controlled trial

- Pediatric Heart Network, Boston Children’s Hospital
  - 21 Centers
- 608 subjects, ages 6 months to 25 yr (mean 11 yr)
- Randomized to:
  - Atenolol, titrated by heart rate (mean dose $\approx 150$ mg in young adults) or
  - Losartan (mean dose $\approx 85$ mg in young adults)
- Followed by echo imaging over 3 years

Change in Aortic Root Diameter and z Score, by Treatment Group

Freedom from Adverse Clinical Outcomes

This trial differed from the others:

- Losartan vs. atenolol, rather than add-on therapy

- Perhaps combination therapy would be more effective than either agent alone…
Marfan-Sartan Trial

- A multi-center (7 French sites), randomized, double-blind, placebo-controlled, trial comparing add-on losartan vs. placebo in Marfan patients already on standard therapy
- 303 patients, age ≥ 10, mean age 29.9 years
  - 86% receiving beta-blockers at baseline
  - Rx losartan 50-100 mg
- Median follow-up 3.5 years
- No change in rate of aortic root growth either by size ($p = 0.36$) or z score ($p = 0.69$)
  - No change in event rates

Pharmacologic Management of Thoracic Aortic Aneurysms in 2017?

- We have yet to define optimal pharmacologic therapy
- For now beta blockers remain the mainstay
  - If intolerant to beta-blockers, consider losartan
  - If room for two agents, it would be reasonable to add losartan to the beta-blocker
Thoracic Aortic Aneurysms: Natural History

Asymptomatic TAA

Growth

Rupture

Dissection

Repair
Indications for Intervention
Weighing the Risk of Aortic Dissection vs. the Risk of Surgery
Rate of Aortic Events vs. Ascending Aortic Diameter

Risk of Aortic Dissection vs. the Risk of Surgery

Mortality of Unoperated Ascending TAA vs. Size

- Acquired
- Congenital
Ascending Aortic Aneurysms: Indications for Aortic Repair

- Idiopathic: ≥ 5.5 cm
    - High risk surgery: ≥ 6.0 cm
- Congenital (e.g., Marfan, familial): ≥ 5.0 cm
    - Low risk for surgery: ≥ 4.5 cm
- BAV: ≥ 5.5 cm
    - Low risk for surgery: ≥ 5.0 cm
- Rapid expansion (≥ 0.5 cm/year)
- Severe AR: Symptoms or LV dysfunction.

J Am Coll Cardiol 2010; 55:e27–e129
J Am Coll Cardiol 2016; 67:724–731
What Are the Surgical Options?

- Ascending thoracic aortic aneurysms
- Root aneurysms
- Arch aneurysms
- Descending thoracic aortic aneurysms
Ascending Thoracic Aortic Aneurysm: Interposition Tube Graft
Root Aneurysm: Valve-Sparing Aortic Root Repair
Arch Aneurysm:
Total Arch Replacement
Descending Thoracic Aortic Aneurysm: Open Surgical Repair
Descending Thoracic Aortic Aneurysm: Endovascular Stent-Graft Repair
Time’s up...