Ascending Aortic Dilatation Associated With Bicuspid Aortic Valve

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introduction

- the clinical presentation of BAV disease remains quite **heterogeneous** with patients presenting from **infancy to late adulthood**
- the heterogeneous presentation of BAV phenotypes may be a more **complex matter** related to **congenital**, **genetic**, and/or **connective tissue abnormalities**
- The reported **prevalence** of BAV- related aortic dilatation ranges from **33%-80%**
- the etiology of aortic dilatation in patients with BAV disease remains **unclear** and as a result, management of these patients remains **controversial**

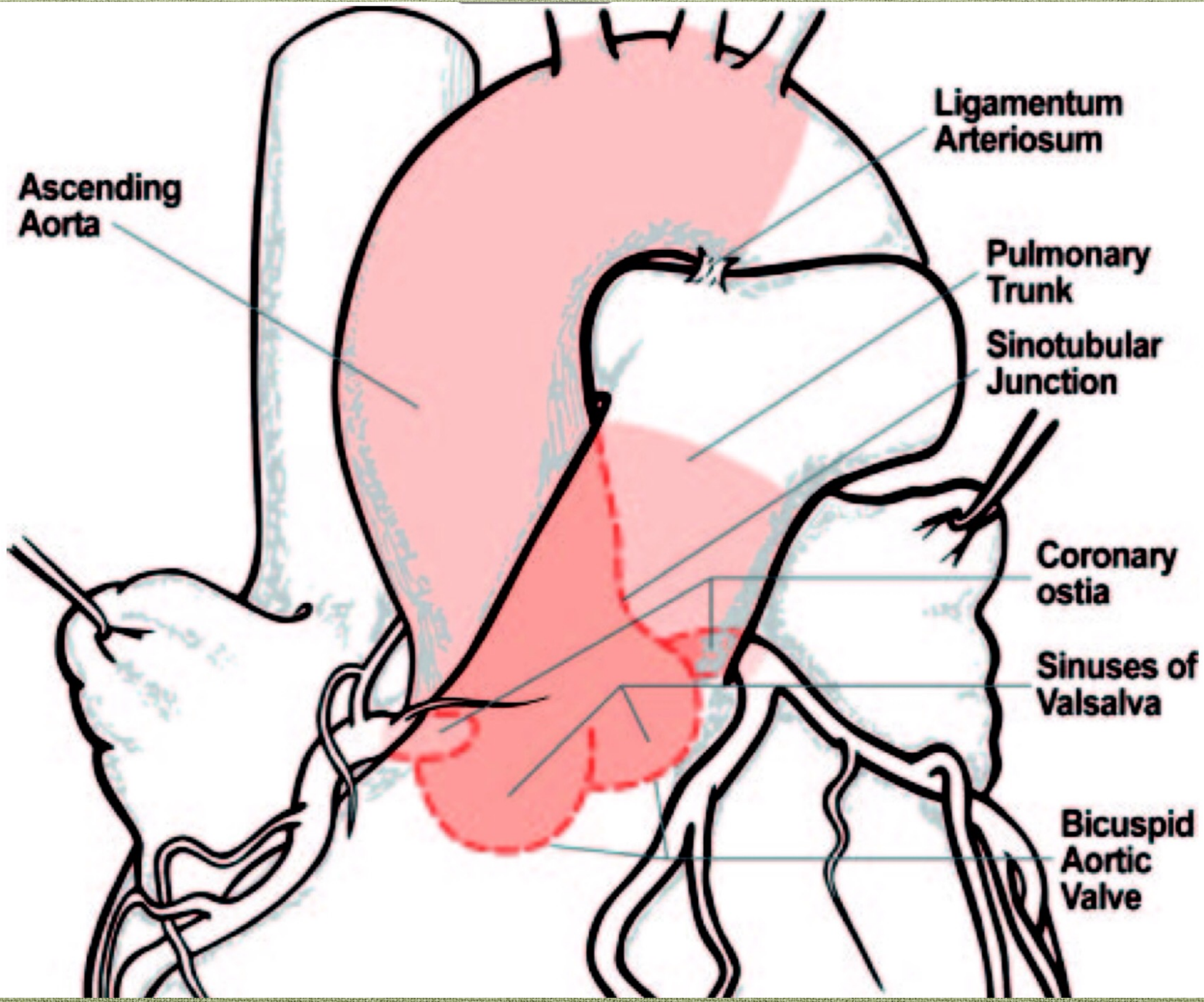
Aortic aneurysm may be related to:

hereditary diseases

- Marfan syndrome
- Loeys –Dietz syndrome
- Ehler-Danlos syndrome
- Arterial Tortuosity Syndrome
- Cutis laxa syndrome
- Alagille syndrome
- Noonan Syndrome
- Turner syndrome

non genetic diseases

- bicuspid aortic valve
- coarctation of aorta
- tetralogy of Fallot
- TGA
- aortitis syndromes



Anatomic Boundaries of BAV Disease

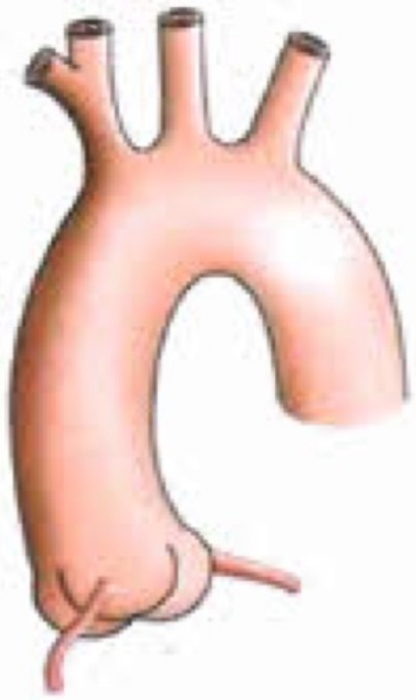
pathophysiology

- Hemodynamic Changes:

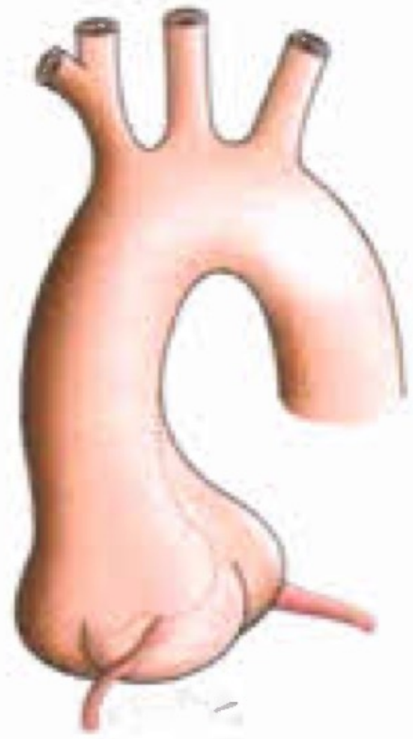
➢ Increased shear stresses on aortic wall play a role in pathogenesis of BAV related aortic dilatation

➢ Anteroposteriorly oriented BAVs are more likely to develop regurgitation ,regurgitant BAVs have higher stroke volumes ,leading to higher wall tension in the ascending aorta(aortic root dilatation)

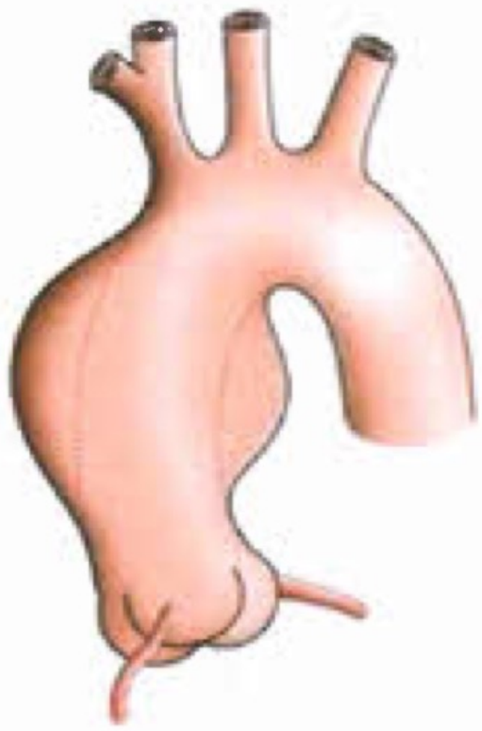
➢ Right- left oriented BAVs are more prone to stenosis, Stenotic BAVs create a high velocity jet that increases shear stress on the anterolateral portion of the ascending aorta



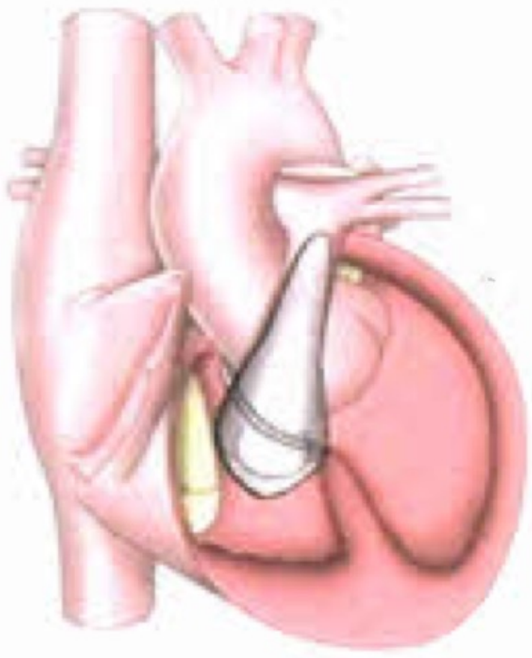
a. Normal



b. Marfan



c. Stenotic BAV



d. Late after TOF repair

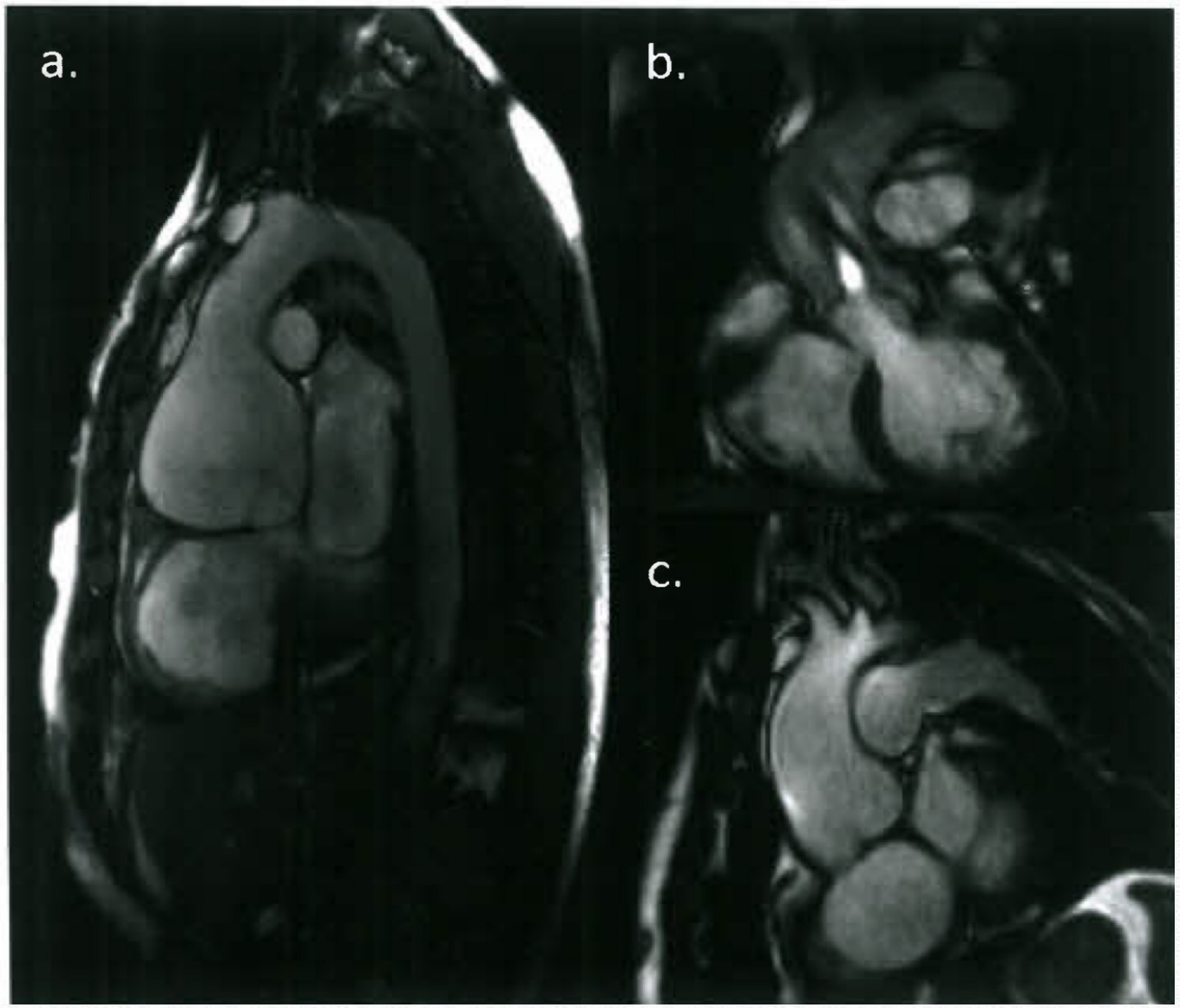


Figure 34.2. Magnetic resonance images of different types of aortic dilation. **A:** Still frame from steady-state free precession image showing the "pear-shaped" aortic dilation seen in Marfan syndrome. A jet of mild aortic regurgitation is seen. **B:** Jet lesion directed to the anterior–lateral portion of the ascending aorta in a stenotic bicuspid aortic valve with asymmetrical dilation of the vessel wall at the same level. **C:** Dilation of the aortic root extending to the sinotubular junction and proximal ascending aorta in a patient with repaired Tetralogy of Fallot.

Pathophysiology (cont.)

- There are some lines of evidence supporting The predominant congenital wall abnormality:

1. In BAV patients (including children) with normally-functioning aortic valve, significant proximal aorta enlargement has been observed

2. Patients with BAV have been shown to have larger A.Ao diameters than patients with TAV even after matching for hemodynamic severity of valvular lesions

3. A.Ao dilatation can occur even after aortic valve replacement

4. pathologic finding has been observed in the aortas of patients with BAV before aneurysm formation occur

5. prevalence of BAV in first-degree relatives

Pathophysiology (cont.)

- Defective protein transport from VSMCs to the extracellular matrix, lack of maintenance of the extracellular protein and increased apoptosis of the VSMCs(medial degeneration)

- increased matrix metalloproteinase activity (proteolytic enzymes,degrade of collagen and elastin),MMPS ⇔ TIMPS

- decreased fibrillin-1 in the aortic wall (Fibrillin-1 is a glycoprotein that helps to maintain the structural integrity of the aortic wall and valve leaflets by tethering VSMCs to a matrix of elastin and collagen)

- Marfan syndrome and BAV disease share common histopathological findings(FBN-1 gene)

- The total thickness of the aortic media is the same for BAV and TAV aortas, but the distance between the elastic lamellae is greater with BAV, and the lamellae themselves are thinner and more fragmented (impaired aortic stiffness)

Table 1

Histopathology of Cystic Medial Degeneration

Characteristic	BAV aneurysm	Marfan aneurysm	TAV aneurysm
Reduction ECM components	Increase VSMC apoptosis: reduction production of ECM proteins		
	Elastin fragmentation: loss of structural support and elasticity		
	FB-1 deficiency: detachment of VSMC from elastin and collagen matrix (matrix disruption)		Lesser degree of changes
Increase matrix degradation enzymes	Increase MMP-2 Increase MMP-9 Increase MMP2/TIMP-1	Increase MMP-12	Increase MMP-13
Spatial CMD distribution	Asymmetrical	Circumferential	Confined to aneurysmal region

BAV, bicuspid aortic valve; CMD, cystic medial degeneration; ECM, extracellular matrix; FB, fibrillin; MMP, matrix metalloproteinase; TAV, tricuspid aortic valve; TIMP, tissue inhibitor of metalloproteinase; VSMC, vascular smooth muscle cells.

Table 1. Abnormalities Associated With BAV Disease

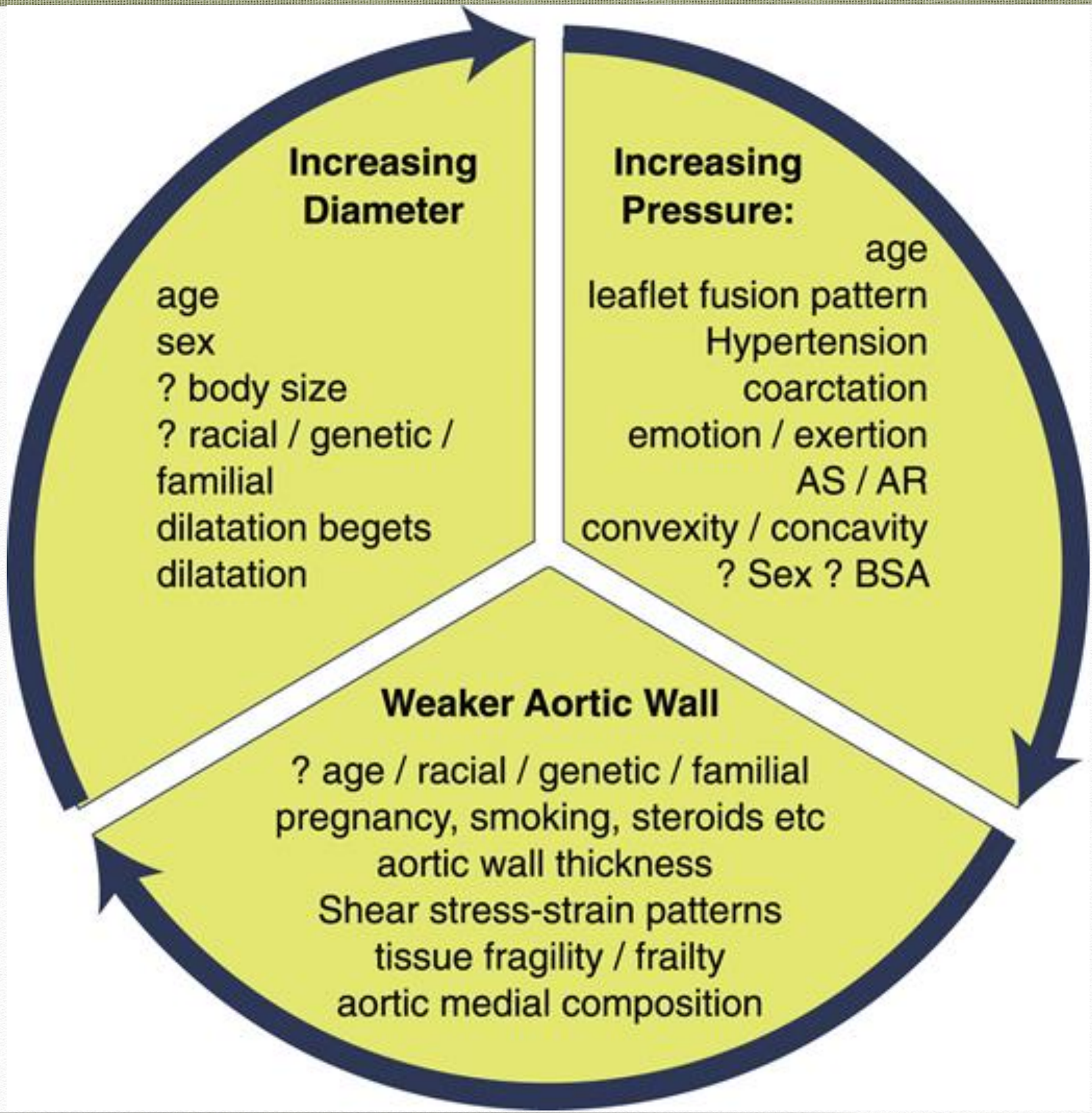
	Result
Genetics	
NOTCH1 mutation	Disrupted intercellular signaling during aortic valve development
UFD1L downregulation	Abnormal development of the cardiac outflow tract
ACTA2 mutation	Decreased VSMC actin α_2 production
eNOS mutation	Abnormal valve and vascular development
Chromosomal linkage detected on 5q, 13q, 18q, 22q	N/A
Histopathology and immunohistochemistry	
Medial degeneration	
VSMC apoptosis	Decreased production of extracellular matrix proteins
Elastin fragmentation	Loss of structural support and elasticity
Differential expression of Bcl-2	Increased VSMC apoptosis
Fibrillin-1 deficiency	Detachment of VSMCs from elastin and collagen matrix
Differential expression of MMPs and TIMPs	Increased degradation of collagen and elastin
Differential expression of PKC	Upregulation of MMPs
Decreased expression of eNOS	Abnormal regulation of vascular remodeling

eNOS indicates endothelial nitric oxide synthase; PKC, protein kinase C; and N/A, not applicable.

TABLE 34.1 Commonest Congenital Heart Disease Lesions Associated with Aortic Root Abnormalities

Heart Defect	Location of AoD	Incidence of AoD	Incidence of Dissection	Recommendations for Ao Replacement
MFS	Sinuses of Valsalva (typical location)	■ 35% by 5 y (24) ■ 68% by 19 y (24)	■ 4.3% in childhood (26) ■ 20% in adolescence (26)	■ >50 mm ■ accelerated aortic growth (>10 mm/y) ■ Development of aortic regurgitation ■ Need for mitral valve surgery
BAV	Ao root and ascending aorta	<19 y, isolated BAV (64) ■ 12% marked AoD ■ 25% moderate AoD	■ Case reports in adolescents (65)	■ >50 mm ■ accelerated aortic growth (>10 mm/y) ■ Need for aortic valve surgery with AoD > 45 mm
TOF	Ao root and ascending aorta	<19 y, repaired TOF (89) ■ 87% at sinus of Valsalva ■ 63% at ascending aorta	■ two case reports in adults with repaired TOF (84,85)	■ ≥ 55 mm, especially when there is an indication for pulmonary valve implantation ■ Development of aortic regurgitation with AoD > 50 mm
CoA	Ascending aorta and site of previous surgical repair	Pediatric and adult population (100) ■ 9% after surgical repair	Pediatric and adult population (100) ■ <1% after surgical repair	■ ~50 mm ■ Accelerated aortic growth (>10 mm/y) ■ Development of aortic regurgitation
Arterial switch	Neoaortic root dilation	■ 33.4% after surgical repair (106)	■ No reports	■ Severe neoaortic root dilation (≥55 mm)

Ao, aortic; AoD, aortic dilation; BAV, bicuspid aortic valve; CoA, coarctation of the aorta; TOF, Tetralogy of Fallot.


Increasing Diameter
age
sex
? body size
? racial / genetic / familial
dilatation begets dilatation
Increasing Pressure:
age
leaflet fusion pattern
Hypertension
coarctation
emotion / exertion
AS / AR
convexity / concavity
? Sex ? BSA
Weaker Aortic Wall
? age / racial / genetic / familial
pregnancy, smoking, steroids etc
aortic wall thickness
Shear stress-strain patterns
tissue fragility / frailty
aortic medial composition

Serial Imaging

- ✓ Aortic dilation is usually silent but may produce symptoms of acute aortic dissection or rupture as aneurysm formation progresses. Thus early identification of aortopathy is important for appropriate follow-up and timely intervention

- ✓ echocardiography recommended 6-12 mo

- ✓ The normal range (AscAo and aortic root diameter<21 mm/m2)

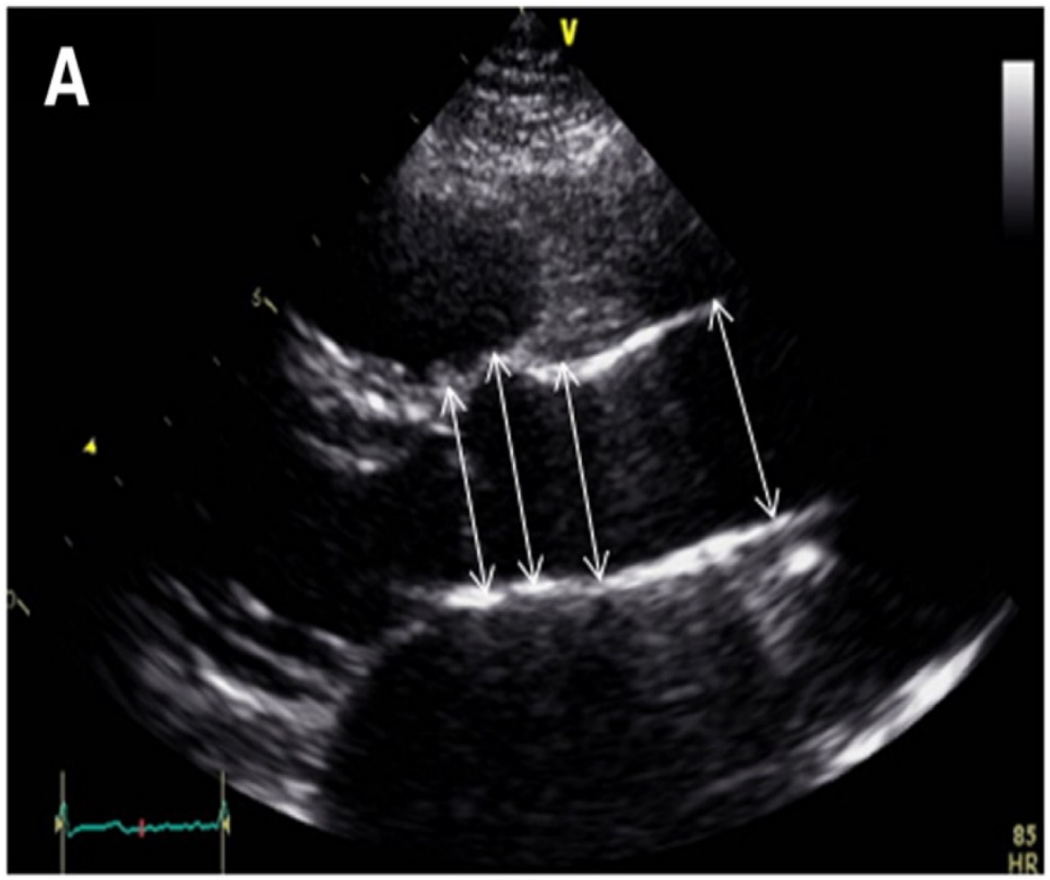
- ✓ Transthoracic echocardiography (TTE) is a noninvasive, cost- effective imaging modality.

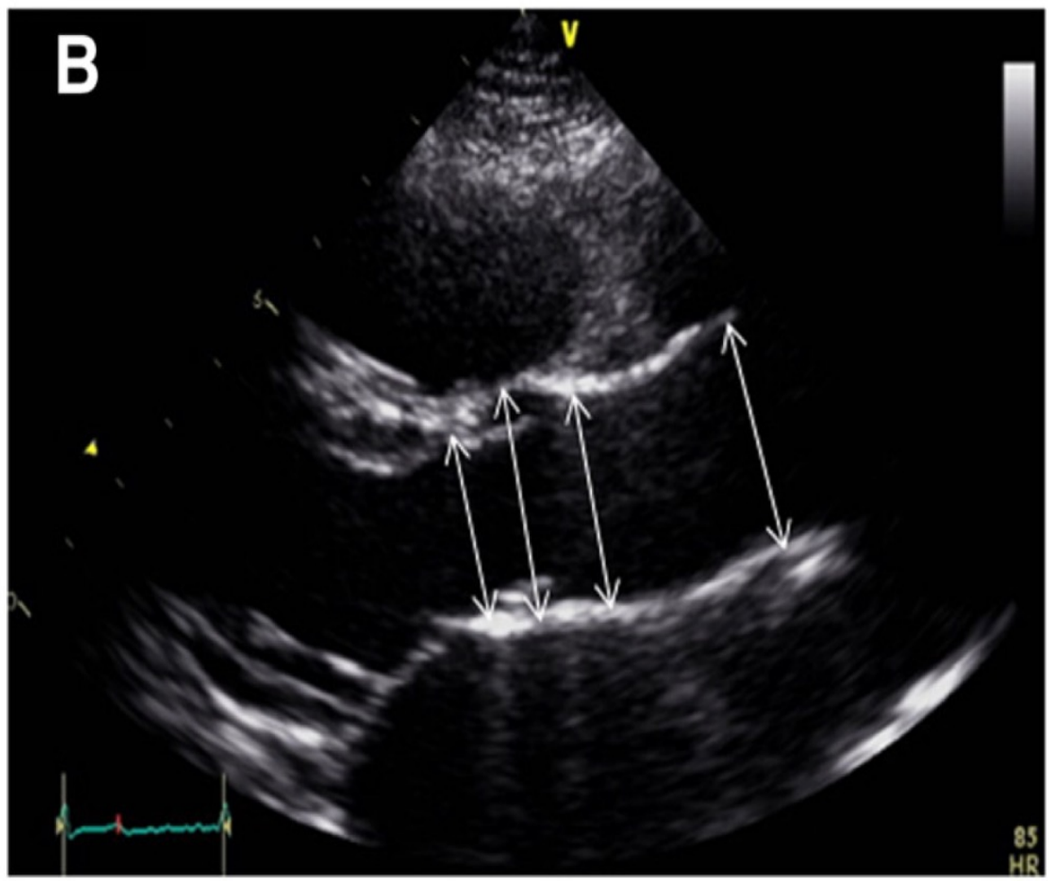
Imaging

- ✓ Measurements of the aortic root, proximal A.AO, and aortic arch by TTE correlate closely with measurements by CT scan ,however, adequate TTE views of the mid and distal A.AO can be difficult to obtain, due to movement of the aorta, especially in those with large body habitus.

- ✓ TTE is an accurate imaging modality, with an insignificant trend toward underestimation of aortic diameter with the use of TTE,CT and MRI measure external diameter, which is 2-4 mm higher compared to the internal diameter measured by echo

A-diastole, leading edge to leading edge
B-systole ,inner edge to inner edge





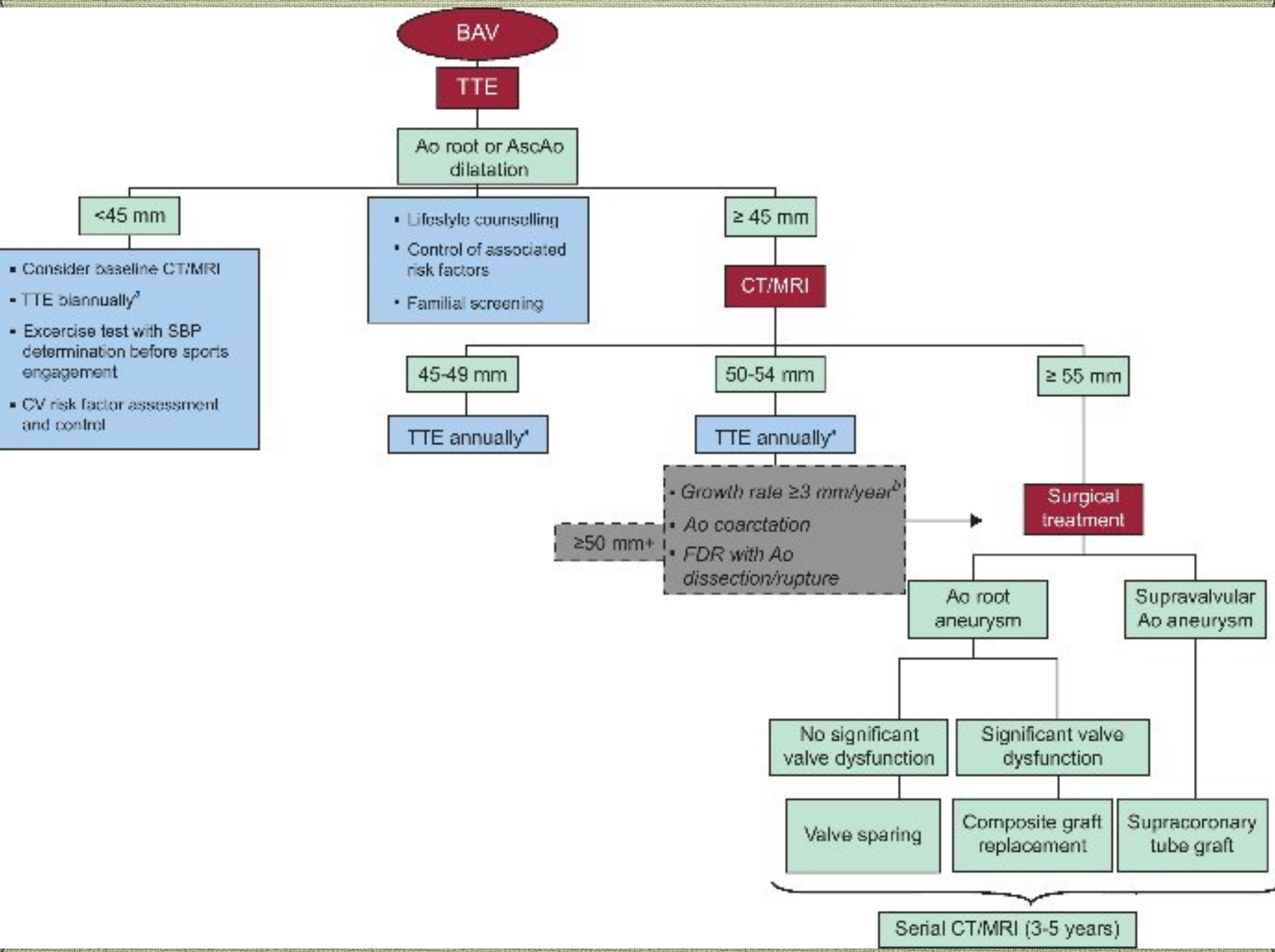
imaging

- if echocardiography provides an indication for surgical intervention, then the images should be remeasured by the initial reader as well as a second reader to ensure accuracy before proceeding to surgery

- If TTE cannot provide measurements from the aortic root up to the mid A.AO, a CT or MRI should be performed.

- Furthermore, if the aortic root or A.AO is 40 mm or more on TTE, a CT or MRI should be performed to evaluate the extent of dilatation as well as screen for COA.

- TEE


BAV
TTE
Ao root or AscAo dilatation
<45 mm
Consider baseline CT/MRI
TTE biannually*
Exercise test with SBP determination before sports engagement
CV risk factor assessment and control
Lifestyle counselling
Control of associated risk factors
Familial screening
≥ 45 mm
CT/MRI
45-49 mm
TTE annually*
50-54 mm
TTE annually*
≥ 55 mm
≥50 mm+
Growth rate ≥3 mm/year*
Ao coarctation
FDR with Ao dissection/rupture
Surgical treatment
Ao root aneurysm
Supravalvular Ao aneurysm
No significant valve dysfunction
Significant valve dysfunction
Valve sparing
Composite graft replacement
Supracoronary tube graft
Serial CT/MRI (3-5 years)

non surgical management

- ✓ BAV is autosomal dominant with reduced penetrance (ninefold in first degree relatives)

- ✓ recent AHA recommendations include echocardiographic screening of first-degree relatives of patients with BAV

non surgical management(cont.)

- ✓ In addition to routine imaging assessment, patients with BAV should receive information on typical symptoms and the risk of aortic dissection

- ✓ Activities or lifestyle should be modified since high intensity competitive and collision sports are potentially dangerous and may precipitate aortic dissection or rupture in more than mild aortic dilatation

non surgical management(cont.)

- ✓ aggressive control of HTN(COA) beta -Blockers and ACE inhibitors or angiotensin II receptor blockers should be considered as first-line agents

- ✓ Prophylactic beta-blocker in BAV disease is recommended in patientswith aortic diameter (>40 mm) without significant aortic regurgitation .

- ✓ losartan has also been shown to reduce the rate of aortic dilatation in marfan (no study in BAV)

- ✓ Statins may potentially limit aortic dilatation by reducing MMP expression and by improving endothelial function via increased endothelial nitric oxide synthase (no clinical use)

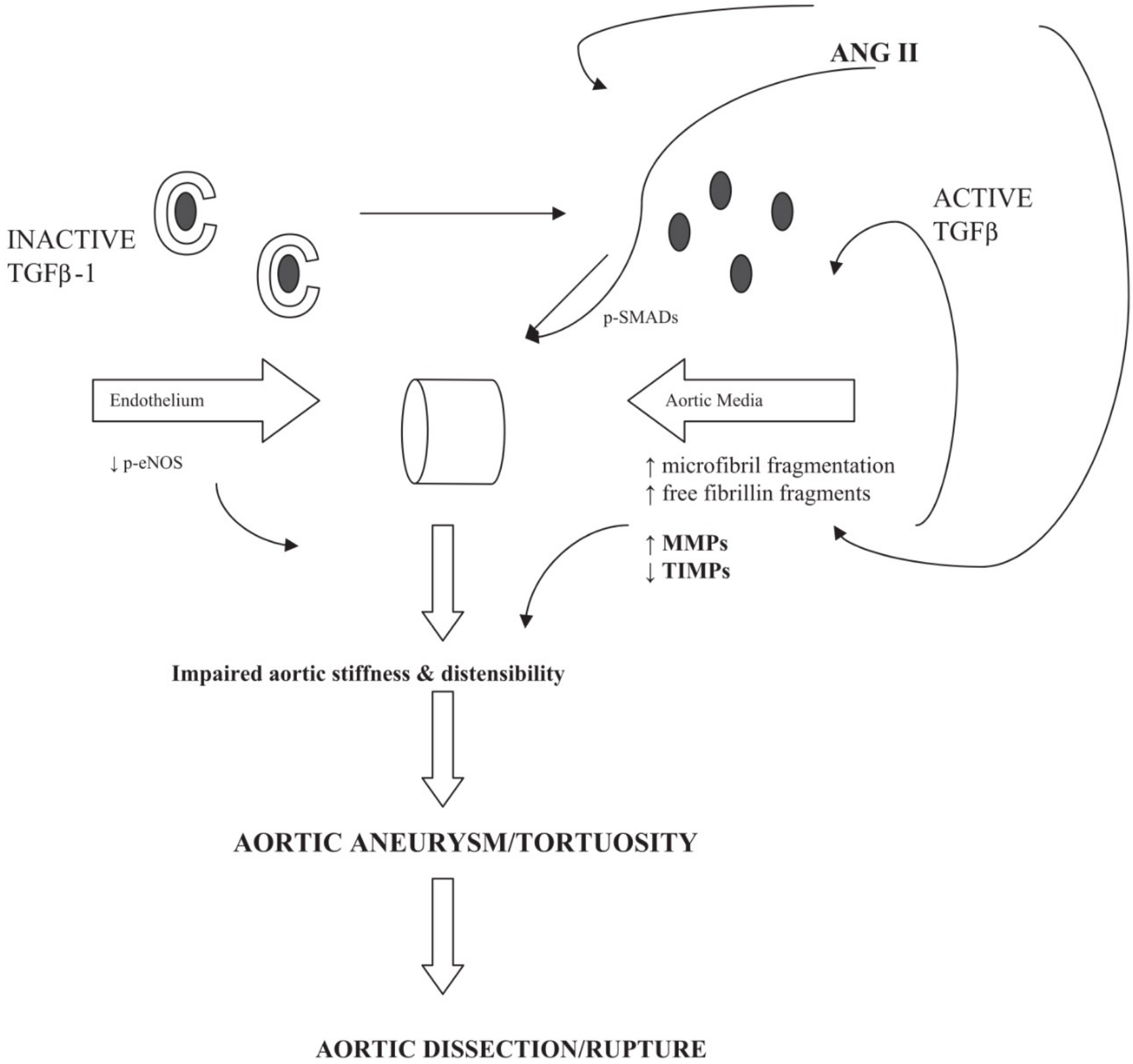


Figure 1 **Summary of Proposed Aneurysm-Promoting Mechanisms and Sites of Medical Therapies**

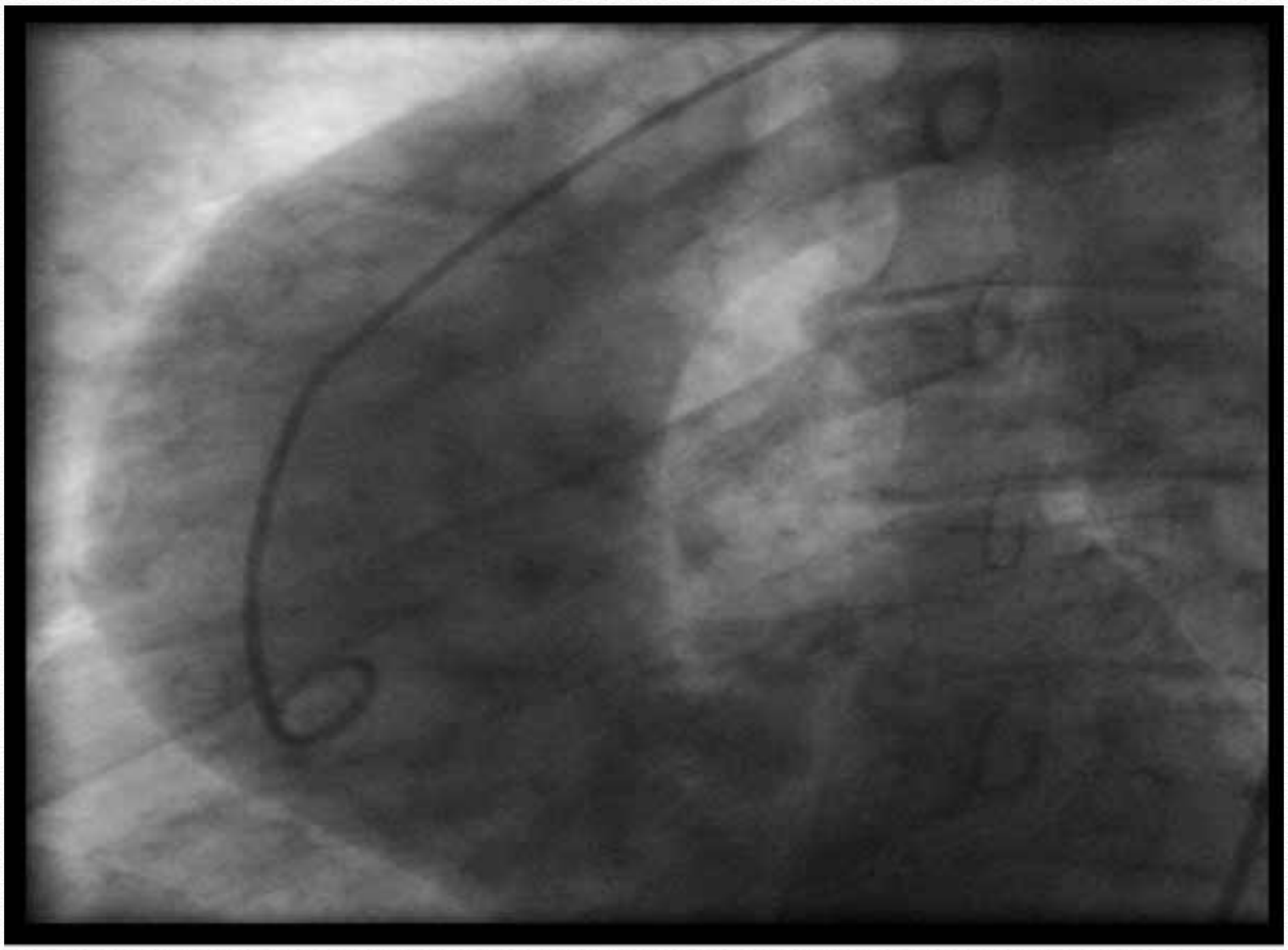


Table 3: Criteria for elective replacement of the ascending aorta in patients with BAV.

AHA/ACC guidelines
Class I
(1) Aortic diameter >5.0 cm
(Level of evidence: B)
(2) Aneurysm growth rate >0.5 cm/year
(Level of evidence: B)
(3) Aortic diameter >4.5 cm with concomitant indication for elective aortic valve repair/replacement
(Level of evidence: B)
Aortic size ratios and indexes
Aortic diameters >4.5 cm and either of the following:
(1) Ratio of aortic area to body height >10 cm^2/m in asymptomatic patients with well-functioning BAV, or 8-9 cm^2/m in symptomatic patients [91]
(2) Ratio of aortic diameter to body surface area >4.5 cm/m^2 [92]
Other criteria (unvalidated)
Aortic diameters >4.5 cm and any of the following:
(1) Aortic coarctation, corrected or uncorrected [93]
(2) First-degree relative with ascending aortic dissection or rupture
(3) Long smoking history, especially with COPD [94, 95]

Table 2
Surgical Options for Bicuspid Aortic Valve Disease

Surgical technique	Considerations
Reduction aortoplasty with /without external synthetic wrapping	• Generally not recommended (risk of recurrent dilatation) • Alternative for patients with high surgical risk (especially if sinuses are not significantly dilated)
Replacement of aortic root and AscAo with reimplantation of coronary ostia (Bentall procedure)	Standard technique in patients with significant valve disease and dilatation of AscAo
Aortic valve replacement and separate supracoronary aortic repair	• Generally not recommended (risk of progressive sinus dilatation) • Alternative for older patients with BAV stenosis, normal sized sinuses and dilatation of supracoronary AscAo
Valve-sparing aortic replacement	Acceptable option for young patients with normally-functioning BAV
Pulmonary autograft	• Generally not recommended (risk of autograft dilatation) • Alternative for children, adolescents or young women who wish to become pregnant
Aortic valve repair	Acceptable option if careful patient selection is made

AscAo, ascending aorta; BAV, bicuspid aortic valve.