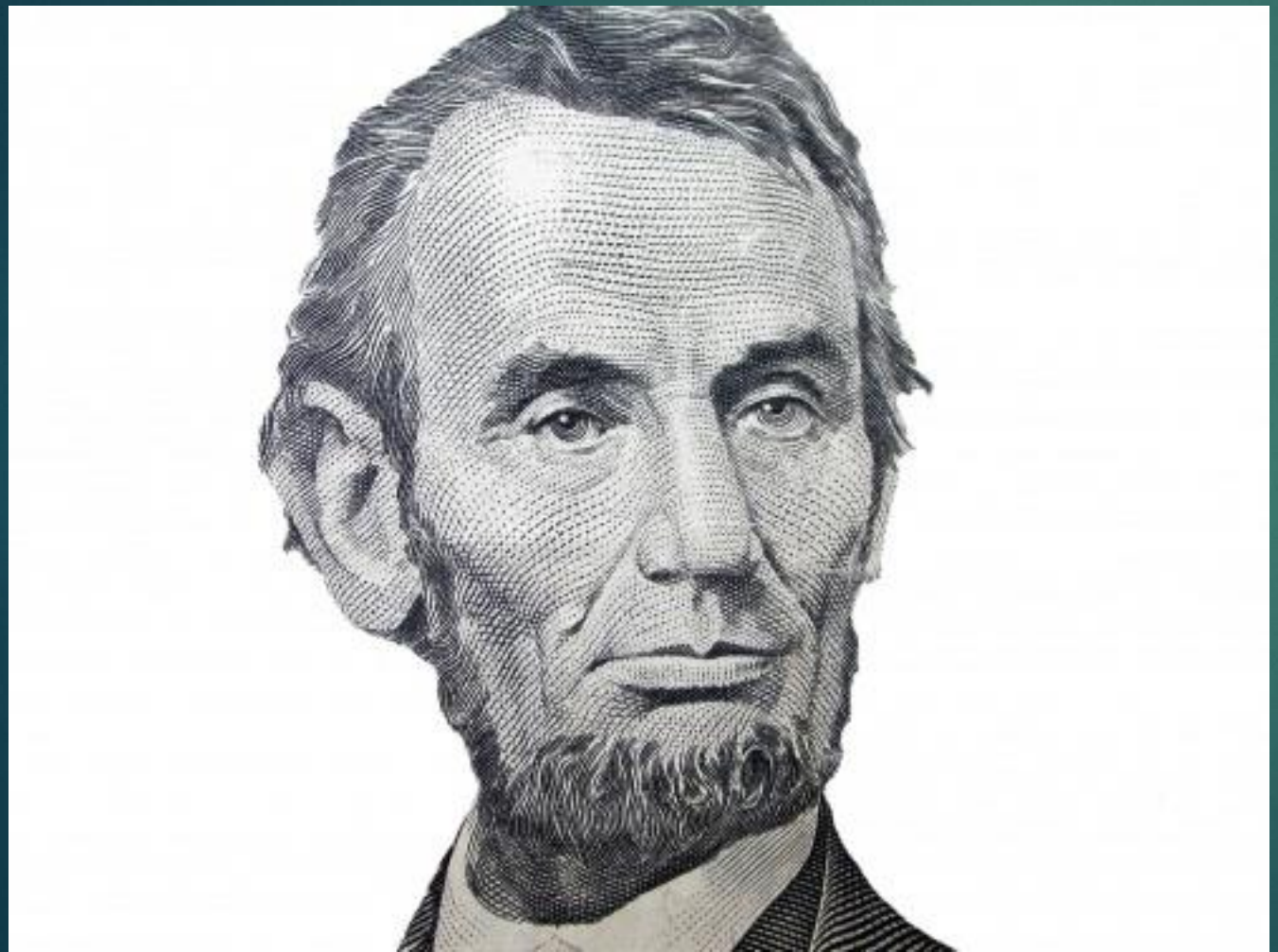
4.7 Aortopathies

PREPARED BY DR. MORHUF AL.SOLIMAN

- He had lean stature, sloping shoulders, long nose, small head, and small eyes which happened to be the visible effects of this disease



SIGNS OF SYNDROME

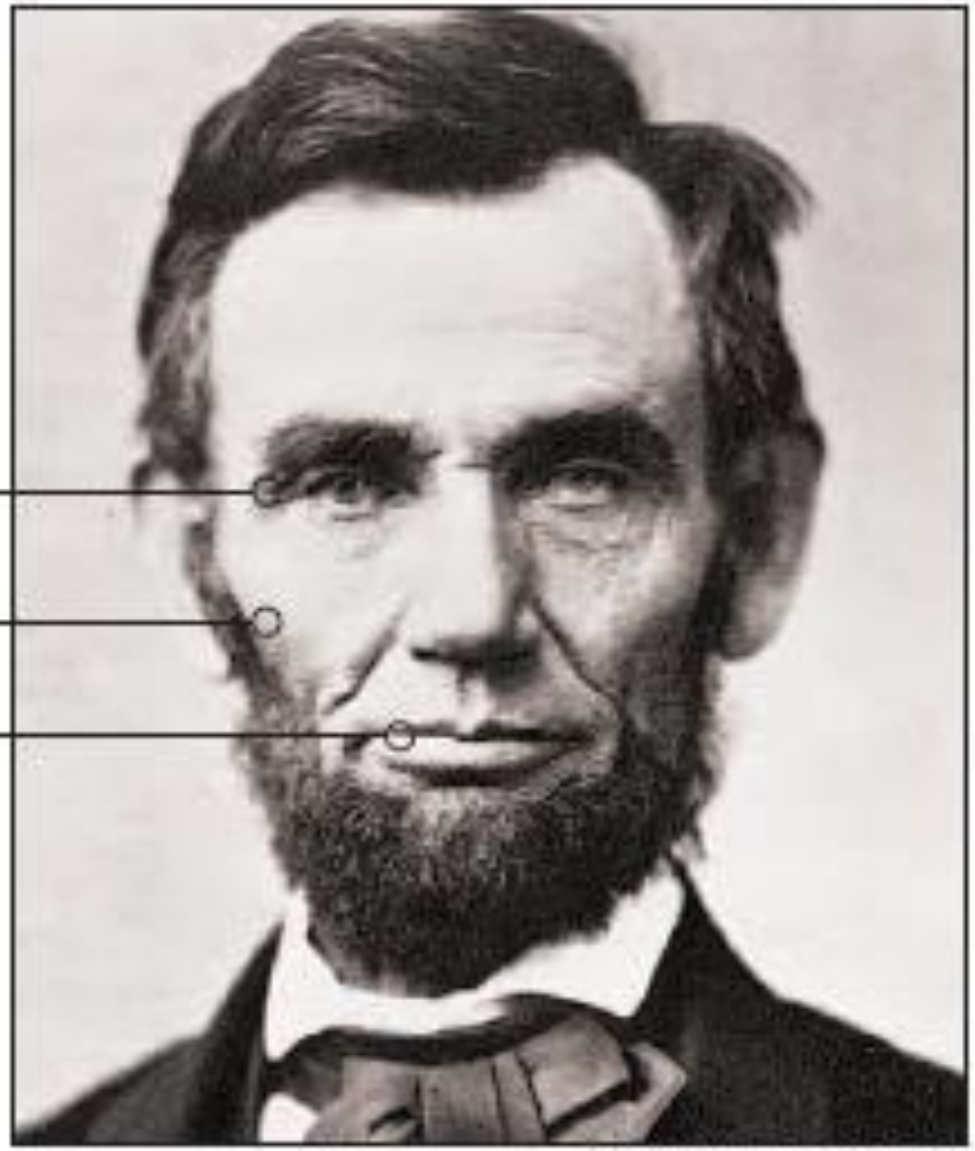
Cardiologist John Sotos says these features of Lincoln bolster his diagnosis of MEN 2B, a genetic disease that causes aggressive thyroid cancer:

Hooded eyes

Asymmetric jaw

Enlarged and lumpy lips

Sotos believes Lincoln was dying from a genetic cancer syndrome when he was shot on April 14, 1865. Only a DNA sample can prove the controversial theory.



LIBRARY OF CONGRESS

4.7.1 Marfan syndrome and related heritable thoracic aortic diseases 4.7.1.1 Introduction and b

- Marfan syndrome is the prototype of syndromic HTAD entities, comprising a clinically and genetically heterogeneous group of disorders with aneurysm or dissection of the thoracic aorta as the common denominator. Both syndromic and non-syndromic (or isolated) forms of HTAD are part of the clinical spectrum, with notable clinical overlap between the various entities
- Since most children with mainly syndromic forms of HTAD will be transferred to ACHD units at adult age
- , these Guidelines focus on specific cardiovascular complications. Marfan syndrome is considered as the model disease other syndromes are mentioned in case of important differences from Marfan syndrome.

4.7.1.2 Clinical presentation and natural history

- Although thoracic aortic disease either aneurysms detected by screening or dissection in an emergency setting is the principal characteristic in Marfan syndrome /HTAD, extra-aortic features in the skeletal/ocular organ system may be the key to diagnosis in some patients.
- Prognosis in all HTAD entities is mainly determined by progressive dilation of the aorta, leading to aortic dissection or rupture.
- Prognosis varies according to the underlying genetic defect.
- The average age at death in untreated Marfan syndrome patients< 40 years,
- but can approach that of the general population in patients in whom the diagnosis is known and who are properly managed.
- More rare cardiovascular causes of death include heart failure and SCD.
- In Marfan syndrome, the major determinant of type A aortic dissection is the aortic root diameter with increased risk of rupture >50 mm.
- Other risk factors include family history of aortic dissection at low diameter, aortic root growth rate, pregnancy, and hypertension. Increasing evidence for gene-based differences in aortic risk are emerging and need to be considered. Other parts of the aorta or in the case of some entities, major branching vessels may also dilate or dissect.

Cont.

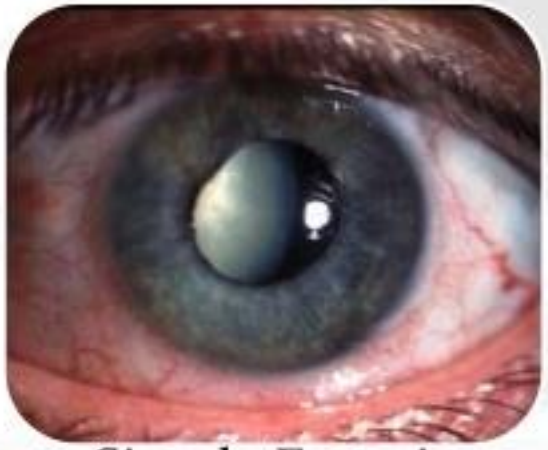
- The presence of significant aortic, tricuspid, or mitral regurgitation usually related to valve prolapse may lead to symptoms of ventricular volume overload.
- However, LV disease may also occur independently of valvular dysfunction and this may be associated with arrhythmia.
- Mitral valve prolapse in patients with Marfan syndrome manifests early and progresses to severe regurgitation, need for surgery, and IE earlier than idiopathic mitral valve prolapse.

4.7.1.3 Diagnostic work-up

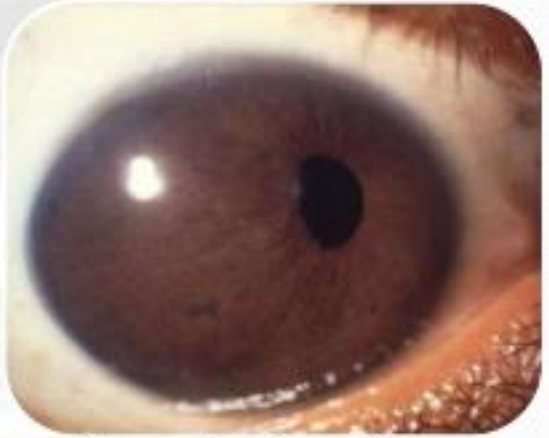
- Early identification and establishment of the correct diagnosis is critical since prophylactic surgery can prevent aortic dissection and rupture. This requires a multidisciplinary team approach with integration of clinical and genetic findings.
- The diagnosis of Marfan syndrome is based on the Ghent criteria, with aortic root aneurysm/dissection and ectopia lentis as cardinal features.
- Criteria for the other HTAD entities are less well defined. Gene panel testing is meaningful for confirmation of the diagnosis and to guide management.
- Mutation pick-up rate in syndromic forms is higher (>90%) than in non-syndromic entities (20-30%).
- Once a pathogenic variant is identified, presymptomatic genetic screening of family members is mandatory to allow early and appropriate management.

Congenital Ectopia Lentis

- Usually bilateral and symmetrical



Simple Ectopia Lentis



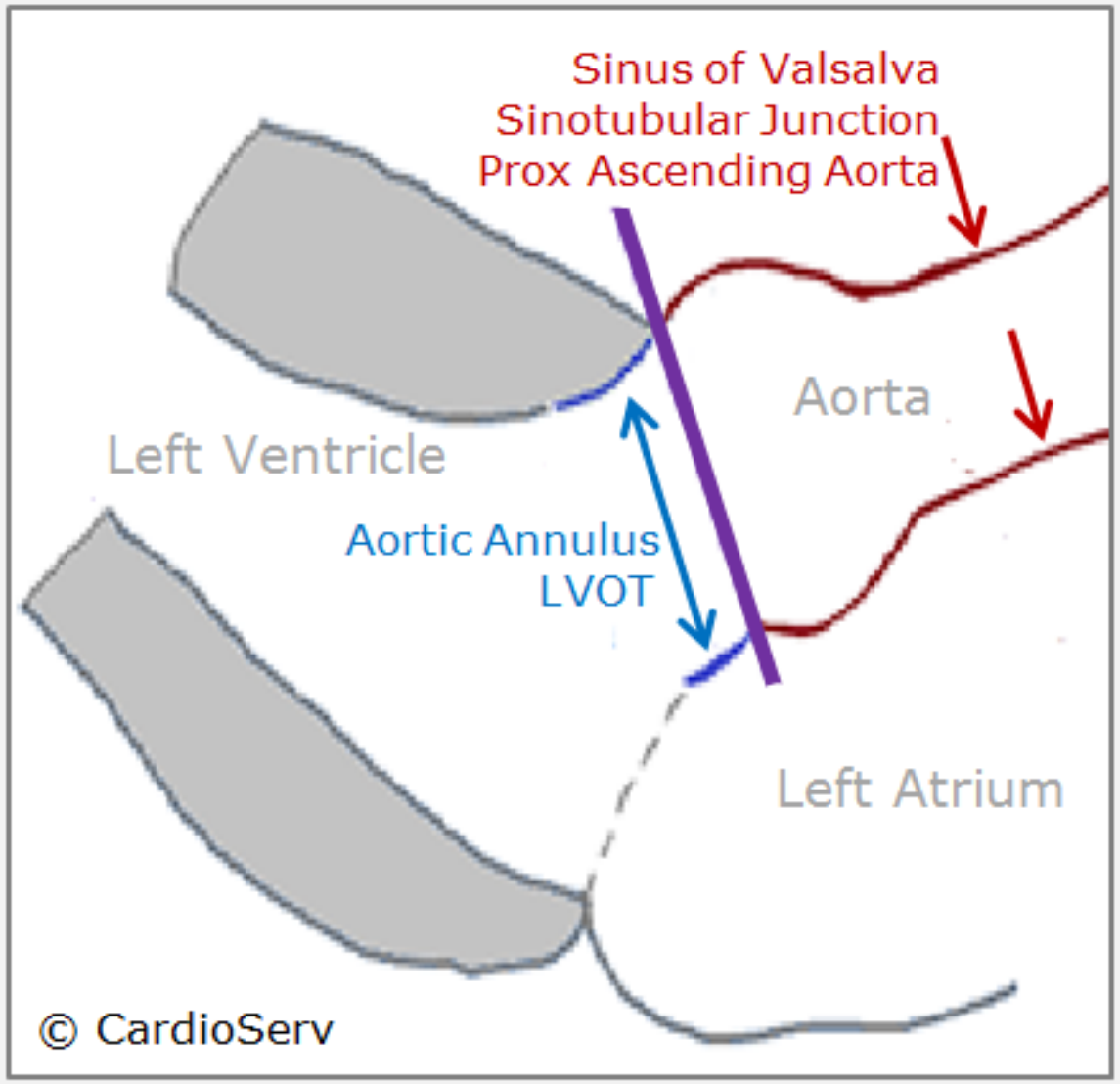
Ectopia Lentis et Pupillae

Laxmi eye institute

System	Major criteria	Minor criteria
Family history	Independent diagnosis in parent, child or sibling	None
Genetics	Mutation FBN1	None
Cardiovascular	Aortic root dilatation, dissection of ascending aorta	Mitral valve prolapse, calcification of the mitral valve (<40 years), dilatation of the pulmonary artery, dilatation/dissection of descending aorta
Ocular	Ectopia lentis	2 needed of the following: flat cornea elongated globe myopia
Skeletal	At least 4 of the following: pectus excavatum needing surgery, pectus carinatum, pes planus, positive wrist or thumb sign, scoliosis >20° or spondylolisthesis, armspan-height ratio >1.05, protrusio acetabulae, diminished extension elbows (<170°)	For the skeletal system to be involved 2–3 major, or 1 major and 2 minor signs should be present: moderate pectus excavatum, high arched palate, typical facial features, joint hypermobility
Pulmonary		Spontaneous pneumothorax, apical bulla
Skin		Striae, recurrent or incisional herniae
Central nervous system	Lumbosacral dural ectasia	

Echocardiographic assessment<<<

- of the aortic root should include measurements at the annulus, sinus, sinotubular junction, distal ascending, arch, and descending thoracic aortic levels.
- In adults, measurement at end diastole using the leadingto-leading edge principle is recommended.
- The values obtained should be corrected for the individual's age, sex, and body size using standardized nomograms.
- Valvular morphology (mitral valve prolapse, BAV) and function must be assessed, as well as the presence of a PDA.
- LV dimension and function should be addressed according to standard recommendations.



Use the aortic annulus as a landmark

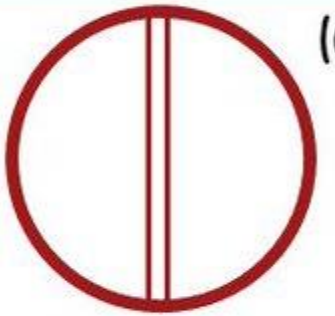
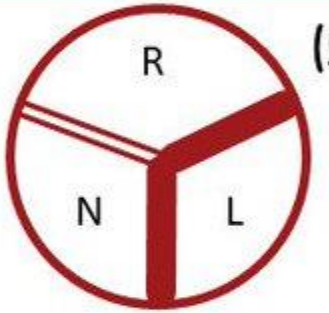
Aortic side of annulus is measured:

- Leading Edge – Leading Edge
- End Diastole

Ventricular side and annulus is measured:

- Inner Edge – Inner Edge
- Mid-Systole

Classification of BAV

Type 0 (0 raphe, true BAV)	Type 1 (1 raphe)	Type 2 (2 raphe)
 (6%)	 (89%)	 (5%)
(4%)  lat (2%)  AP	Type 1a (71%)  R-L Type 1b (15%)  R-N Type 1c (3%)  L-N	(functionally unicuspid)

Adapted from Sievers HH, Schmidtke C. J Thorac Cardiovasc Surg 2007; 133:1226-1233

Cont.

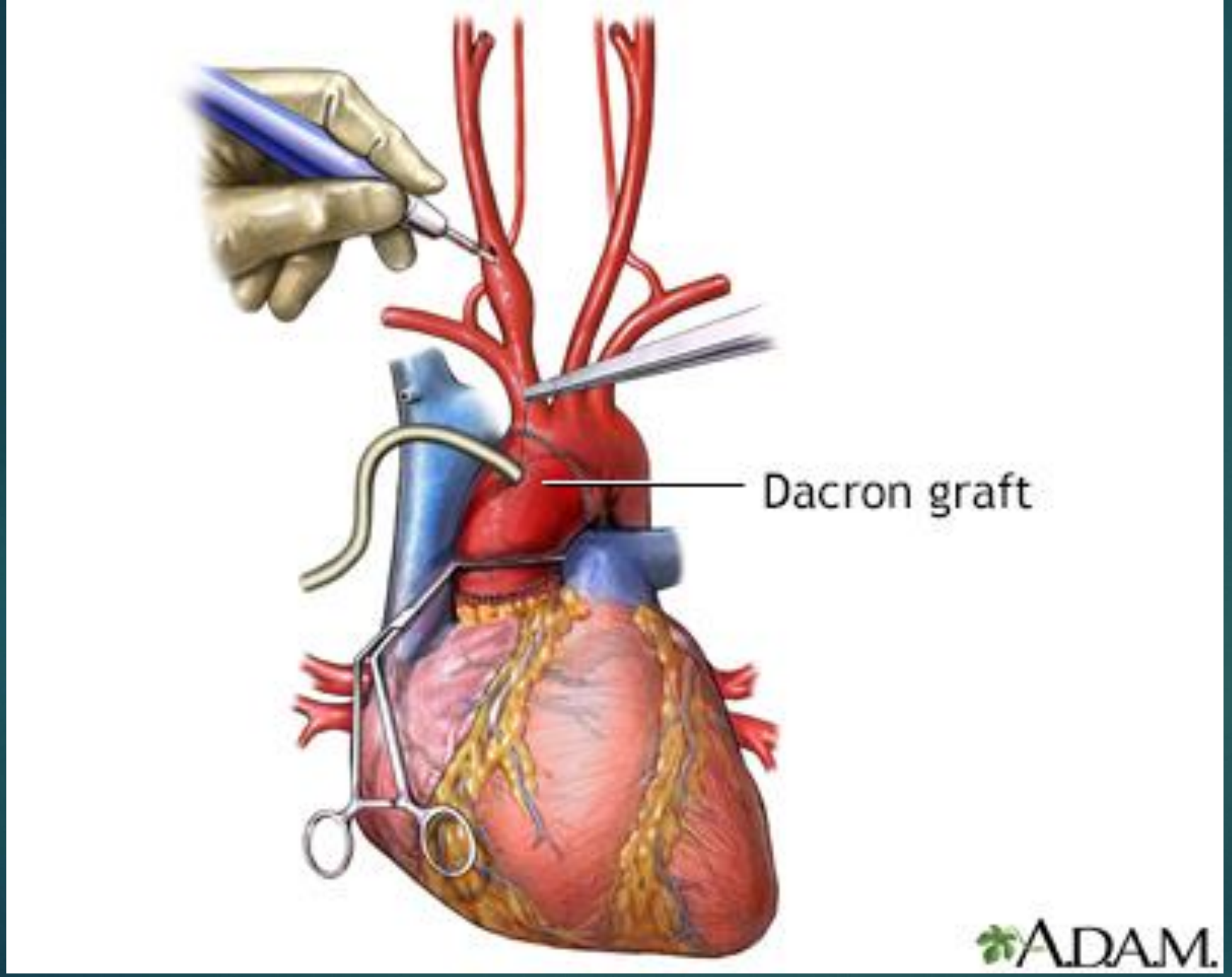
- • CMR or CCT angiography from head to pelvis should be performed in every patient at baseline, providing imaging of the entire aorta and branching vessels.
- In addition to measuring aortic diameters, information on aortic/vertebral artery tortuosity is important for diagnostic and prognostic purposes.2
- • Holter monitoring should be performed in symptomatic patients, as ventricular arrhythmias, conduction disturbances, and SCD can occur.

4.7.1.4 Medical therapy

- Although ~~no reduction in mortality or dissection rate has been established in any trial~~, beta blockers remain the mainstay for medical treatment in Marfan/HTAD patients, reducing wall shear stress and aortic growth rate.
- Rigorous antihypertensive medical treatment aimed at a 24-h ambulatory systolic blood pressure

4.7.1.5 Surgical treatment

- Indications for intervention are summarized in the Recommendations for aortic surgery in aortopathies table**. Prophylactic aortic root surgery is the only definitive treatment for the prevention of aortic dissection in Marfan syndrome and related HTADs**.
- In patients with anatomically normal aortic valves and low-grade regurgitation, a valve-sparing aortic root replacement by a **Dacron prosthesis** and reimplantation of the coronary arteries into the prosthesis (David procedure) has become the preferred surgical procedure with good long-term outcome, including in Marfan patients.
- Composite graft replacement, usually with a **mechanical valve**, is a more durable alternative but does ~~require lifelong anticoagulation~~.
- The decision on which technique to use should be made on an individual basis, and patient preferences and surgical experience should be taken into account.
- Marfan and related HTADs are associated with a risk of redissection and recurrent aneurysm in the **distal aorta**, especially in patients with previous dissection. With improved life expectancy, these complications now occur more frequently.
- **Open aortic surgery** remains the reference method for treatment of distal aortic disease, although hybrid procedures with endovascular stenting where proximal and distal landing is possible in a Dacron tube could be considered in selected cases.


Dacron graft
A.D.A.M.

4.7.1.6 Follow-up recommendations

- Lifelong and regular multidisciplinary follow-up at an expert centre is required. Echocardiography and CCT/CMR are the principal examinations.

4.7.1.7 Additional considerations

- Exercise/sports: patients should be advised to avoid exertion at maximal capacity, competitive, contact, and isometric sports. Risk estimation based on aortic size has been suggested by Budts et al. 24
- • Pregnancy: in genetically confirmed Marfan/HTAD, there is a 50% transmission risk for both men and women. Proper and timely genetic counselling is needed.
- Women with an aortic root diameter >45 mm are strongly discouraged from becoming pregnant without prior repair because of the increased risk of dissection.
- An aortic root diameter < 40 mm rarely presents a problem, although a completely safe diameter does not exist.
- With an aortic root 40-45 mm, previous aortic growth and family history are important factors when considering repair prior to pregnancy.
- After repair of the ascending aorta, Marfan patients remain at risk for dissection of the **residual aorta** .
- • IE prophylaxis: recommended only for high-risk patients .

4.7.2 Bicuspid aortic disease

- Depending on the reported series, 20-84% of patients with a BAV will **develop** ascending aortic dilatation, indicating that BAV should be regarded as part of a spectrum of valvluo-aortopathy and that bicuspid aortic disease may be a more appropriate term.
- Although the relative contribution of intrinsic/genetic wall abnormalities and altered haemodynamics remains debated, both factors are probably involved.
- In the absence of significant valvular dysfunction, aortic dilatation in the setting of bicuspid aortic disease typically evolves asymptomatically.
- With increasing diameters, however, the risk for acute aortic dissection rises. Compared with the general population, the dissection incidence in bicuspid aortic disease patients is **eight times higher**, which is in absolute numbers still a low risk (31/100 000 patient years) and **much lower** than in Marfan/HTAD.
- Observational studies indicate that the clinical outcome in bicuspid aortic disease patients is more similar to that of the general population with aneurysms and represents a **more benign** aortopathy than Marfan/ HTAD.

- CoA is associated with an increased risk for dissection

- To this date**, no evidence for medical treatment of aortic dilatation in the setting of bicuspid aortic disease is available,** but it may be reasonable to consider beta blockers or ARBs as first-line treatment for arterial hypertension.

- Indications for intervention are summarized in the Recommendations for aortic surgery in aortopathies table.
- Familial occurrence of BAV has clearly been established with rates of 5-10% in first-degree relatives in various studies.
- Echocardiographic screening in first-degree relatives of BAV patients is recommended and may be appropriate, particularly in **boys**, in **athletes**, and if hypertension is present. Rare pathogenic variants in a number of genes account for < 5% of all bicuspid aortic disease cases and routine genetic testing in this setting is not indicated but may be considered in familial cases.
- There are no data on the risk for dissection related to pregnancy in women with a dilated aorta.
- According to the 2018 ESC Guidelines for the management of cardiovascular disease during pregnancy, women should be counselled against pregnancy when the aortic diameter is >50 mm.

4.7.3 Turner syndrome

- Turner syndrome is caused by a partial or complete monosomy of the X-chromosome and occurs in 1 in 2500 live-born females.
- Turner syndrome is associated with short stature, delayed puberty, ovarian dysgenesis, hypergonadotropic hypogonadism, infertility, congenital malformations of the heart, diabetes mellitus, osteoporosis, and autoimmune disorders. CHD, occurring in approximately 50% of women with Turner syndrome, includes a high incidence of BAV, CoA, partial anomalous pulmonary venous connection, left SVC, elongated transverse aortic arch, dilatation of the brachiocephalic arteries, and aortic dilatation.
- Given this high prevalence of abnormalities, every woman with Turner syndrome should be seen by a **cardiologist** at least once.
- Even in the absence of CHD, all individuals with Turner syndrome have a generalized arteriopathy and Turner syndrome alone is an independent risk factor for thoracic aortic dilation.
- Aortic dissection (both type A and type B) occurs in approximately >>>>>>>>>
- 40 per 100 000 person-years compared with 6 per 100 000 person-years in the general population.

For diagnostic work-up see section 4.7.1.3. I

- Indications for intervention are summarized in the Recommendations for aortic surgery in aortopathies table.
- With advances in assisted reproductive technology and oocyte donation, an increasing number of women with Turner syndrome are now able to become pregnant.
- The presence of aortic dilatation and CHD increases the risks of pregnancy and Turner syndrome women are also at increased risk of hypertensive disorders, including pre-eclampsia.
- All women with Turner syndrome should be counselled about the increased cardiovascular risk of pregnancy and fertility treatment.

Recommendations for aortic surgery in aortopathies

Recommendations	Class[a]	Level[b]
Marfan syndrome and HTAD		
Aortic valve repair, using the reimplantation or remodelling with aortic annuloplasty technique, is recommended in young patients with Marfan syndrome or related HTAD with aortic root dilation and tricuspid aortic valves, when performed by experienced surgeons.	I	C
Surgery is indicated in patients with Marfan syndrome who have aortic root disease with a maximal aortic sinus diameter ≥50 mm.[c]	I	C
Surgery should be considered in patients with Marfan syndrome who have aortic root disease with maximal aortic sinus diameter ≥45 mm[c] and additional risk factors.[d]	IIa	C
Surgery should be considered in patients with a *TGFBR1* or *TGFBR2* mutation (including Loeys–Dietz syndrome) who have aortic root disease with maximal aortic sinus diameter >45mm.[c]	IIa	C

Bicuspid aortic disease		
Aortic surgery should be considered if the ascending aorta is: • ≥50 mm in the presence of a bicuspid valve with additional risk factors[e] or coarctation. • ≥55 mm for all other patients.	**IIa**	**C**
Turner syndrome		
Elective surgery for aneurysms of the aortic root and/or ascending aorta should be considered for women with Turner syndrome who are >16 years of age, have an ascending aortic size index >25 mm/m^2, and have associated risk factors for aortic dissection.[f]	**IIa**	**C**
Elective surgery for aneurysms of the aortic root and/or ascending aorta may be considered for women with Turner syndrome who are >16 years of age, have an ascending aortic size index >25 mm/m^2, and do not have associated risk factors for aortic dissection.[f]	**IIb**	**C**


Thank you

Ee Family history of aortic dissection at a low diameter (or personal history of spontaneous vascular dissection), progressive AR, desire for pregnancy, uncontrolled hypertension, and/or aortic size increase >3 mm/year (on repeated measurements using the same ECG-gated imaging technique measured at the same level of the aorta with side-by-side comparison and confirmed by another technique).