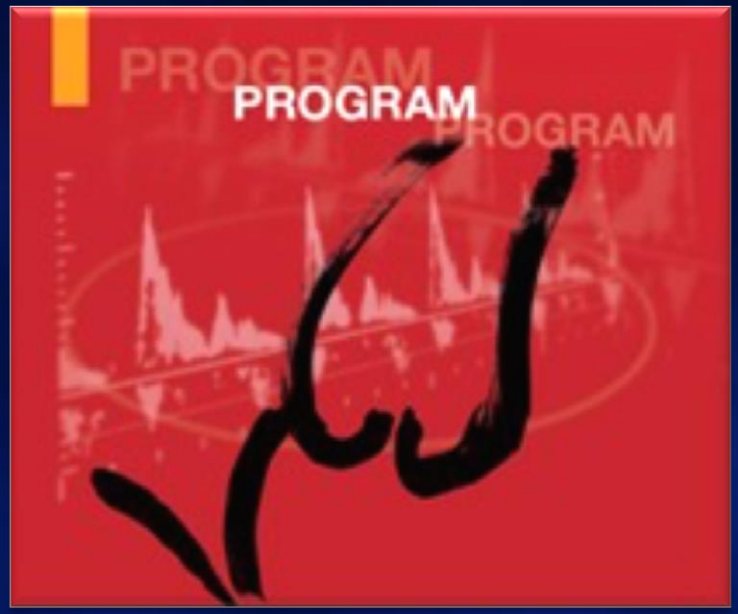


Aortic Aneurysm // AR

Hector I. Michelena, MD, FACC, FASE

Professor of Medicine
Director, Intra-operative Echocardiography
Mayo Clinic

NO DISCLOSURES

EXCEPT HONORED and frustrated…

"There is no disease more conducive to clinical humility than aneurysm of the aorta"

-William Osler

TAA Epidemiology and Definitions

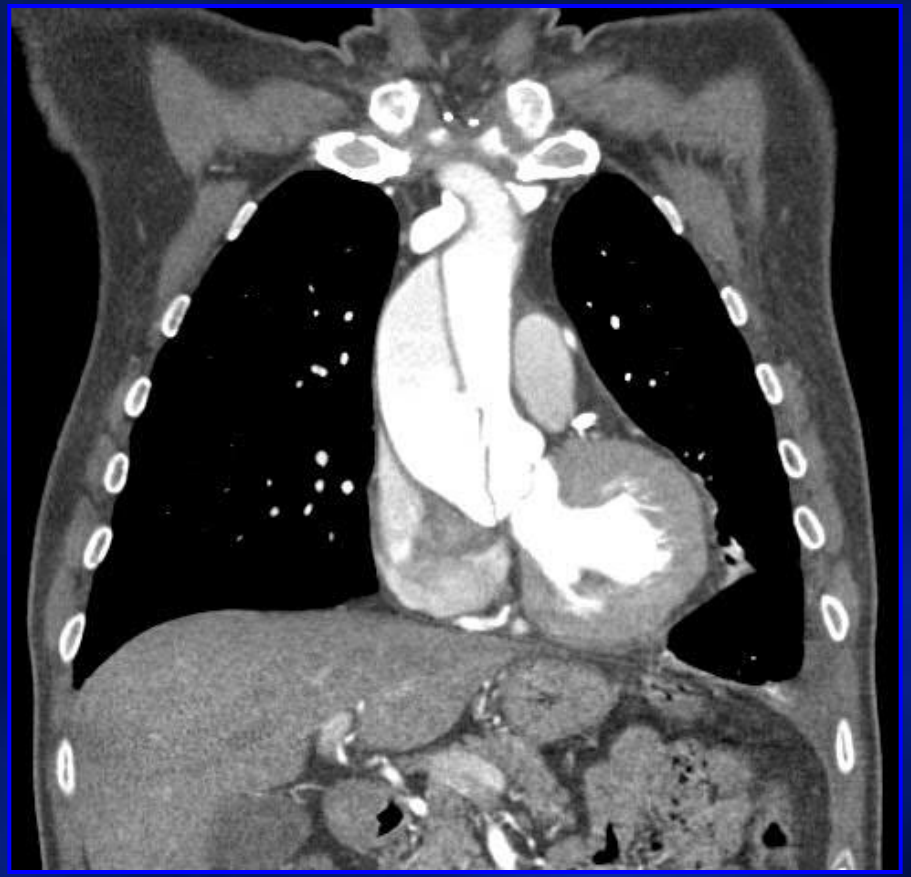
- TAA incidence 6/100,000
- Aneurysm

  Localized arterial dilation >50% ↑ in diameter
- Dissection

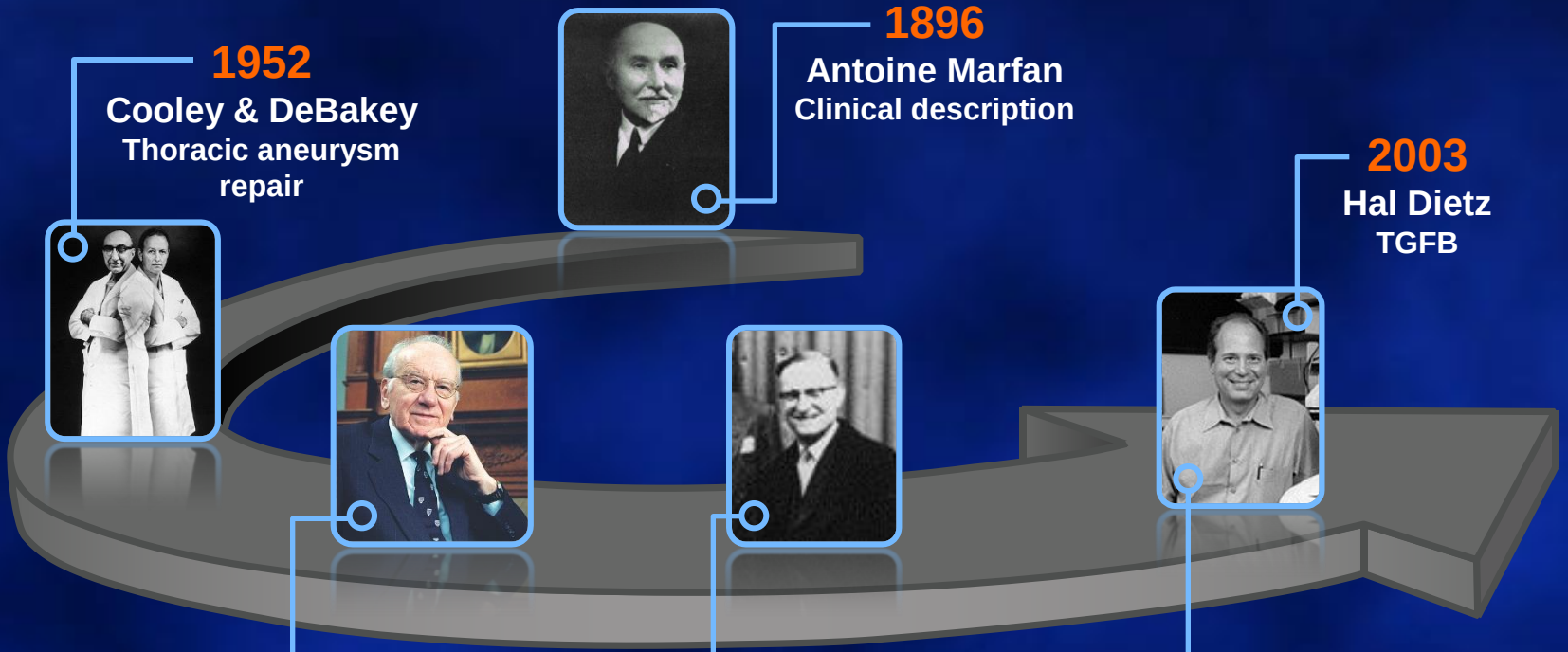
  Entry of column of blood through an intimal tear with layer separation → false lumen

Acute Aortic Dissection

- Potentially fatal condition
- 2 - 3.5/100,000 person years
- High mortality
  - 40% immediate
  - 1% per hour – first 48 hrs
  - 70% - first 2 weeks
- Correct diagnosis <50%
- Goal – rapid early Dx and Rx



Thoracic Aortic Aneurysm Milestones



1896
Antoine Marfan
Clinical description

1952
Cooley & DeBakey
Thoracic aneurysm repair

1956
Victor McKusick
Heritable Disorders of Connective Tissue

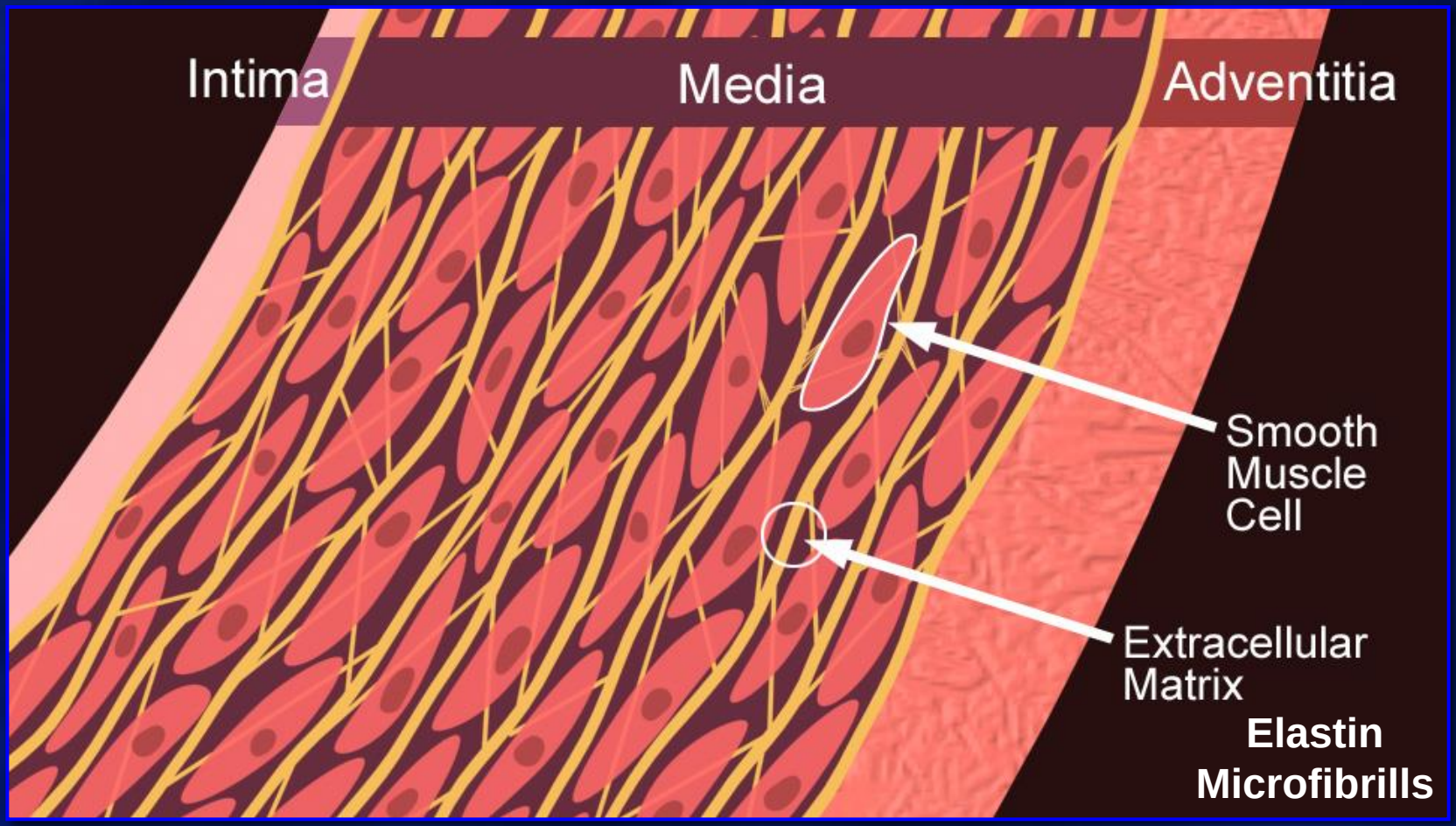
1968
Hugh Bentall
Composite graft

1991
Hal Dietz
Fibrillin gene

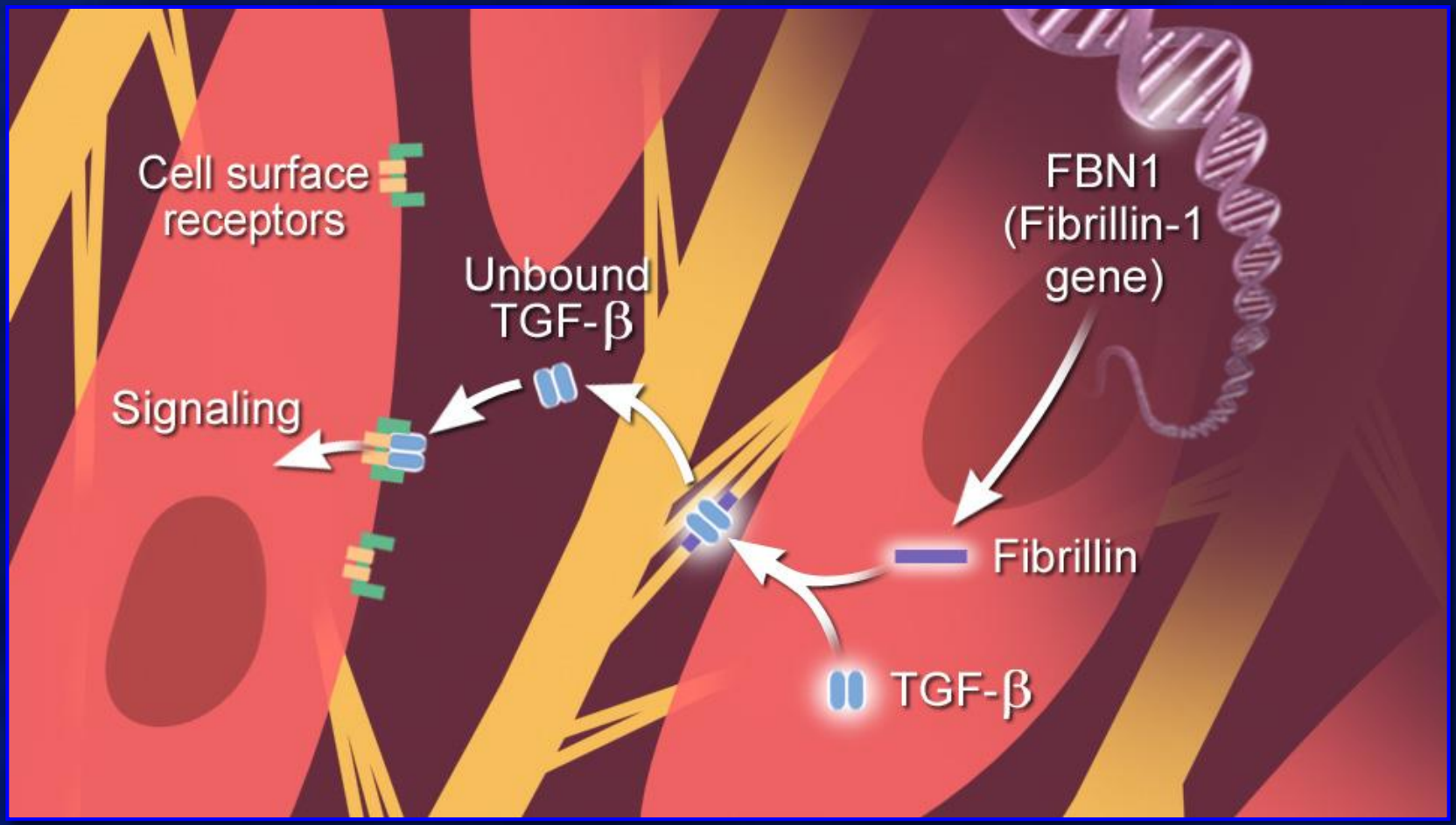
2003
Hal Dietz
TGFB

MAYO CLINIC

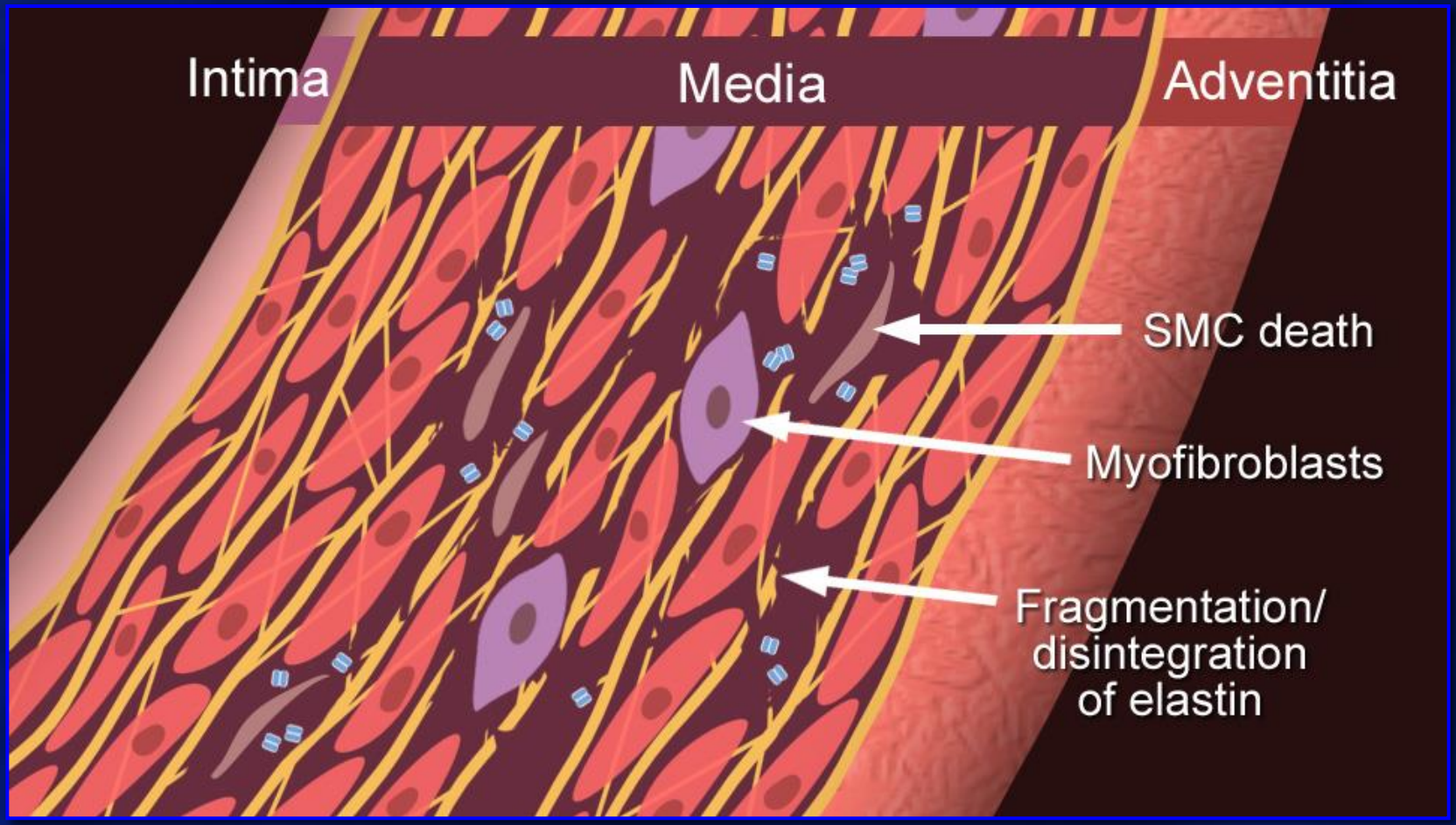
The Aorta

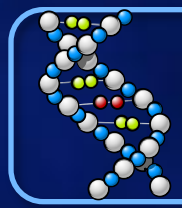


How it Works

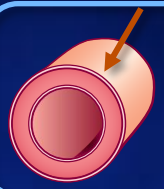


Medial Disease





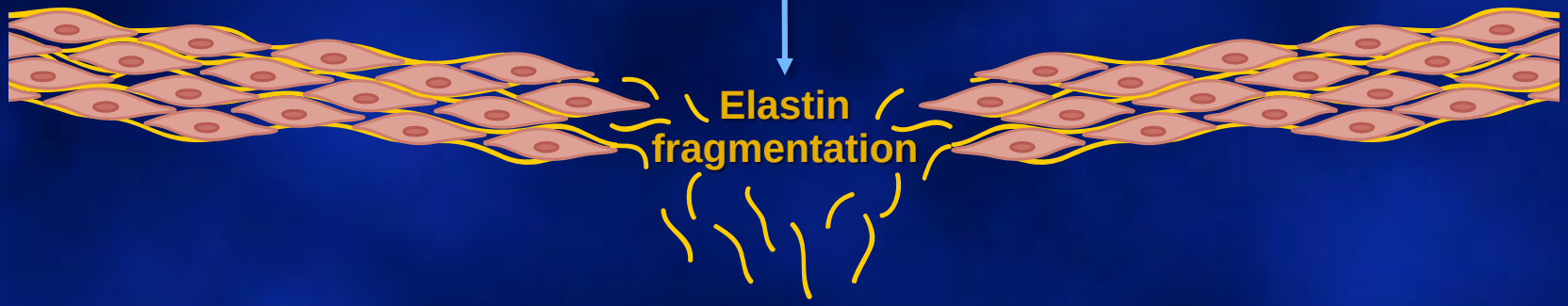
Gene mutations



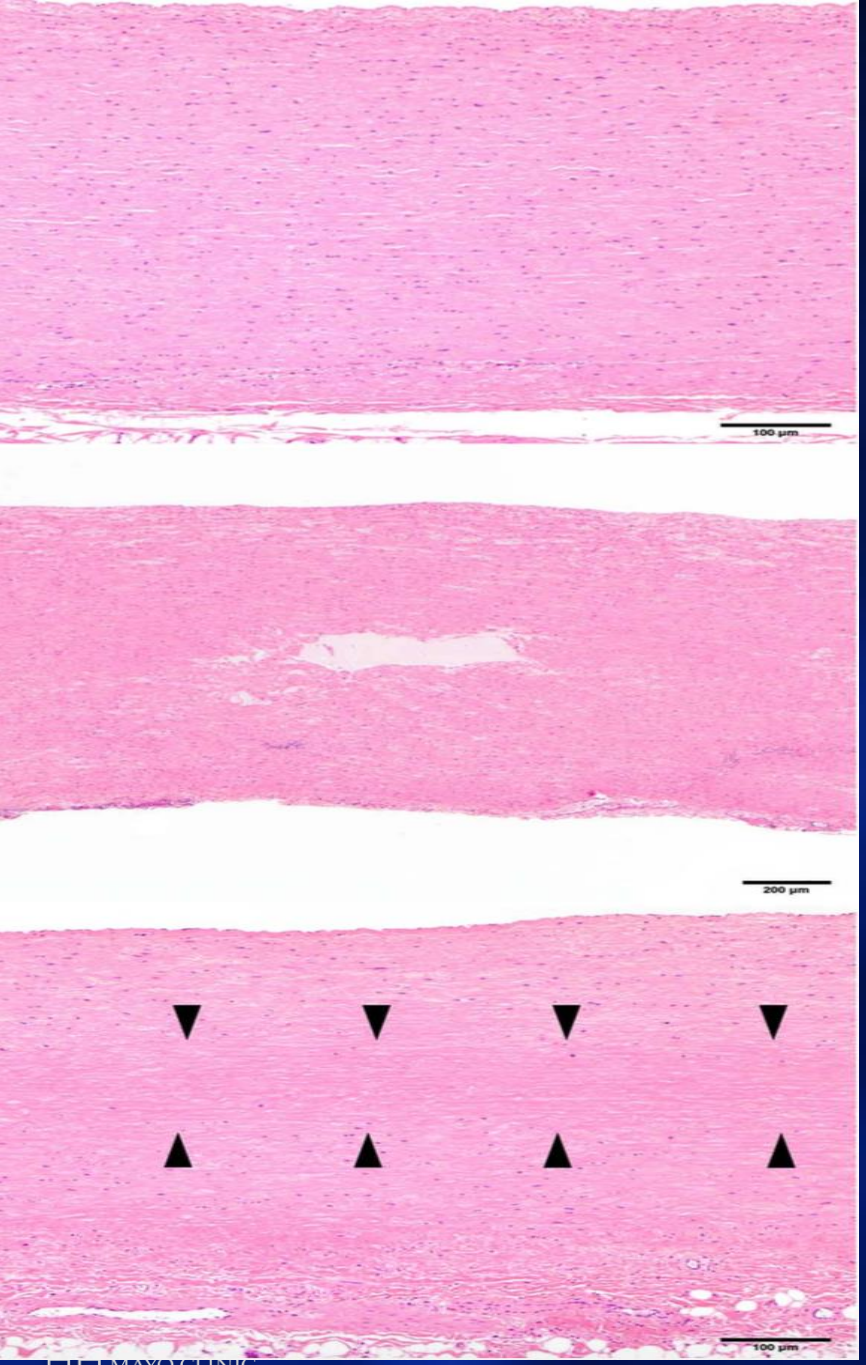
Increased vascular wall stress

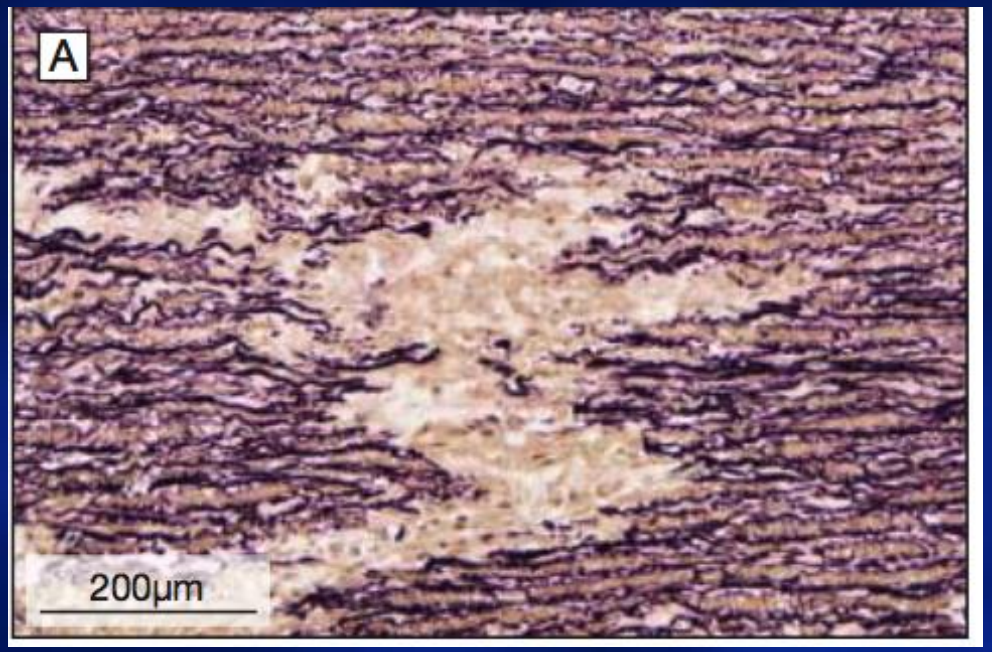
Age
HTN
Smoking
Atheroma

SMC contractile dysfunction/overload



Aneurysm // Dissection





Michelena et al. JAMA 2011;306:1104-13

MAYO CLINIC

Eleid, Michelena

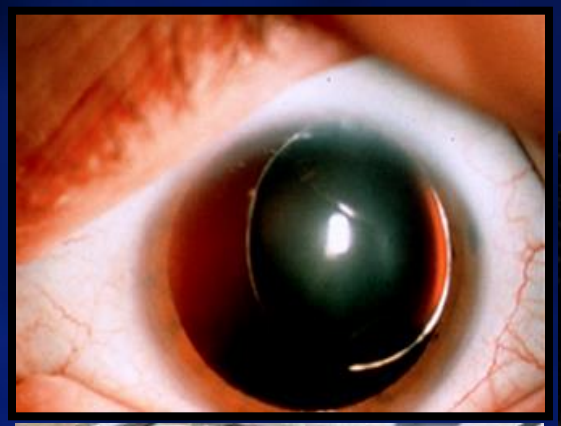
Heart 2013;**99**:1668–1674.

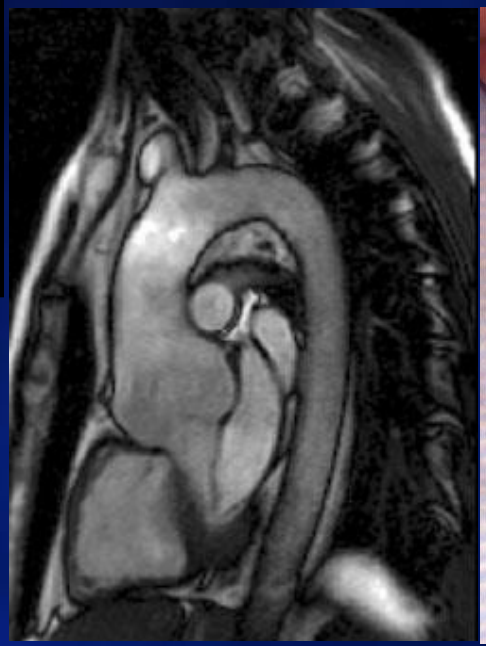
Thoracic Aortic Aneurysms

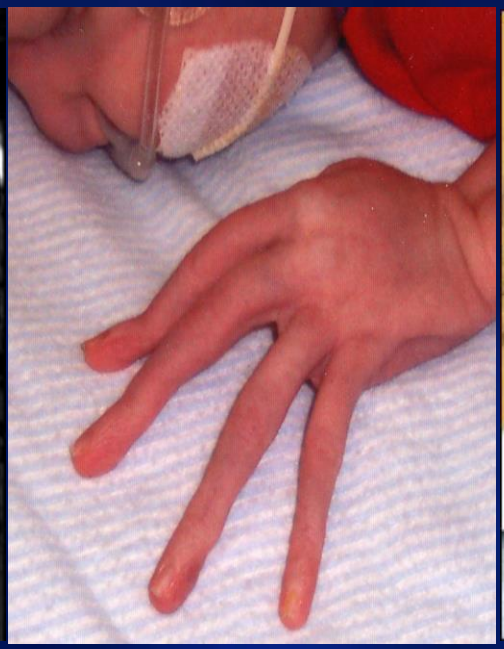
Syndromic	**<5%**
Marfan	*FBN1*
Turner	45,X
Loeys-Dietz	*TGFBR 1, 2*
Vascular Ehlers-Danlos	*COL3A1*
Aneurysm-osteoarthritis	*SMAD3*
Bicuspid aortic valve	***Notch-1* GATA5 ACTA2 and ?**
Familial	**15-20%** *TGFBR 2, MYH11, ACTA2*
Sporadic	**80% (age > 60)**

Examples

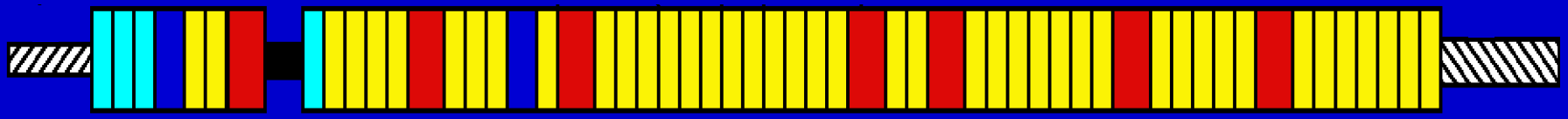
Marfan syndrome





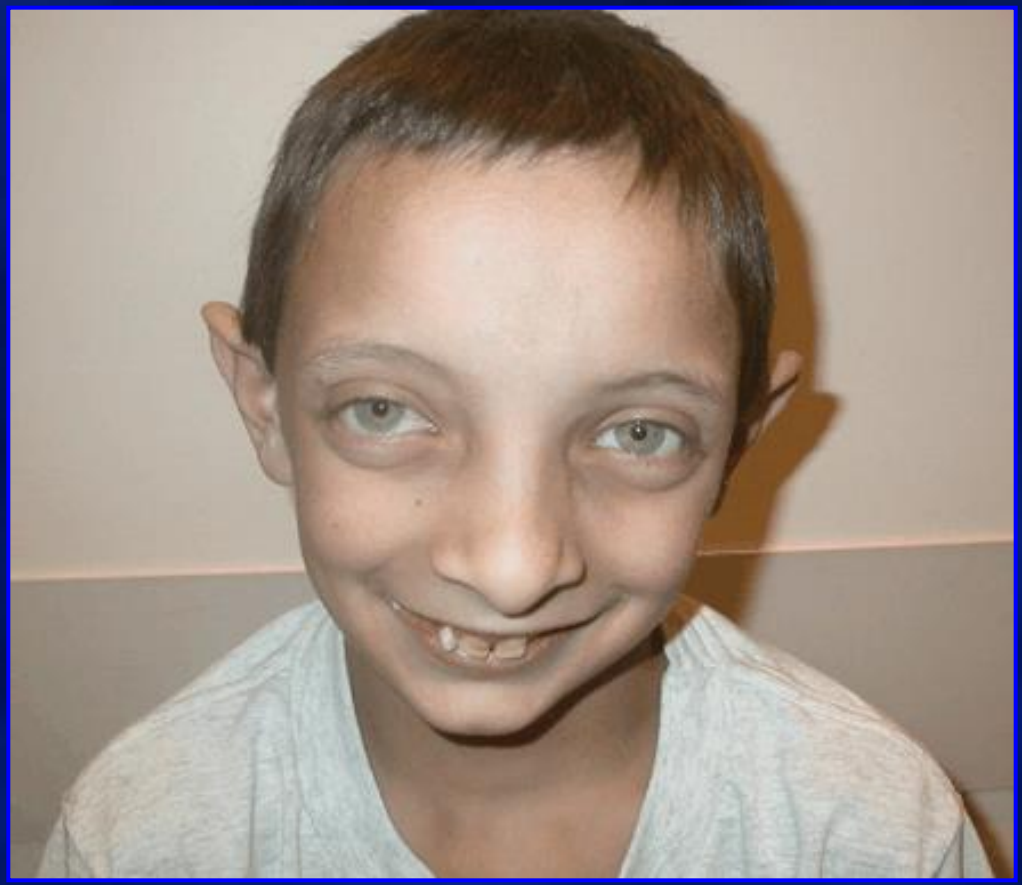


Fibrillin-1



Dietz…Francomano Nature, 1991

Loeys-Dietz Syndrome

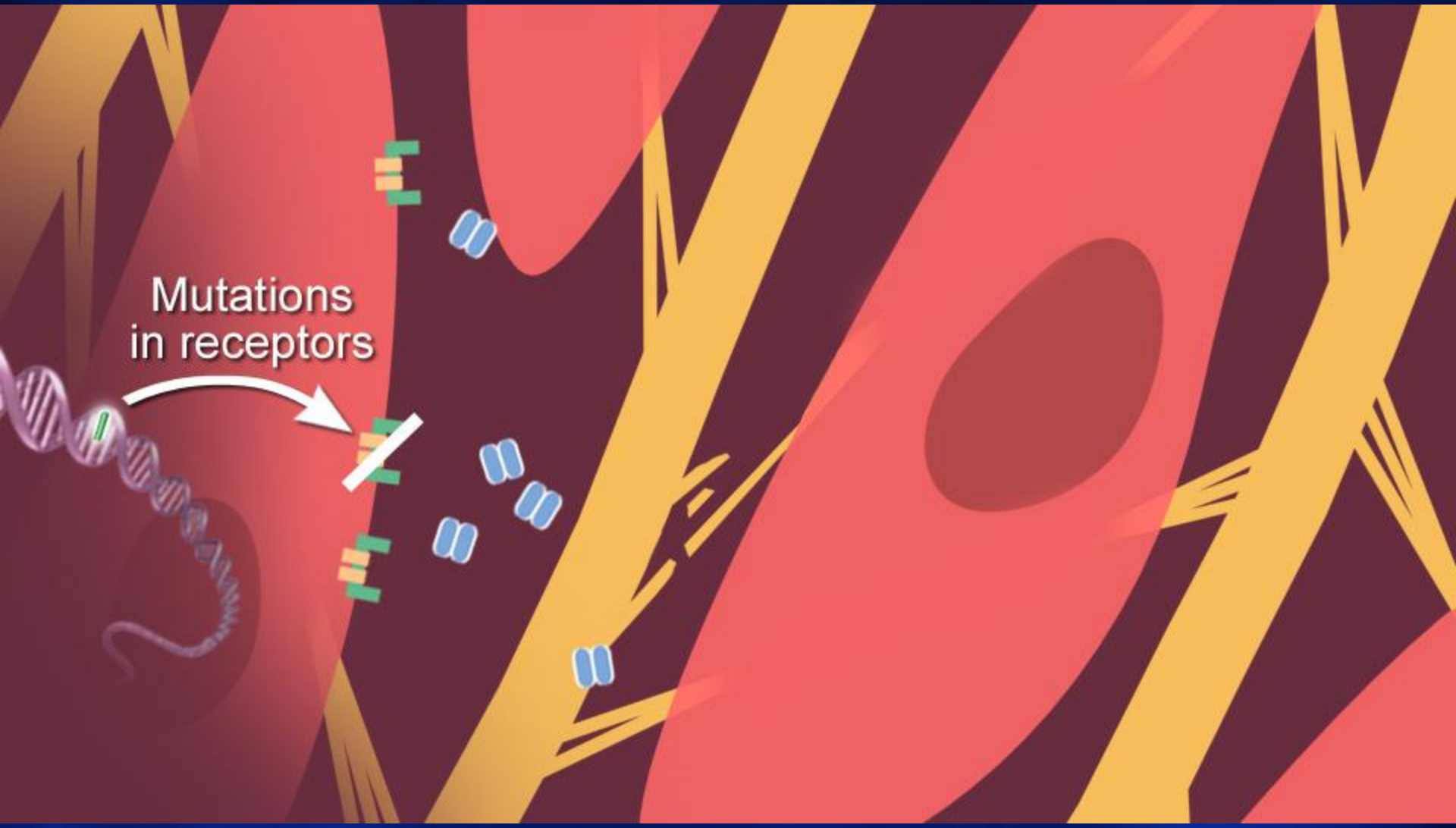


Williams et al, 2007

Loeys et al, 2006

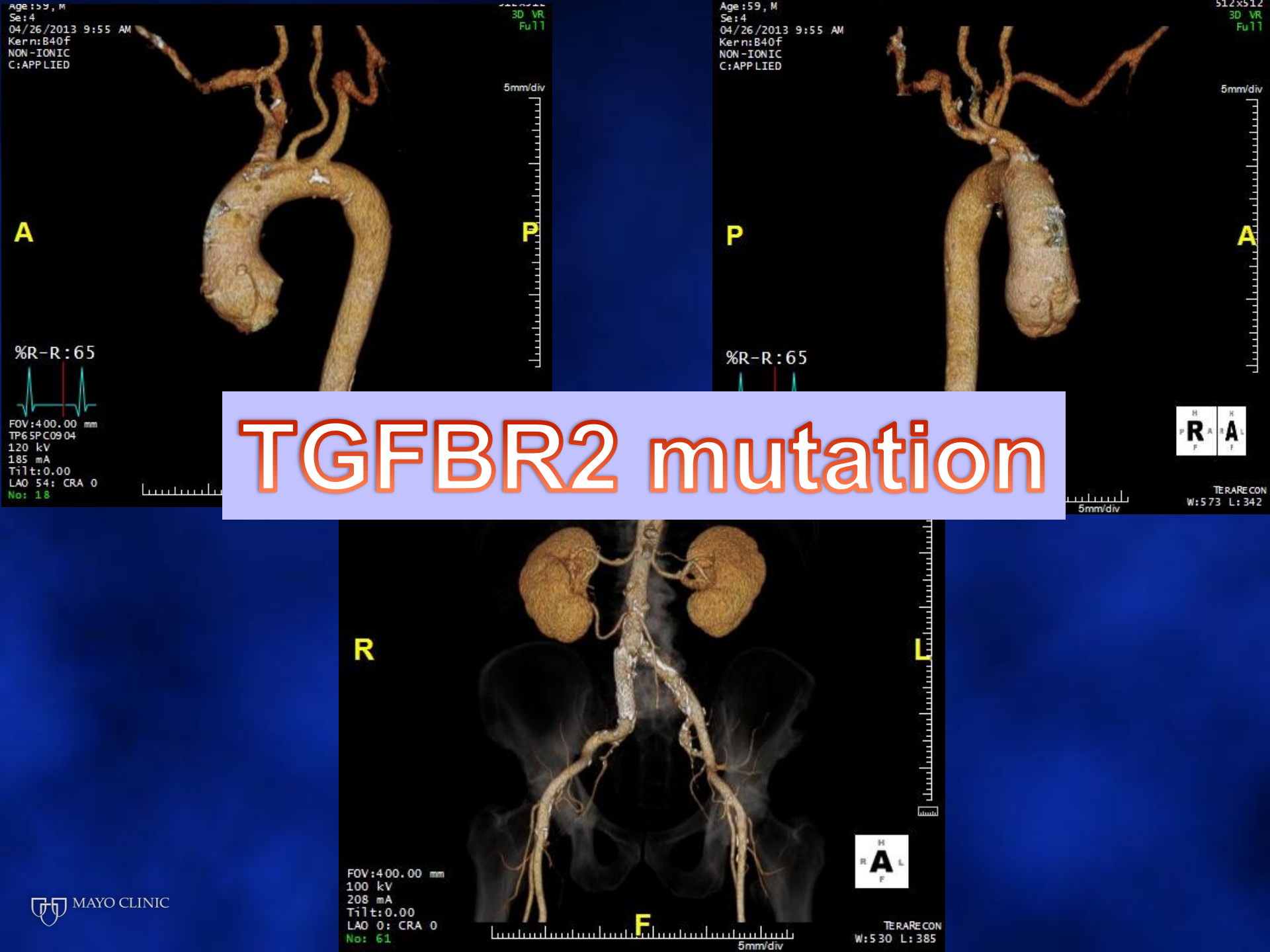
MAYO CLINIC

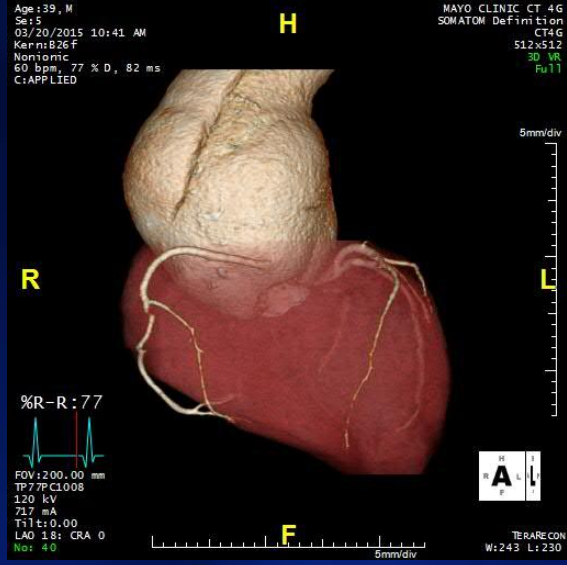
Loeys-Dietz Syndrome



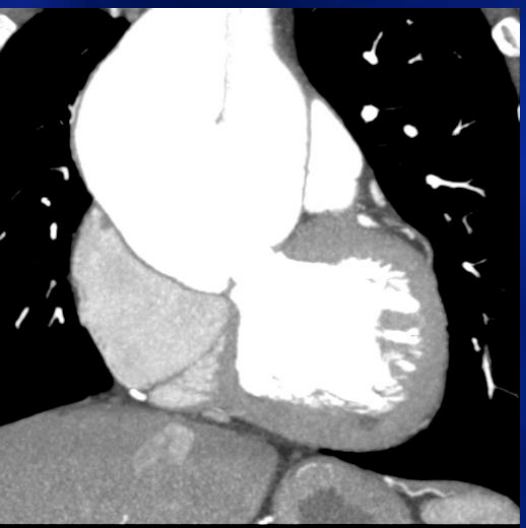
60 yo man –Normal appearance/ 2013

- Mod COPD
- S/P iliac aneurysm endograft 2006
- S/P CABG 2007
- Root 55mm, asc ao 44mm since 2010
- Surgical consult 2010: continue to observe
- Grandfather died iliac aneurysm
- What to do?

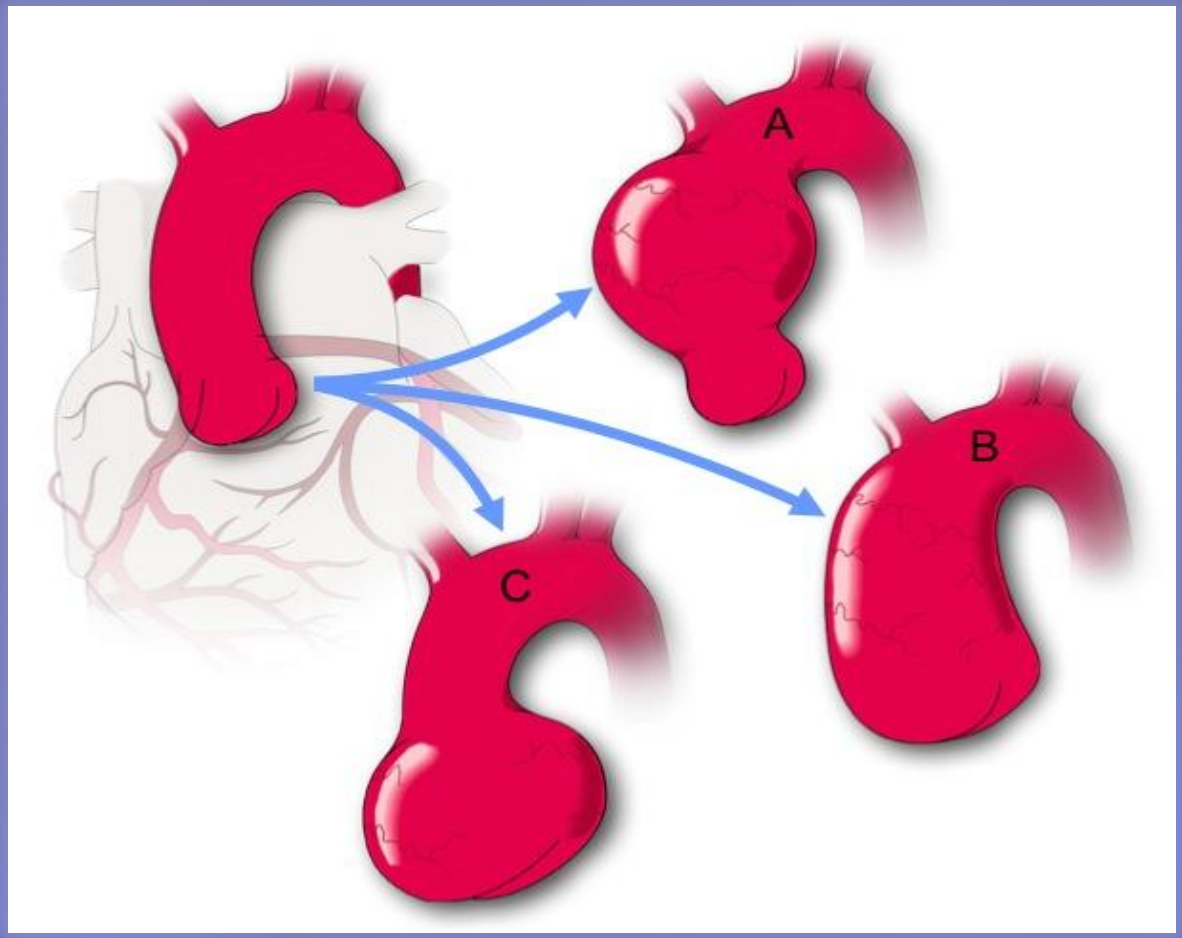

Age:59, M
Se:4
04/26/2013 9:55 AM
Kern:B40f
NON-IONIC
C:APPLIED
3D VR
Full
5mm/div
A
P
%R-R:65
FOV:400.00 mm
TP65PC0904
120 kV
185 mA
Tilt:0.00
LAO 54: CRA 0
No: 18
TERARECON
W:573 L:342
R
L
F
FOV:400.00 mm
100 kV
208 mA
Tilt:0.00
LAO 0: CRA 0
No: 61
W:530 L:385
TGFBR2 mutation
MAYO CLINIC



Critical #1 Imaging!!

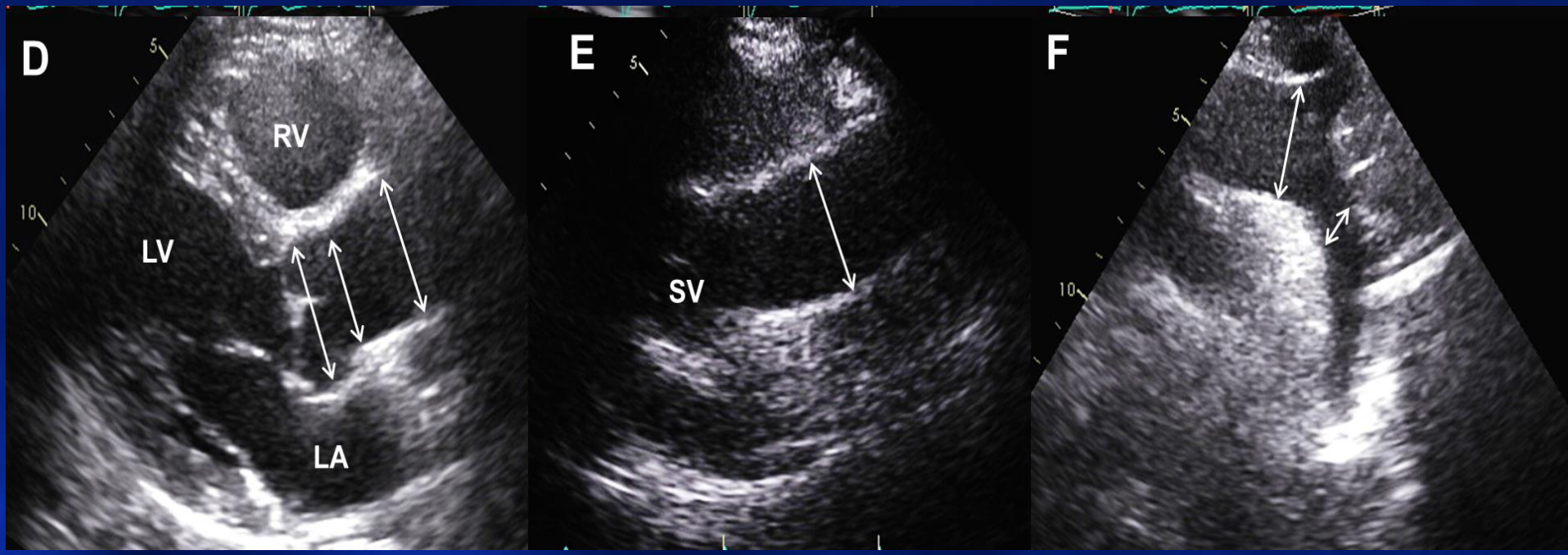


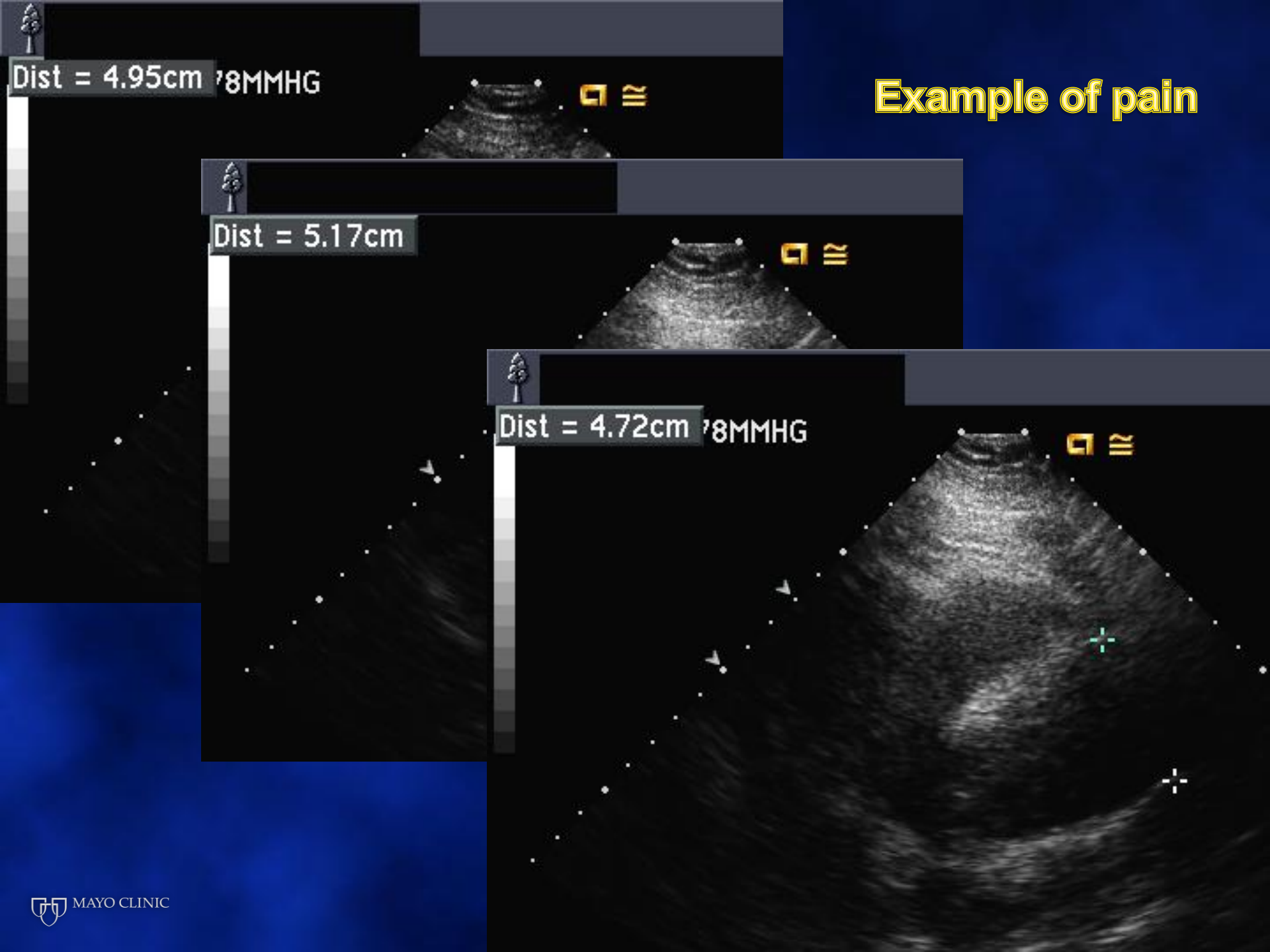
Root ≠ Asc Ao !!



MAYO CLINIC

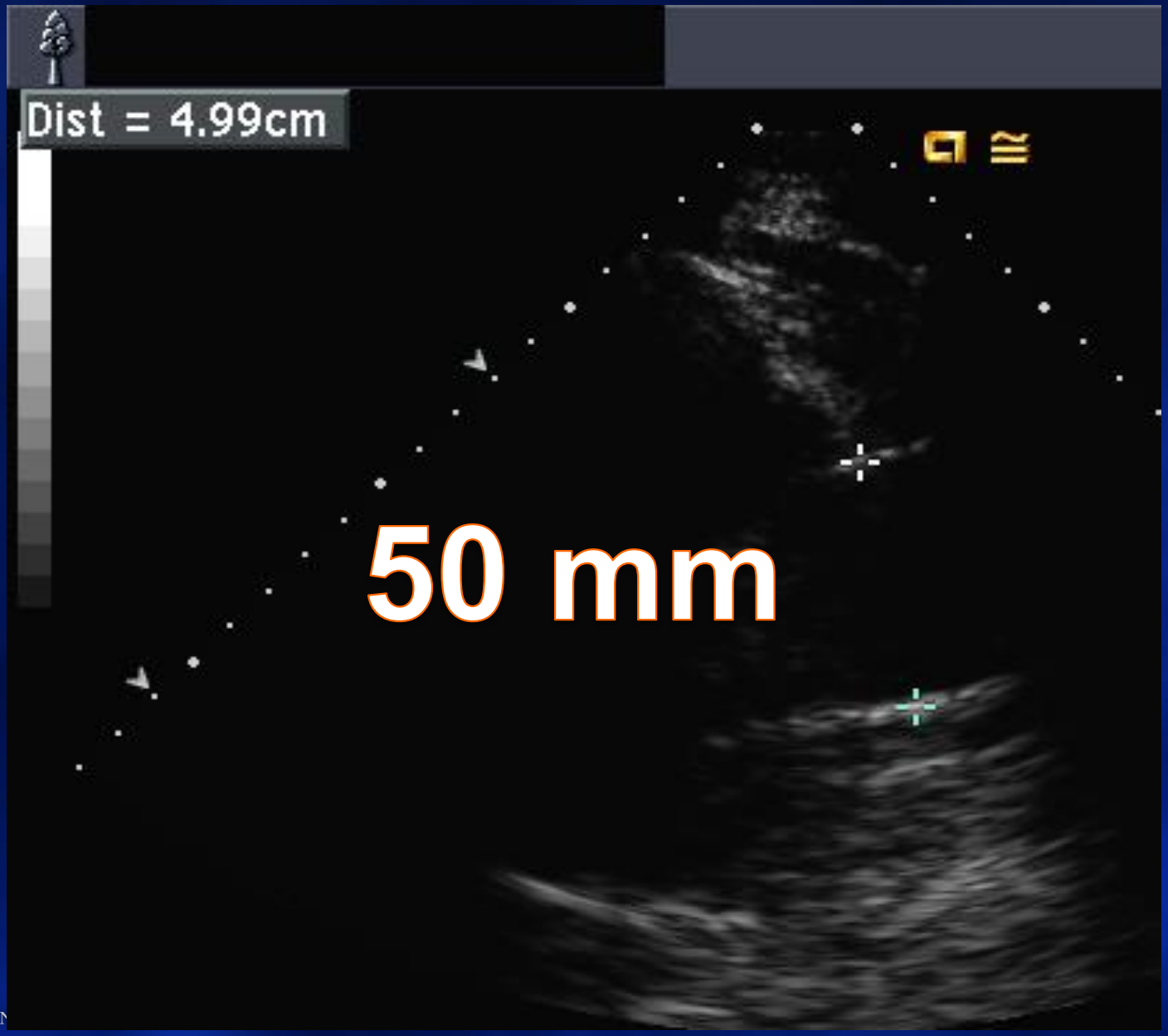
Michelena et al. Circulation 2014;129:2691

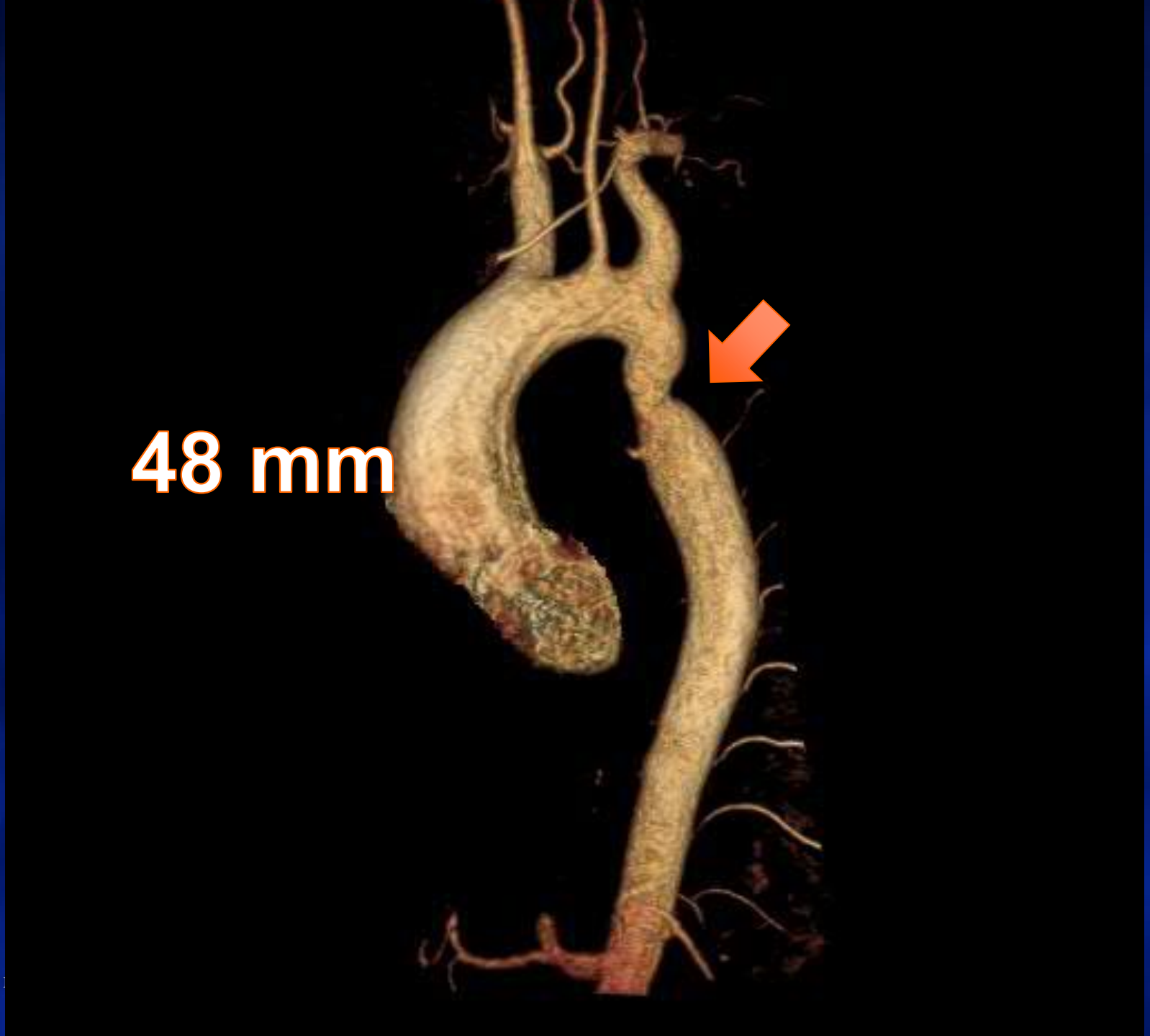

D
RV
LV
LA
E
SV
F



Example of pain

Careful measurement

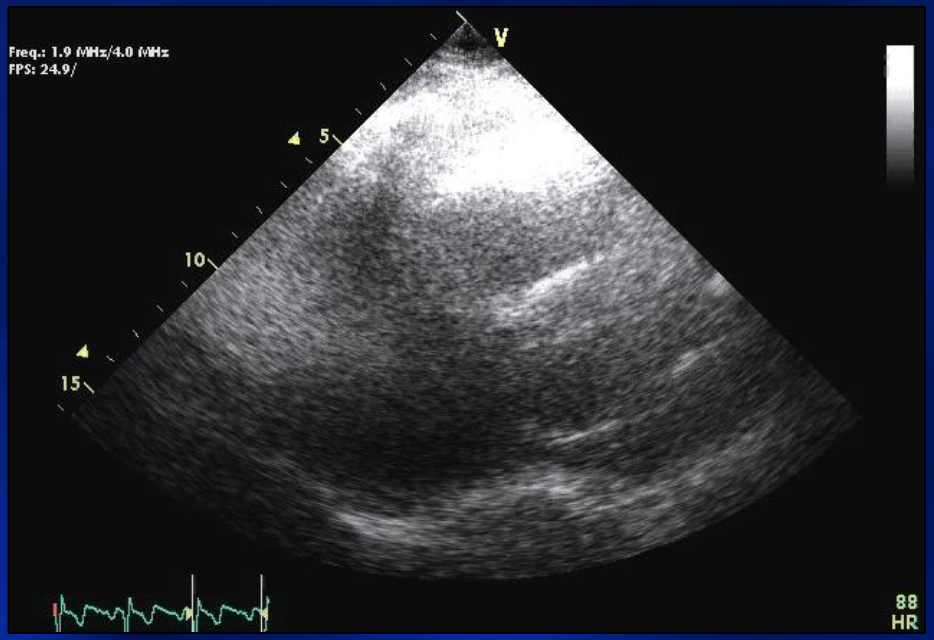


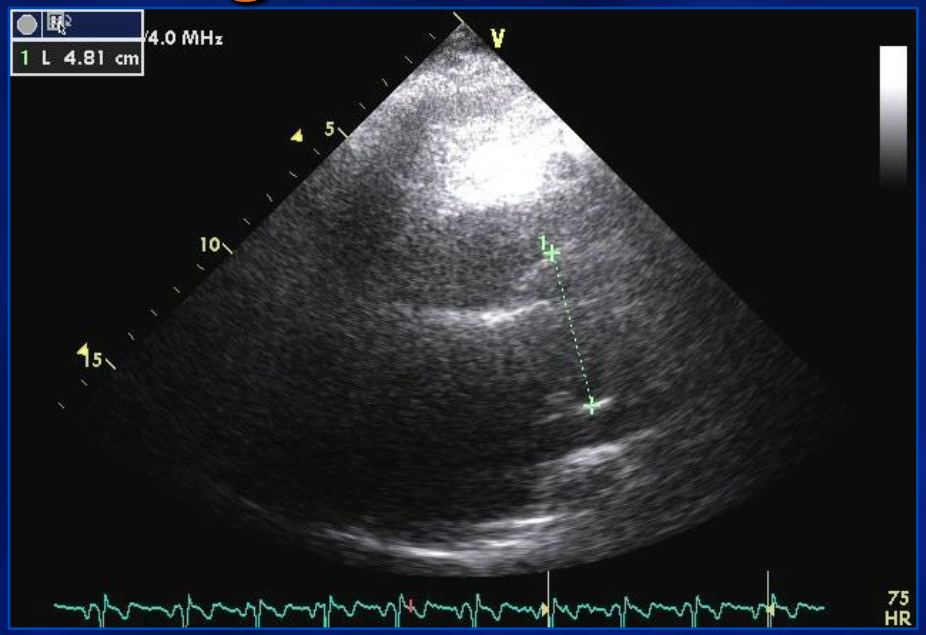

48 mm

Another Example of pain

22-Year-Old Female with MFS

26 Weeks Pregnant



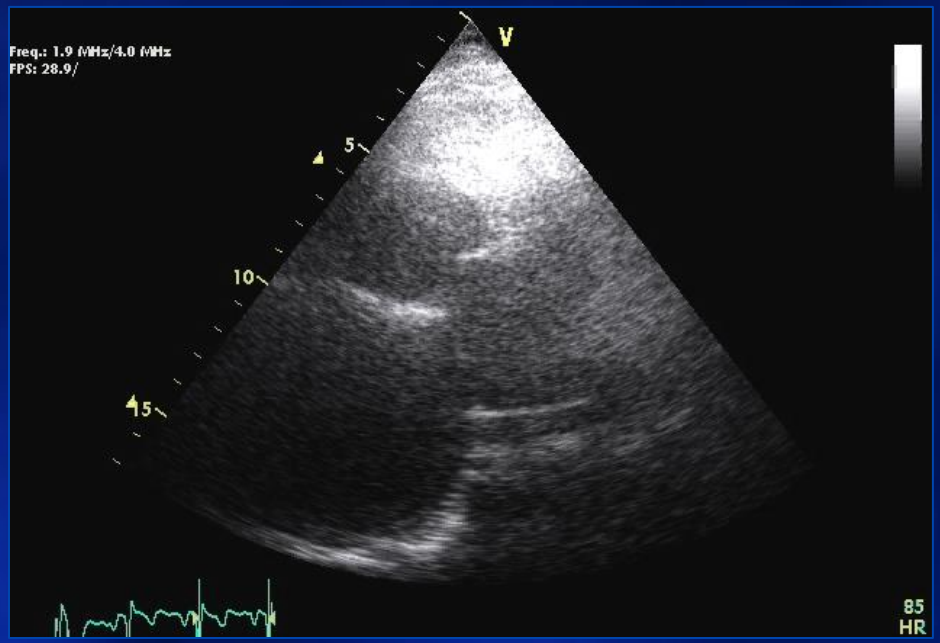


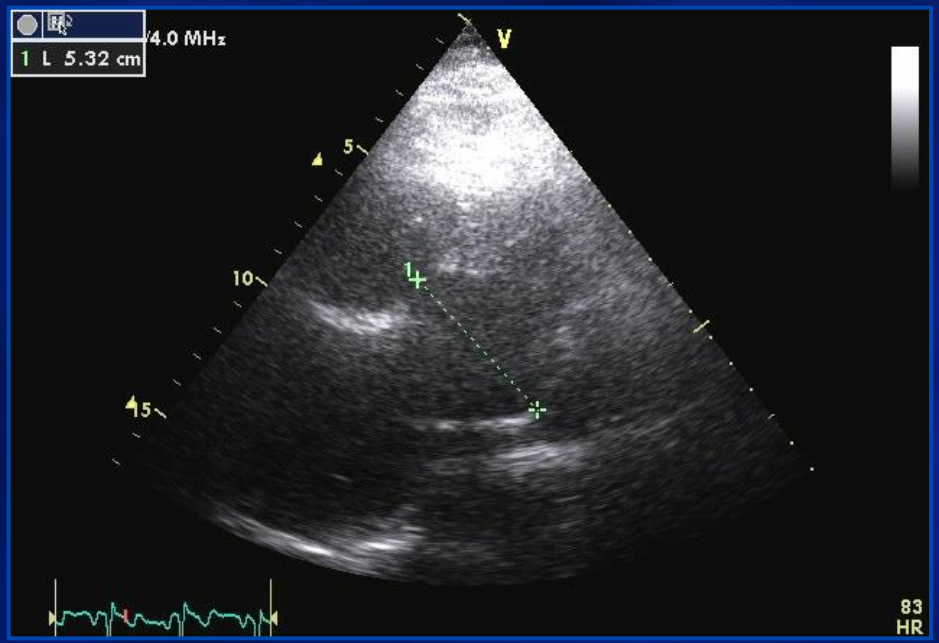
Sinus = 47 mm

4 Weeks Later

22-Year-Old Female with MFS

30 Weeks Pregnant





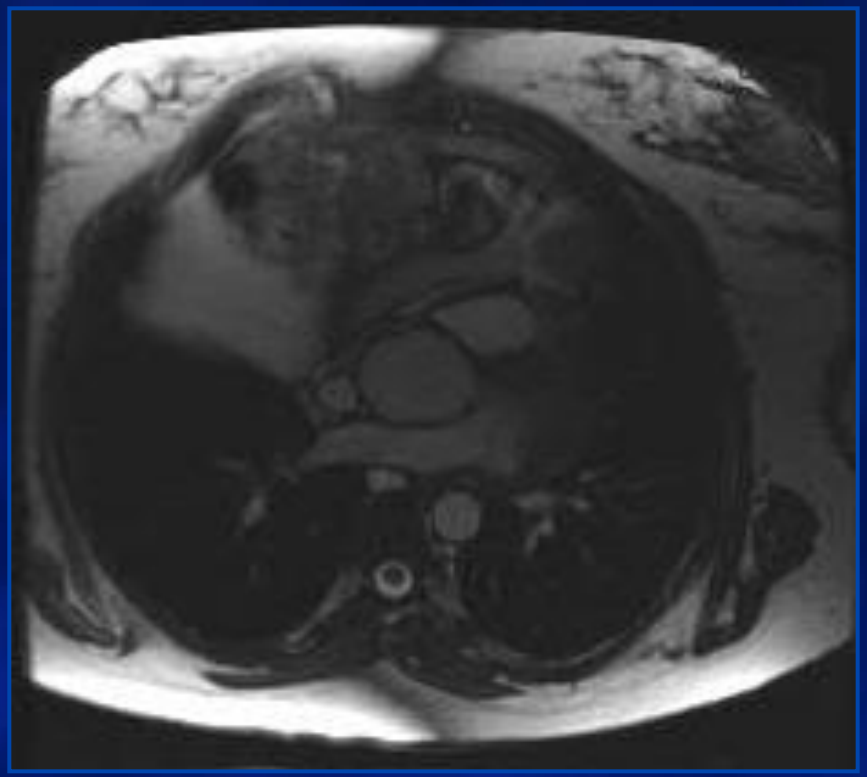
Sinus = 53 mm

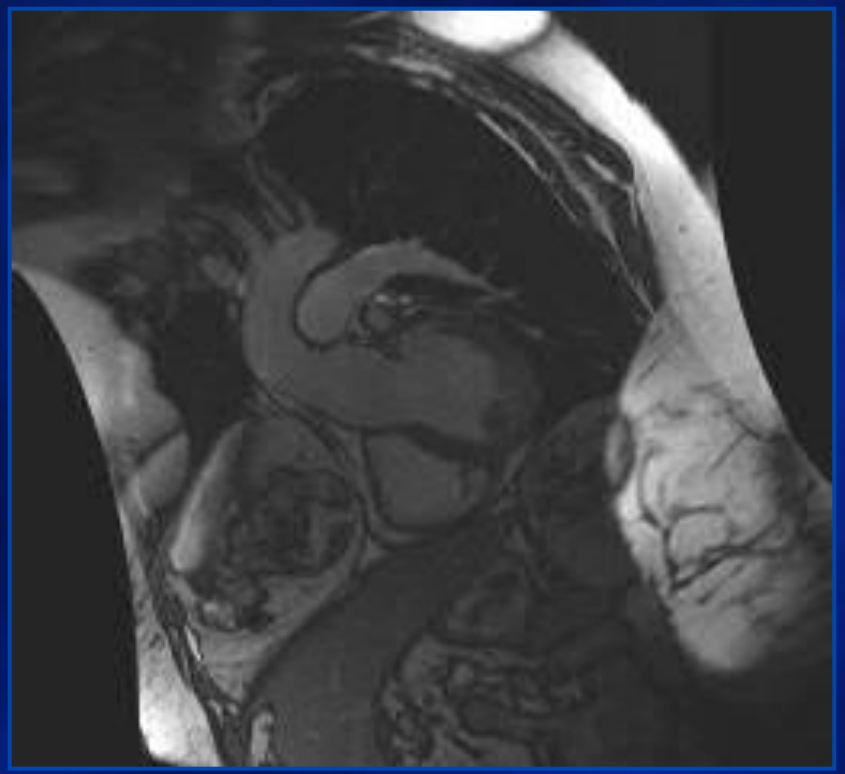
What would you recommend?

1. Emergency surgery – aorta and cesarean
2. Emergency surgery – aorta only
3. Continue observation (yeah right…)
4. Other

22-Year-Old Female with MFS

Additional Imaging





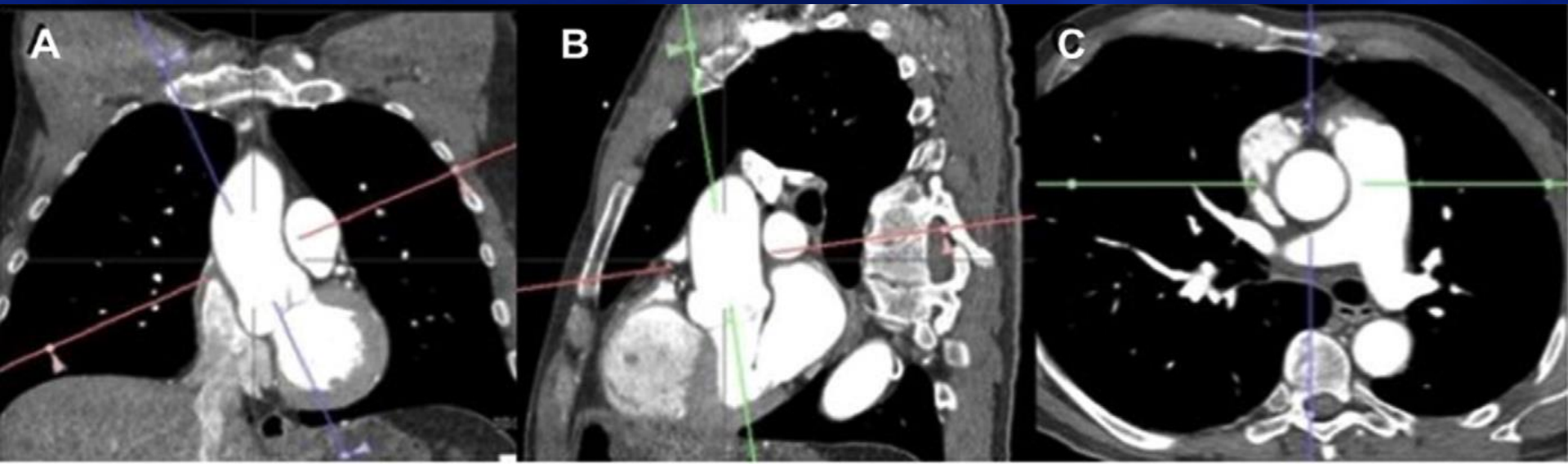
MRI Aortic Root = 47 mm

…continued observation

It is evident …
For aortic imaging

- TRY USING SAME TECHNIQUE (ECHO, CT, MR)
  - SAME MEASUREMENT METHOD WITHIN THE TECHNIQUE
    - REPEATED MEASUREMENTS
      - SAME AORTIC LEVEL
    - SIDE-BY-SIDE COMPARISON BY EXPERT

WHEN ECHO DOES NOT MAKE SENSE OR LARGE AORTA (>45-50mm): CHECK CT OR MRI



2014 ESC Guidelines on the diagnosis and treatment of aortic diseases

European Heart Journal (2014) **35**, 2873–2926

Recommendations for the management of aortic root dilation in patients with bicuspid aortic valve

Recommendations	Class[a]	Level[b]
Patients with known BAV should undergo an initial TTE to assess the diameters of the aortic root and ascending aorta.	I	C
Cardiac MRI or CT is indicated in patients with BAV when the morphology of the aortic root and the ascending aorta cannot be accurately assessed by TTE.	I	C
Serial measurement of the aortic root and ascending aorta is indicated in every patient with BAV, with an interval depending on aortic size, increase in size and family history	I	C
In the case of a diameter of the aortic root or the ascending aorta >45 mm or an increase >3 mm/year measured by echocardiography, annual measurement of aortic diameter is indicated.	I	C
In the case of aortic diameter >50 mm or an increase >3 mm/year measured by echocardiography, confirmation of the measurement is indicated, using another imaging modality (CT or MRI).	I	C

Essentially valid for any non-syndromic aortopathy

MAYO

Critical #2 Screening

2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease

Hiratzka *et al.*
2010 Guidelines on Thoracic Aortic Disease

5.1.6. Recommendations for Familial Thoracic Aortic Aneurysms and Dissections

CLASS I

1. Aortic imaging is recommended for first-degree relatives of patients with thoracic aortic aneurysm and/or dissection to identify those with asymptomatic disease. (126,127) (*Level of Evidence: B*)
2. If the mutant gene (*FBN1, TGFBR1, TGFBR2, COL3A1, ACTA2, MYH11*) associated with aortic aneurysm and/or dissection is identified in a patient, first-degree relatives should undergo counseling and testing. Then, only the relatives with the genetic mutation should undergo aortic imaging. (*Level of Evidence: C*)

2014 ESC Guidelines on the diagnosis and treatment of aortic diseases

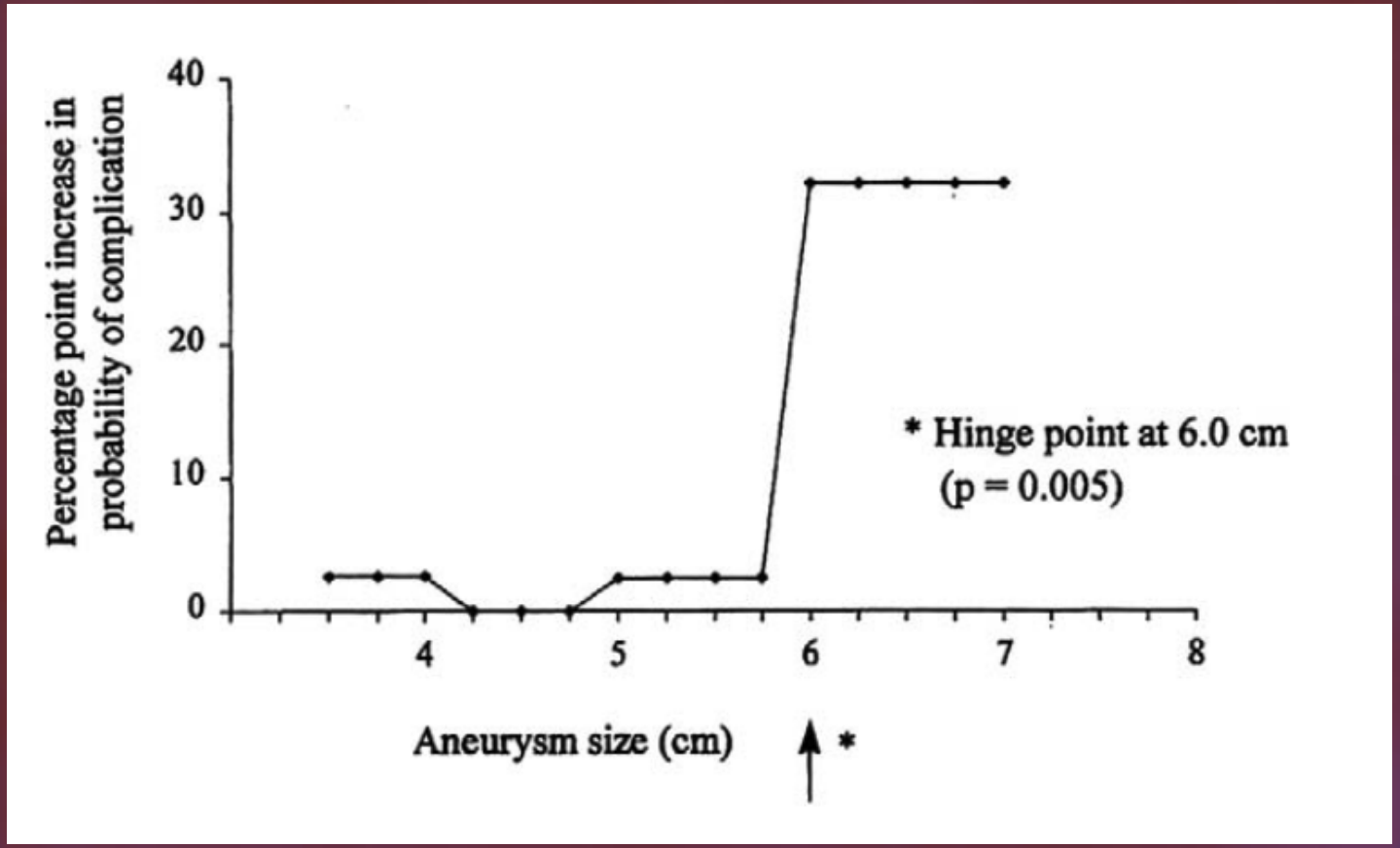
European Heart Journal (2014) **35**, 2873–2926

Recommendations on genetic testing in aortic diseases

Recommendations	Class[a]	Level[b]
It is recommended to investigate first-degree relatives (siblings and parents) of a subject with TAAD to identify a familial form in which relatives all have a 50% chance of carrying the family mutation/disease.	I	C
Once a familial form of TAAD is highly suspected, it is recommended to refer the patient to a geneticist for family investigation and molecular testing.	I	C
Variability of age of onset warrants screening every 5 years of 'healthy' at-risk relatives until diagnosis (clinical or molecular) is established or ruled out.	I	C

Critical #3 size!!

55 mm is appropriate cut-off for elective repair



Elefteriades. Ann Thorac Surg 2002;74:1877-80

Table 2. Incidence of Aortic Dissection per 10 000 Patient-Years

Category	Incidence (95% CI)
Men	4.5 (0.7-13.8)
Women	0 (N/A)

0.03% patient-year
Age-adjusted relative-risk of aortic dissection in BAV is 8.4[2.1-33.5] compared to the general population (p=0.003)

Thus, the incidence of dissection if baseline aneurysm is ~ 0.45% per patient-year

ORIGINAL CONTRIBUTION

Michelena et al. JAMA 2011;306:1104-13

Incidence of Aortic Complications in Patients With Bicuspid Aortic Valves

2014 ESC Guidelines on the diagnosis and treatment of aortic diseases

European Heart Journal (2014) **35**, 2873–2926

Recommendations on interventions on ascending aortic aneurysms

Recommendations	Class[a]	Level[b]
Surgery is indicated in patients who have aortic root aneurysm, with maximal aortic diameter[c] ≥50 mm for patients with Marfan syndrome.	I	C
Surgery should be considered in patients who have aortic root aneurysm, with maximal ascending aortic diameters: • ≥45 mm for patients with Marfan syndrome with risk factors.[d] • ≥50 mm for patients with bicuspid valve with risk factors.[e,f] • ≥55 mm for other patients with no elastopathy.[g,h]	IIa	C
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.	IIb	C

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Aortic Event Rate in the Marfan Population

A Cohort Study

Guillaume Jondeau, MD, PhD; Delphine Detaint, MD; Florence Tubach, MD, PhD; Florence Arnoult, MD; Olivier Milleron, MD; Francois Raoux, MD; Gabriel Delorme, MD; Lea Mimoun, MD; Laura Krapf, MD; Dalil Hamroun, PhD; Christophe Beroud, PharmD, PhD; Carine Roy, MD; Alec Vahanian, MD; Catherine Boileau, PharmD, PhD

Background—Optimal management, including timing of surgery, remains debated in Marfan syndrome because of a lack of data on aortic risk associated with this disease.

Methods and Results—We used our database to evaluate aortic risk associated with standardized care. Patients who fulfilled the international criteria, had not had previous aortic surgery or dissection, and came to our center at least twice were included. Aortic measurements were made with echocardiography (every 2 years); patients were given systematic β-blockade and advice about sports activities. Prophylactic aortic surgery was proposed when the maximal aortic diameter reached 50 mm. Seven hundred thirty-two patients with Marfan syndrome were followed up for a mean of 6.6 years. Five deaths and 2 dissections of the ascending aorta occurred during follow-up. Event rate (death/aortic dissection) was 0.17%/y. Risk rose with increasing aortic diameter measured within 2 years of the event: from 0.09%/y per year (95% confidence interval, 0.00–0.20) when the aortic diameter was $<$40 mm to 0.3% (95% confidence interval, 0.00–0.71) with diameters of 45 to 49 mm and 1.33% (95% confidence interval, 0.00–3.93) with diameters of 50 to 54 mm. The risk increased 4 times at diameters $\geq$50 mm. The annual risk dropped below 0.05% when the aortic diameter was $<$50 mm after exclusion of a neonatal patient, a woman who became pregnant against our recommendation, and a 72-year-old woman with previous myocardial infarction.

Conclusions—Risk of sudden death or aortic dissection remains low in patients with Marfan syndrome and aortic diameter between 45 and 49 mm. Aortic diameter of 50 mm appears to be a reasonable threshold for prophylactic surgery. **(*Circulation*. 2012;125:226-232.)**

2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease

Hiratzka *et al.*
2010 Guidelines on Thoracic Aortic Disease

CLASS IIa

1. Elective aortic replacement is reasonable for patients with Marfan syndrome, other genetic diseases, or bicuspid aortic valves, when the ratio of maximal ascending or aortic root area (πr^2) in cm^2 divided by the patient's height in meters exceeds 10. (16,143) (*Level of Evidence: C*)
2. It is reasonable for patients with Loeys-Dietz syndrome or a confirmed *TGFBR1* or *TGFBR2* mutation to undergo aortic repair when the aortic diameter reaches 4.2 cm or greater by transesophageal echocardiogram (internal diameter) or 4.4 to 4.6 cm or greater by computed tomographic imaging and/or magnetic resonance imaging (external diameter). (78) (*Level of Evidence: C*)

Svensson et al. J Thorac Cardiovasc Surg 2003;126(3):892-3.
Wojnarski et al. The Annals of thoracic surgery 2015;100:1666-74.

Aortic Cross-Sectional Area/Height Ratio and Outcomes in Patients With a Trileaflet Aortic Valve and a Dilated Aorta

Circulation. 2016;134:1724–1737.

Table 4. Multivariable Cox Proportional Hazard Analysis for the Primary End Point of Longer-Term Death in the Entire Study Sample (n=771)

Variable	χ^2	Hazard Ratio With 95% Confidence Interval	*P* Value
Model A: With aortic root area/height ratio in the model			
Aortic root area/height ratio≥10 cm^2/m	51.14	4.04 (2.69–6.23)	<0.001
Aortic surgery during follow-up	31.38	0.47 (0.27–0.81)	<0.001
Right ventricular systolic pressure (for 10 mm Hg increase)	13.68	1.34 (1.14–1.63)	<0.001
Society of Thoracic Surgeons score (for every 1% increase)	11.10	2.01 (1.35–3.00)	0.001
Interaction between aortic surgery during follow-up and aortic root area/height ratio≥10 cm^2/m	6.20	0.37 (0.17–0.82)	0.01
Angiotensin receptor blockers	4.38	0.77 (0.57–0.99)	0.04
Inherited aortic syndromes	4.23	1.53 (1.03–2.31)	0.04
Model B: With ascending aortic area/height ratio in the model			
Ascending aortic area/height ratio≥10 cm^2/m	19.27	2.42 (1.32–4.04)	<0.001
Right ventricular systolic pressure (for 10 mm Hg increase)	18.27	1.42 (1.19–1.70)	<0.001
Society of Thoracic Surgeons score (for every 1% increase)	17.41	2.22 (1.48–3.32)	<0.001
Aortic surgery during follow-up	8.91	0.60 (0.34–0.90)	0.02
Inherited aortic syndromes	6.27	1.93 (1.09–3.57)	0.02
Interaction between aortic surgery during follow-up and ascending aortic area/height ratio≥10 cm^2/m	5.21	0.51 (0.28–0.94)	0.04
Angiotensin receptor blockers	4.98	0.69 (0.46–0.98)	0.04

Aortic Cross-Sectional Area/Height Ratio and Outcomes in Patients With a Trileaflet Aortic Valve and a Dilated Aorta

Circulation. 2016;134:1724–1737.

Table 5. Incremental Prognostic Utility of Aortic Area/Height Ratio and Aortic Surgery for the Primary Outcome of Death in the Entire Study Sample (n=771)

	Model 1: Clinical Factors	Model 2: Clinical Factors + Aortic Root Area/Height Ratio ≥10 cm^2/m	*P* Value for Difference Between Models 1 and 2	Model 3: Clinical Factors + Aortic Root Area/Height Ratio ≥10 cm^2/m + Aortic Surgery	*P* Value for Difference Between Models 2 and 3
With aortic root area/height ratio ≥10 cm^2/m					
C-statistic	0.57 (0.35–0.77)	0.65 (0.52–0.73)	0.03	0.72 (0.61–0.84)	0.02
Categorical NRI	0.17 (0.02–0.31)	0.23 (0.04–0.34)	0.01	0.19 (0.05–0.32)	0.02
With ascending aortic area/height ratio ≥10 cm^2/m					
C-statistic	0.57 (0.35–0.77)	0.63 (0.47–0.77)	0.04	0.70 (0.58–0.83)	0.03
Categorical NRI	0.17 (0.02–0.31)	0.20 (0.03–0.33)	0.03	0.18 (0.03–0.36)	0.03

Aortic Cross-Sectional Area/Height Ratio and Outcomes in Patients With a Trileaflet Aortic Valve and a Dilated Aorta

Circulation. 2016;134:1724–1737.

- Retrospective
- Referral bias
- Selection bias
- Only total death
- Not possible to analyze dissection

A lot of patients // Clean association index-death
Noise

Wonders of size..!!

Rain on everyone's parade…

Aortic Diameter ≥5.5 cm Is Not a Good Predictor of Type A Aortic Dissection

Observations From the International Registry of Acute Aortic Dissection (IRAD)

Circulation 2007

	All	Ascending <5.5 cm	Ascending ≥5.5 cm	*P*
No. (%)	591	349 (59.1)	242 (40.9)	
Demographics				
Age, n (SD)	60.8 (14.4)	60.5 (13.6)	61.2 (15.5)	0.61
Male, n (%)	390 (66.0)	226 (64.8)	164 (67.8)	0.45
History				
Hypertension, n (%)	407 (71.2)	247 (72.4)	160 (69.3)	0.41
Marfan syndrome, n (%)	28 (4.9)	11 (3.2)	17 (7.5)	0.02
Known aortic aneurysm, n (%)	70 (12.4)	41 (12.0)	29 (12.9)	0.75
Prior aortic dissection, n (%)	22 (3.9)	15 (4.4)	7 (3.1)	0.44
BAV (n=383), n (%)*	16 (4.2)	6 (2.6)	10 (6.5)	0.06

Ao size did not predict death

2014 ESC Guidelines on the diagnosis and treatment of aortic diseases

European Heart Journal (2014) **35**, 2873–2926

In cases of BAV, surgery of the ascending aorta is indicated in case of:

- aortic root or ascending aortic diameter >55 mm.
- aortic root or ascending aortic diameter >50 mm in the presence of other risk factors.[c]
- aortic root or ascending aortic diameter >45 mm when surgical aortic valve replacement is scheduled.

[c]Coarctation of the aorta, systemic hypertension, family history of dissection, or increase in aortic diameter >3 mm/year (on repeated measurements using the same imaging technique, measured at the same aortic level, with side-by-side comparison and confirmed by another technique).

Oliver et al. Am J Cardiol;104:1001-06

Bicuspid aortic valve aortopathy in adults: Incidence, etiology, and clinical significance

International Journal of Cardiology, 2015

Hector I. Michelena [a,*], Alessandro Della Corte [b], Siddharth K. Prakash [c], Dianna M. Milewicz [c], Artur Evangelista [d], Maurice Enriquez-Sarano [a]

Root/ascending aorta 50-54 mm *(Confirm by CTA or MRA)*

Root/ascending aorta ≥55 mm *(Confirm by CTA or MRA)*

No risk factors

Risk factors *(Any one or more)*
- Family history of dissection
- ≥3 mm/year dilatation
- Uncontrolled HTN
- Root phenotype
- Personal history of coarctation

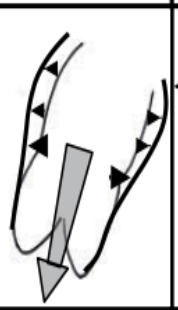
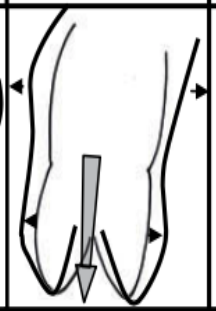
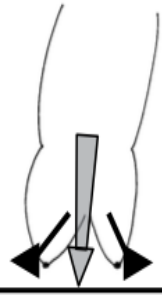
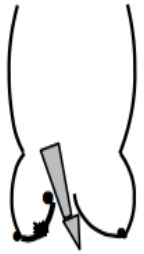
Elective surgical repair
- Consider aortic valve sparing if valve tissue appropriate
- Consider center of excellence

Aortic regurgitation Link with AA??

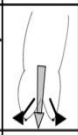
Repair-oriented classification of aortic insufficiency: Impact on surgical techniques and clinical outcomes

Munir Boodhwani, MD, MMSc, Laurent de Kerchove, MD, David Glineur, MD, Alain Poncelet, MD, Jean Rubay, MD, Parla Astarci, MD, Robert Verhelst, MD, Philippe Noirhomme, MD, and Gébrine El Khoury, MD

The Journal of Thoracic and Cardiovascular Surgery • Volume 137, Number 2

AI Class	Type I Normal cusp motion with FAA dilatation or cusp perforation				Type II Cusp Prolapse	Type III Cusp Restriction
	Ia	Ib	Ic	Id		
Mechanism						
Repair Techniques (Primary)	STJ remodeling *Ascending aortic graft*	Aortic Valve sparing: *Reimplantation or Remodeling with SCA*	SCA	Patch Repair *Autologous or bovine pericardium*	Prolapse Repair *Plication* *Triangular resection* *Free margin Resuspension* *Patch*	Leaflet Repair *Shaving* *Decalcificatio* *Patch*

Type 1

AI Class	Type I: Normal cusp motion with FAA dilatation or cusp perforation				Type II: Cusp Prolapse	Type III: Cusp Restriction
	Ia	Ib	Ic	Id		
Mechanism						
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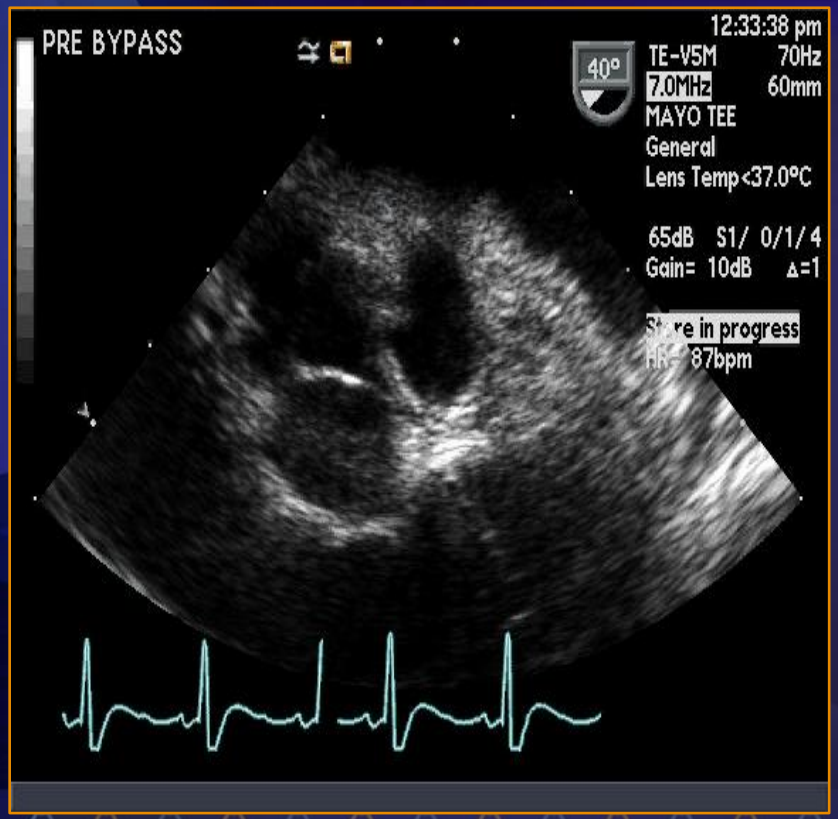
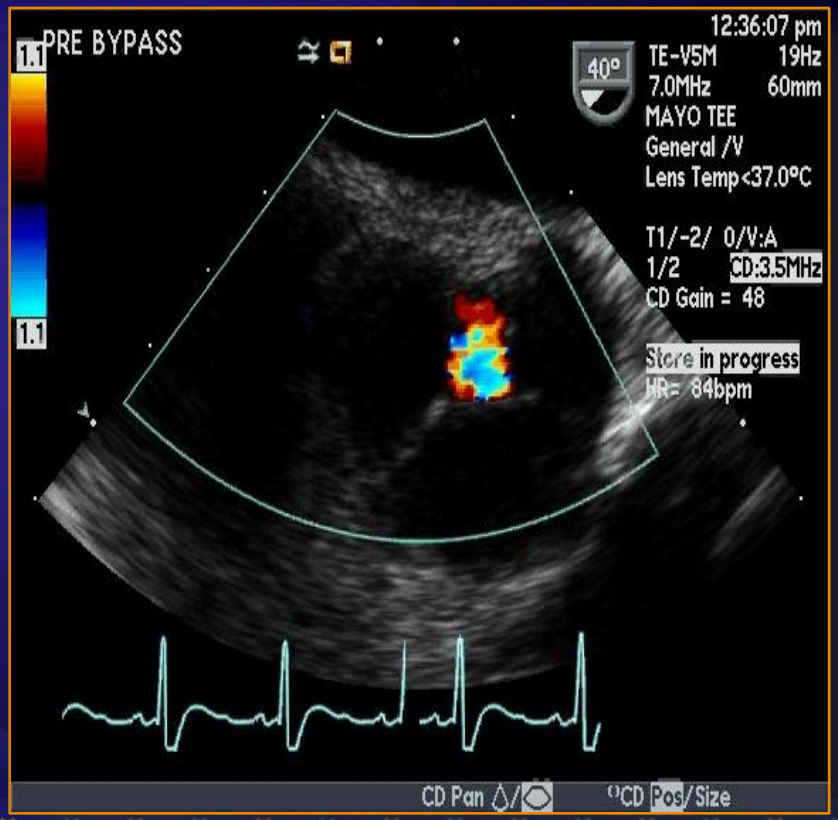
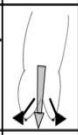
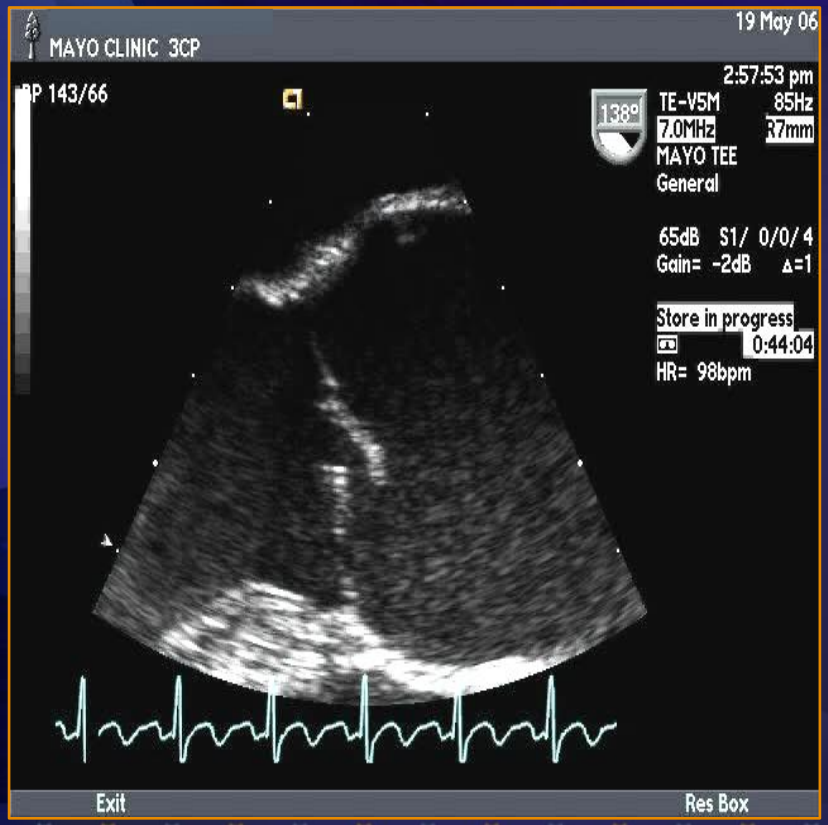
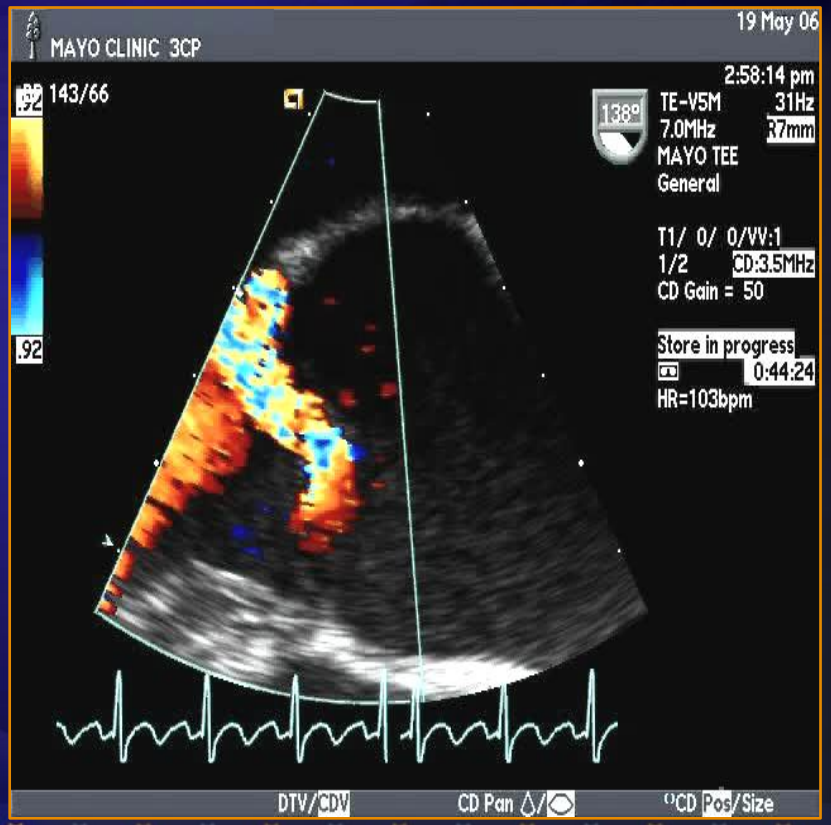




Type 2

AI Class	Type I: Normal cusp motion with FAA dilatation or cusp perforation				Type II	Type III
	Ia	Ib	Ic	Id	Cusp Prolapse	Cusp Restriction
Mechanism						
Repair Techniques (Primary)	STJ remodeling *Ascending aortic graft*	Aortic Valve sparing: *Reimplantation or Remodeling with SCA*	SCA	Patch Repair *Autologous or bovine pericardium*	Prolapse Repair *Plication* *Triangular resection* *Free margin Resuspension* *Patch*	Leaflet Repair *Shaving* *Decalcificatio* *Patch*





Predictors of ascending aortic dilatation with bicuspid aortic valve: a wide spectrum of disease expression☆

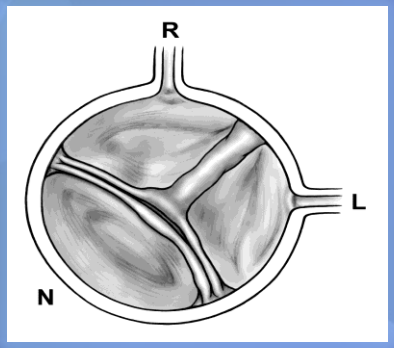
Alessandro Della Corte*,1, Ciro Bancone, Cesare Quarto, Giovanni Dialetto, Franco E. Covino, Michelangelo Scardone, Giuseppe Caianiello, Maurizio Cotrufo

European Journal of Cardio-thoracic Surgery 31 (2007) 397–405

Heart 2008;**94**:1634–1638.

The bicuspid aortic valve: an integrated phenotypic classification of leaflet morphology and aortic root shape

B M Schaefer,[1] M B Lewin,[2] K K Stout,[1,2] E Gill,[1] A Prueitt,[2] P H Byers,[1] C M Otto[1]



BAV Root phenotype AR

Aortic dilatation patterns and rates in adults with bicuspid aortic valves: a comparative study with Marfan syndrome and degenerative aortopathy

Delphine Detaint,[1,2] Hector I Michelena,[3] Vuyisile T Nkomo,[3] Alec Vahanian,[1,4] Guillaume Jondeau,[1,2,4] Maurice Enriquez Sarano[3]

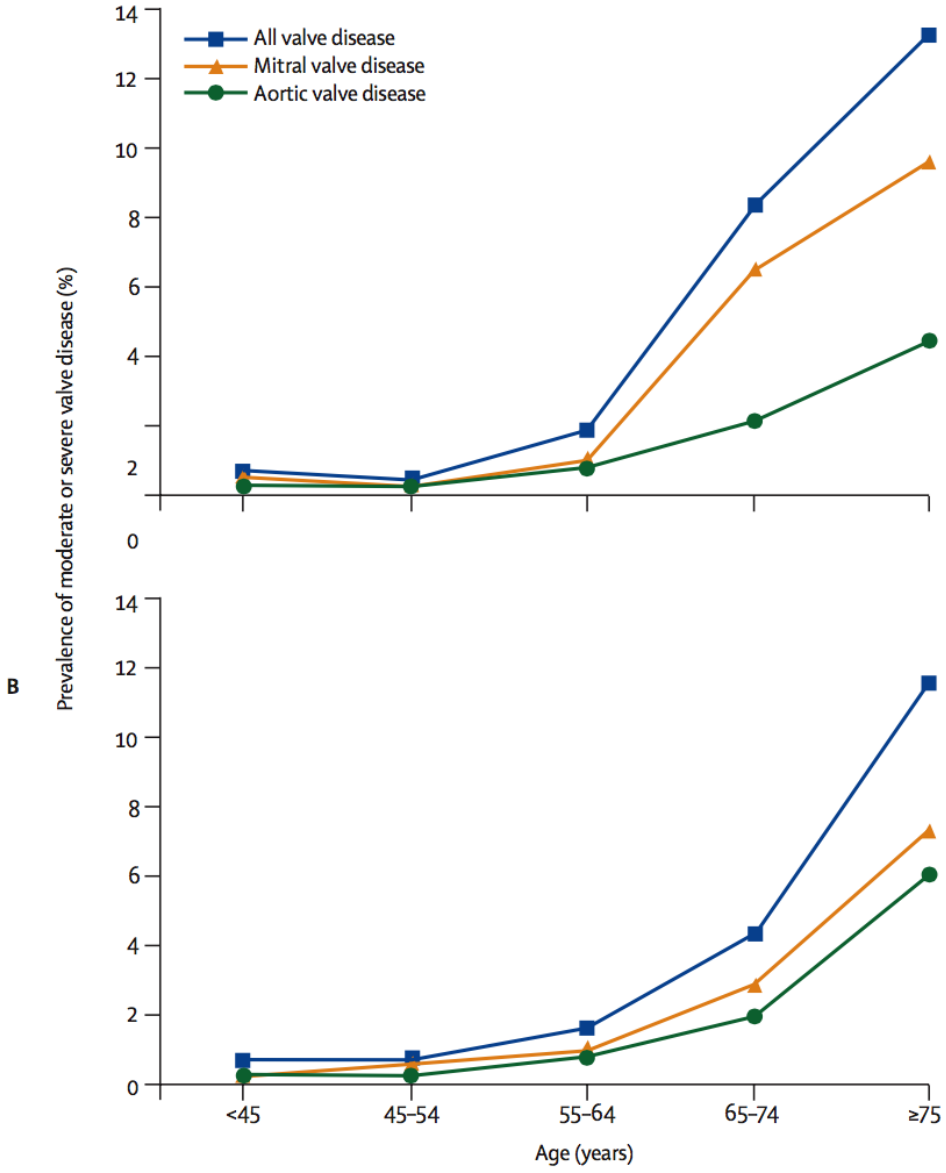
Heart 2014;100:126–134.

- **Most common dilatation irrespective of BAV type-Asc Ao**
- **Root dilatation linked to R-L fusion, male gender (p=0.0001)**
- **R-L fusion annulus/root/STJ enlargement**
- **AR related to root progression**

Burden of valvular heart diseases: a population-based study

Vuyisile T Nkomo, Julius M Gardin, Thomas N Skelton, John S Gottdiener, Christopher G Scott, Maurice Enriquez-Sarano

Lancet 2006; 368: 1005–11



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Vuyisile T Nkomo, Julius M Gardin, Thomas N Skelton, John S Gottdiener, Christopher G Scott, Maurice Enriquez-Sarano

Lancet 2006; 368: 1005–11

	Age (years)	Valvular heart diseases diagnosed in Olmsted County				p value for trend
	18–44	45–54	55–64	65–74	≥75	
Residents, n	49 957	16 306	10 241	6686	6663	..
Residents examined, n (% men)	4310 (38%)	2737 (48%)	2847 (53%)	2798 (53%)	3851 (41%)	..
Mitral regurgitation (n=874)	57, 0·1% (0·1–0·2)	62, 0·4% (0·3–0·5)	93, 0·9% (0·7–1·1)	186, 2·8% (2·4–3·3)	476, 7·1% (6·5–7·8)	<0·0001
Mitral stenosis (n=33)	5, 0·01% (0–0·02)	3, 0·02% (0–0·05)	3, 0·03% (0·01–0·1)	8, 0·1% (0·05–0·2)	14, 0·2% (0·1–0·4)	<0·0001
Aortic regurgitation (n=282)	55, 0·1% (0·08–0·1)	38, 0·2% (0·2–0·3)	33, 0·3% (0·2–0·5)	41, 0·6% (0·4–0·8)	115, 1·7% (1·4–2·1)	<0·0001
Aortic stenosis (n=547)	51, 0·1% (0·08–0·1)	35, 0·2% (0·2–0·3)	57, 0·6% (0·4–0·7)	96, 1·4% (1·2–1·8)	308, 4·6% (4·1–5·2)	<0·0001

	Age (years)	Prevalence of valvular heart diseases in population-based studies				p value for trend
	18–44	45–54	55–64	65–74	≥75	
Participants (n)	4351	696	1240	3879	1745	..
Male, n (%)	1959 (45%)	258 (37%)	415 (33%)	1586 (41%)	826 (47%)	..
Mitral regurgitation (n=449)	23, 0·5% (0·3–0·8)	1, 0·1% (0–0·8)	12, 1·0% (0·5–1·8)	250, 6·4% (5·7–7·3)	163, 9·3% (8·1–10·9)	<0·0001
Mitral stenosis (n=15)	0, 0% (0–0·1)	1, 0·1% (0–0·8)	3, 0·2% (0·1–0·7)	7, 0·2% (0·1–0·4)	4, 0·2% (0·1–0·6)	0·006
Aortic regurgitation (n=90)	10, 0·2% (0·1–0·4)	1, 0·1% (0–0·8)	8, 0·7% (0·3–1·3)	37, 1·0% (0·7–1·3)	34, 2·0% (1·4–2·7)	<0·0001
Aortic stenosis (n=102)	1, 0·02% (0–0·1)	1, 0·1% (0–0·8)	2, 0·2% (0·6–1·9)	50, 1·3% (1·0–1·7)	48, 2·8% (2·1–3·7)	<0·0001

Critical #1 AR
Why ESD??

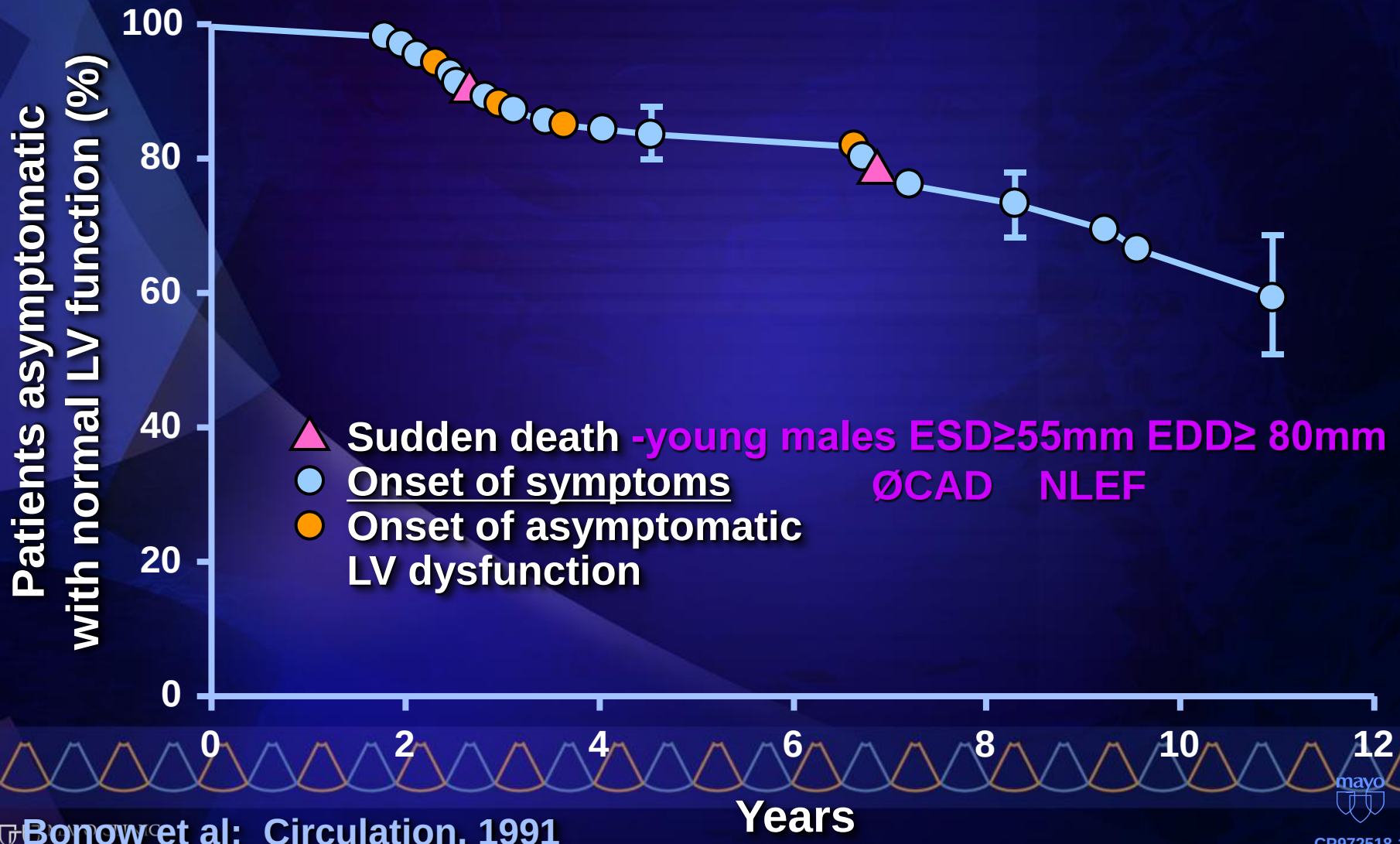
Serial Long-term Assessment of the Natural History of Asymptomatic Patients With Chronic Aortic Regurgitation and Normal Left Ventricular Systolic Function

Robert O. Bonow, MD; Edward Lakatos, PhD;
Barry J. Maron, MD; and Stephen E. Epstein, MD

Circulation 1991;84:1625-1635

- 104 asymptomatic, 86% male, mean 36 y
- EF≥ 45%, 3+ to 4+ AR
- Mean FU 8 y
- Surgery if symptoms or ↓LVEF
- Sudden death 0.4%/y
- Events 5%/y

Aortic Regurgitation
Natural History: Composite Outcome



Bonow et al: Circulation, 1991

Serial Long-term Assessment of the Natural History of Asymptomatic Patients With Chronic Aortic Regurgitation and Normal Left Ventricular Systolic Function

Robert O. Bonow, MD; Edward Lakatos, PhD;
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Circulation 1991;84:1625-1635

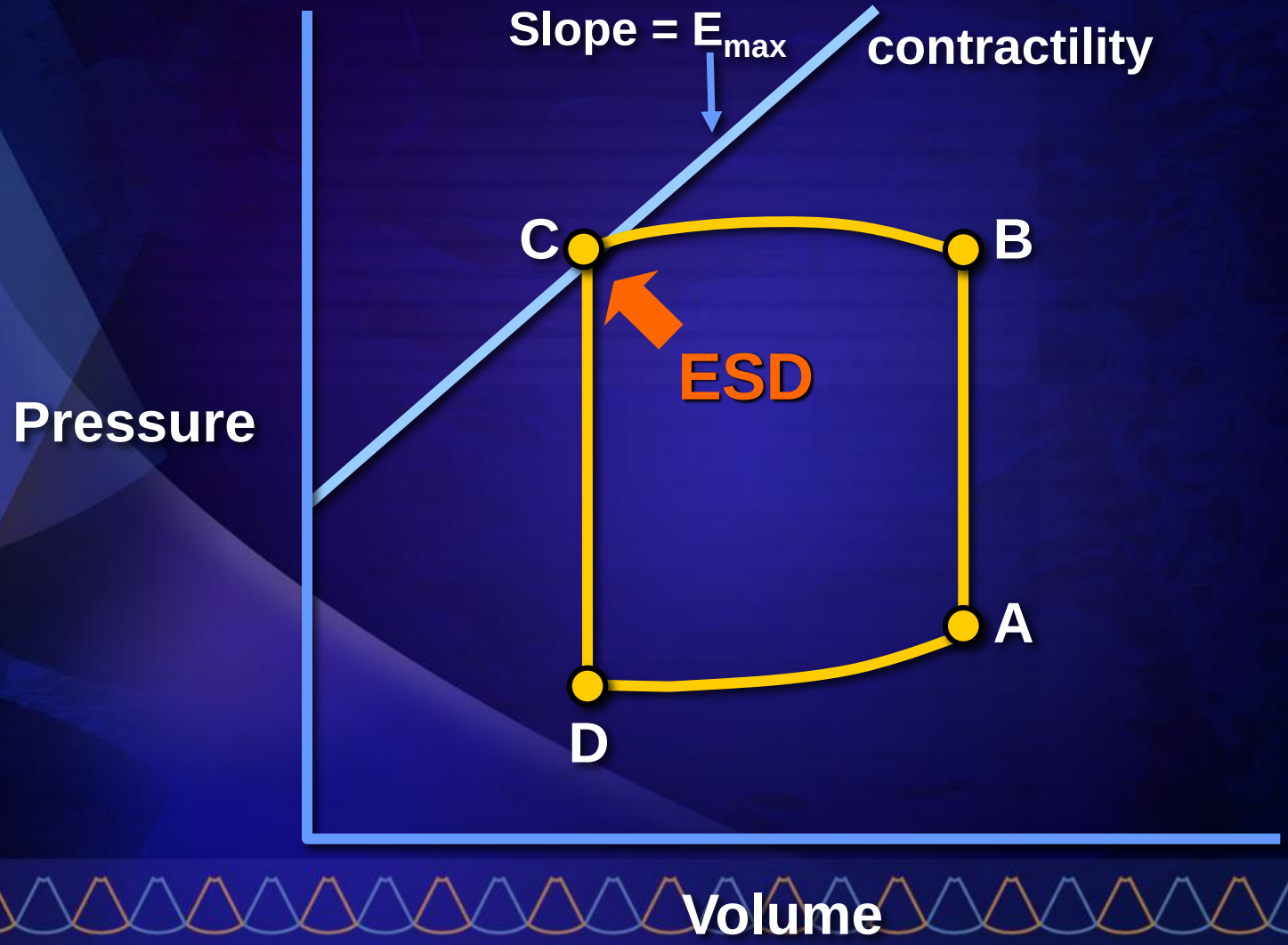
TABLE 2. Risk Stratification Based on Kaplan-Meier Life Table Analysis of Measurements at Initial Study

Variable	Value	Likelihood of death, symptoms, or LV dysfunction
LV end-systolic dimension	>50 mm	19% per year
	40–49 mm	6% per year
	<40 mm	0% per year
LV end-diastolic dimension	≥70 mm	10% per year
	<70 mm	2% per year
LV ejection fraction response to exercise	Decrease >5%	12% per year
	Decrease 0–5%	4% per year
	Increase >0%	1% per year

LV, left ventricular.

Why ESD?

Pressure Volume Relationship



Critical #2 AR

Almost never too late…

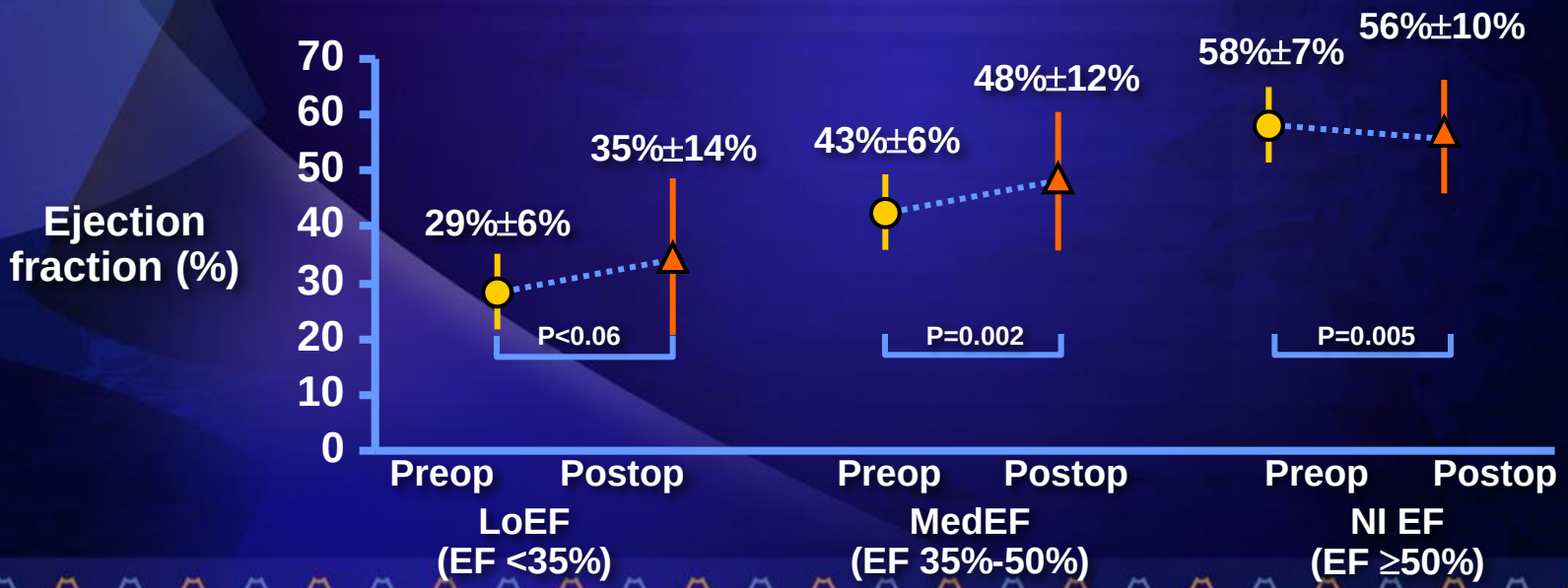
AR: Volume & pressure overload

Outcomes After Aortic Valve Replacement in Patients With Severe Aortic Regurgitation and Markedly Reduced Left Ventricular Function

Hari P. Chaliki, MD; Dania Mohty, MD; Jean-Francois Avierinos, MD; Christopher G. Scott, MS; Hartzell V. Schaff, MD; A. Jamil Tajik, MD; Maurice Enriquez-Sarano, MD

Circulation 2002;106:2687-2693

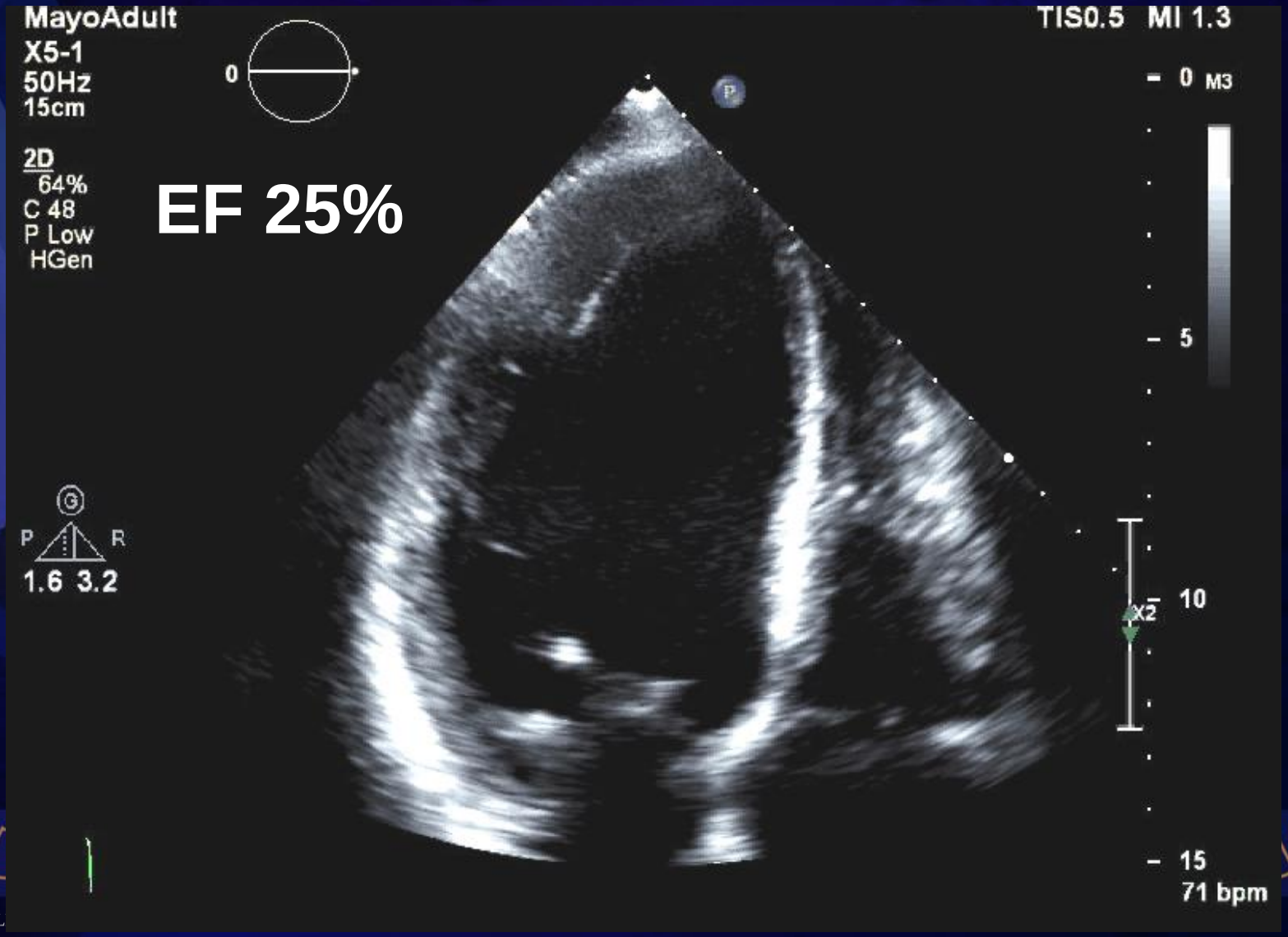
- 450 patients 1980-1995, men

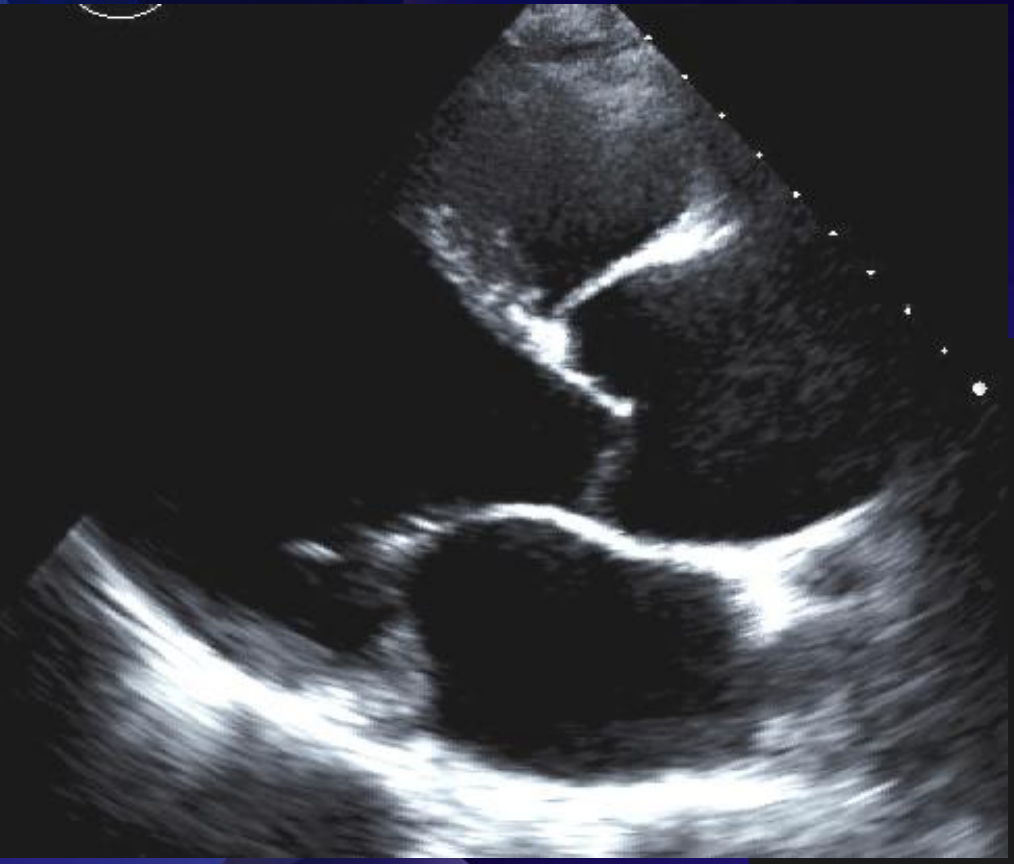


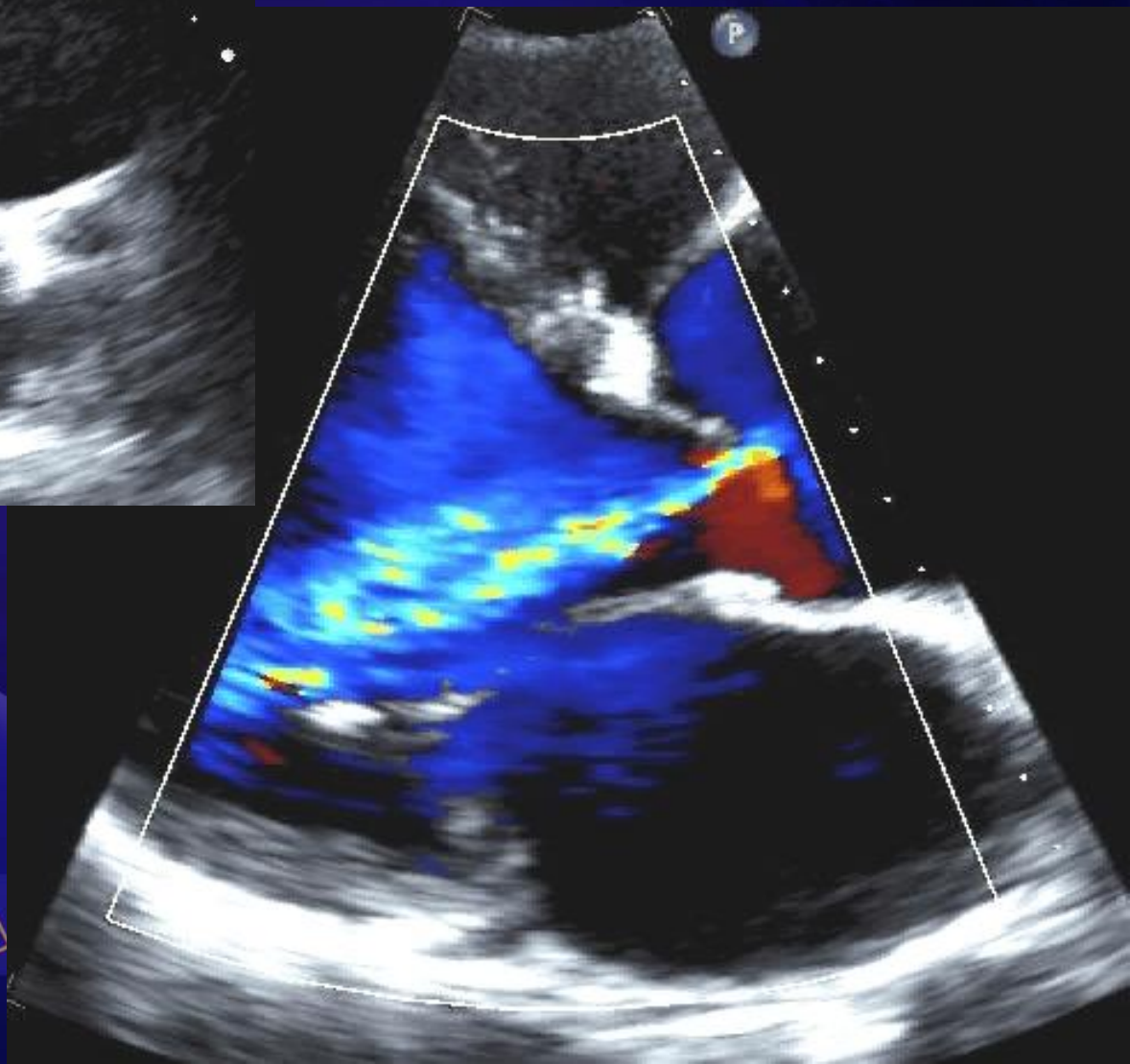
AVR for symptomatic patients with low EF has almost no cut-off

- Even EF < 25% may benefit
- Prognosis without surgery very poor

72 yo SOB, Hx Afib on amio, now sinus rhythm, aneurysm

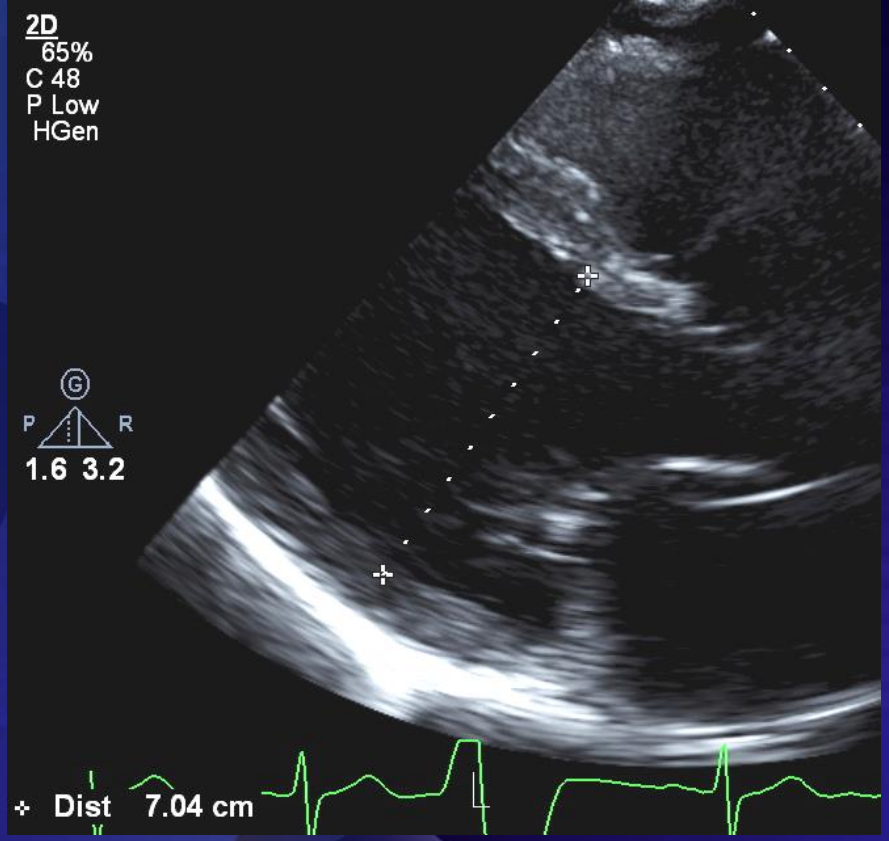


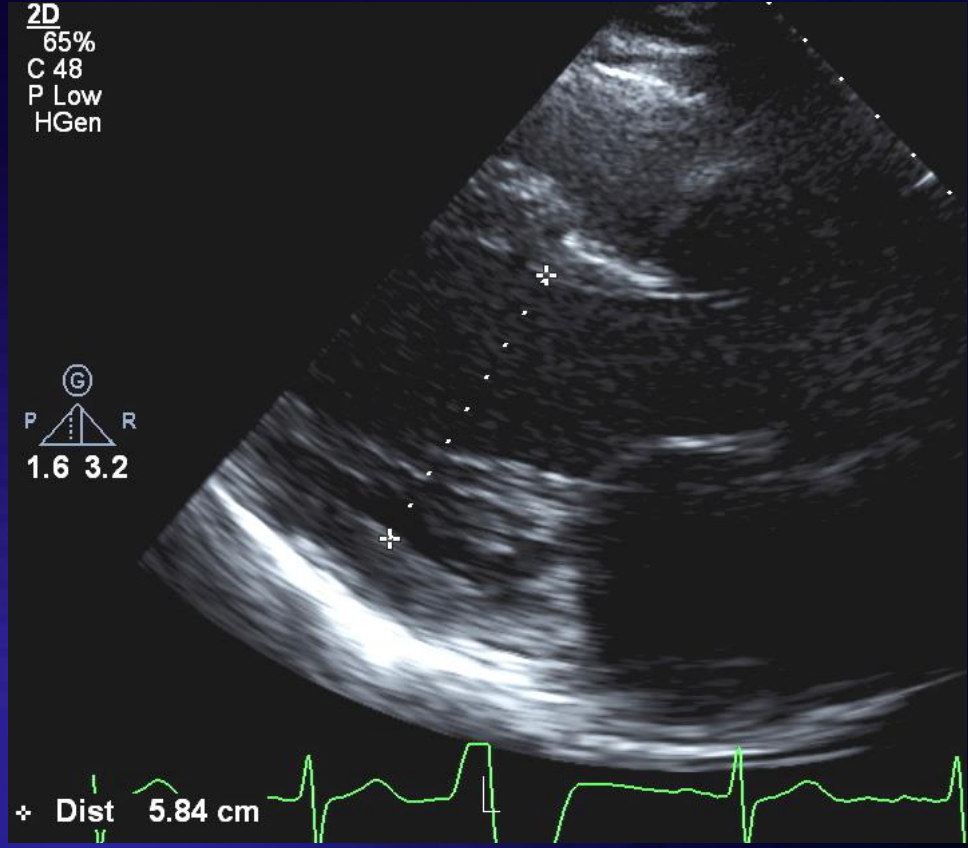


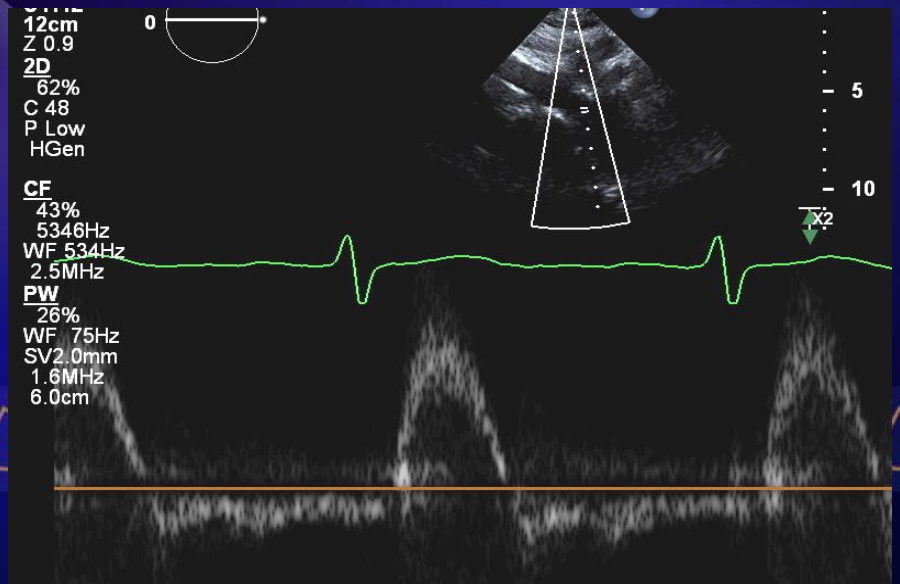


Root 56mm
Asc Ao 60mm

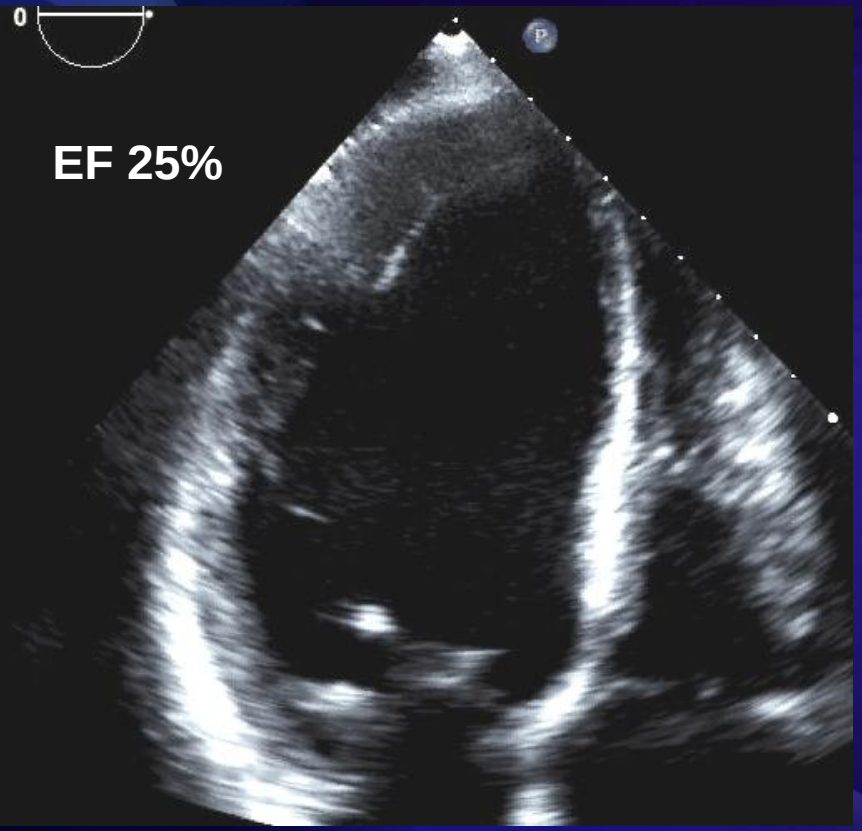
MAYO CLINIC

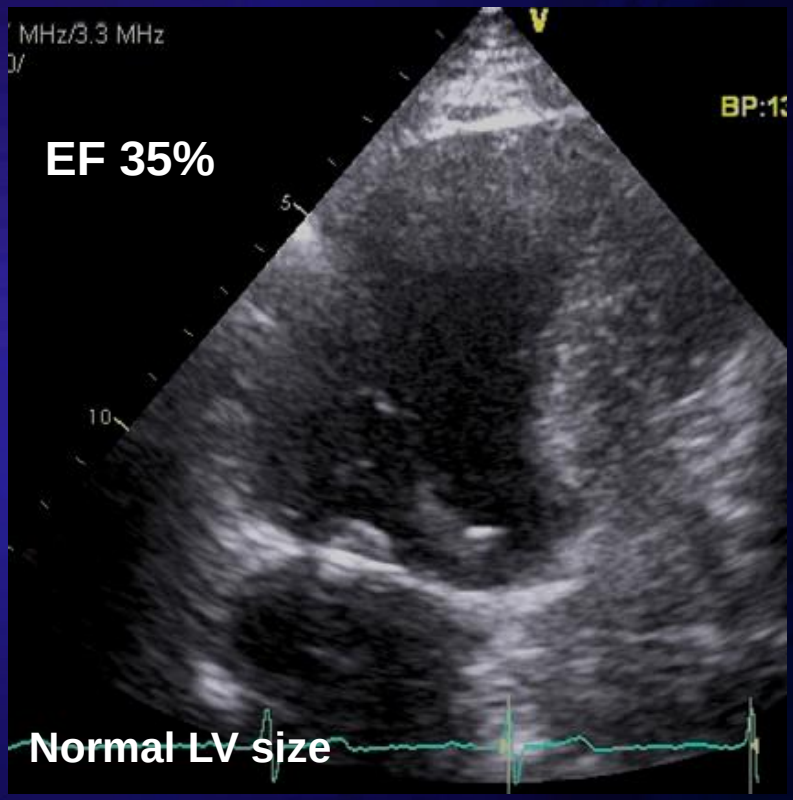

2D
65%
C 48
P Low
HGen
P R
1.6 3.2
Dist 7.04 cm


2D
65%
C 48
P Low
HGen
P R
1.6 3.2
Dist 5.84 cm


12cm
Z 0.9
2D
62%
C 48
P Low
HGen
CF
43%
5346Hz
WF 534Hz
2.5MHz
PW
26%
WF 75Hz
SV2.0mm
1.6MHz
6.0cm
0
5
10
X2

72 yo 11/2 years post Sx





Critical #3 AR

Women…Be careful !!

Surgery for Aortic Regurgitation in Women
Contrasting Indications and Outcomes Compared With Men

E Klodas, M Enriquez-Sarano, A. Jamil Tajik, C Mullany, K Bailey, J Seward

Circulation. 1996;94:2472-2478

- 249 (51 women, 198 men severe AR 1980-89)

Variable	Men	Women	*P*
BSA, m^2	1.99	1.68	<.0001
LVD, mm	70.7	61.9	<.0001
LVS, mm	49.4	41.8	<.0001
EF, %	51.1	53.4	NS

Surgery for Aortic Regurgitation in Women

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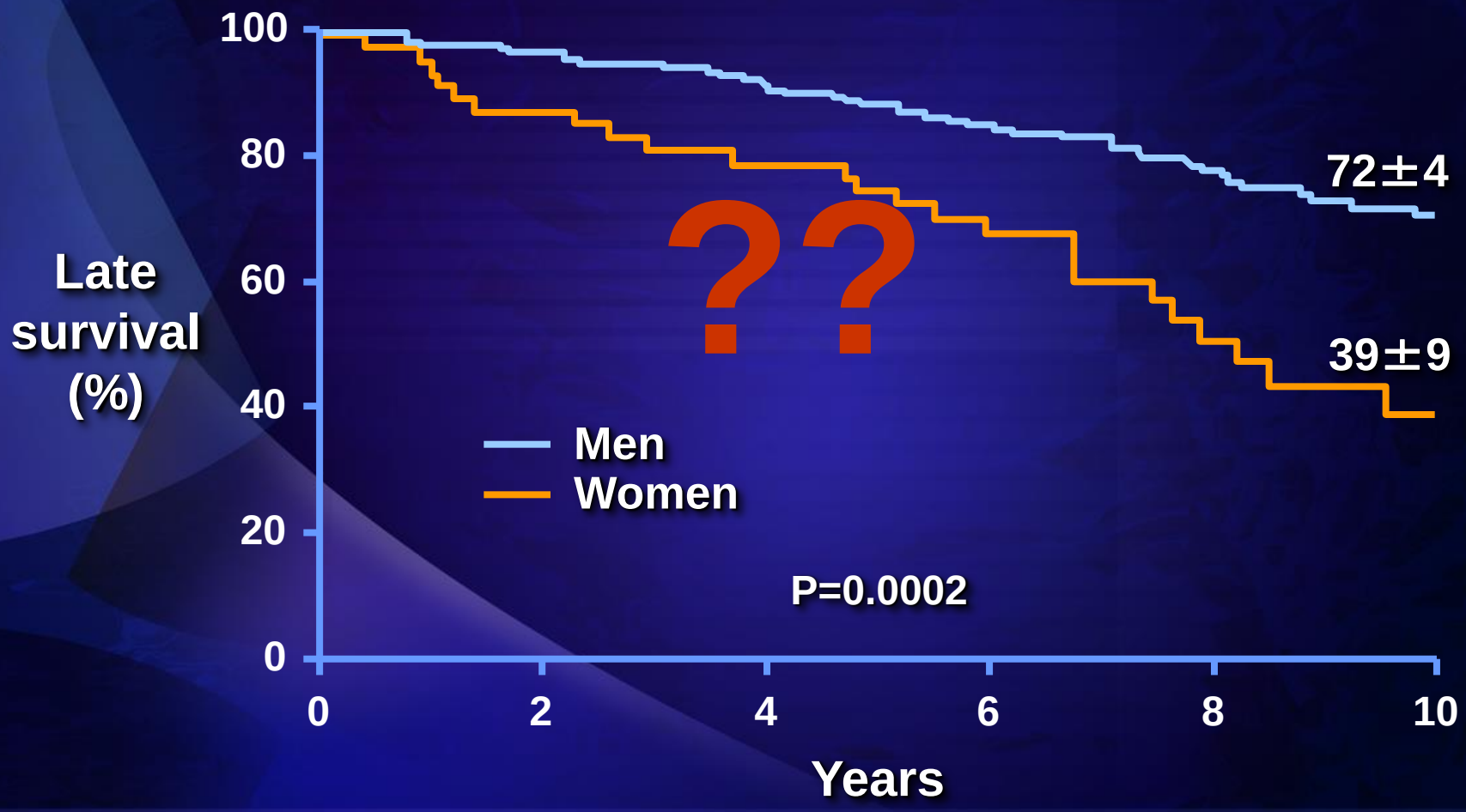


Men	n= 187	181	179	176	169	151	128	116	96	75	63
Women	n= 49	48	44	41	40	36	30	24	16	13	8

Surgery for Aortic Regurgitation in Women

Contrasting Indications and Outcomes Compared With Men

E Klodas, M Enriquez-Sarano, A. Jamil Tajik, C Mullany, K Bailey, J Seward

Circulation. 1996;94:2472-2478

- 2/3 women class III or IV dyspnea
- 1/3 men class III or IV dyspnea
- 1 in 10 women preoperative end-systolic dimension 55 mm
- 1 in 3 men preoperative end-systolic dimension 55 mm

Sex Differences and Survival in Adults With Bicuspid Aortic Valves: Verification in 3 Contemporary Echocardiographic Cohorts

Hector I. Michelena, MD; Rakesh M. Suri, MD, D.Phil; Ognjen Katan, MD; Mackram F. Eleid, MD; Marie-Annick Clavel, DVM, PhD; Mathew J. Maurer, MS; Patricia A. Pellikka, MD; Douglas Mahoney, MS; Maurice Enriquez-Sarano, MD

Background—Sex-related differences in morbidity and survival in bicuspid aortic valve (BAV) adults are fundamentally unknown. Contemporary studies portend excellent survival for BAV patients identified at early echocardiographic-clinical stages. Whether BAV adults incur a survival disadvantage throughout subsequent echocardiographic-clinical stages remains undetermined.

Methods and Results—Analysis was done of 3 different cohorts of consecutive patients with echocardiographic diagnosis of BAV identified retrospectively: (1) a community cohort of 416 patients with first BAV diagnosis (age 35±21 years, follow-up 16±7 years), (2) a tertiary clinical referral cohort of 2824 BAV adults (age 51±16 years, follow-up 9±6 years), and (3) a surgical referral cohort of 2242 BAV adults referred for aortic valve replacement (AVR) (age 62±14 years, follow-up 6±5 years). For the community cohort, 20-year risks of aortic regurgitation (AR), AVR, and infective endocarditis were higher in men (all $P \leq 0.04$); for a total BAV-related morbidity risk of 52±4% vs 35±6% in women ($P=0.01$). The cohort's 25-year survival was identical to that in the general population ($P=0.98$). AR independently predicted mortality in women ($P=0.001$). Baseline AR was more common in men ($P \leq 0.02$) in the tertiary cohort, with 20-year survival lower than that in the general population ($P<0.0001$); age-adjusted relative death risk was 1.16 (95% confidence interval [CI] 1.05-1.29) for men versus 1.67 (95% CI 1.38-2.03) for women ($P=0.001$). AR independently predicted mortality in women ($P=0.01$). Baseline AR and infective endocarditis were higher in men (both ≤0.001) for the surgical referral cohort, with 15-year survival lower than that in the general population ($P<0.0001$); age-adjusted relative death risk was 1.34 (95% CI 1.22-1.47) for men versus 1.63 (95% CI 1.40-1.89) for women ($P=0.026$). AR and NYHA class independently predicted mortality in women (both $P \leq 0.04$).

Conclusions—Within evolving echocardiographic-clinical stages, the long-term survival of adults with BAV is not benign, as both men and women incur excess mortality. Although BAV-related morbidity is higher in men in the community, and AR and infective endocarditis are more prevalent in men, women exhibit a significantly higher relative risk of death in tertiary and surgical referral cohorts, which is independently associated with AR. **(*J Am Heart Assoc.* 2016;5:e004211 doi: 10.1161/JAHA.116.004211)**

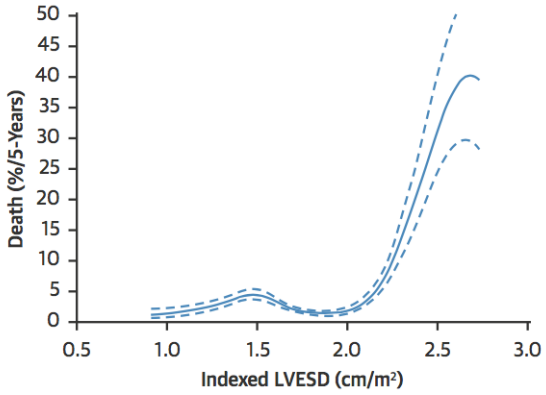
- ESD ≥25 mm/m² AR

Long-Term Outcomes in Patients With Aortic Regurgitation and Preserved Left Ventricular Ejection Fraction

Amgad Mentias, MD, Ke Feng, MD, Alaa Alashi, MD, L. Leonardo Rodriguez, MD, A. Marc Gillinov, MD, Douglas R. Johnston, MD, Joseph F. Sabik, MD, Lars G. Svensson, MD, PhD, Richard A. Grimm, MD, Brian P. Griffin, MD, Milind Y. Desai, MD

(J Am Coll Cardiol 2016;68:2144-53)

FIGURE 1 Mortality Risk



In the subgroup that did not undergo aortic valve surgery, in order to assess the possible nonlinear relationship between iLVESD and risk of death, we modeled the covariate predicted iLVESD as a quadratic spline. Based upon the visual analysis of the curves, patients with iLVESD <2 cm/m^2 had excellent 5-year survival. However, the risk of death significantly and continuously rose as iLVESD increased beyond 2 cm/m^2. **Solid line** = 5-year parametric estimates of instantaneous risk of death; **dotted lines** = 68% confidence interval. iLVESD = indexed left ventricular end-systolic dimension.

AR Management

Indications for AVR for Chronic AR

Class I

Class IIa

Aortic regurgitation

Severe AR
(stages C and D)
Vena contracta >0.6 cm
Holodiastolic aortic flow reversal
RVol ≥60 mL/beat
RF ≥50%
ERO ≥0.3 cm^2
LV dilation

Progressive AR
(stage B)
Vena contracta ≤0.6 cm
RVol <60 mL/beat
RF <50%
ERO <0.3 cm^2

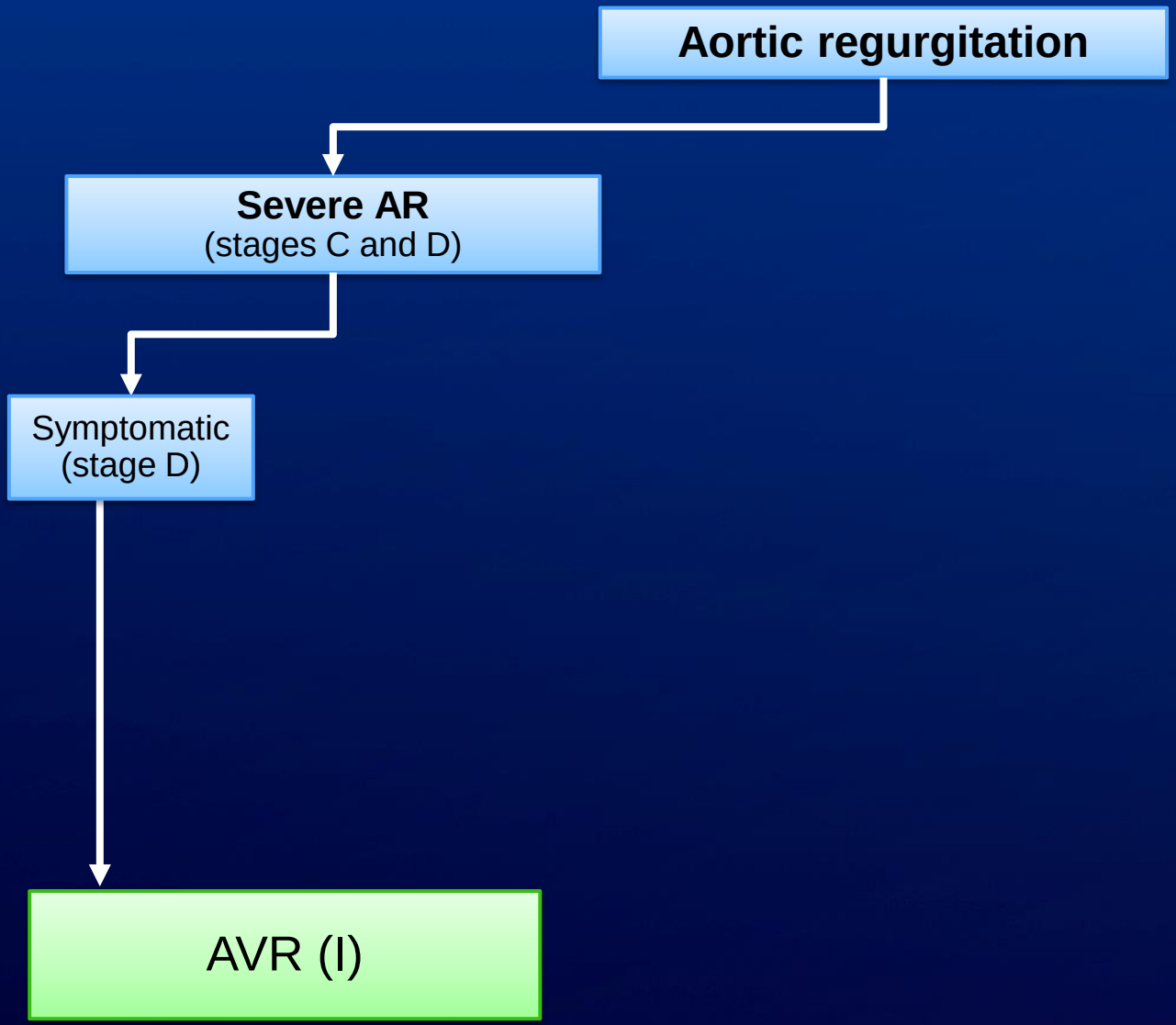
MAYO CLINIC

ACC/AHA VHD Guidelines 2014

Indications for AVR for Chronic AR

Class I

Class IIa



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ACC/AHA VHD Guidelines 2014

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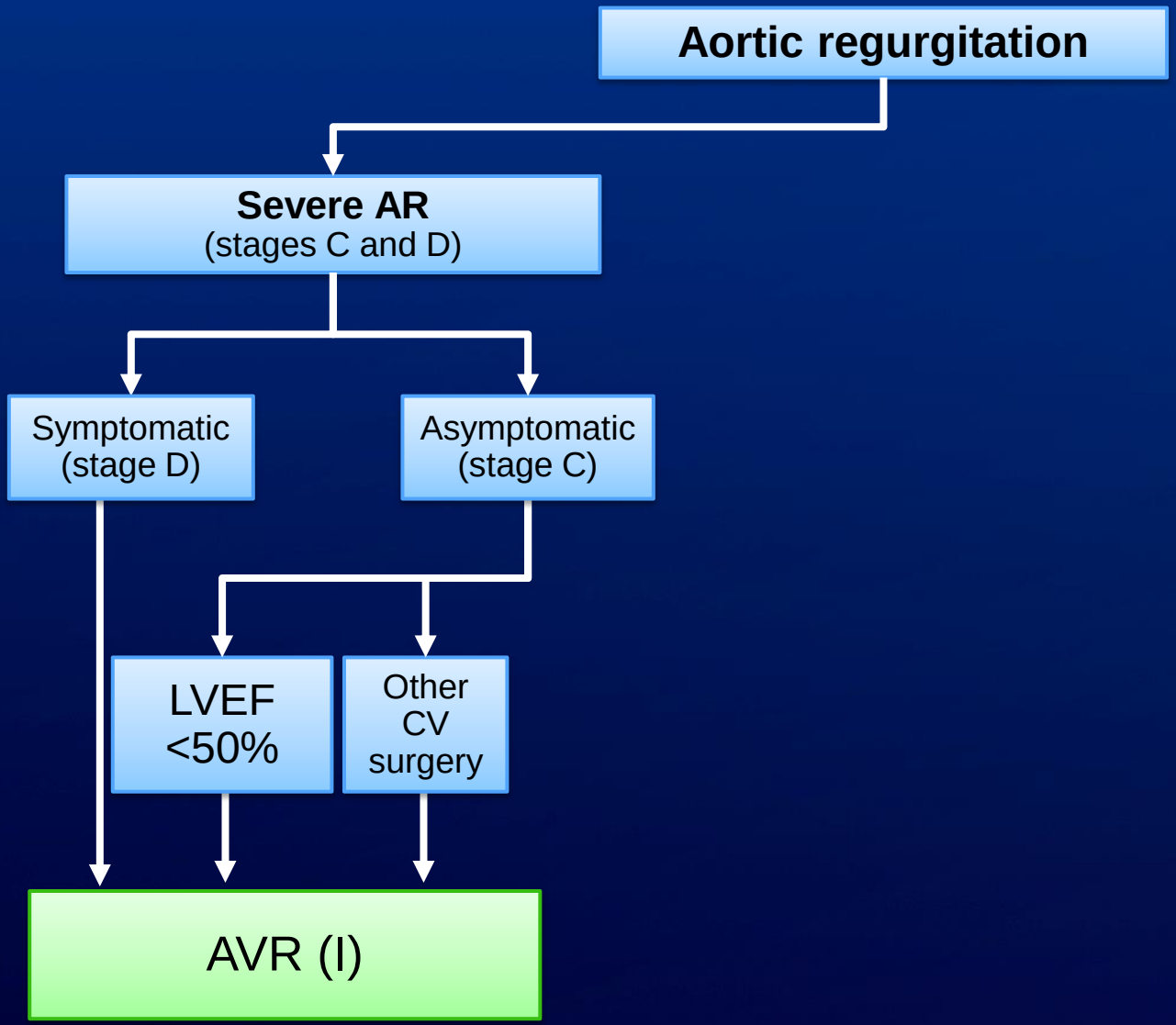

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ACC/AHA VHD Guidelines 2014

Indications for AVR for Chronic AR

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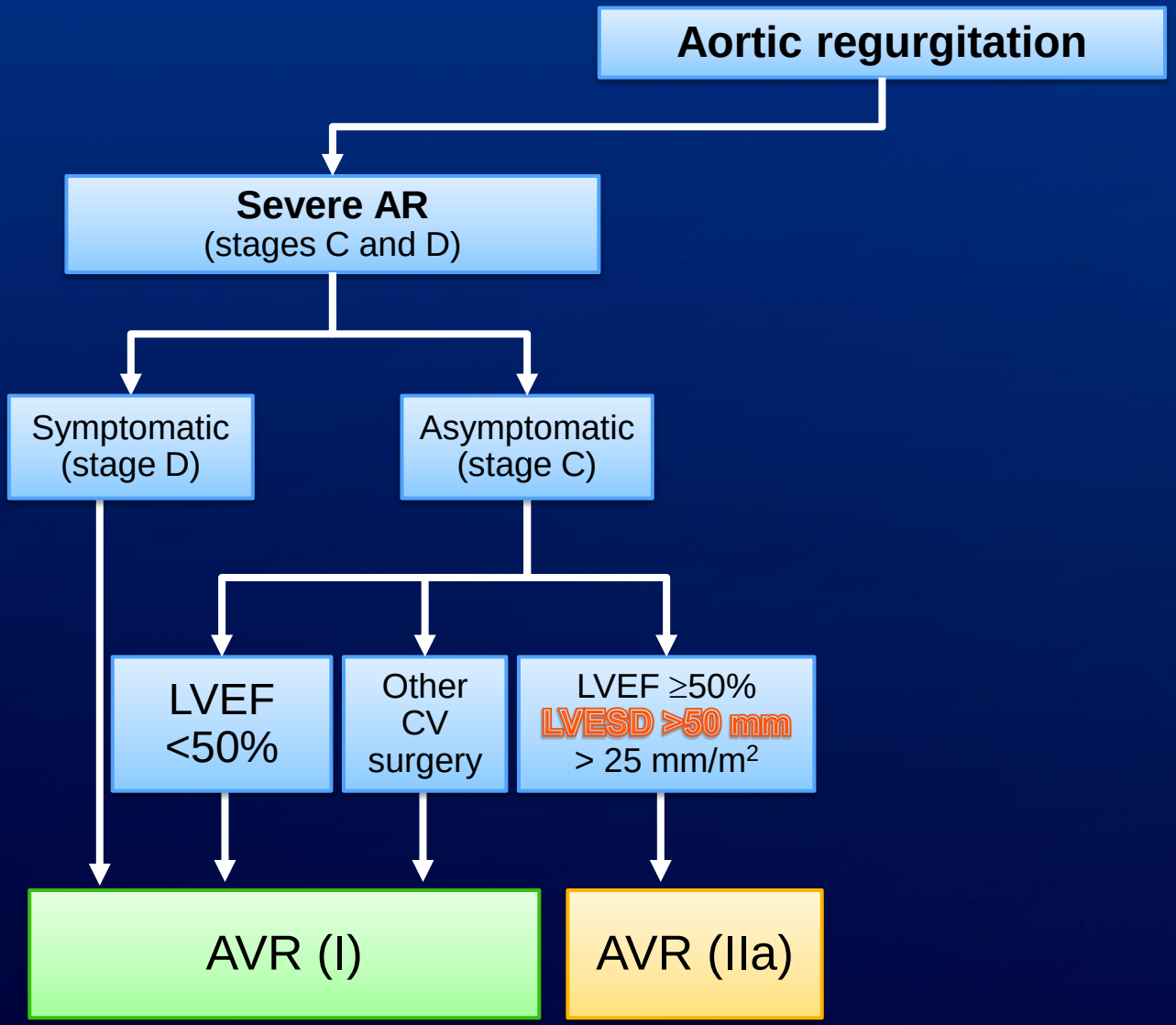


Take Home Points

MAYO CLINIC

- Imaging AA: TTE, CT/MR
- Screening family members / genetics
- The importance / limitations of size
- The importance of other risk factors

- Link between AR/AA
- Importance of ESD
- Almost never too late to fix
- Importance of women

In life we cannot save people, we can only love them.
In medicine, we may have a chance to both save them and love them.

Michelena.hector@mayo.edu

European Heart Journal (2011) **32**, 3147–3197
doi:10.1093/eurheartj/ehr218

ESC GUIDELINES

ESC Guidelines on the management of cardiovascular diseases during pregnancy

The Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC)

Endorsed by the European Society of Gynecology (ESG), the Association for European Paediatric Cardiology (AEPC), and the German Society for Gender Medicine (DGesGM)

Regitz-Zagrosek V, Lundqvist C, Borghi C, et al.

Management of Aortic Disease In Pregnancy

ESC Guidelines 2011

Surgical treatment pre-pregnancy should be considered in women with aortic disease associated with a bicuspid aortic valve when the aortic diameter is >50mm (or >27 mm/m^2 BSA).	IIa	C
Prophylactic surgery should be considered during pregnancy if the aortic diameter is ≥50 mm and increasing rapidly.	IIa	C

Aortic Dilatation in Patients with Bicuspid Aortic Valve

Subodh Verma, M.D., Ph.D., and Samuel C. Siu, M.D.

N Engl J Med 2014;370:1920-9.

Table S 2: Management of Pregnant Women with Bicuspid Aortopathy*

Prior to Pregnancy

- Women with a bicuspid aortic valve should undergo imaging of the entire aorta before pregnancy[10]
- Prepregnancy evaluation in women with bicuspid aortic valve and aortopathy should be

- Women with ascending aorta and/or root dimension >45 mm should be advised against pregnancy[11,12]
- Women with mildly dilated ascending aorta/root (40-45 mm) likely represent an intermediate risk group for which pregnancy is relatively contraindicated and who will require close medical surveillance during pregnancy[12]
- Threshold for surgery prior to pregnancy is similar to that of the general population of individuals with bicuspid aortopathy without concomitant valvular dysfunction (50-55 mm) [10,12]

surface area index has been proposed as an alternative threshold for pre-pregnancy surgical consideration but the suggested threshold was extrapolated from women with Turner's syndrome[10]

Even in pregnancy
BAV ≠ Marfan

Aortic Dissection in Pregnancy: Analysis of Risk Factors and Outcome

(Ann Thorac Surg 2003;76:309–14)

Franz F. Immer, MD, Anne G. Bansi, MD, Alexsandra S. Immer-Bansi, MD, Jane McDougall, MD, Kenton J. Zehr, MD, Hartzell V. Schaff, MD, and Thierry P. Carrel, MD

Table 2. Type A Dissections (Prepartum)

	Marfan Syndrome	BAVD	*p* Value
Patients	16	4	
Age (years)	29.8 ± 4.1	27.8 ± 3.7	ns
Gravida	1.6 ± 0.9	1.3 ± 0.5	ns
Para	0.4 ± 0.6	0	ns
Systemic disease	16	0	< 0.05
Hypertensive	3	1	ns
Aortic regurgitation	10	1	< 0.05
Severe (IV)	3	1	ns
Aortic root (cm)	4.8 ± 0.8	5.3 ± 1.1	ns
Gestation (weeks)	31.5 ± 5.9	26.8 ± 7.6	< 0.05
Delivery			
Spontaneous vaginal	2[a]	2[a]	ns
Cesarean section	14	2	< 0.05
Maternal outcome			
Maternal death	0	1	ns
Fetal outcome			
Fetal death	3	3	ns
Poor	1	0	ns

All case-reports from 1983-2002 PLUS the Mayo and Bern experience

MAYO

Frequency of Cardiovascular Events in Women With a Congenitally Bicuspid Aortic Valve in a Single Community and Effect of Pregnancy on Events

Stephen H. McKellar, MD[a], Ryan J. MacDonald, BS[a], Hector I. Michelena, MD[b], Heidi M. Connolly, MD[b], and Thoralf M. Sundt III, MD[a,*]

(Am J Cardiol 2011;107:96–99)

- 1980-1999
- 88 women age 35 years BAV
- Median FU 12 years
- 216 preg, 186 deliveries
- No dissections
- 6% Ao >40mm baseline…

Abnormal Extracellular Matrix Protein Transport Associated With Increased Apoptosis of Vascular Smooth Muscle Cells in Marfan Syndrome and Bicuspid Aortic Valve Thoracic Aortic Aneurysm

Maria Nataatmadja, Malcolm West, Jenny West, Kim Summers, Philip Walker, Michio Nagata and Teruo Watanabe

Circulation 2003, 108:II-329-II-334

Marfan-like Bad

Indications for elective surgery BAV + Marfan

Bonow et al. *J Am Coll Cardiol*, 2006; 48:1-148
Beckman et al. *Circulation 2010, 121:e266-e369*

Aortic size ≥50 mm

Rate of ↑ ≥5 mm/yr

Predictors of dissection

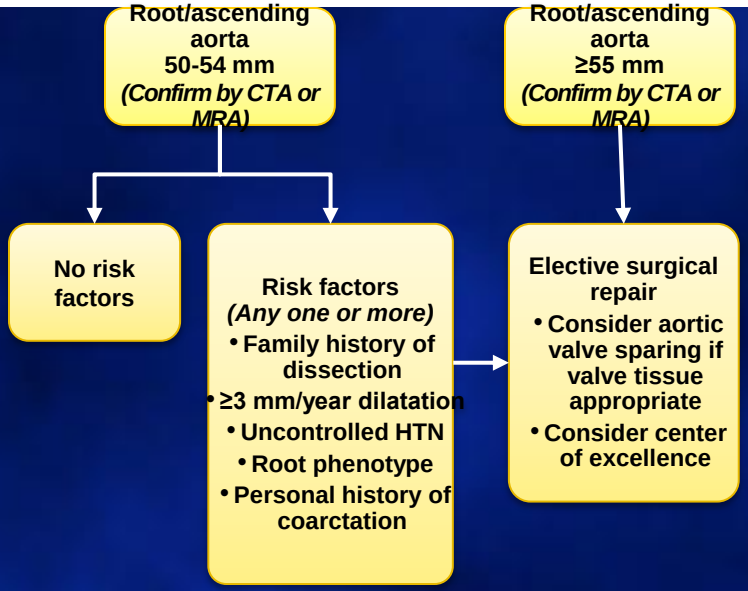
Family history of aortic complications

ACC/AHA GUIDELINES CLARIFICATION

JACC 2016

Surgery for Aortic Dilatation in Patients With Bicuspid Aortic Valves

COR	LOE	RECOMMENDATIONS
I	B-NR	1. Operative intervention to repair or replace the aortic root (sinuses) or replace the ascending aorta is indicated in asymptomatic patients with BAV if the diameter of the aortic root or ascending aorta is 5.5 cm or greater (4-8).
IIa	B-NR	1. Operative intervention to repair or replace the aortic root (sinuses) or replace the ascending aorta is reasonable in asymptomatic patients with BAV if the diameter of the aortic root or ascending aorta is 5.0 cm or greater and an additional risk factor for dissection is present (e.g., family history of aortic dissection or aortic growth rate ≥0.5 cm per year) or if the patient is at low surgical risk and the surgery is performed by an experienced aortic surgical team in a center with established expertise in these procedures (2,7-9).



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IIa	C-EO	2. Replacement of the ascending aorta is reasonable in patients with BAV undergoing AVR because of severe aortic stenosis or aortic regurgitation when the diameter of the ascending aorta is greater than 4.5 cm (13-17).

Rain on everyone's parade…

Aortic Diameter ≥5.5 cm Is Not a Good Predictor of Type A Aortic Dissection

Observations From the International Registry of Acute Aortic Dissection (IRAD)

Circulation 2007

	All	Ascending <5.5 cm	Ascending ≥5.5 cm	*P*
No. (%)	591	349 (59.1)	242 (40.9)	
Demographics				
Age, n (SD)	60.8 (14.4)	60.5 (13.6)	61.2 (15.5)	0.61
Male, n (%)	390 (66.0)	226 (64.8)	164 (67.8)	0.45
History				
Hypertension, n (%)	407 (71.2)	247 (72.4)	160 (69.3)	0.41
Marfan syndrome, n (%)	28 (4.9)	11 (3.2)	17 (7.5)	0.02
Known aortic aneurysm, n (%)	70 (12.4)	41 (12.0)	29 (12.9)	0.75
Prior aortic dissection, n (%)	22 (3.9)	15 (4.4)	7 (3.1)	0.44
BAV (n=383), n (%)*	16 (4.2)	6 (2.6)	10 (6.5)	0.06

Ao size did not predict death

Multimod imaging !!

What do guidelines say??

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Regitz-Zagrosek V, Lundqvist C, Borghi C, et al.

Management of Aortic Disease In Pregnancy

ESC Guidelines 2011

Recommendations	Class[a]	Level[b]
Women with Marfan syndrome or other known aortic disease should be counselled about the risk of aortic dissection during pregnancy and the recurrence risk for the offspring.	I	C
Imaging of the entire aorta (CT/MRI) should be performed before pregnancy in patients with Marfan syndrome or other known aortic disease.	I	C
Women with Marfan syndrome and an ascending aorta >45 mm should be treated surgically pre-pregnancy.	I	C

Preconceptual Counseling in MFS

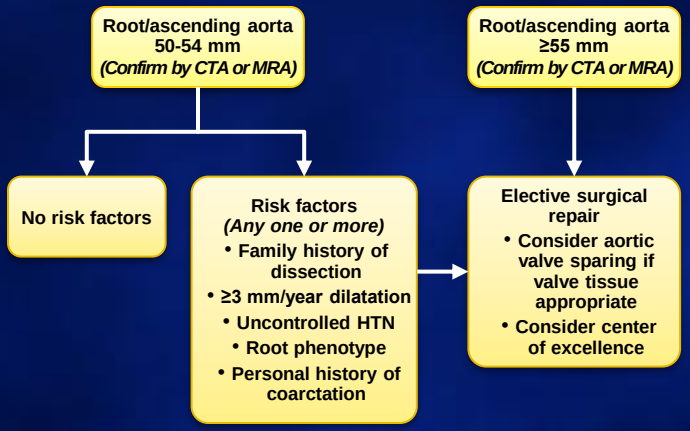
Advise against pregnancy

- Aortic dimension >45 mm
- Aortic dimension ≤45 mm

  FH of ao dissection

  High risk features
- Prior aortic dissection

Pregnancy risk factor BAV??



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You don't wanna get there!!!!!

PRENATAL COUNSELING

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