

Thoracic Aorta Disease Update: Etiology, Diagnosis, and Management

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Presenter Disclosure Information



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- No relationships to disclose

Objectives



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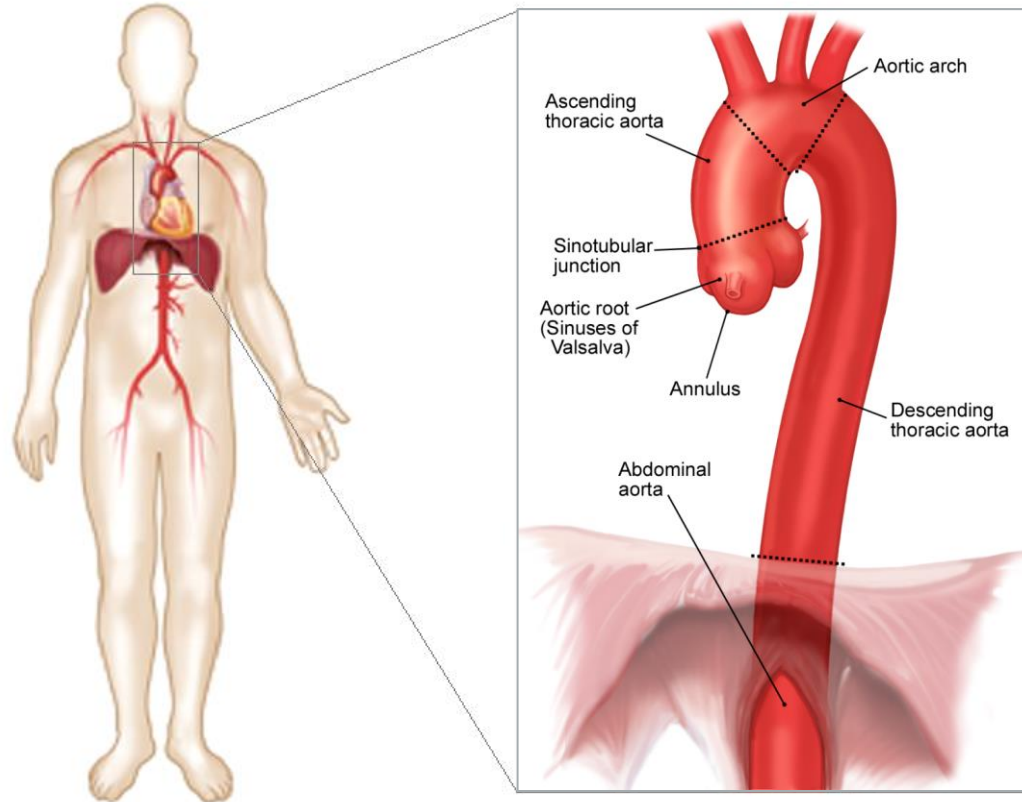
1. Recognize the risk factors for thoracic aortic aneurysms
2. Know the importance of screening family members
3. Understand how to choose among the imaging modalities
4. Consider the data on medical therapies
5. Be aware of the size thresholds for aortic repair
6. Be familiar with the available surgical and endovascular options.

Aortic Anatomy 101



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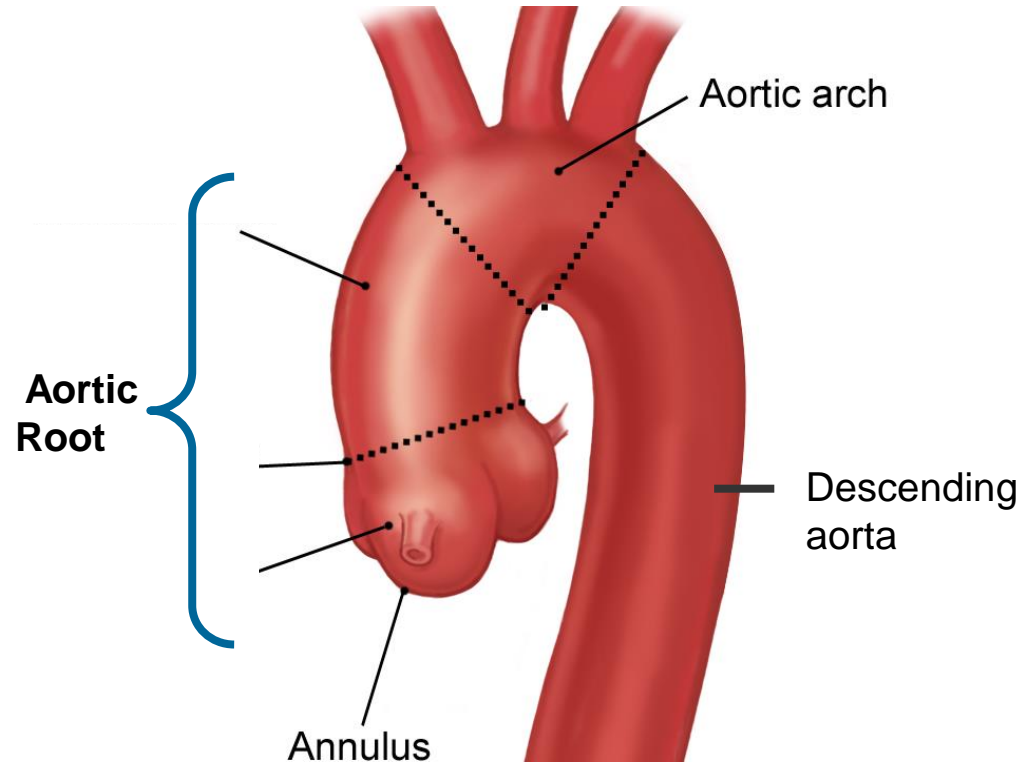


Thoracic Aortic Anatomy: Nomenclature



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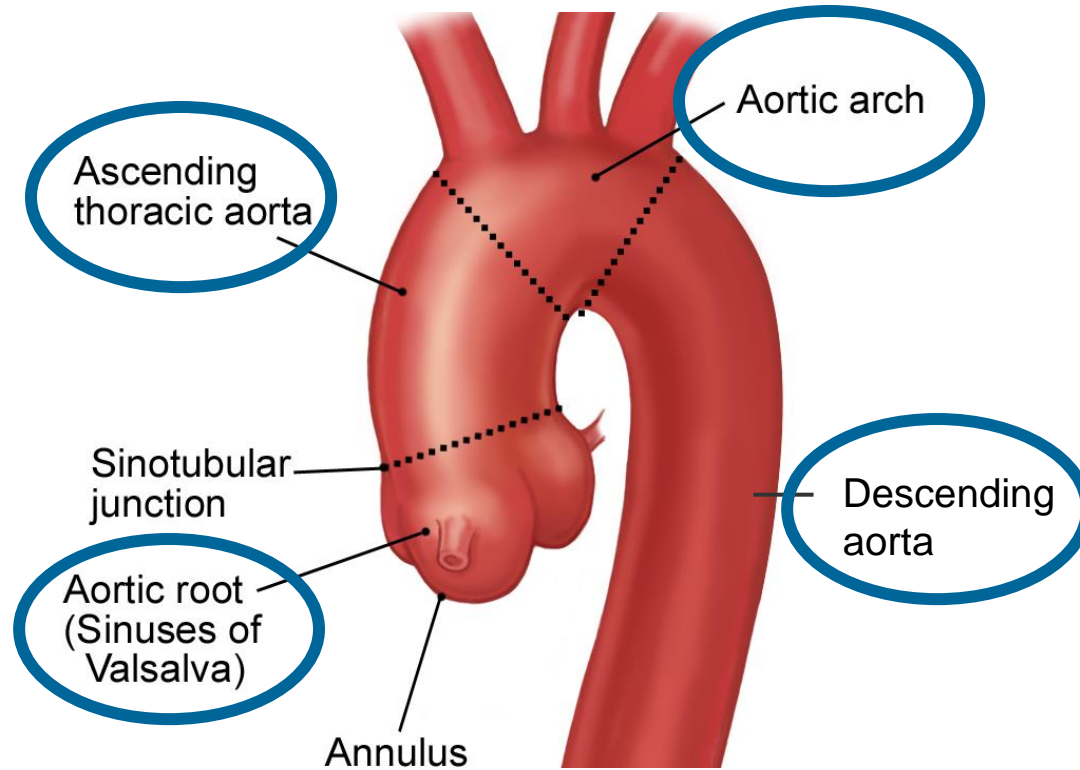


Thoracic Aortic Anatomy: Nomenclature



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Be wary of poorly worded imaging reports



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- Actual prevalence of thoracic aortic aneurysms is unknown
 - There are no agreed upon definitions of “dilation” or “aneurysm” of the aortic root or ascending aorta
- Diagnosis rate
 - 10-16 cases per 100,000 men per year
 - 5-9 cases per 100,000 women per year
- Diagnosis rate is increasing
 - Aging population
 - Improved diagnostic imaging techniques
 - More frequent use of imaging

Olsson C, et al. Circulation 2006;114:2611

McClure RS, et al. J Thorac Cardiovasc Surg 2018;155:2254-64

Thoracic Aortic Aneurysms: Etiology



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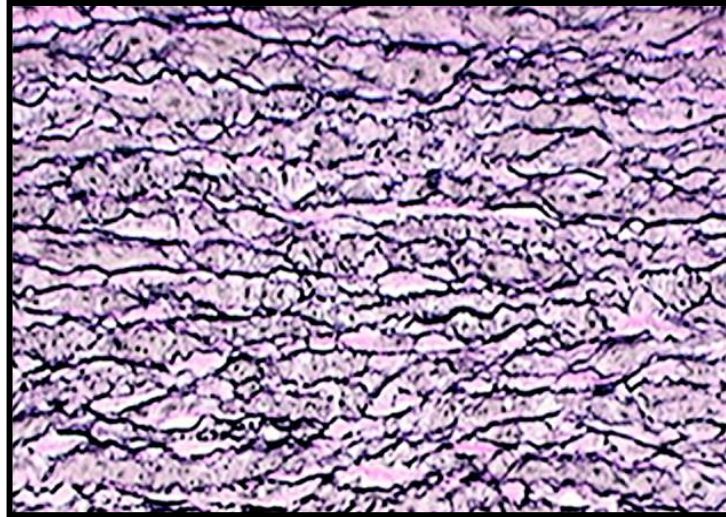
- The most common underlying pathology = medial degeneration
 - Fragmentation and loss of elastic fibers
 - Smooth muscle apoptosis
 - Elastic fiber and smooth muscle cell disorganization
 - Mucoïd extracellular matrix accumulation
- Aortic wall becomes weak
- Aorta dilates.

Medial Degeneration of the Aorta

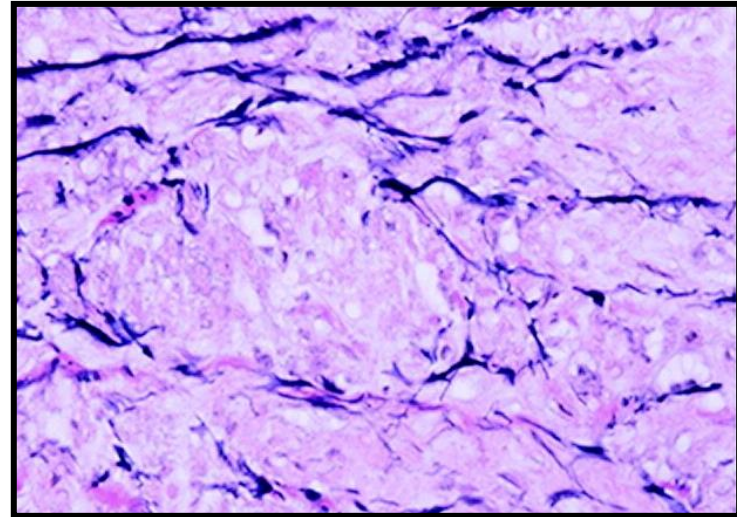


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Normal



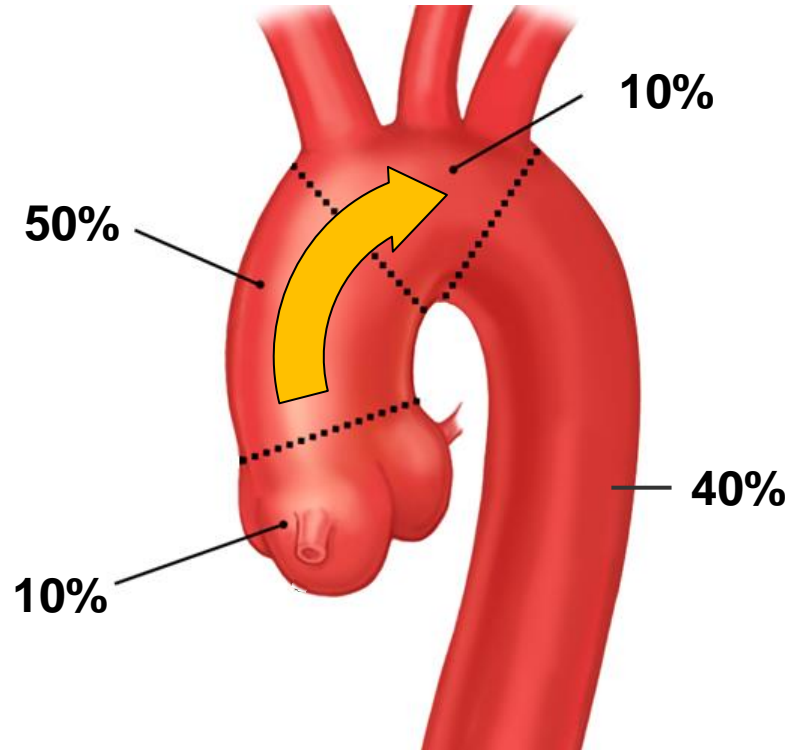
Loss of elastic fibers
Smooth muscle cell apoptosis
Mucoid extracellular matrix
accumulation

Thoracic Aortic Anatomy: Aneurysm Involvement by Segment



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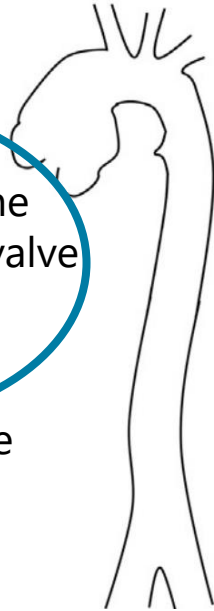
Root/Ascending (Proximal) vs. Descending (Distal) Aneurysms



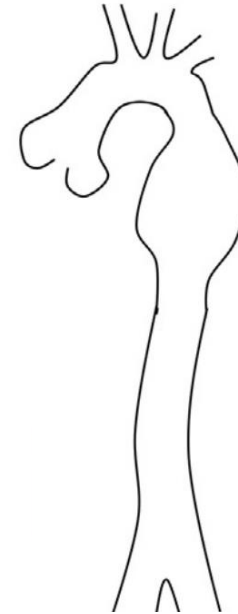
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- Marfan syndrome
- Bicuspid aortic valve
- Familial thoracic aortic aneurysm
- Turner syndrome
- Loeys-Dietz
- vEDS
- Sporadic



Root/ascending
TAA



Descending
TAA

- Advanced age
- Hypertension
- Atherosclerosis
- Smoking

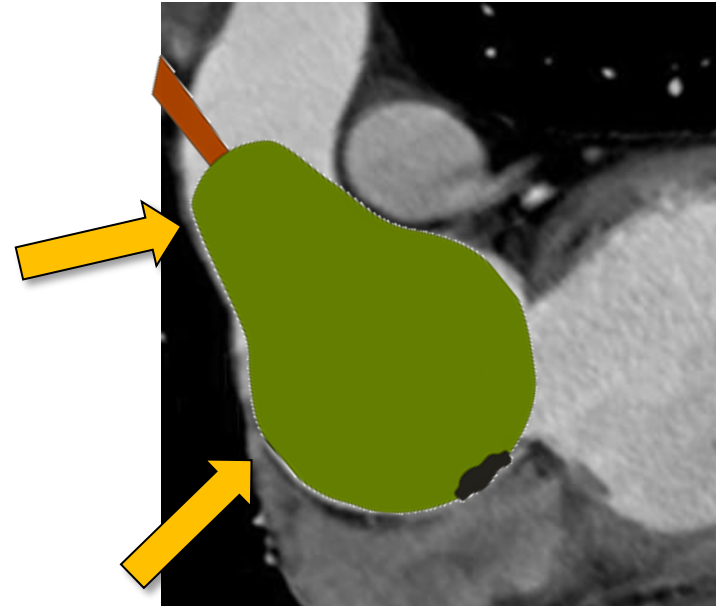
Congenital Medial Degeneration: Marfan Syndrome



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- Autosomal dominant disorder of connective tissue
- Associated with aneurysms of the aortic root, sparing the ascending aorta
 - *Annuloaortic ectasia*
- Due to mutations in the gene for fibrillin-1 (FBN1).



Congenital Aneurysms: Bicuspid Aortic Valve



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- 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, AR, or normally functioning BAV
 - Medial degeneration is again the culprit
- Several patterns of involvement:
 - 60% ascending aorta; 10% aortic root; 30% both.

Familial Thoracic Aortic Aneurysm and Dissection Syndrome



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- Medial degeneration is seen in ascending aneurysms or dissection in the absence of known risk factors
 - Cases may be sporadic, but are often familial
 - $\approx 20\%$ 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 $\approx 30\%$ of families:
 - *ACTA2* (17%), *TGFBR2* (2%), *MYH11* (1%).

Congenital Thoracic Aortic Aneurysms



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- 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



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- Vascular Ehlers-Danlos syndrome (type IV)
- Loeys-Dietz syndrome
- Turner syndrome
- Vasculitis
 - Takayasu's arteritis
 - Giant cell arteritis
 - IgG4-related aortitis
- Infectious aortitis (mycotic aneurysm)
- Syphilitic aortitis
- Trauma.

Presentation and Detection



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- Symptoms are uncommon
- Few are detectable on physical exam
 - Not palpable
 - Diastolic murmur of AR may be present
- Large majority are discovered incidentally
 - Routine CXR, CT, or echocardiogram
- Others go undetected until they dissect or rupture.

Thoracic Aortic Aneurysms: Diagnostic Modalities



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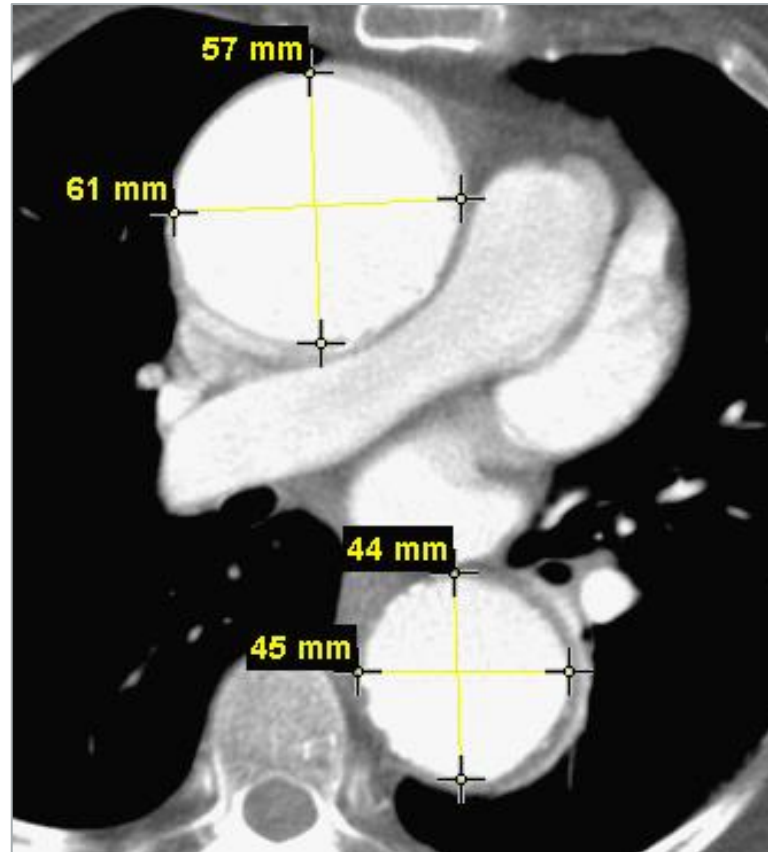
- Contrast-enhanced CT scanning (CTA)
- Magnetic resonance imaging (MRI and MRA)
- Echocardiography (TTE and TEE)

Contrast-enhanced CT Scanning: Standard Axial Imaging



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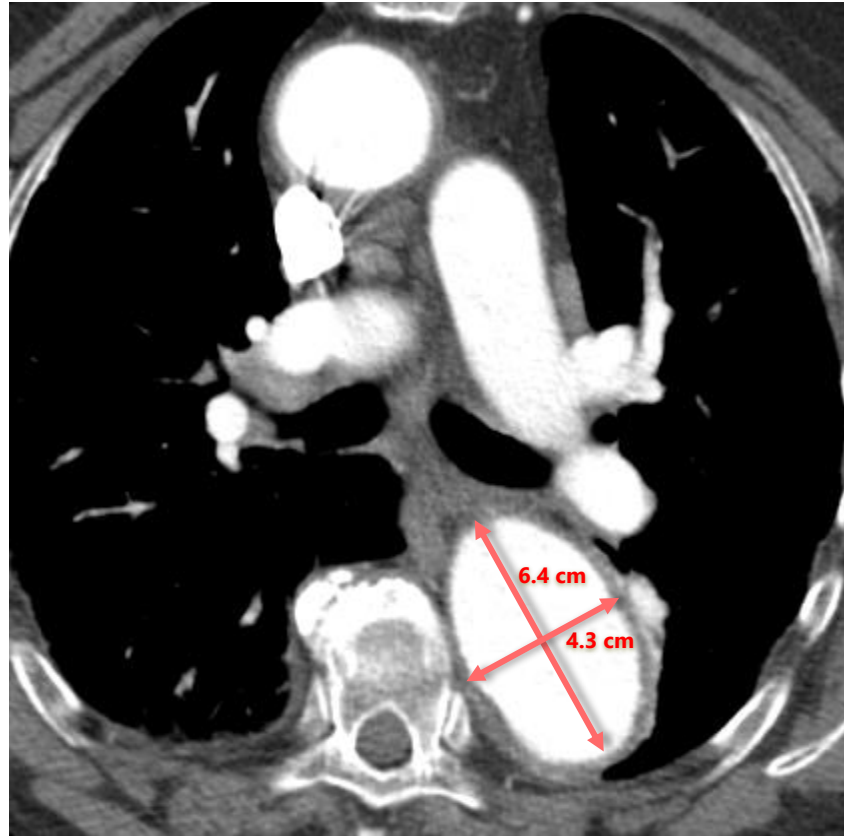


A Limitation of Axial CT: The Risk of Mismeasurement



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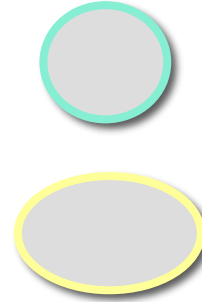
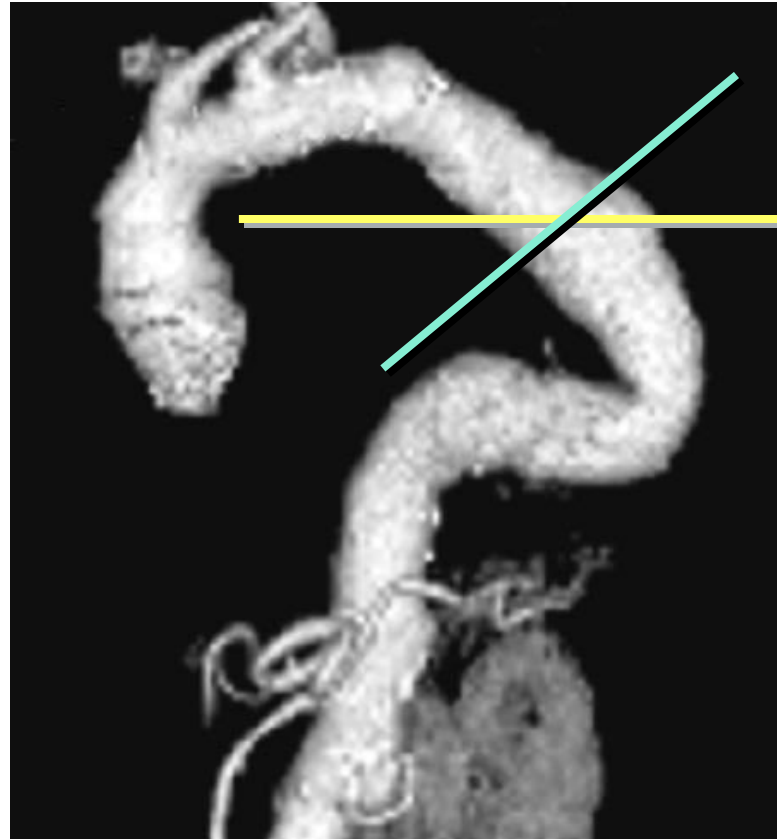


CTA with 3-D Reconstruction Better Defines True Aortic Anatomy



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CTA with Planar Reformats

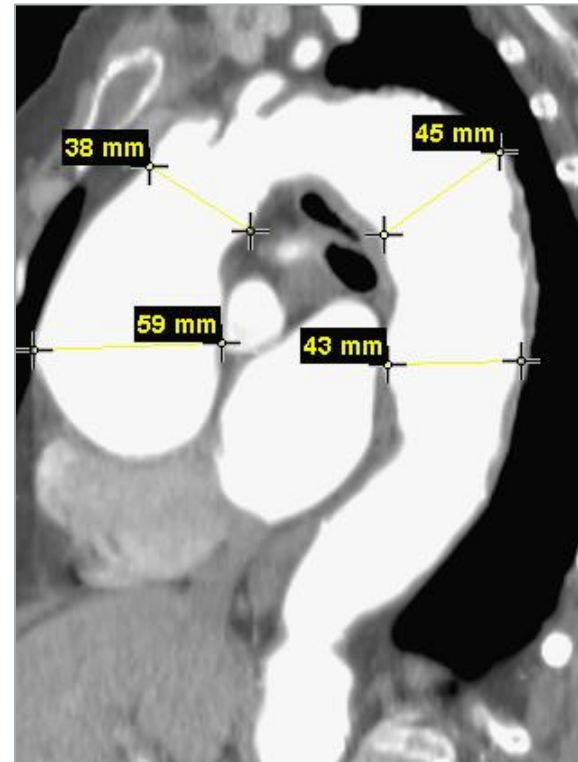


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Coronal



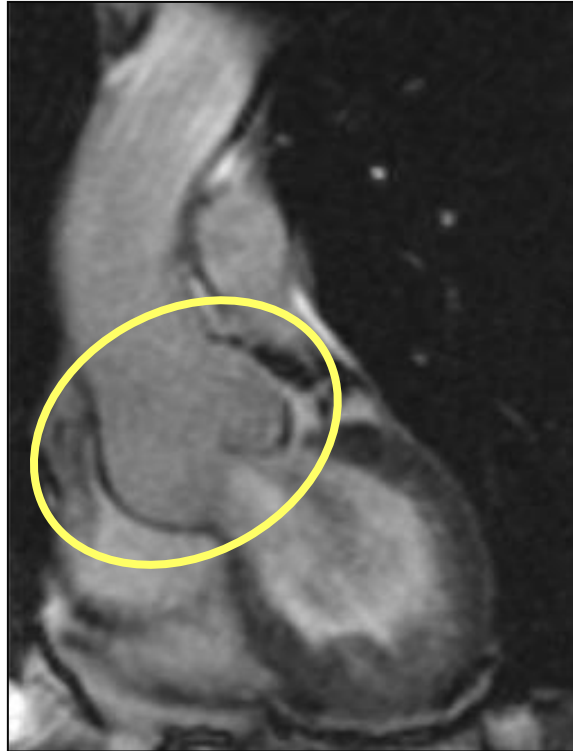
Sagittal

MRA (MRI with gadolinium): Aortic Root Aneurysm

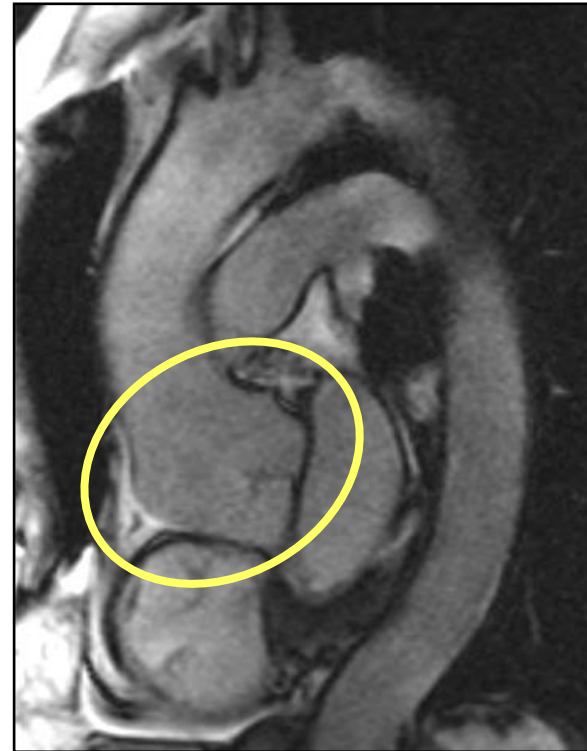


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Coronal



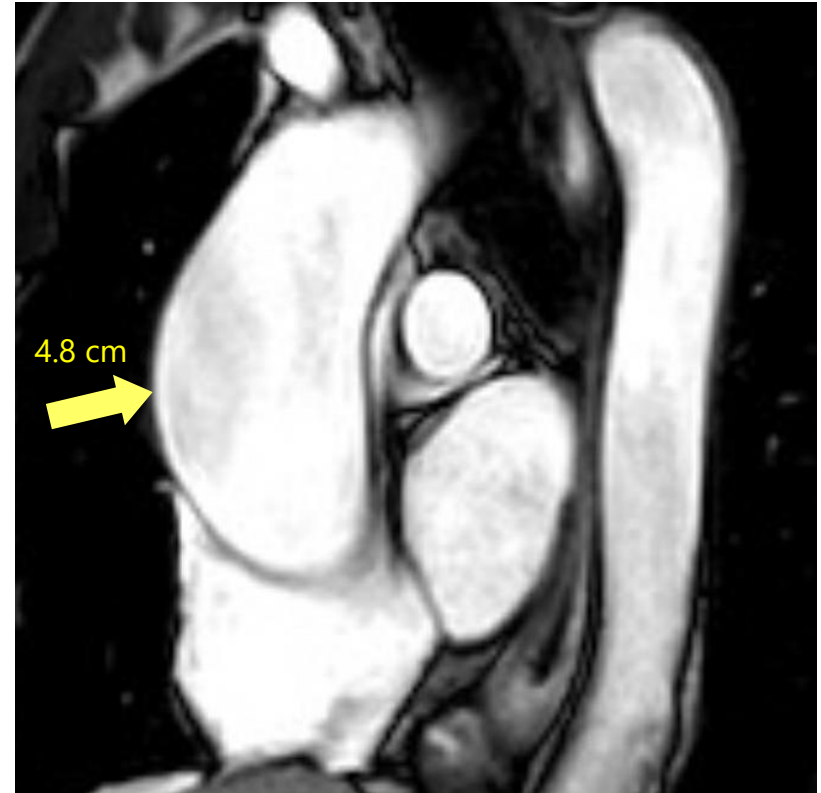
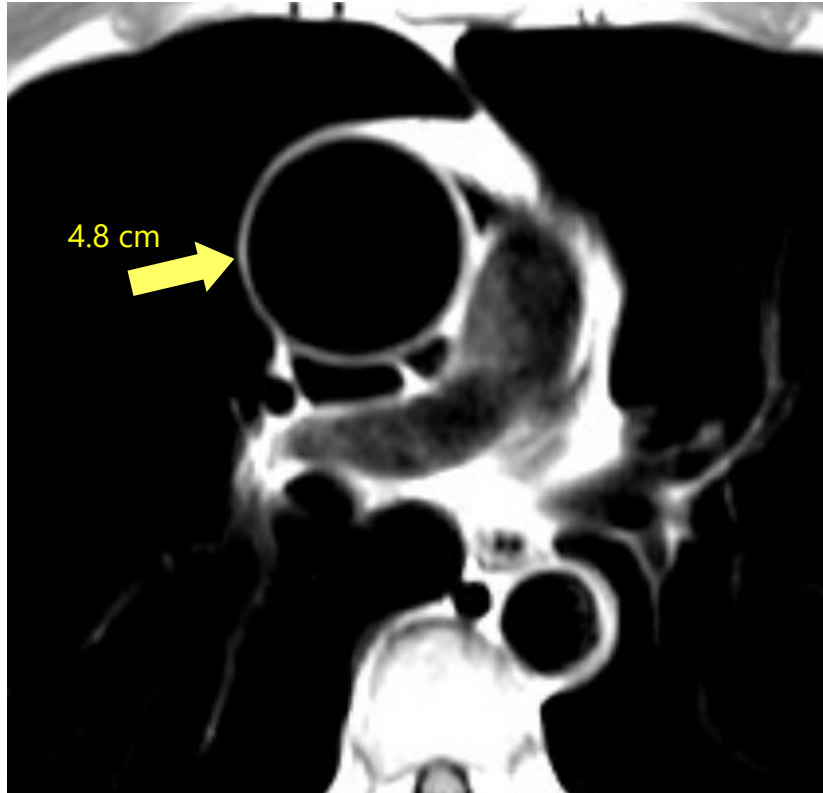
Sagittal

MRI without Contrast: Black Blood and Bright Blood Imaging



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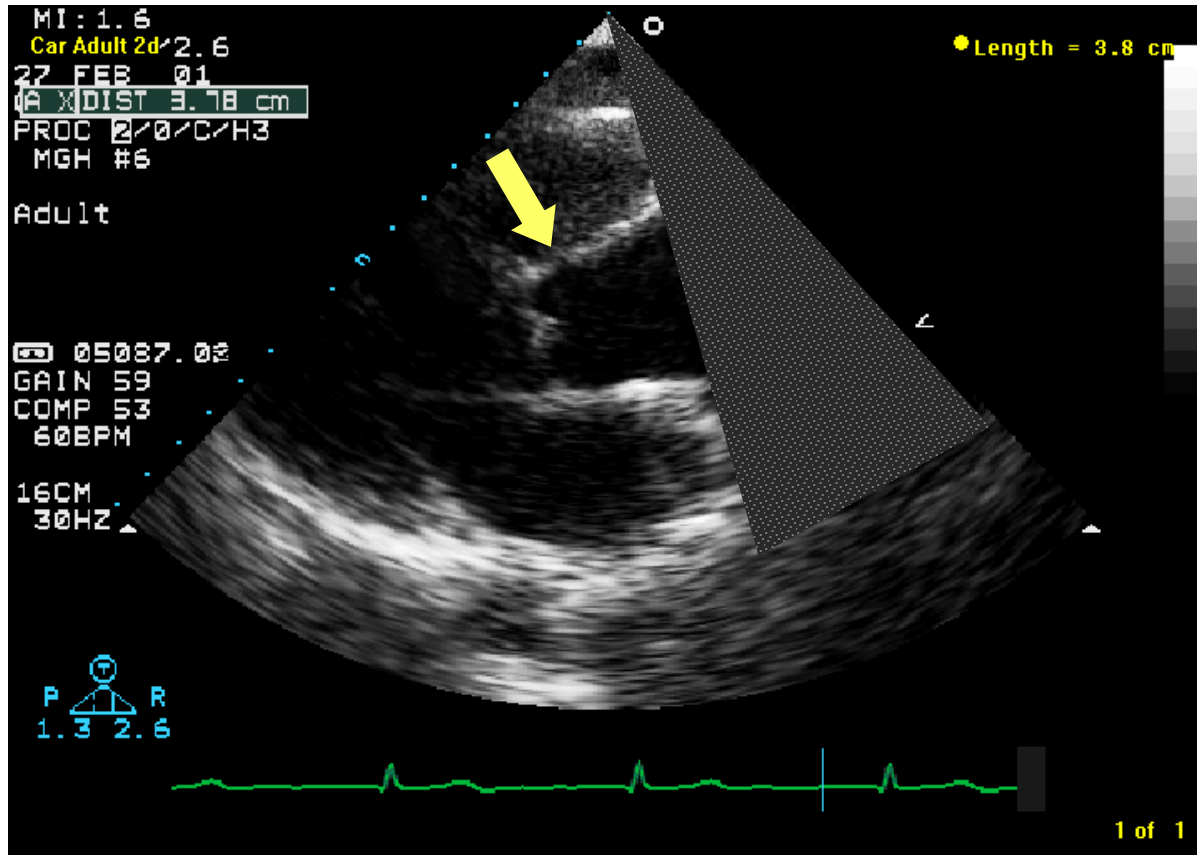


Transthoracic Echocardiography



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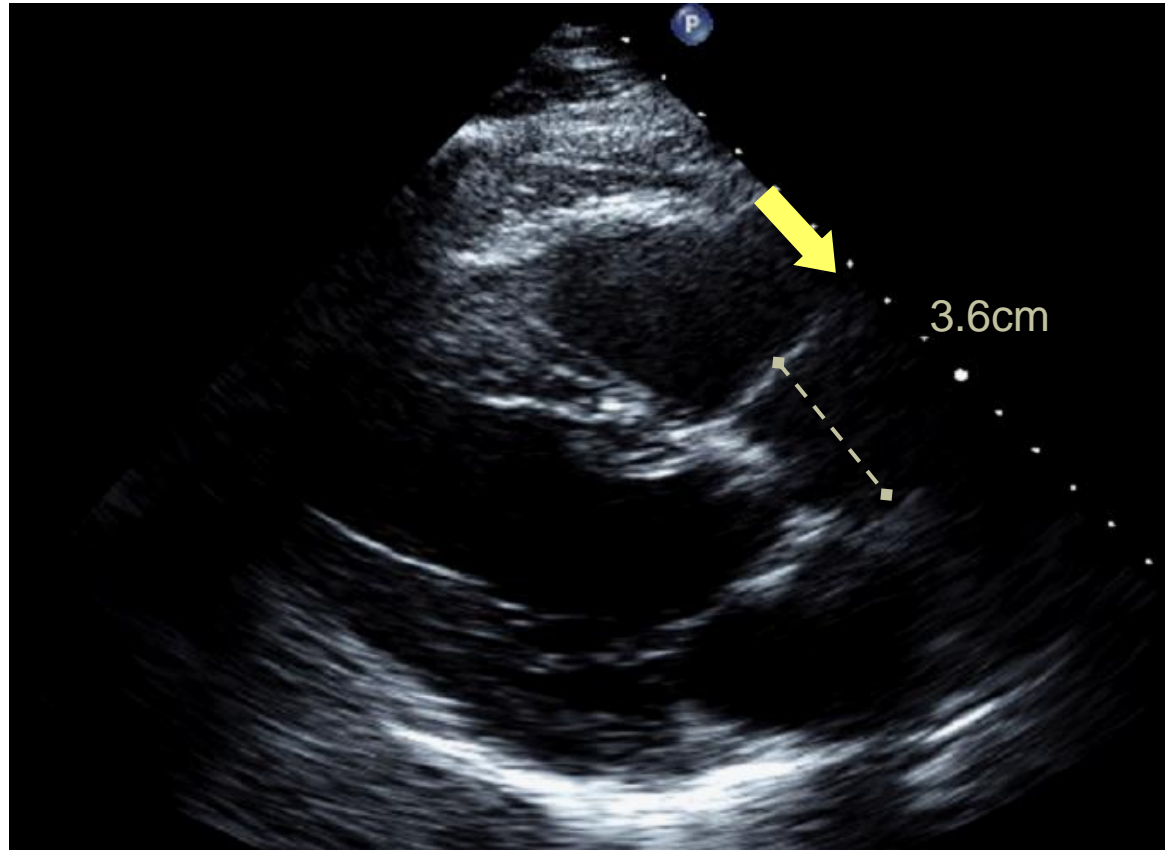


Transthoracic Echocardiography: Aortic root visualized, but not ascending aorta



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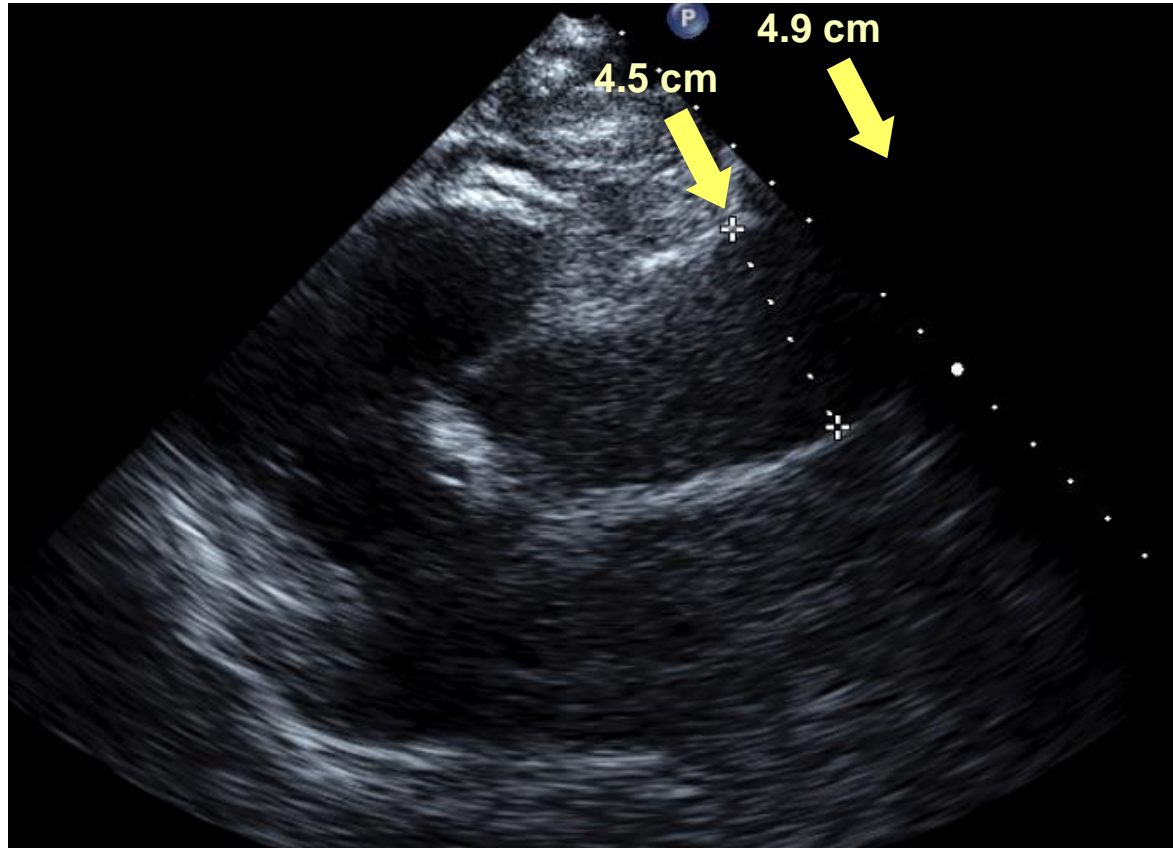


Transthoracic Echo: Ascending aorta visualized, but ? underestimate



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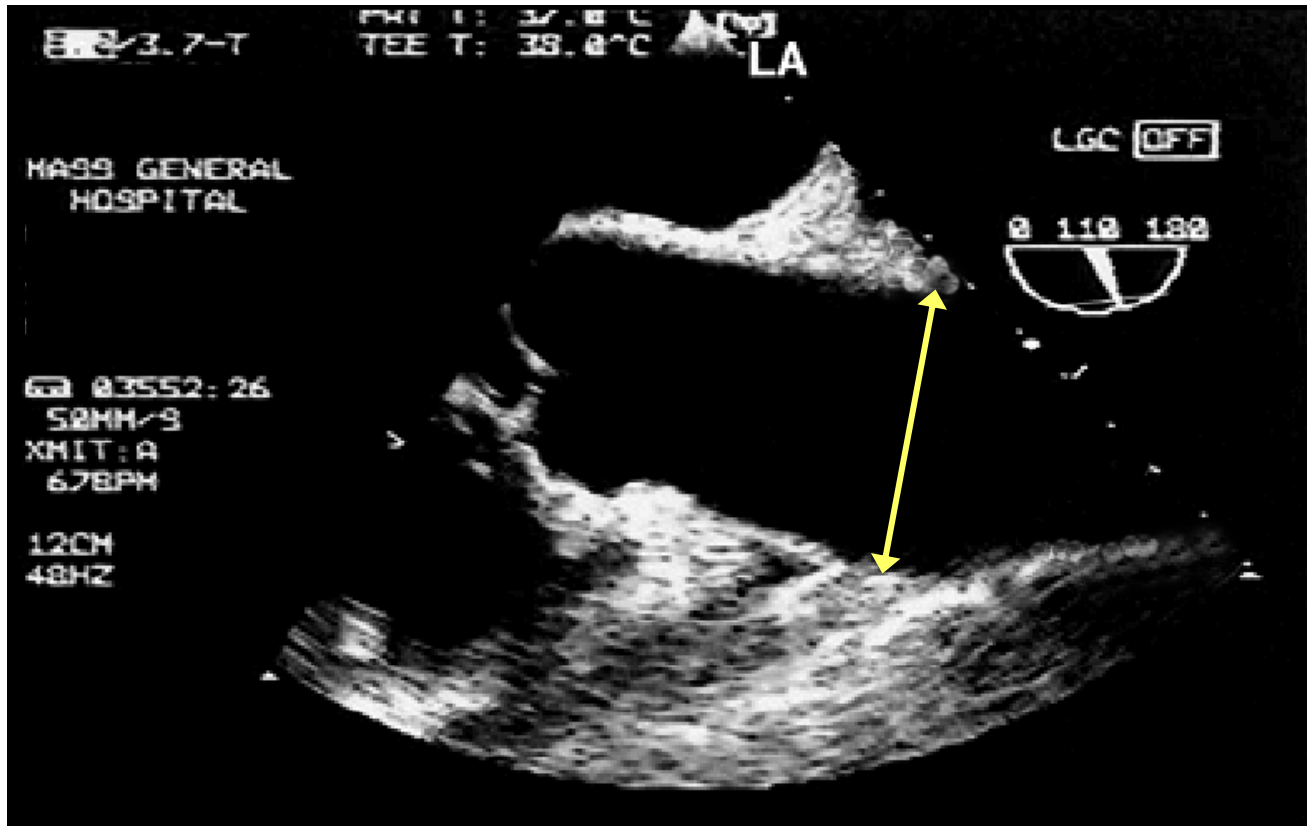


Transesophageal Echocardiography



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Which Modality to Choose: A General Guideline



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Routine TAA	Contrast-enhanced CT
Disease of the aortic root	Echocardiogram
Tortuous aorta or arch aneurysm	CTA (3-D reconstruction) or MRA
Allergy to iodinated contrast	MRA
Renal insufficiency	Non-contrast MRI or Non-contrast CT

Thoracic Aortic Aneurysms: Natural History



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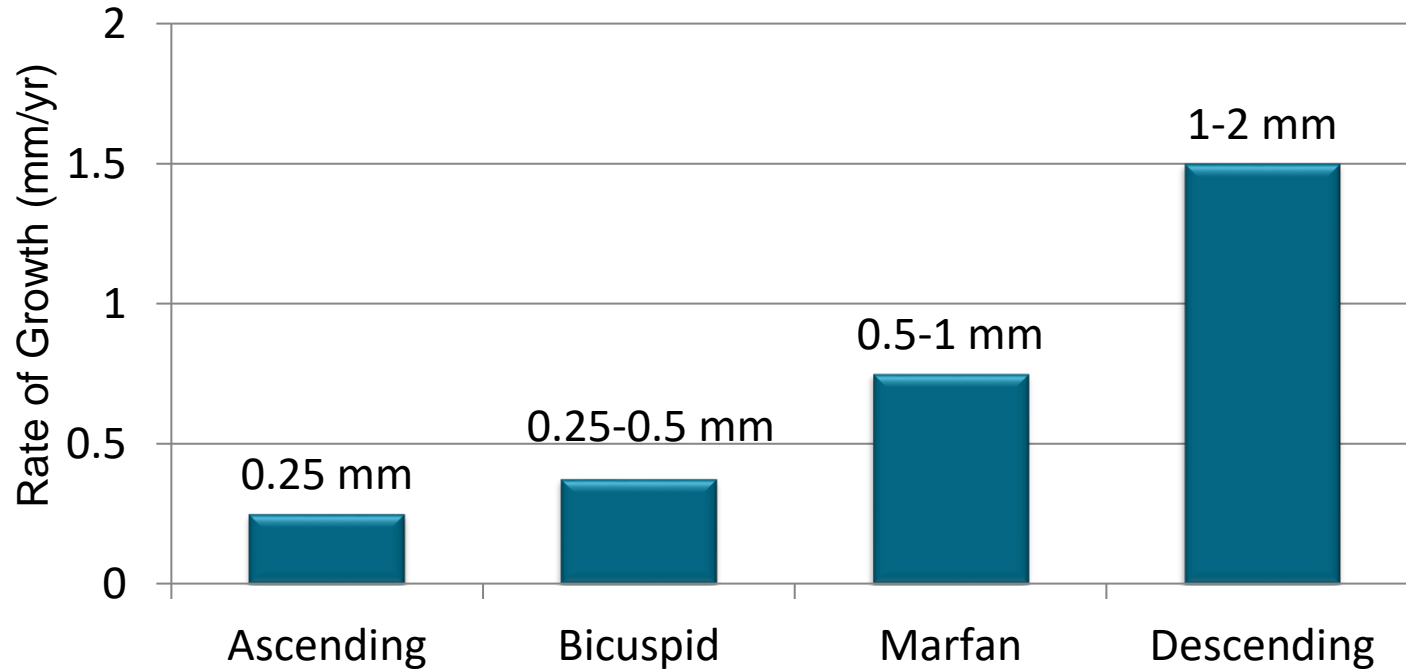
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Asymptomatic
TAA



Growth

Rates of Growth



Kim JB, et al. J Am Coll Cardiol 2016;69:1209-19

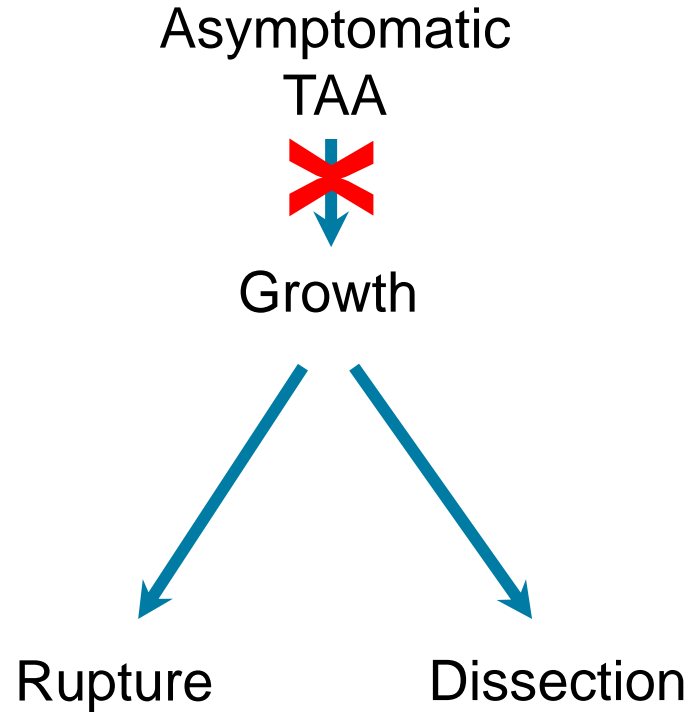
Coady MA, et al. J Thorac Cardiovasc Surg 1997;113:476-91

Thoracic Aortic Aneurysms: Natural History



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Medical Management of Thoracic Aortic Aneurysms



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Beta Blockers

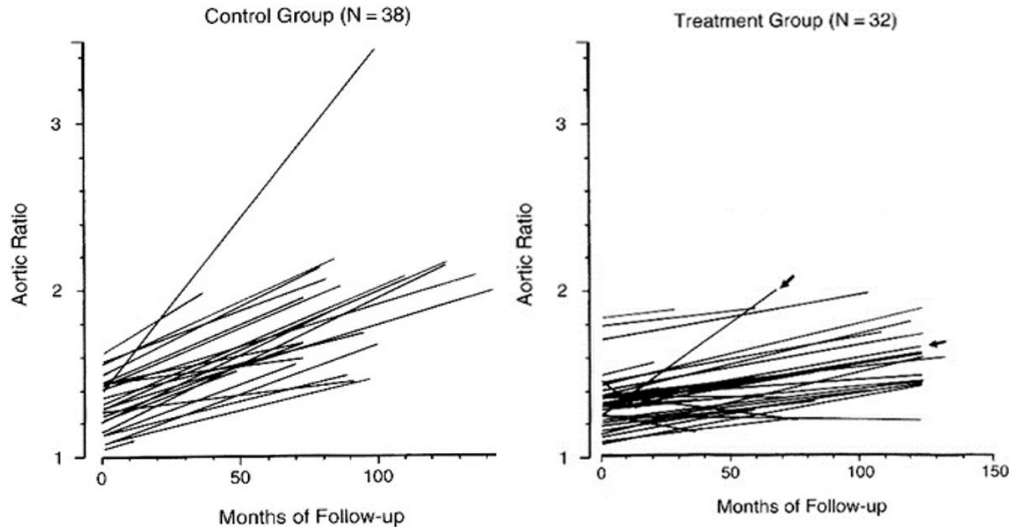


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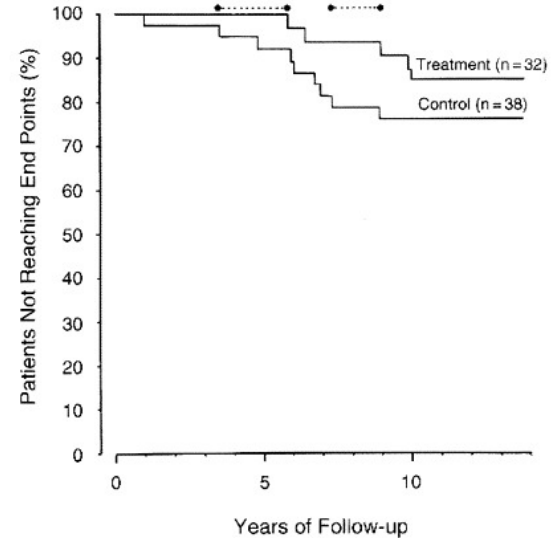
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- Demonstrated benefit in Marfan syndrome

Changes in the aortic size ratio (measured/expected)



Survival free of death, AoD, HF,
or aortic surgery



Potential Alternative Therapeutic Strategy For Treating Marfan Syndrome



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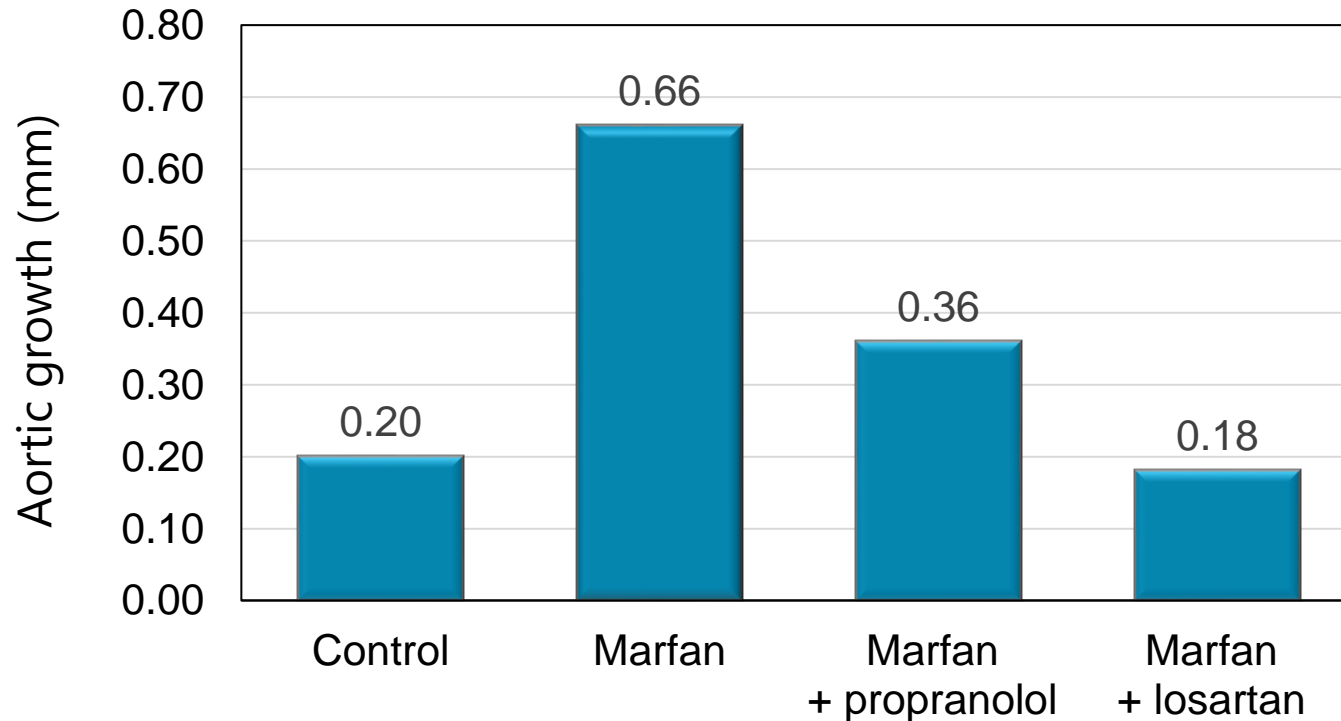
- Hal Dietz, et al
 - In Marfan syndrome, deficiency of fibrillin-1 results in overactivity of TGF- β , which in turn is associated with aortic medial degeneration
- Anti-TGF- β antibody blunted aortic growth in mice
- Previous studies had shown that losartan, an angiotensin II type 1 receptor (AT1) blocker, inhibits activity of TGF- β
- So Dietz et al studied the effect of losartan therapy on aortic root growth in a mouse model of MFS.

Efficacy of Losartan in Mouse Model of MFS: Aortic Growth Over 6 Months



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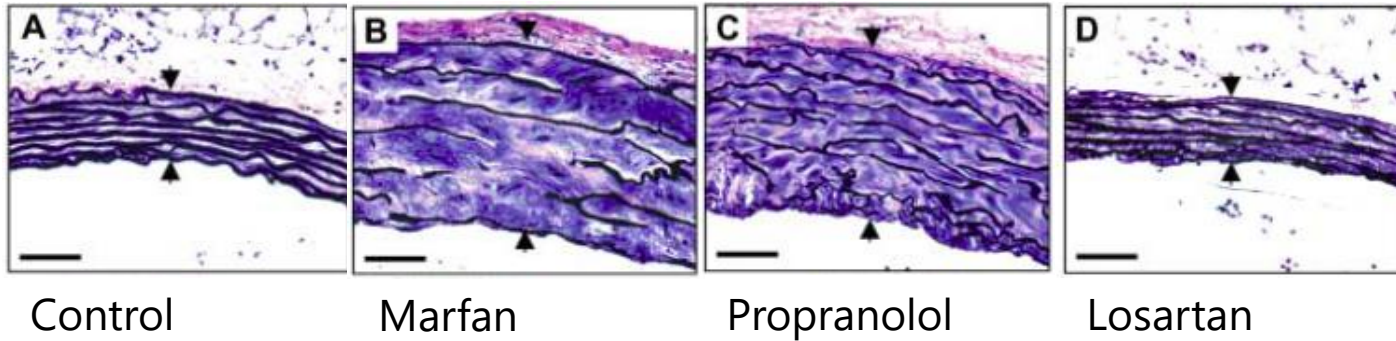


Efficacy of Losartan in Mouse Model of MFS: Aortic Wall Architecture



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Atenolol vs. losartan for MFS: A randomized blinded controlled trial



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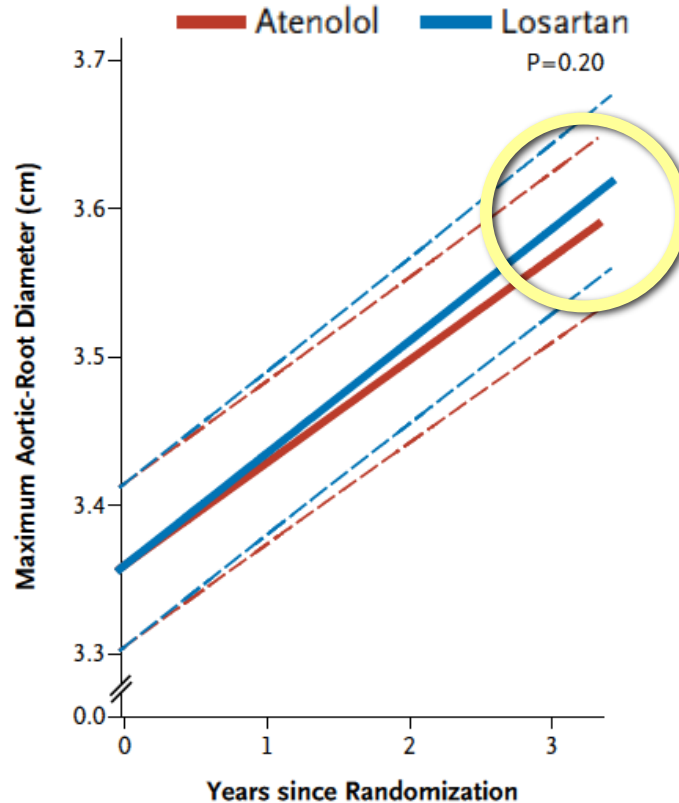
- Pediatric Heart Network, Boston Children's Hospital
 - 21 Centers
- 608 subjects, ages 6 months to 25 yr (mean 11 yr)
- Randomized to:
 - Atenolol (mean dose \approx 150 mg in young adults) vs.
 - Losartan (mean dose \approx 85 mg in young adults)
- Followed by echo imaging over 3 years

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



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Sobering Reminder



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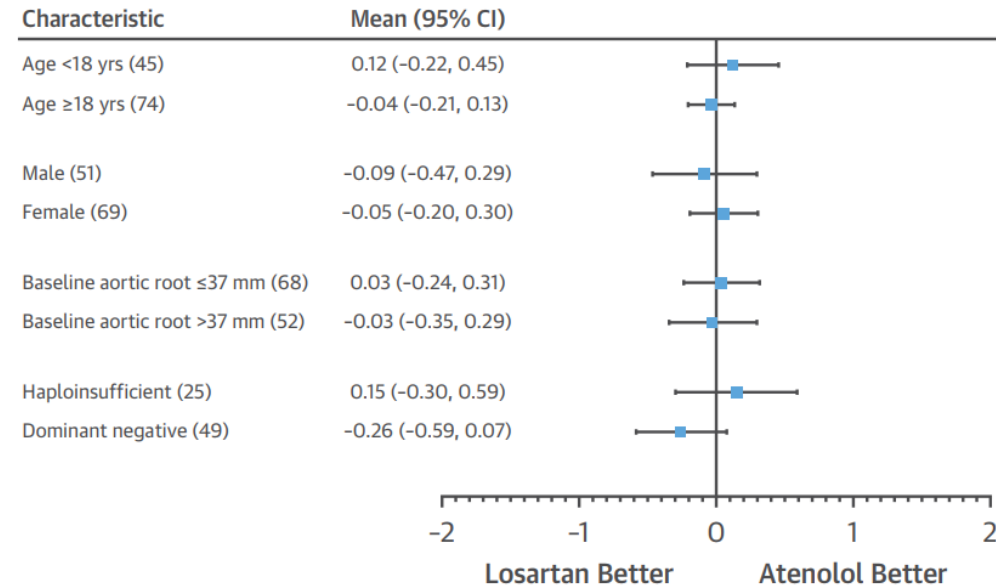
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Longer term 9-year trial of losartan vs. atenolol in 128 Marfan patients



FIGURE 2 Effect of Losartan Compared to Atenolol on Aortic Root Dilatation Rate in Subgroups of Marfan Patients



Fluoroquinolone Risk



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- Fluoroquinolone antibiotics are known to be associated with an increased risk of tendinitis and tendon rupture
 - Possibly related to an adverse effect on collagen
 - There was an FDA black box warning regarding the risk of tendon rupture
- In 2015 and 2018 three observational studies raised concern that fluoroquinolone antibiotics increase the risk of aortic aneurysm or dissection
 - All reported a twofold increased risk of aortic aneurysm or dissection within 60 days from start of treatment.

Lee C-C, et al. JAMA Intern Med. 2015;175(11):1839-1847

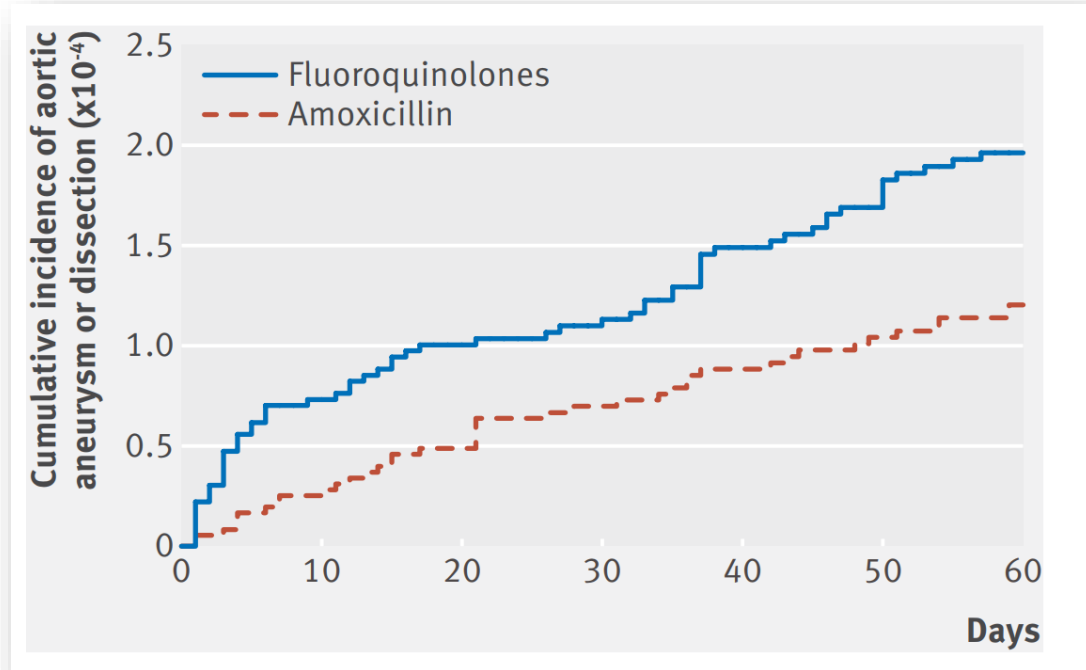
Daneman N, et al. BMJ Open. 2015 Nov 18; 5(11):e010077

Pasternak B, et al. BMJ 2018;360:k678

Fluoroquinolone use and risk of aortic aneurysm and dissection



Cumulative incidence of aortic aneurysm or dissection within 60-day risk period from start of study treatment



U.S. FDA Issued Warning in 12/2018



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The screenshot shows the FDA website's 'Drugs' section. The main heading is 'FDA warns about increased risk of ruptures or tears in the aorta blood vessel with fluoroquinolone antibiotics in certain patients'. A large text box is overlaid on the page, containing the following text: 'Fluoroquinolones should not be used in patients at increased risk unless there are no other treatment options available.' Below this, the text continues: 'People at increased risk include those with a history of blockages or aneurysms (abnormal bulges) of the aorta or other blood vessels, high blood pressure, certain genetic disorders that involve blood vessel changes, and the elderly. We are requiring that a new warning about this risk be added to the [prescribing information](#) and patient [Medication Guide](#) for all fluoroquinolones.'

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Drugs

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Postmarket Information Providers

Information

Medication

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Drug Recalls

Drug Supply Chain Integrity

FDA warns about increased risk of ruptures or tears in the aorta blood vessel with fluoroquinolone antibiotics in certain patients

Fluoroquinolones should not be used in patients at increased risk unless there are no other treatment options available. People at increased risk include those with a history of blockages or aneurysms (abnormal bulges) of the aorta or other blood vessels, high blood pressure, certain genetic disorders that involve blood vessel changes, and the elderly. We are requiring that a new warning about this risk be added to the [prescribing information](#) and patient [Medication Guide](#) for all fluoroquinolones.

Educate patients to avoid them



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FLUOROQUINOLONES

FDA

WARNING

Medical Management in 2022



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- Beta blockers are mainstay
- ARBs are good alternative
- If blood pressure room, prescribe both agents
- Target systolic blood pressure 110-125 mmHg
 - Add additional antihypertensives, as needed
- Avoid fluoroquinolones, when possible.

Educate patients about exercise



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- Light and moderate aerobic exercise (without sprint or burst episodes) is safe
- When heavy weightlifting requires Valsalva, there is an increase in intrathoracic pressure followed by an increase in SBP to ≥ 300 mmHg
 - So heavy weightlifting and competitive athletics involving isometric exercise should be avoided
 - Those who wish to do weight training should focus on light to moderate weights with lots of reps (if they can breathe or talk while lifting, it should be safe).

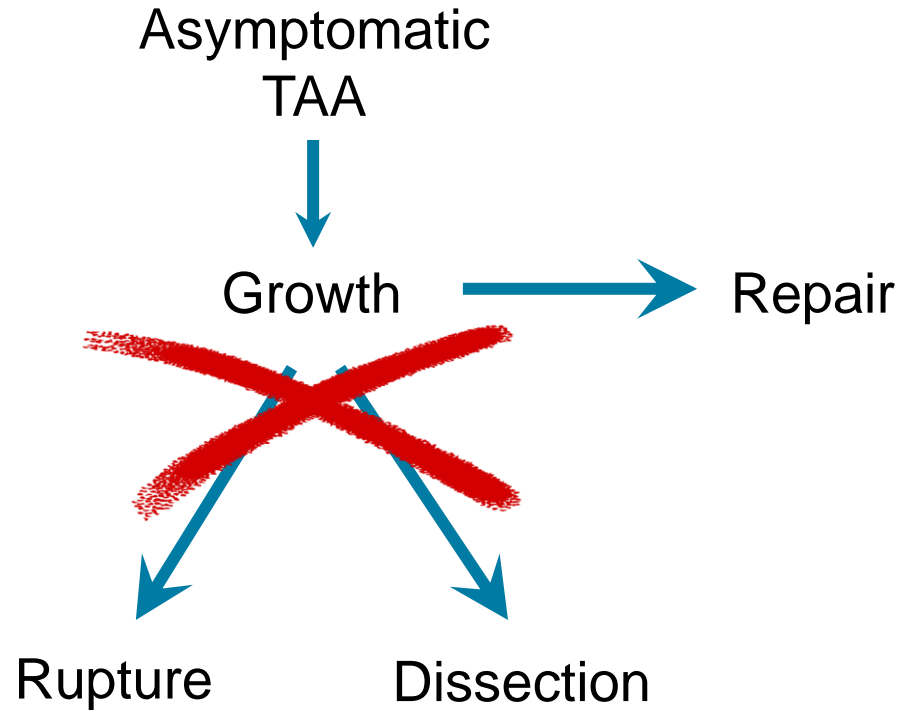


Thoracic Aortic Aneurysms: Natural History



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Weighing the Risk of Aortic Dissection vs. the Risk of Intervention



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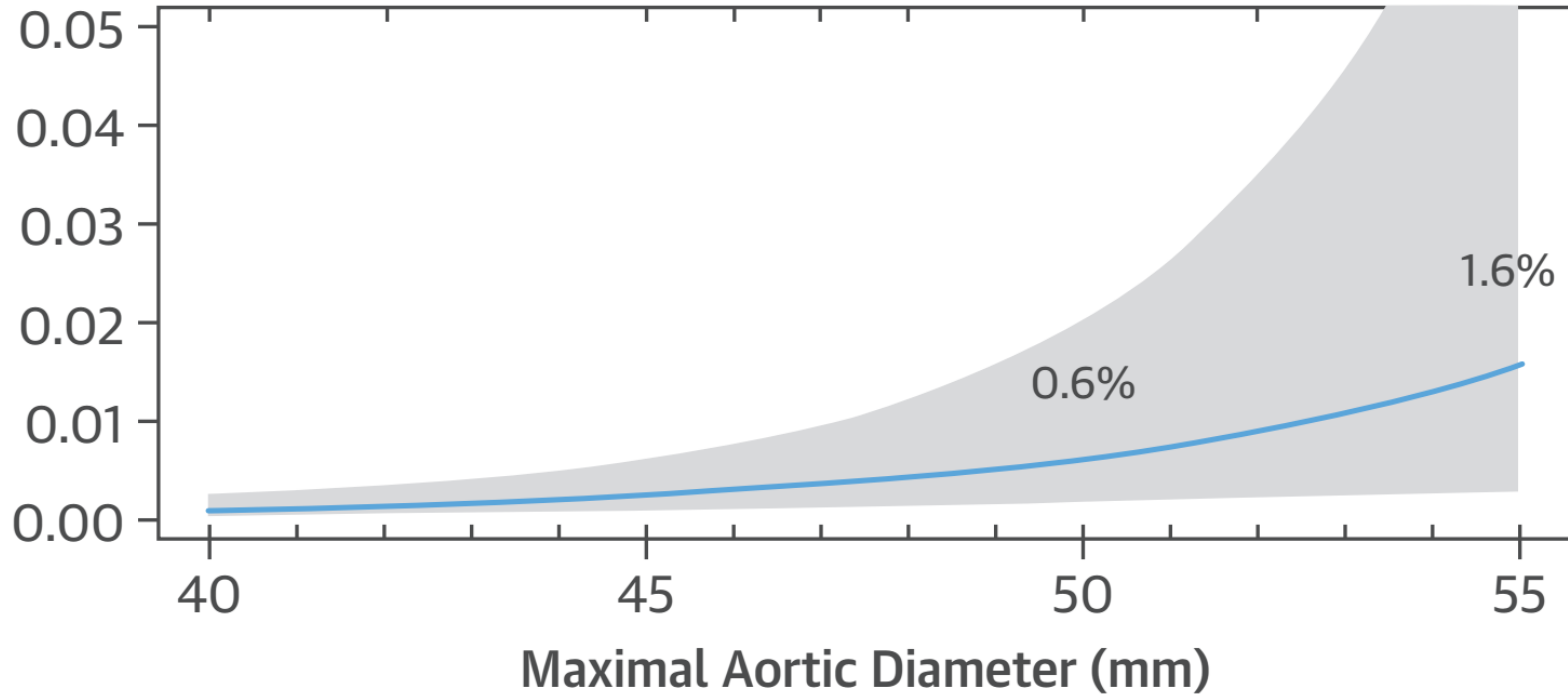


Rate of Aortic Events vs. Ascending Aortic Diameter



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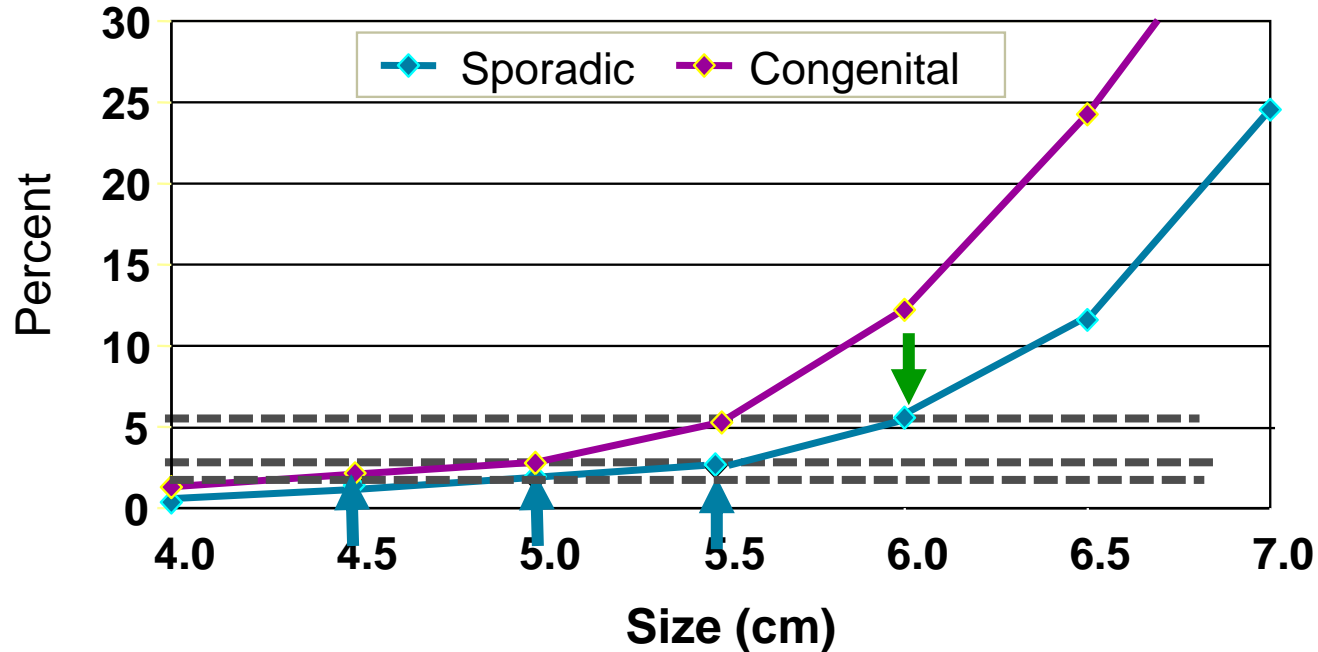
Risk of Aortic Dissection vs. the Risk of Surgery



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Mortality of Unoperated Ascending TAA vs. Size



Indications for Intervention



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Ascending Aortic Aneurysms: Indications for Aortic Repair



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- Idiopathic/sporadic, BAV-related: ≥ 5.5 cm
 - High risk surgery: ≥ 6.0 cm
- Genetic (e.g., Marfan, familial): ≥ 5.0 cm
 - Low risk for surgery ≥ 4.5 cm
- Rapid expansion
 - ≥ 0.5 cm/year
 - ≥ 0.3 cm/year x several years (extrapolated from ESC guidelines)
- Severe AR: Symptoms or LV dysfunction.

ACC/AHA Guidelines for Management of Thoracic Aortic Disease. J Am Coll Cardiol 2010; 55:e27-e129

A Statement of Clarification From the ACC/AHA. J Am Coll Cardiol 2016; 67:724-731

European Guidelines. Heart J 2014; 35:2873–2926

What Are the Surgical Options?



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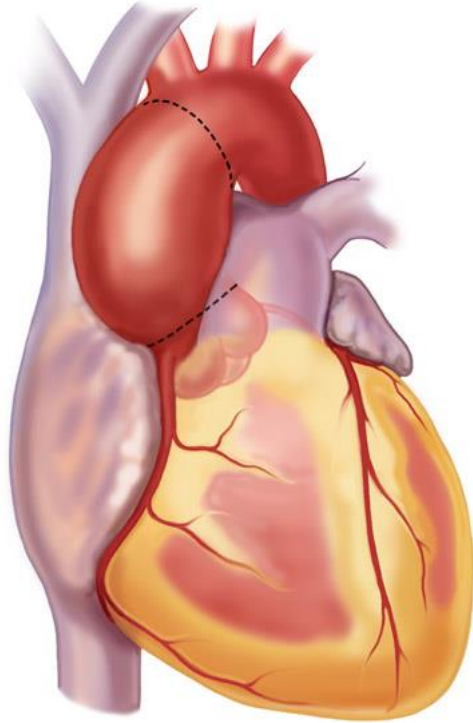
- Ascending thoracic aortic aneurysms
- Root aneurysms
- Arch aneurysms
- Descending thoracic aortic aneurysms

Ascending Thoracic Aortic Aneurysm: Interposition Tube Graft



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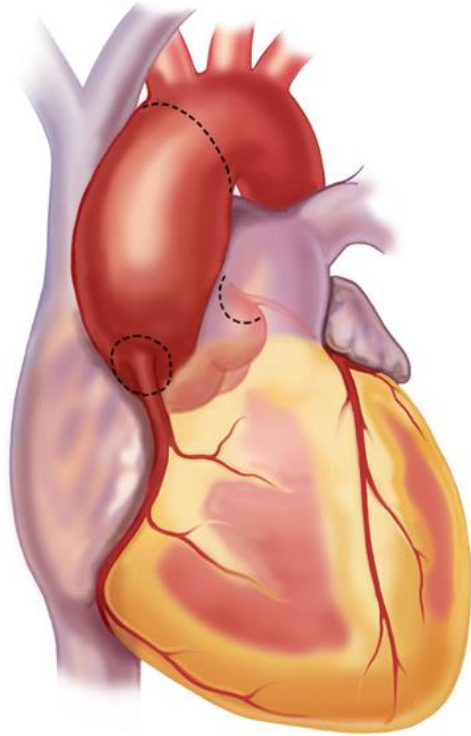


Root Aneurysm: Composite Aortic Graft



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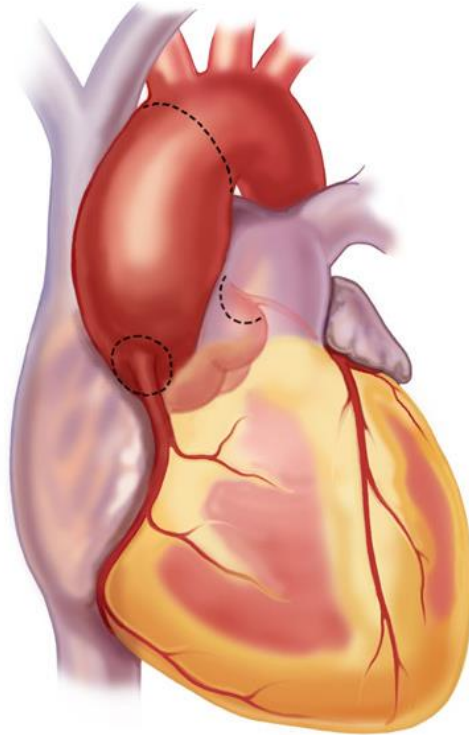


Root Aneurysm: Valve-Sparing Aortic Root Repair



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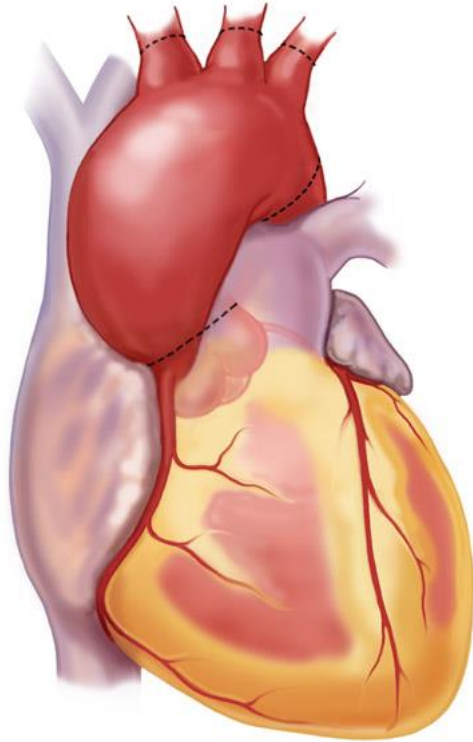


Arch Aneurysm: Total Arch Replacement



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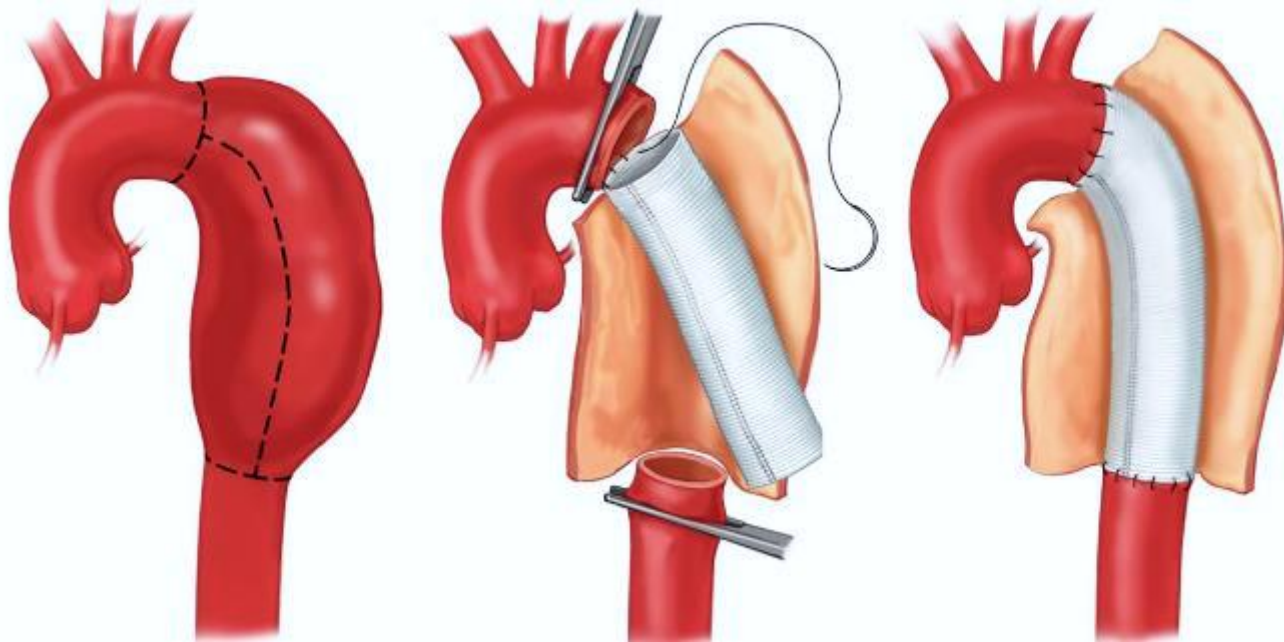


Descending Thoracic Aortic Aneurysm: Open Surgical Repair



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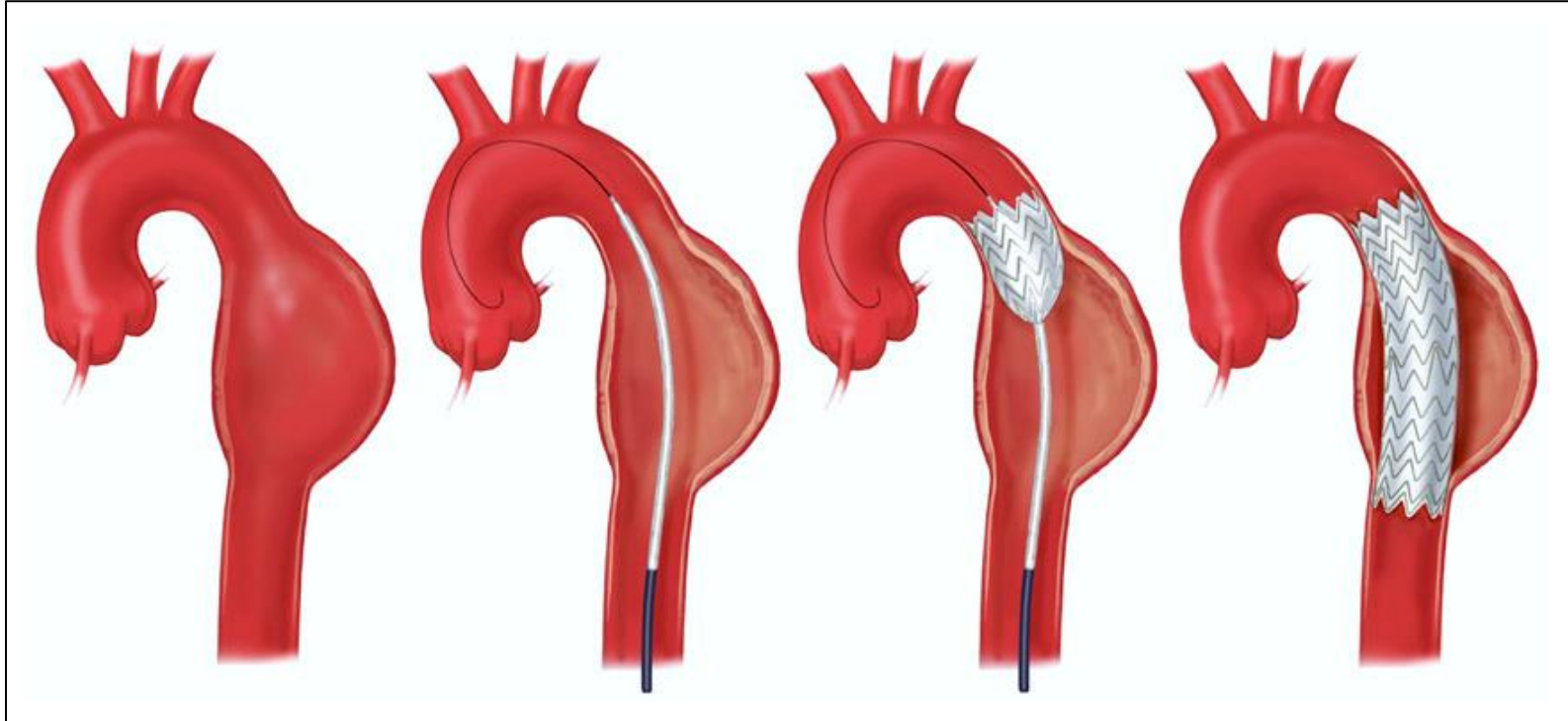


Descending Thoracic Aortic Aneurysm: Endovascular Stent-Graft Repair



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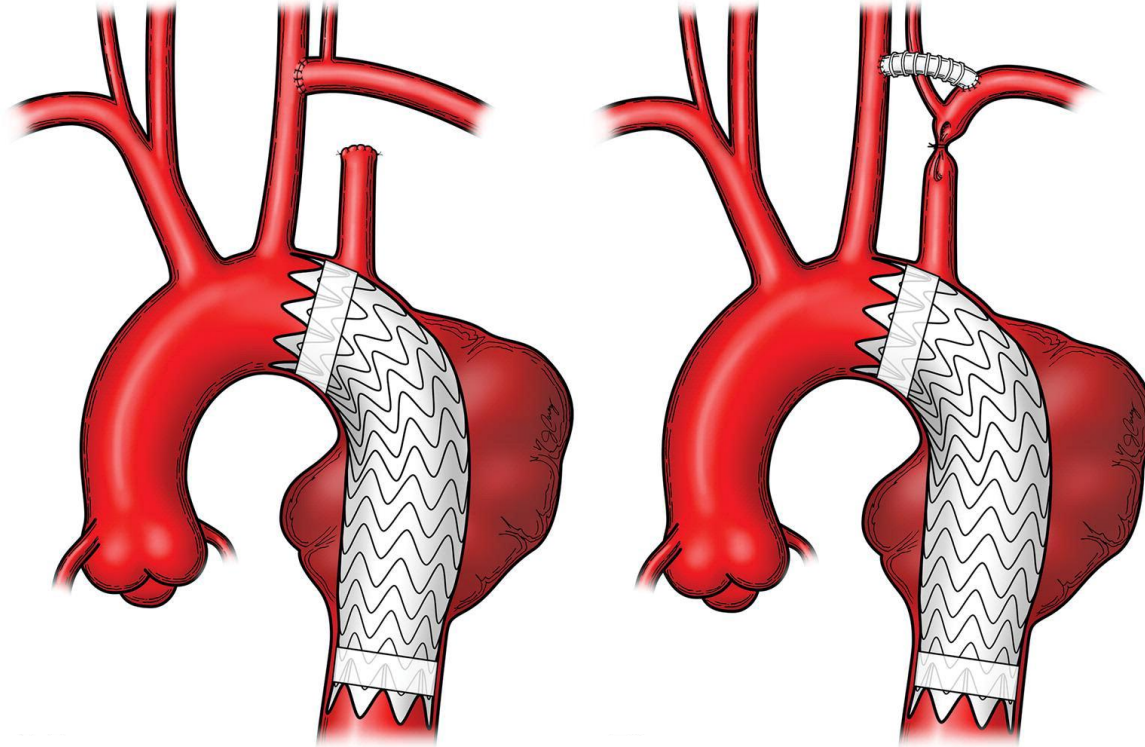


Left Subclavian to Carotid Transposition or Bypass



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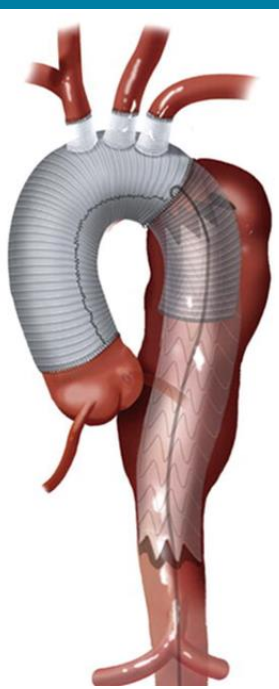


And Many More Individualized Options

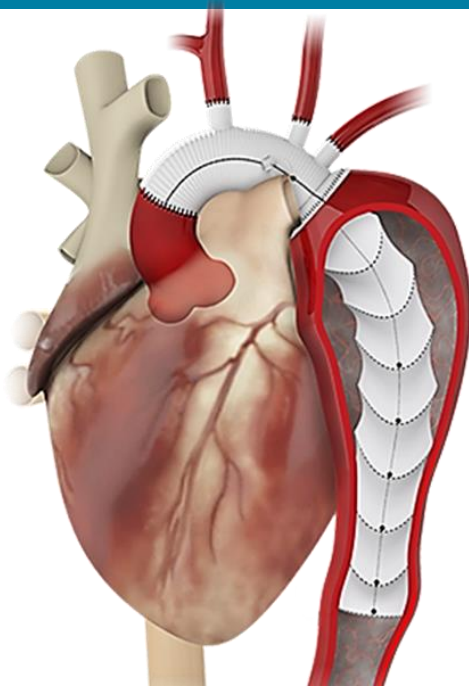


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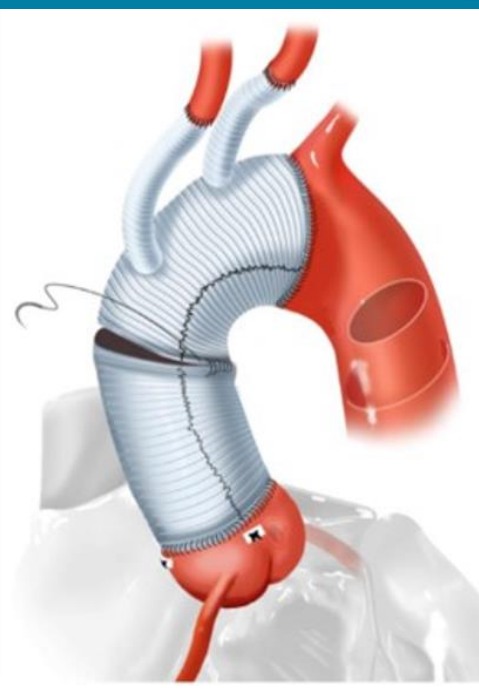
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Elephant
trunk



Frozen elephant
trunk



Zone 2 aortic
arch repair



Fenestrated
endograft

And Finally...



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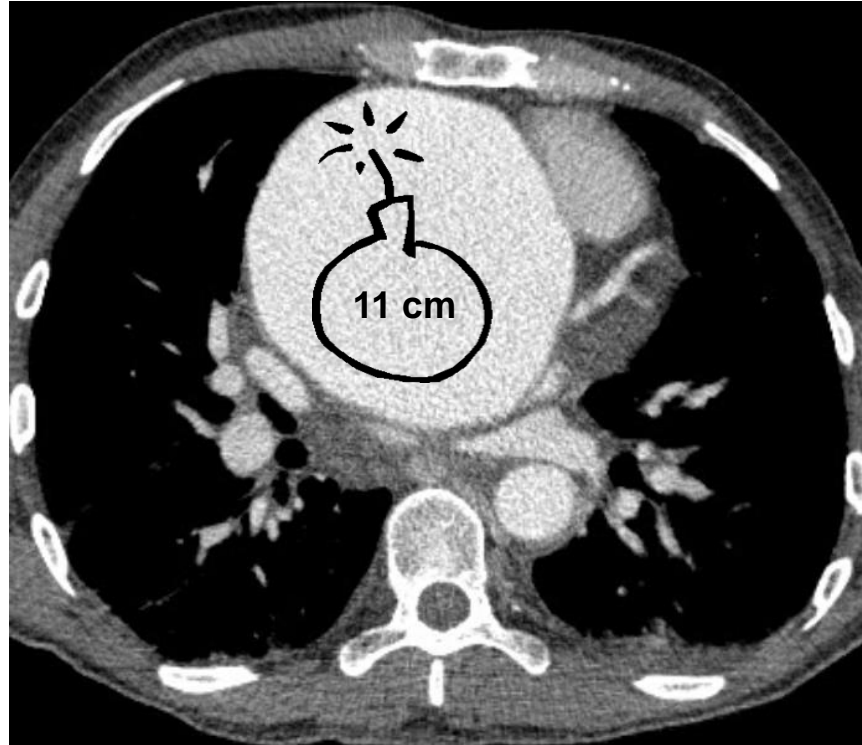
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Time is up!



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Take Home Points



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1. Patients with bicuspid aortic valve are at increased risk for root and ascending aneurysms, so make sure to image their aortas
2. Screen first-degree relatives of all patients with aortic root and/or ascending aortic aneurysms
3. Follow thoracic aortic aneurysms with surveillance imaging
4. Beta-blockers remain the mainstay of medical therapy
5. The most common threshold for surgery is a diameter of 5.5 cm.

Thoracic Aorta Disease Update: Etiology, Diagnosis, and Management

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Director, MGH Healthcare Transformation Lab

Associate Professor of Medicine, Harvard Medical School



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