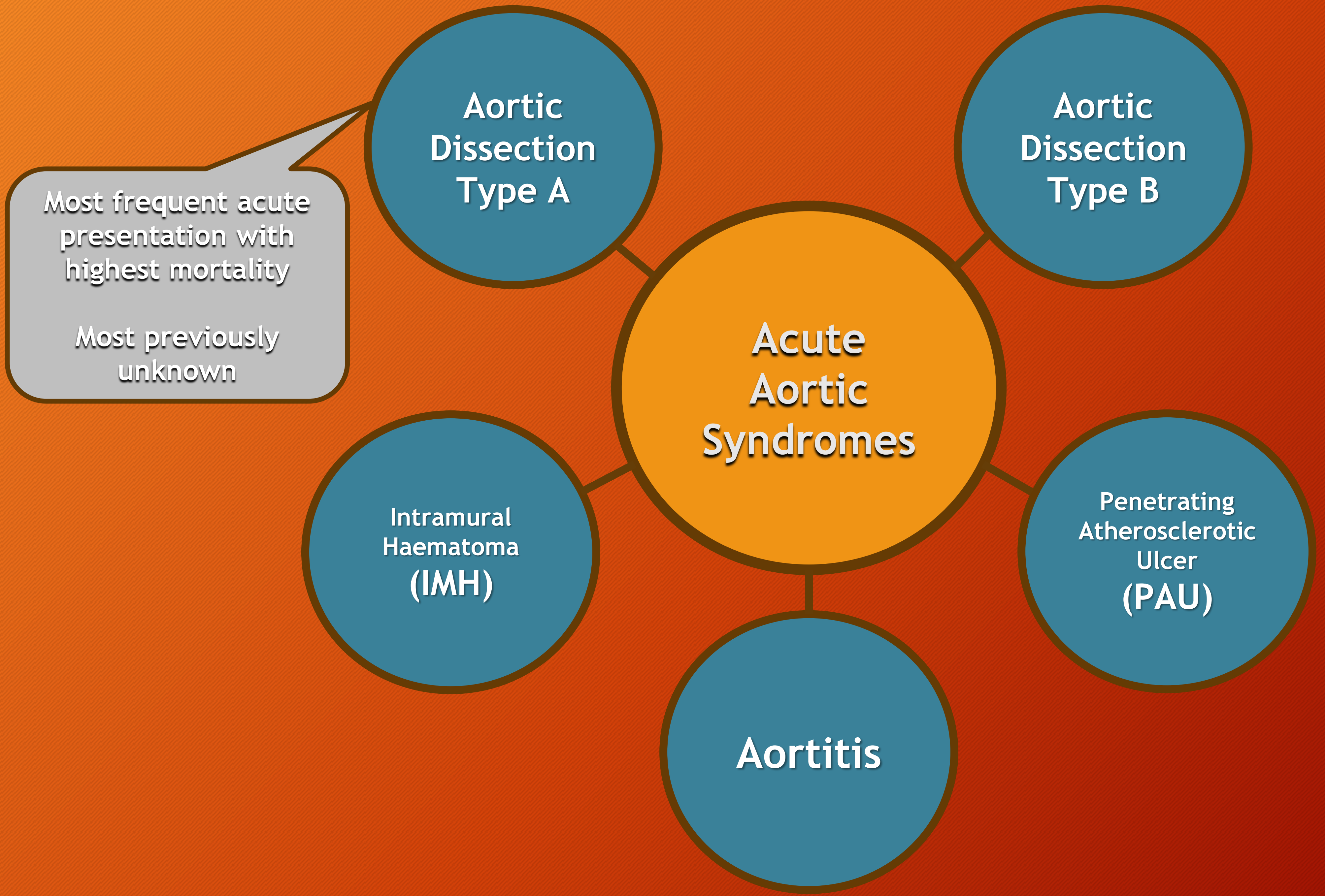
Aorta and Pericardial Disease

Diseases of the Aorta

Dr Julie Humphries

ECHO AUSTRALIA

17-19 March 2025


Acute Aortic Syndromes
Aortic Dissection Type A
Most frequent acute presentation with highest mortality
Most previously unknown
Aortic Dissection Type B
Intramural Haematoma (IMH)
Penetrating Atherosclerotic Ulcer (PAU)
Aortitis

Aortic Size
>5.0cm

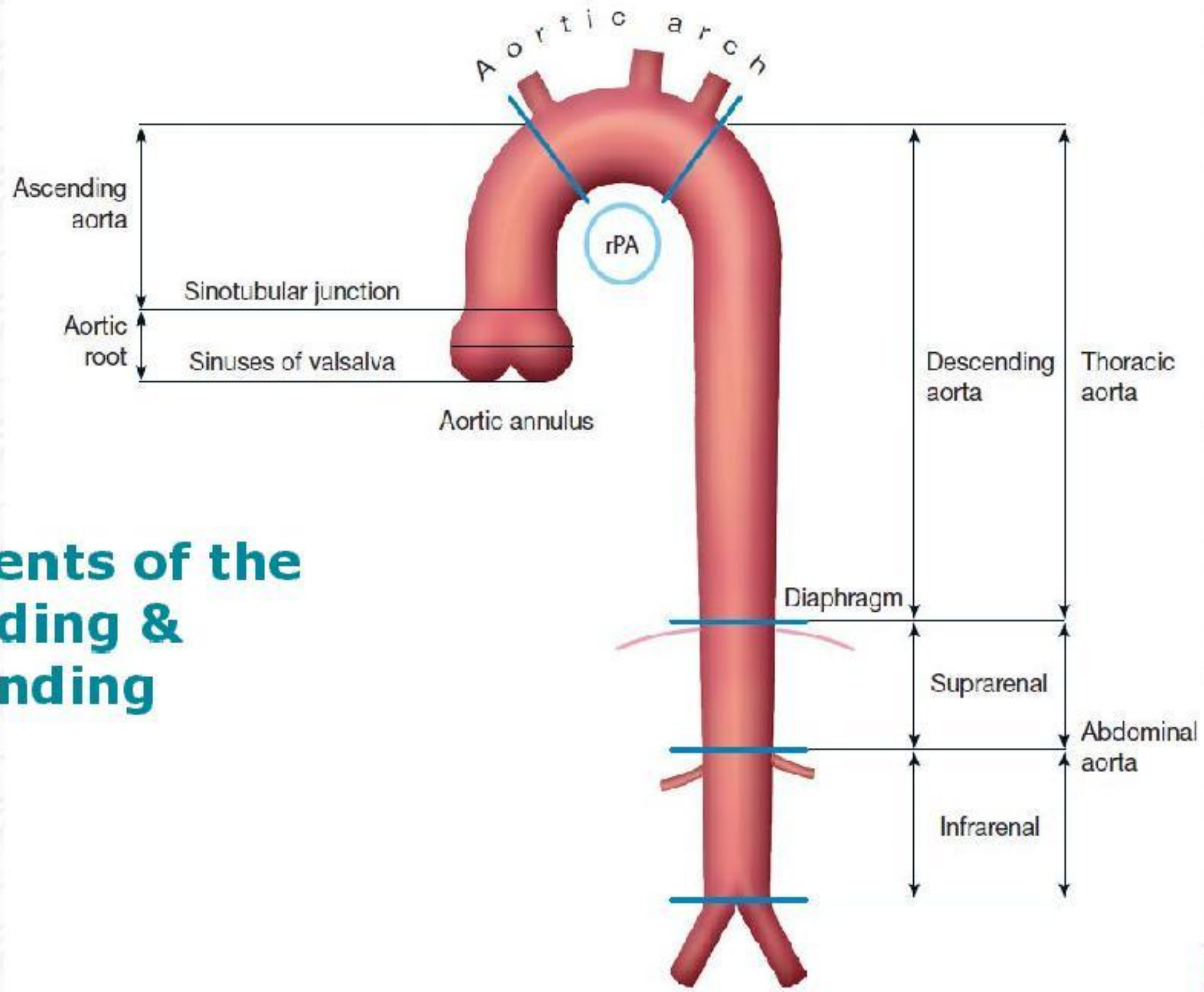
Predictors
of
Dissection

Rate of
Increase
>0.5cm/year

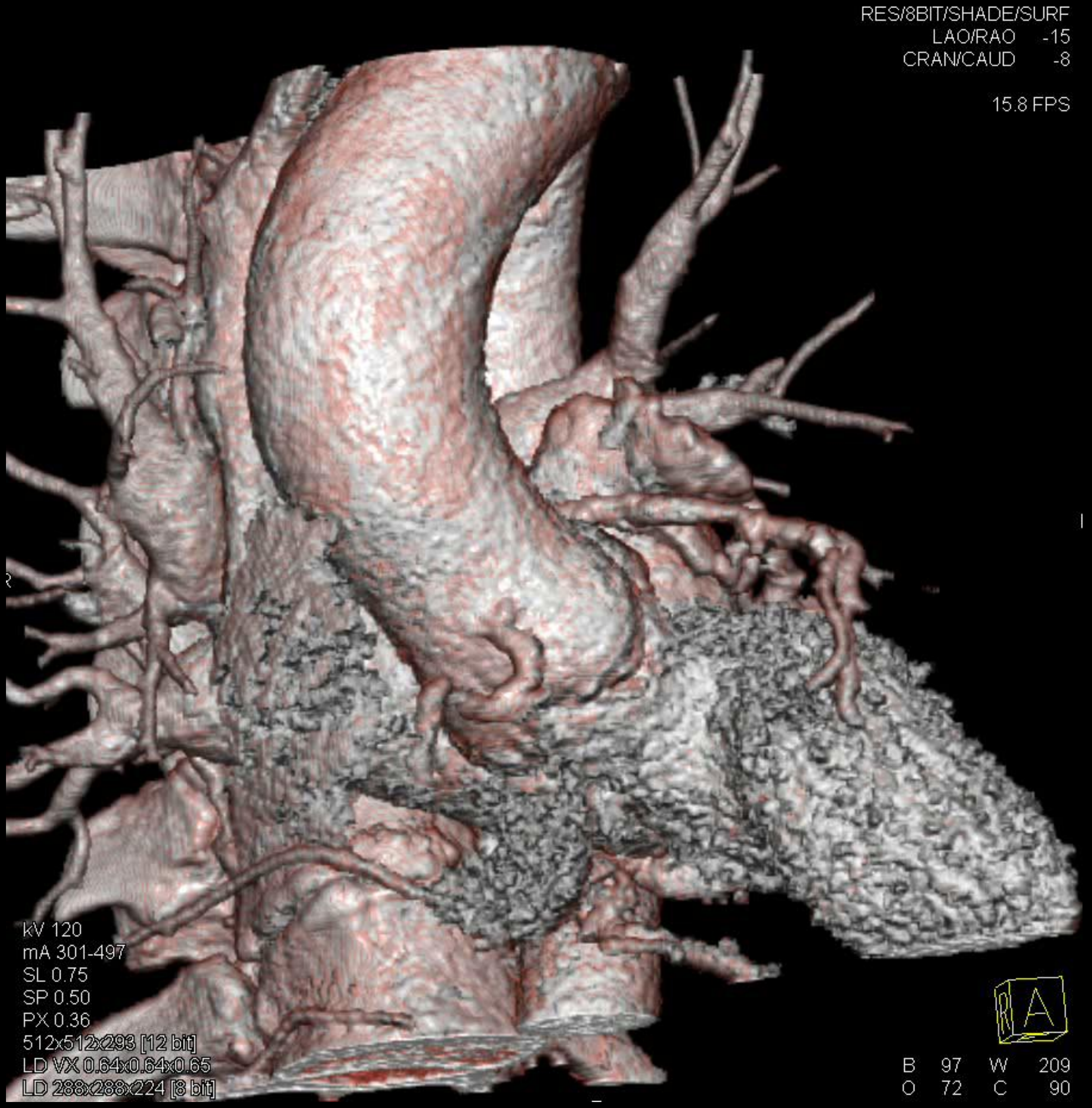
Genetic testing
for heritability

Family History of early
Aortic Complications

Segments of the ascending & descending aorta



Anatomical Considerations



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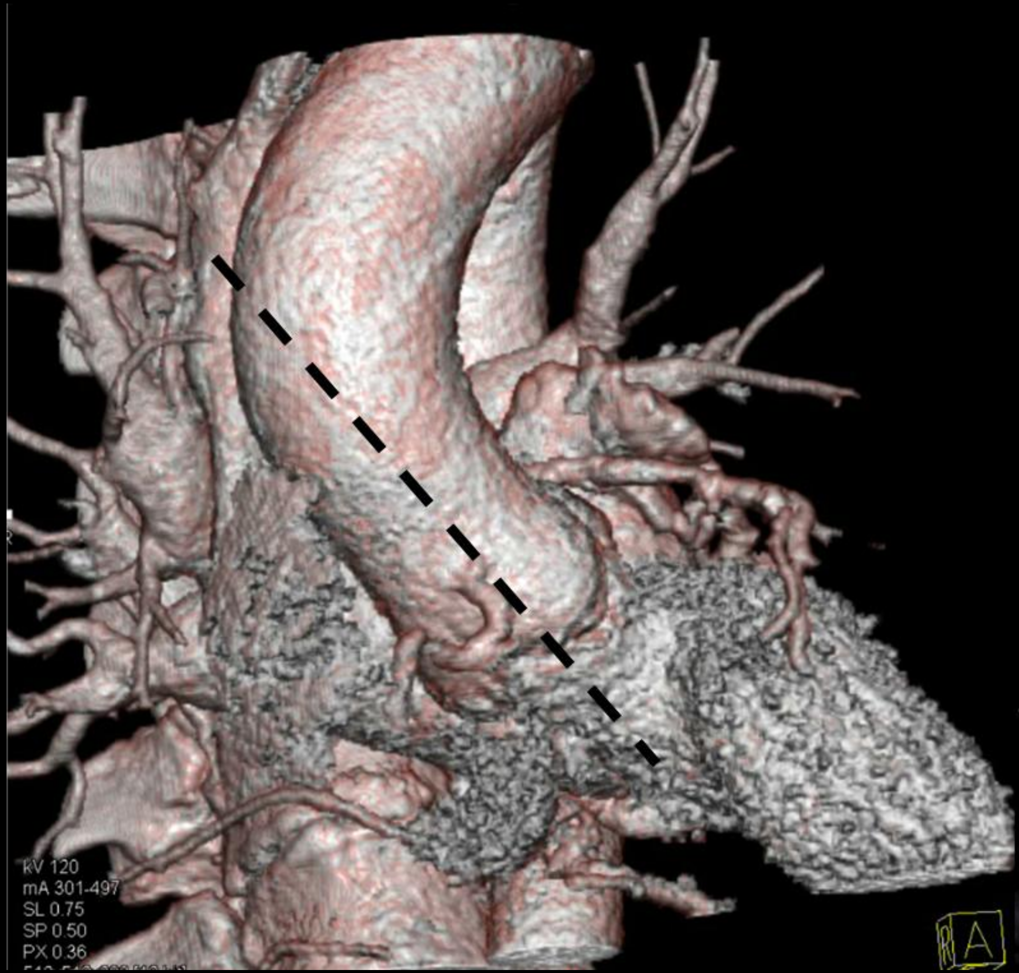
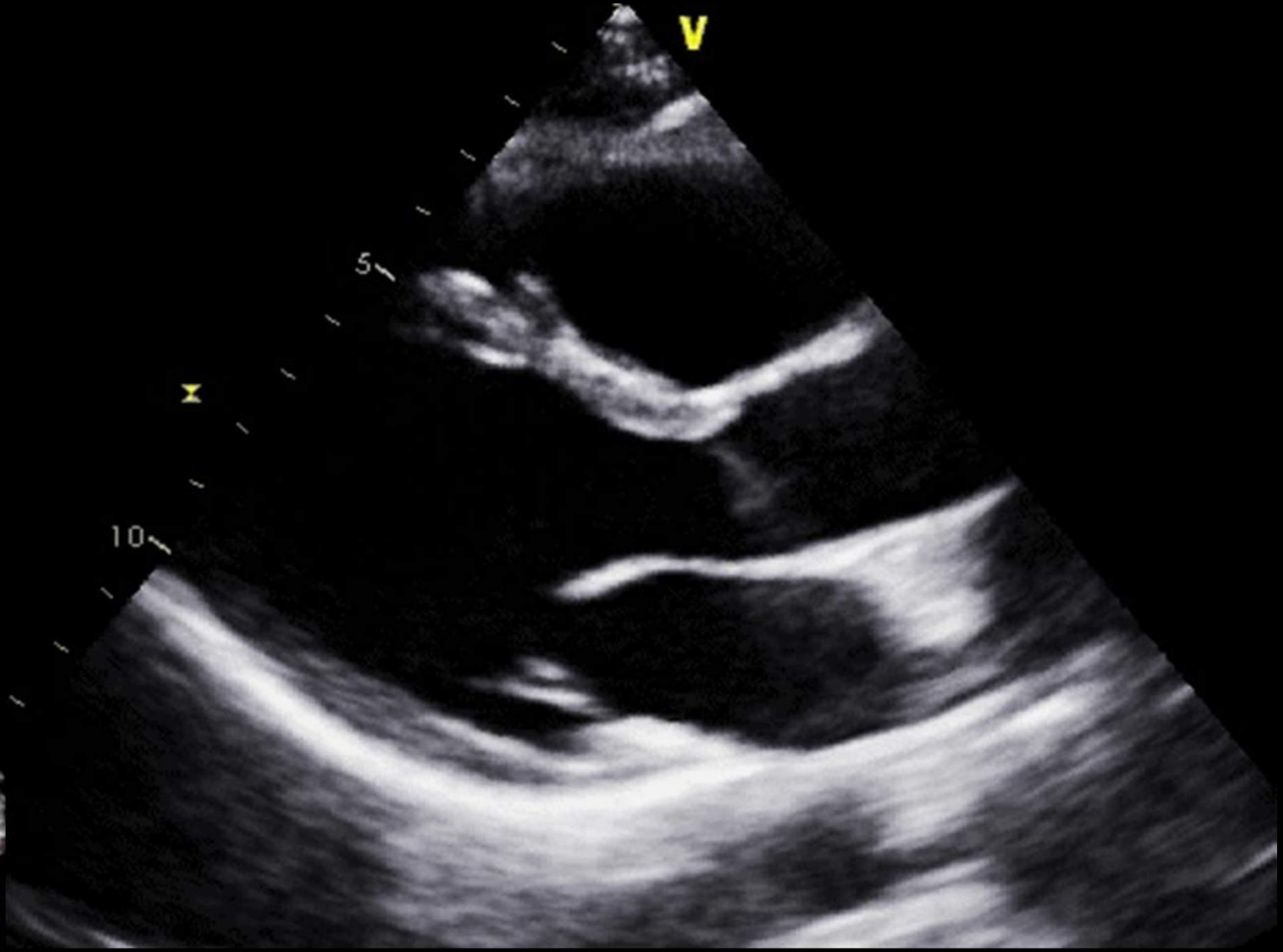
Anatomical Considerations – Ao root/STJ





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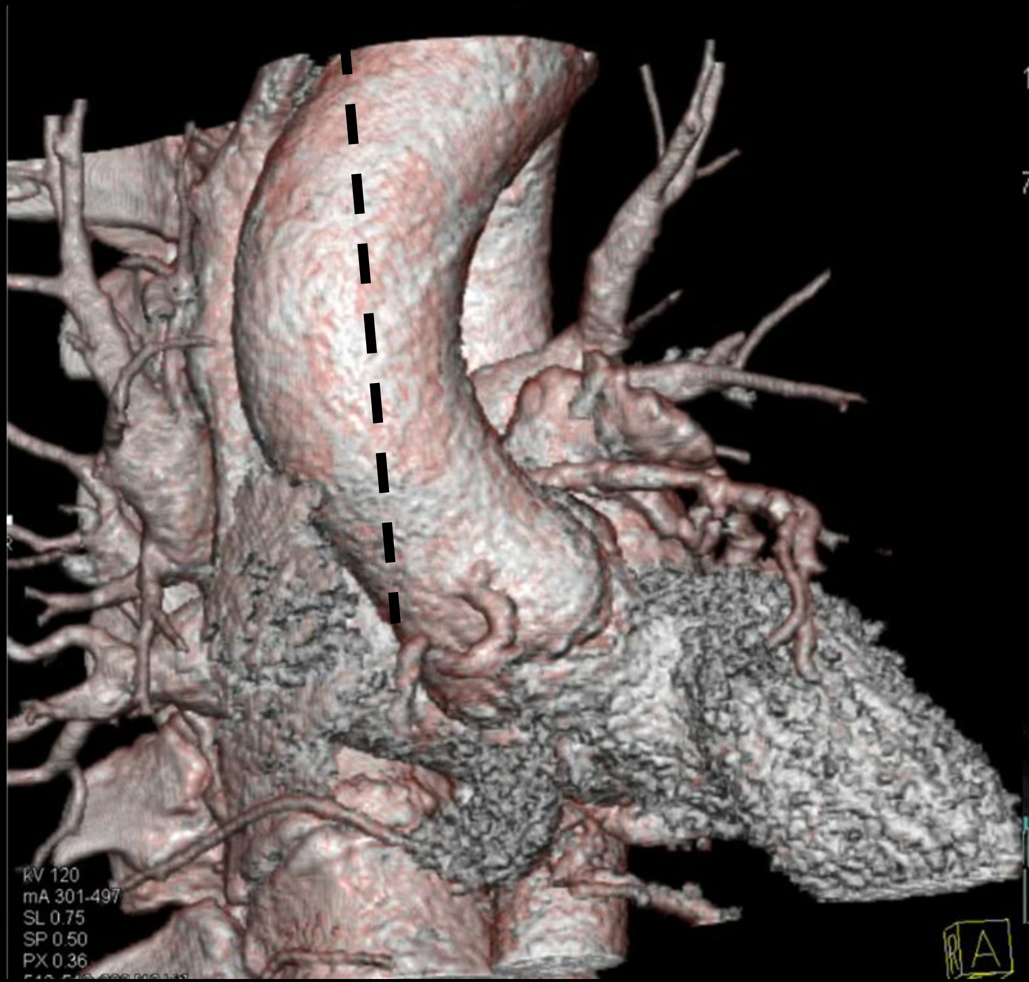
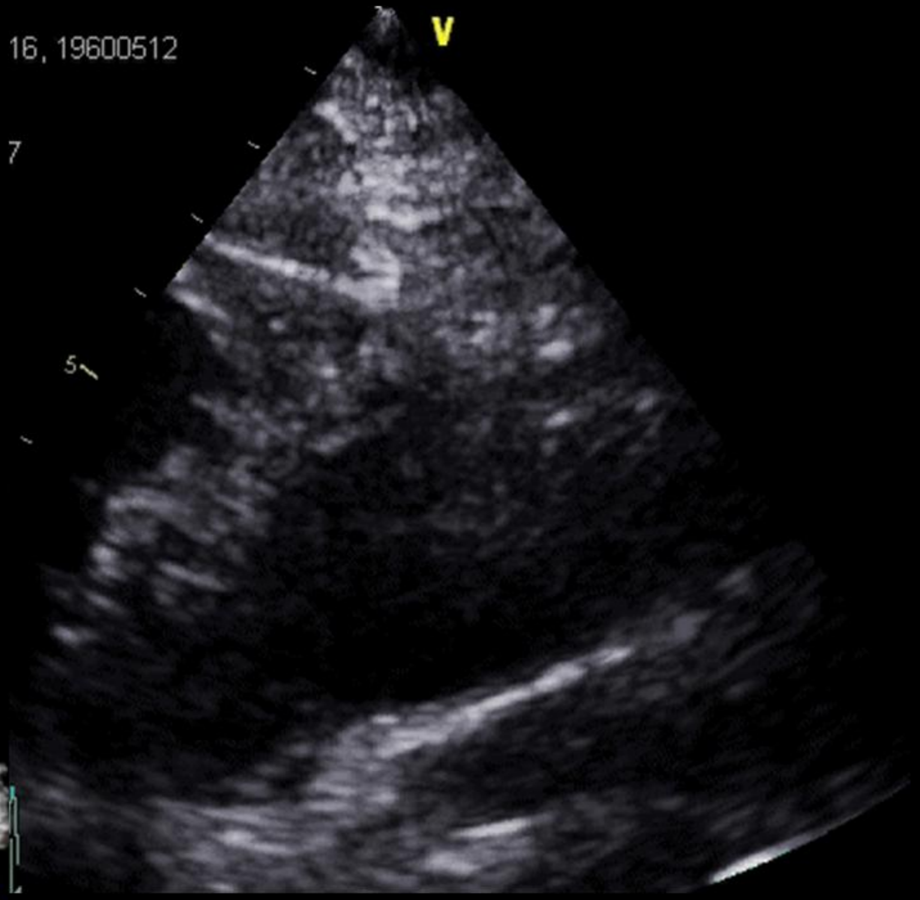
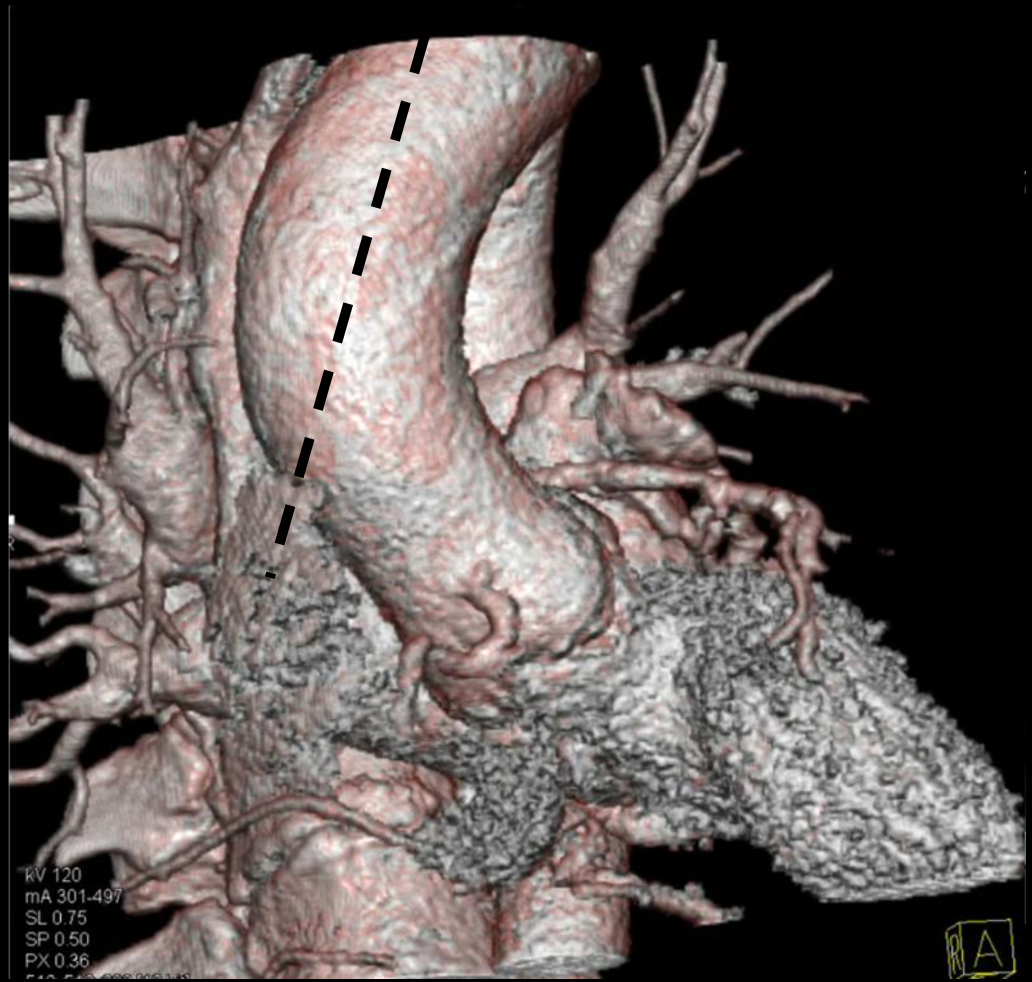
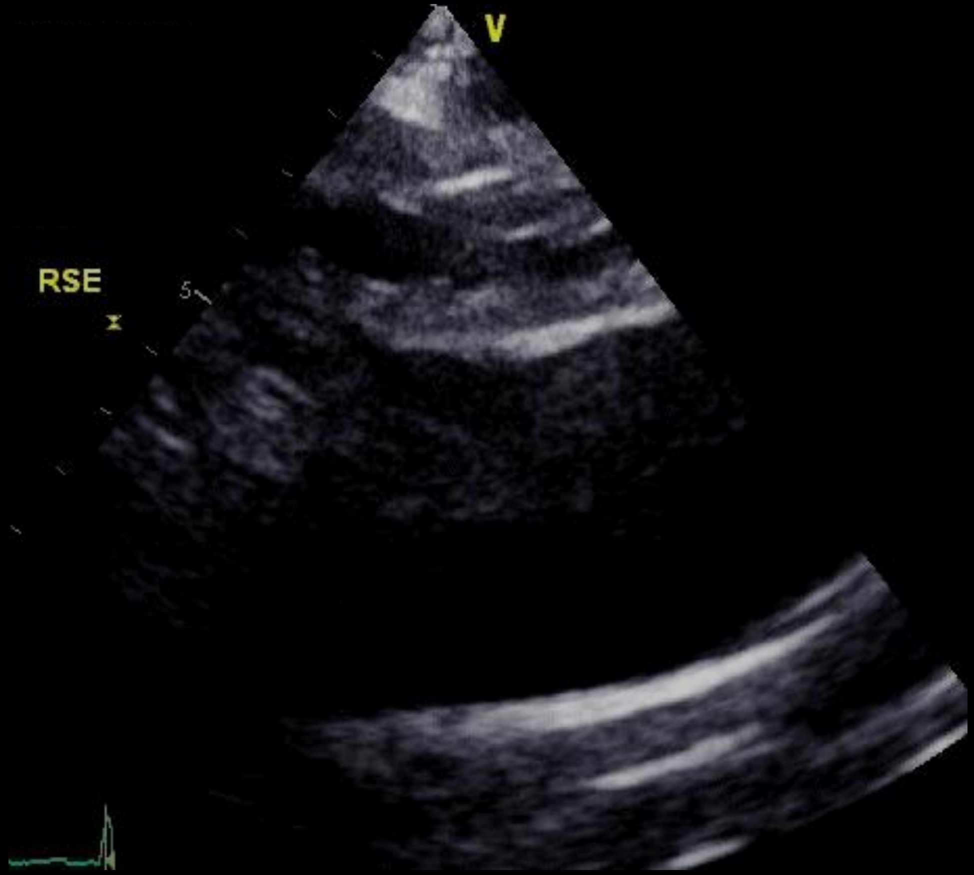
Anatomical Considerations – Asc Ao (LSE)



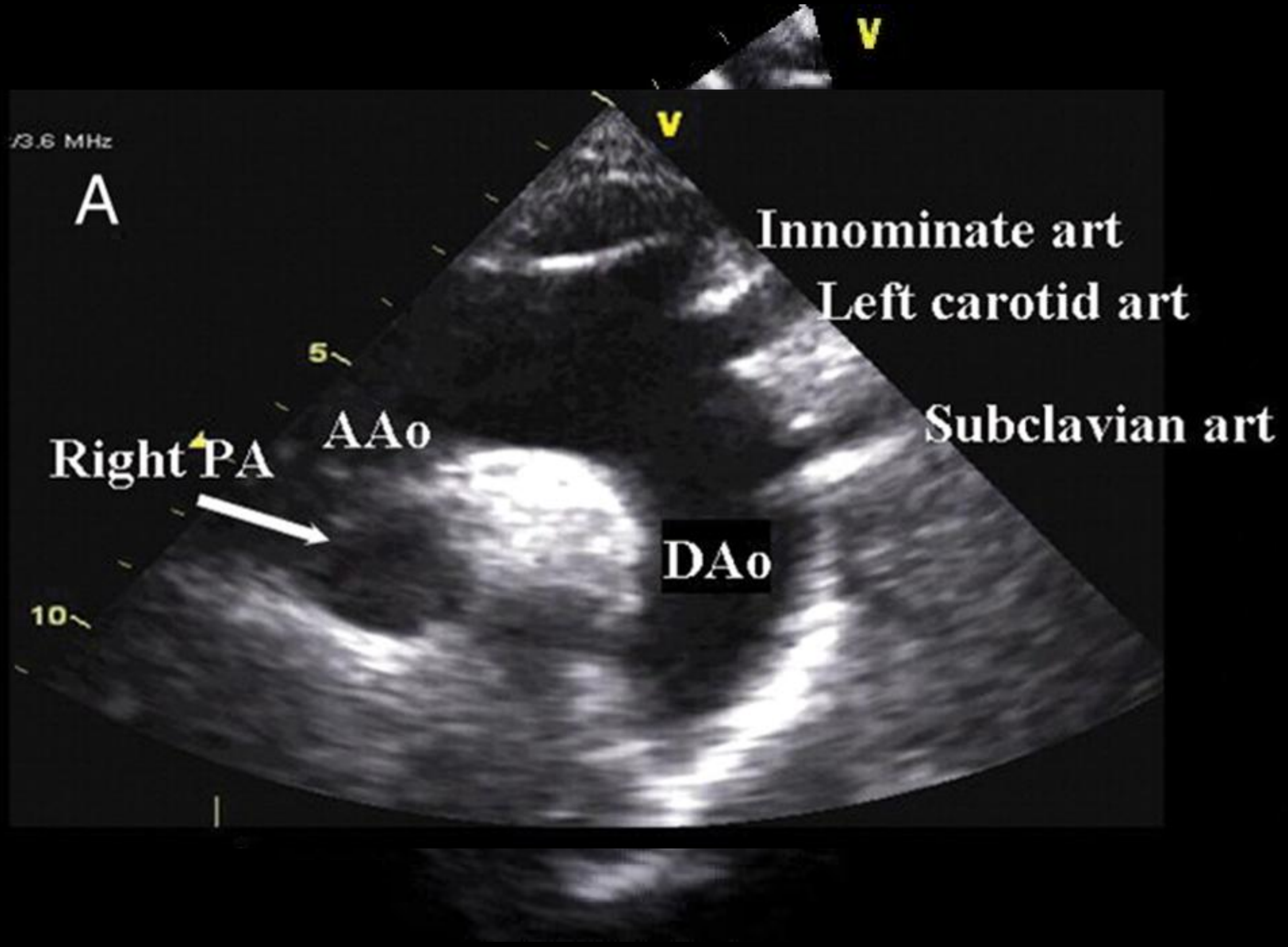


Anatomical Considerations – Asc Ao (RSE)



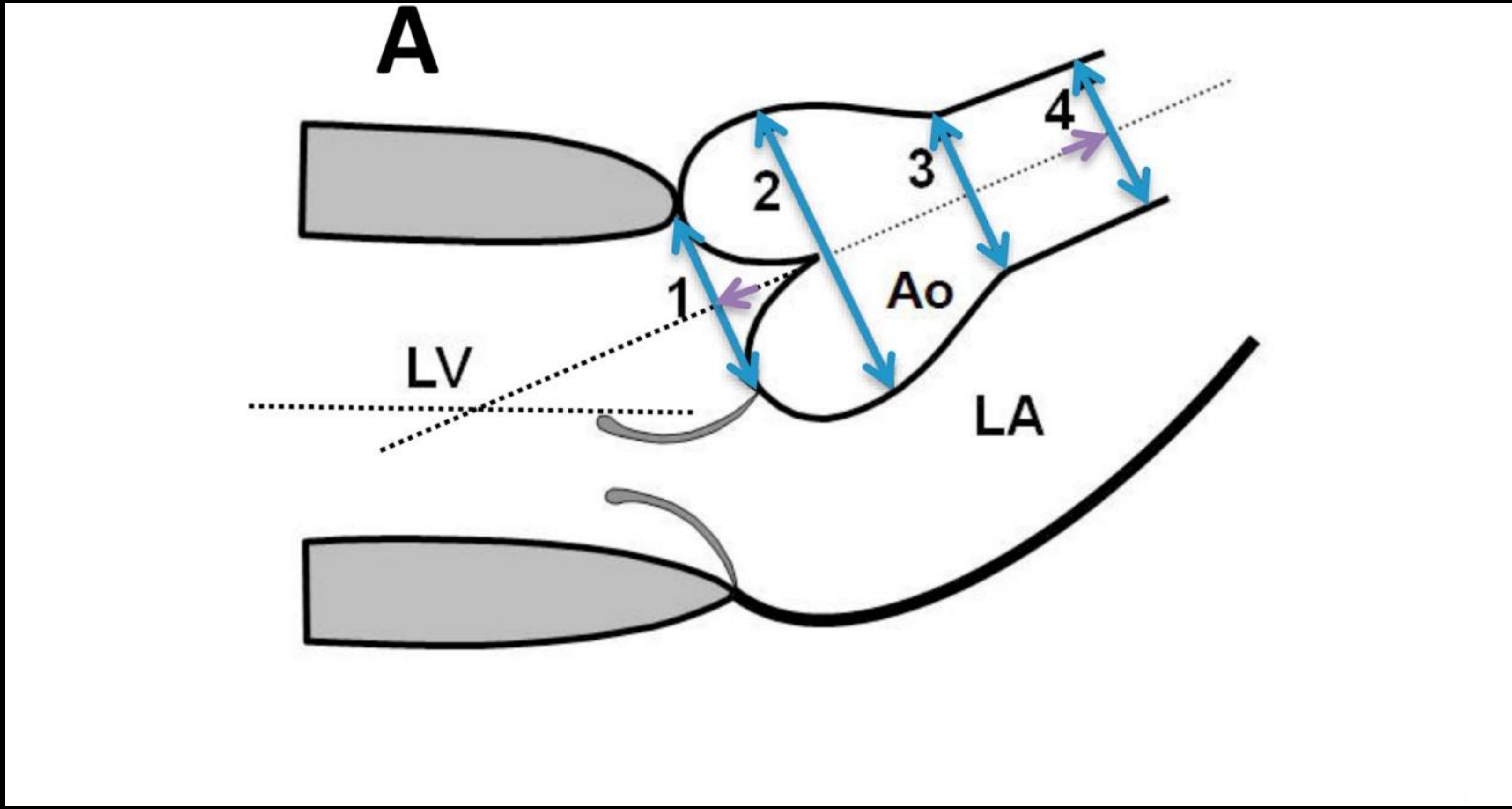


Anatomical Considerations - Arch/Desc Ao



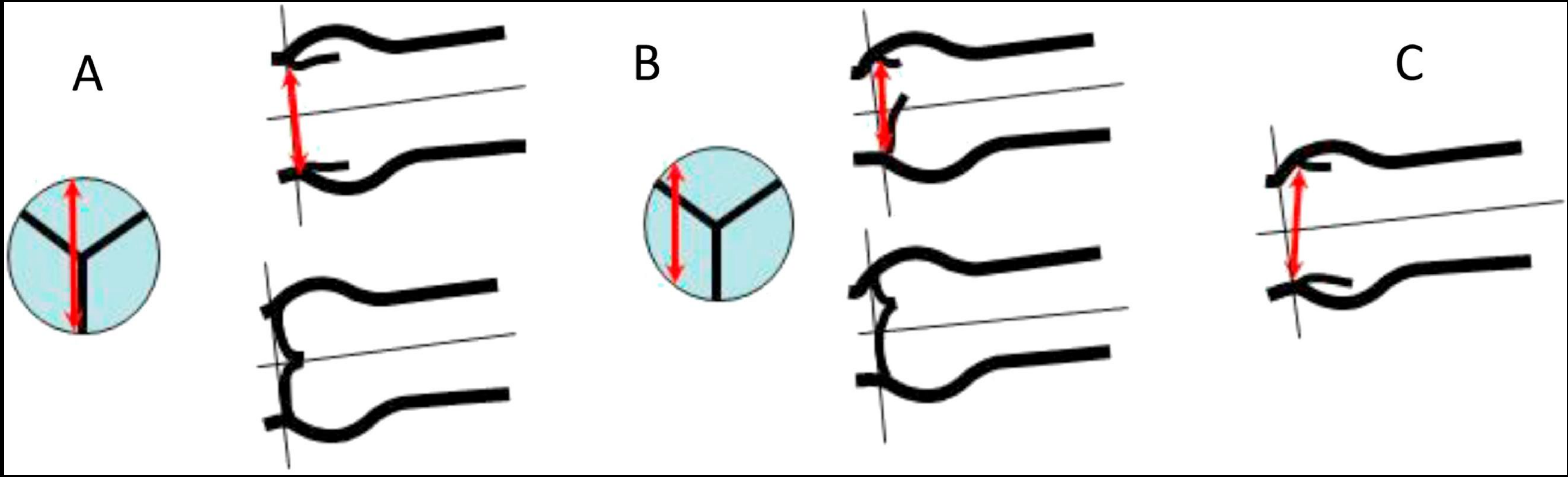
The Comprehensive Echocardiographic Assessment of the Aorta

ASE Recommendations 2015



Journal of the American Society of Echocardiography 2015 28, 1-39.e14
DOI: (10.1016/j.echo.2014.10.003)

ASE Recommendations 2015



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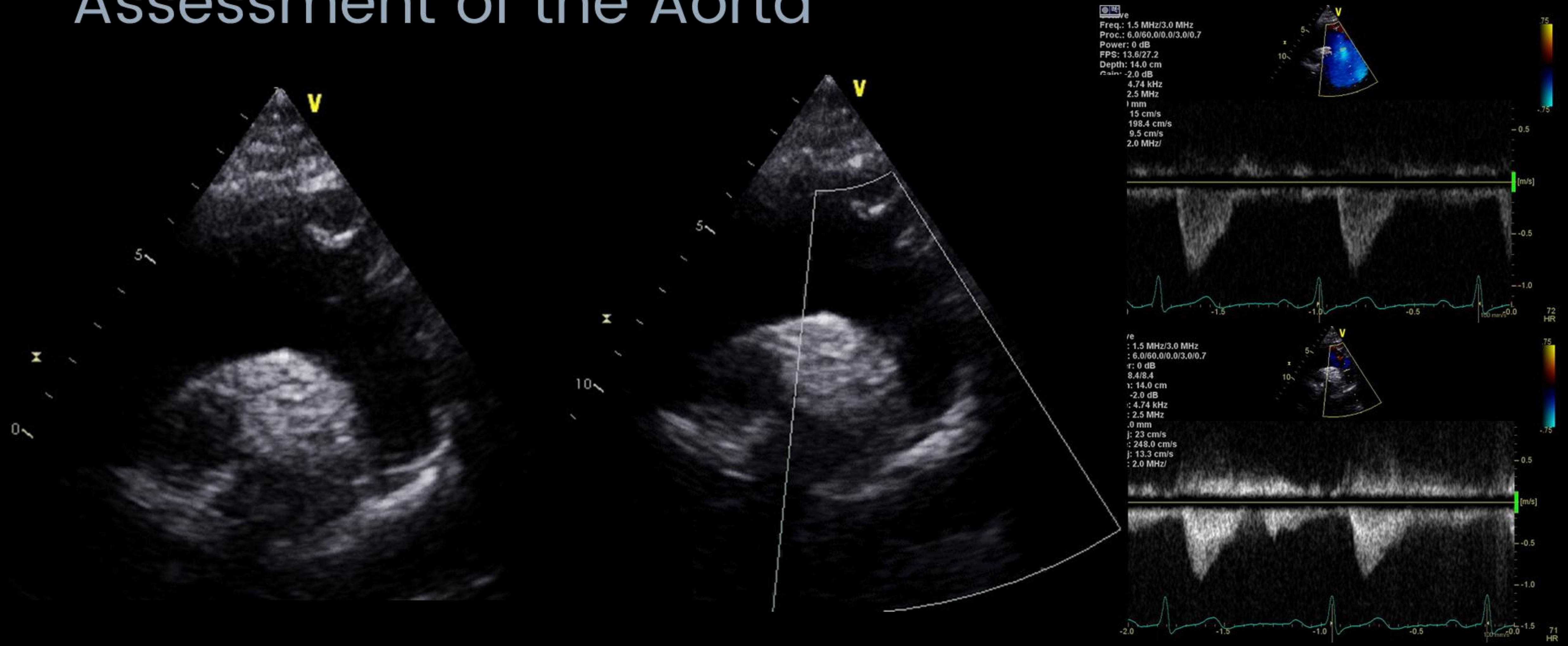
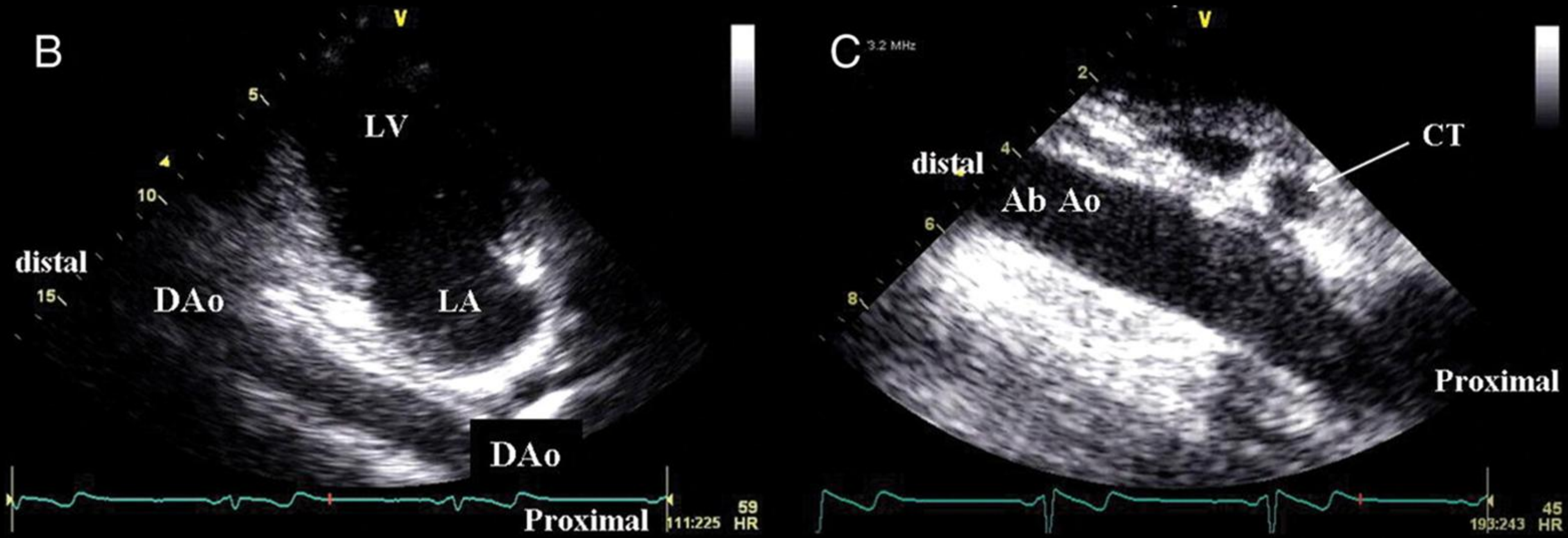
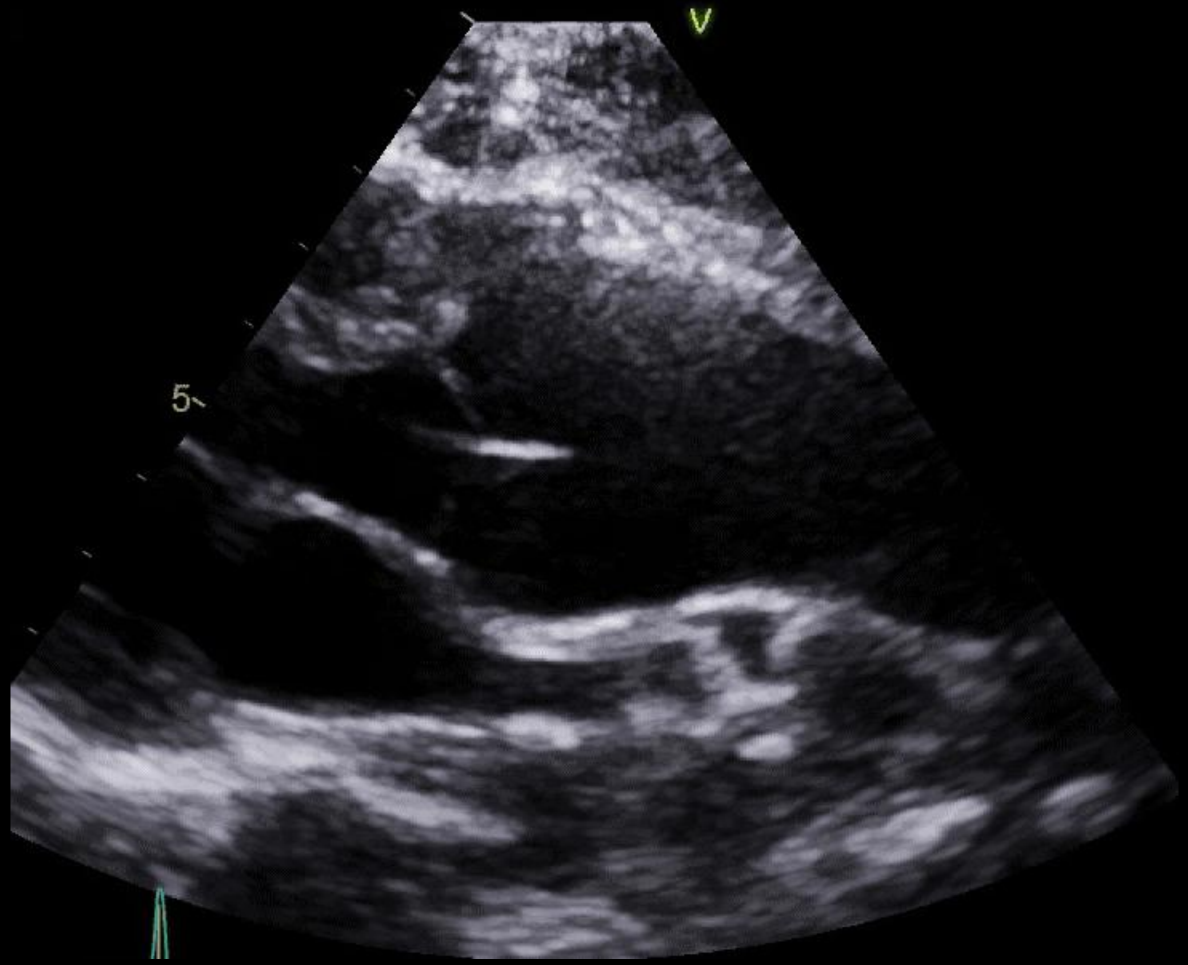
The Comprehensive Echocardiographic Assessment of the Aorta



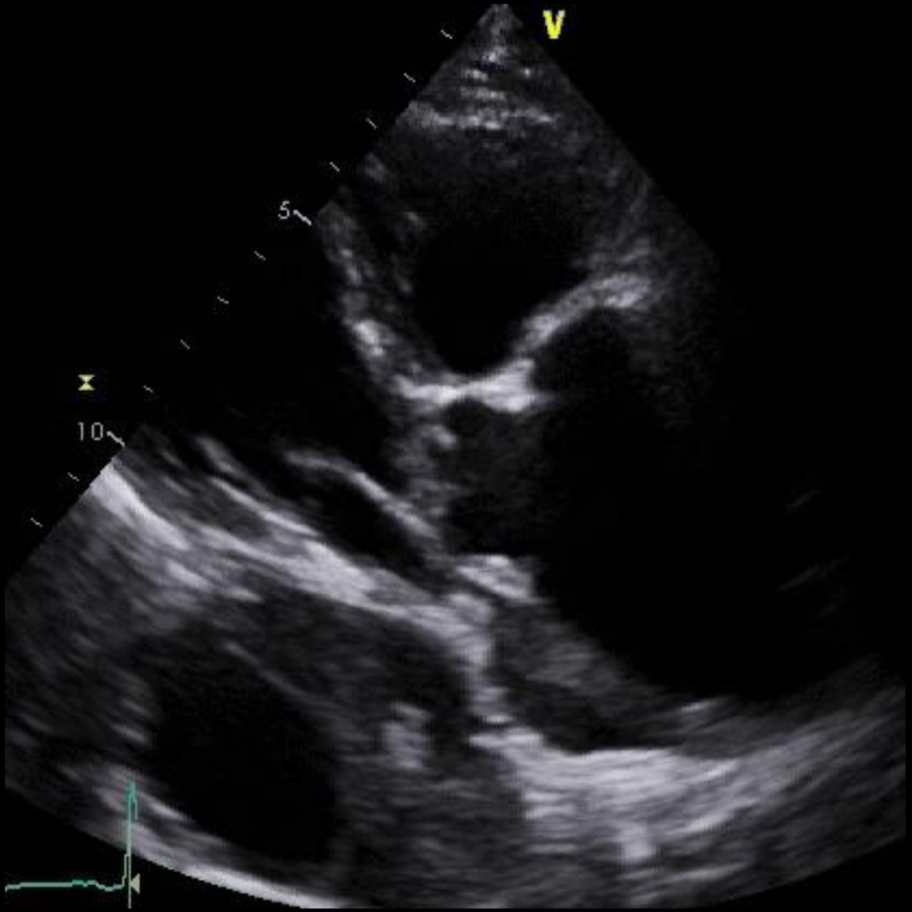
The Comprehensive Echocardiographic Assessment of the Aorta



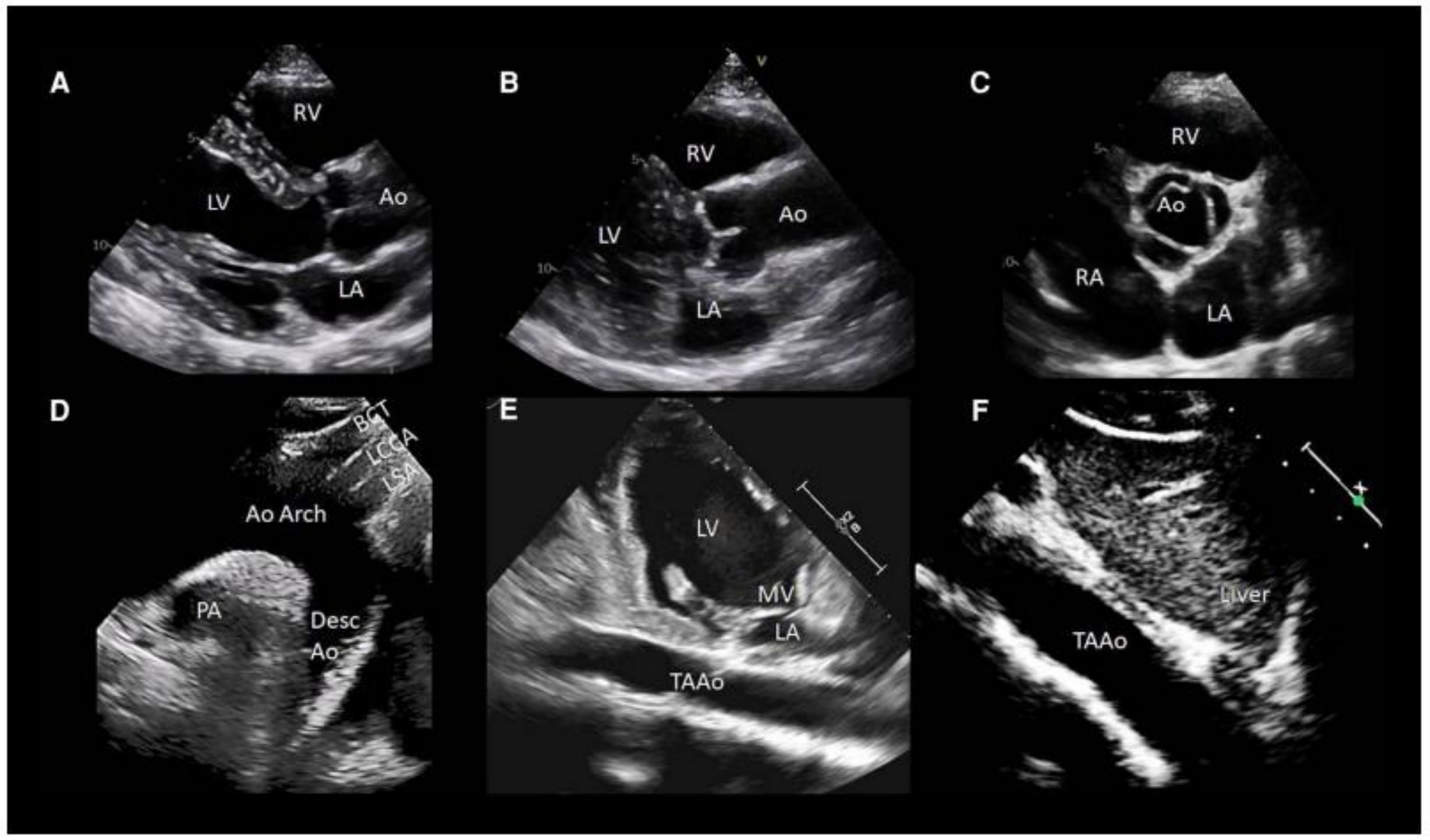
Sinotubular Effacement



Ascending Aortic Dilatation



TTE standard views for Assessment of AAS



EACVI
European Association of Cardiovascular Imaging
European Society of Cardiology

Eur Heart J Cardiovasc Imaging, Volume 24, Issue 5, May 2023, Pages e65–e85

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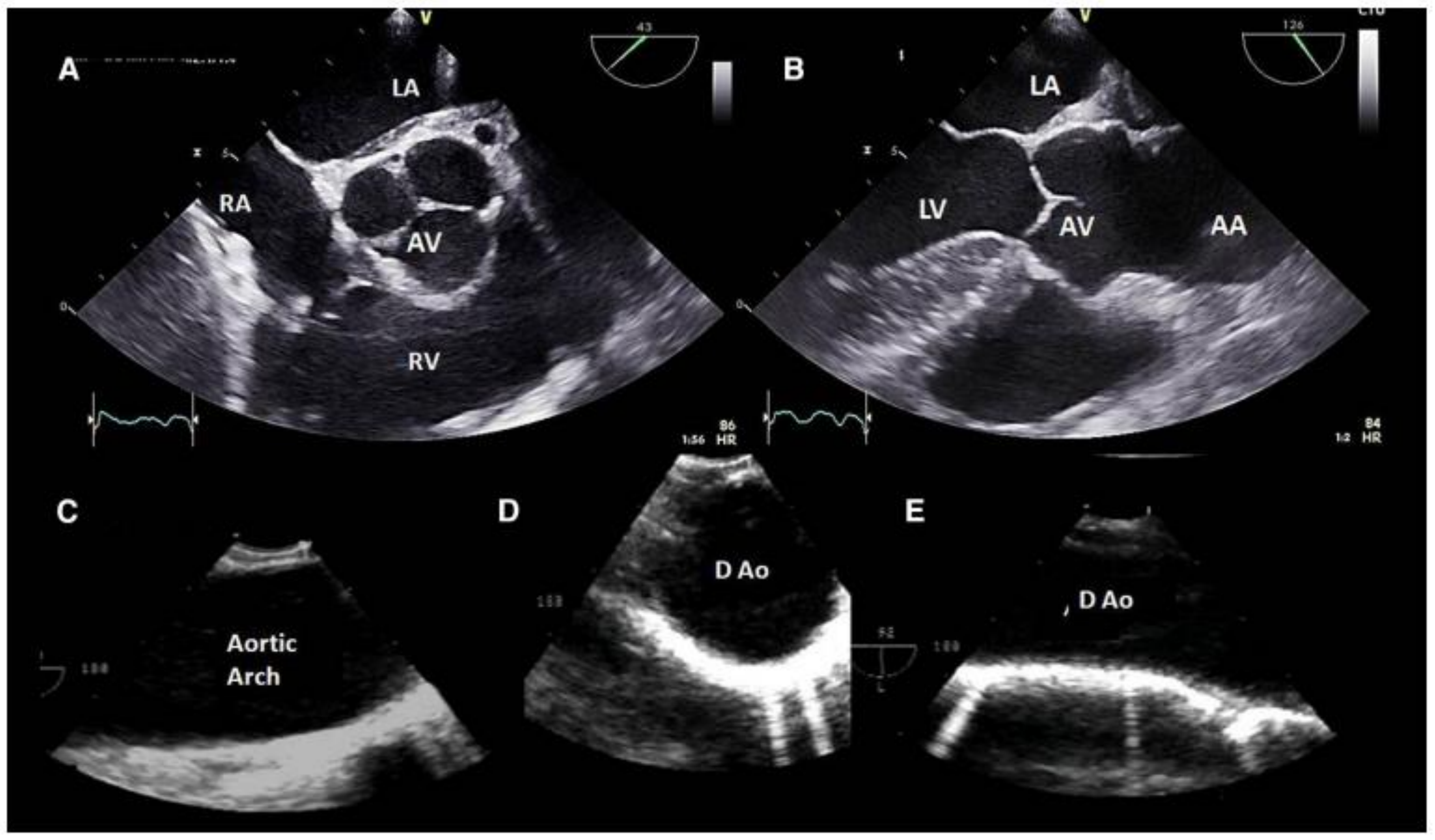
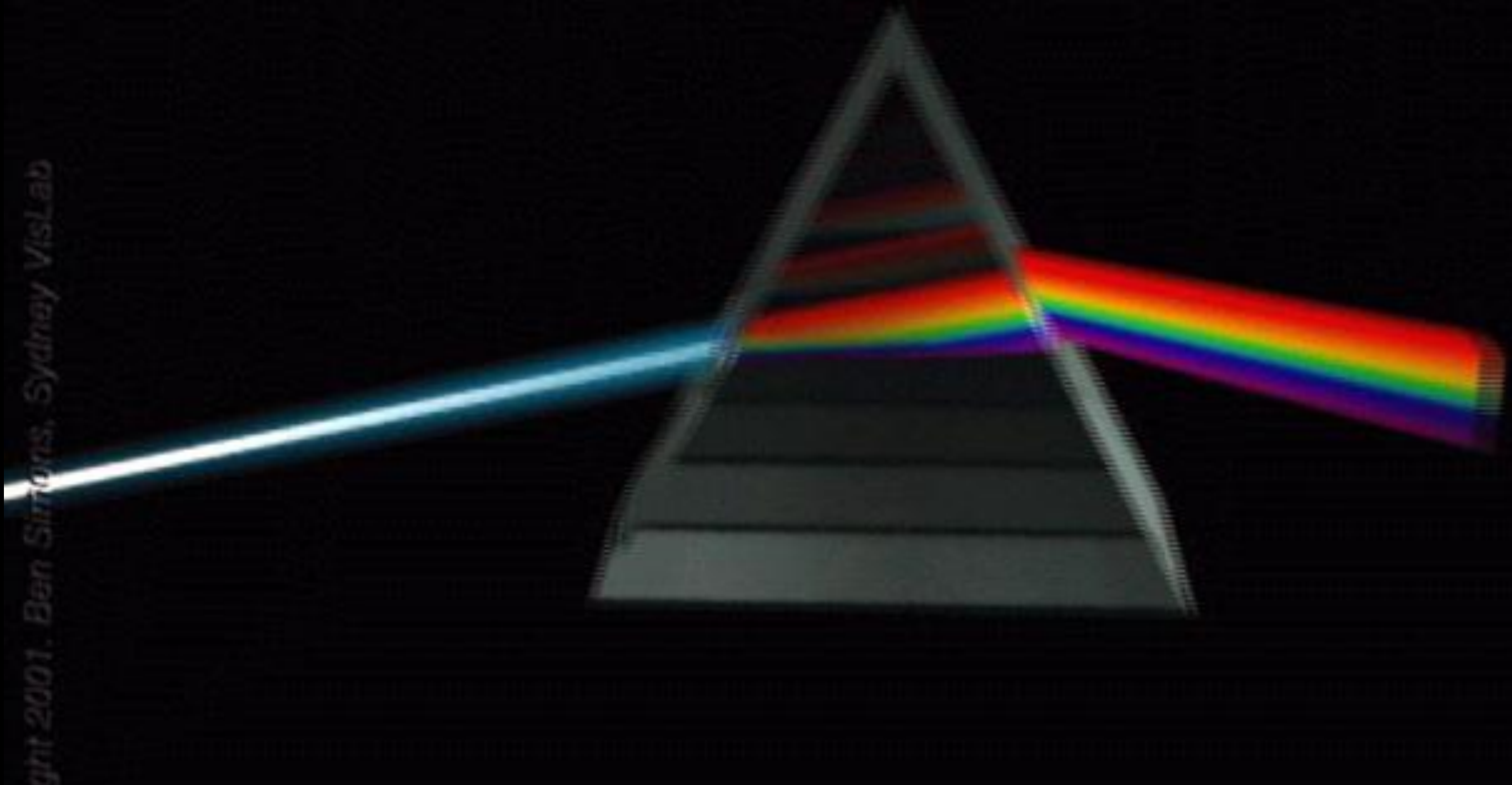
TOE standard views for Assessment of AAS



Eur Heart J Cardiovasc Imaging, Volume 24, Issue 5, May 2023, Pages e65–e85

Spectrum of Genotypic and Phenotypic Expression



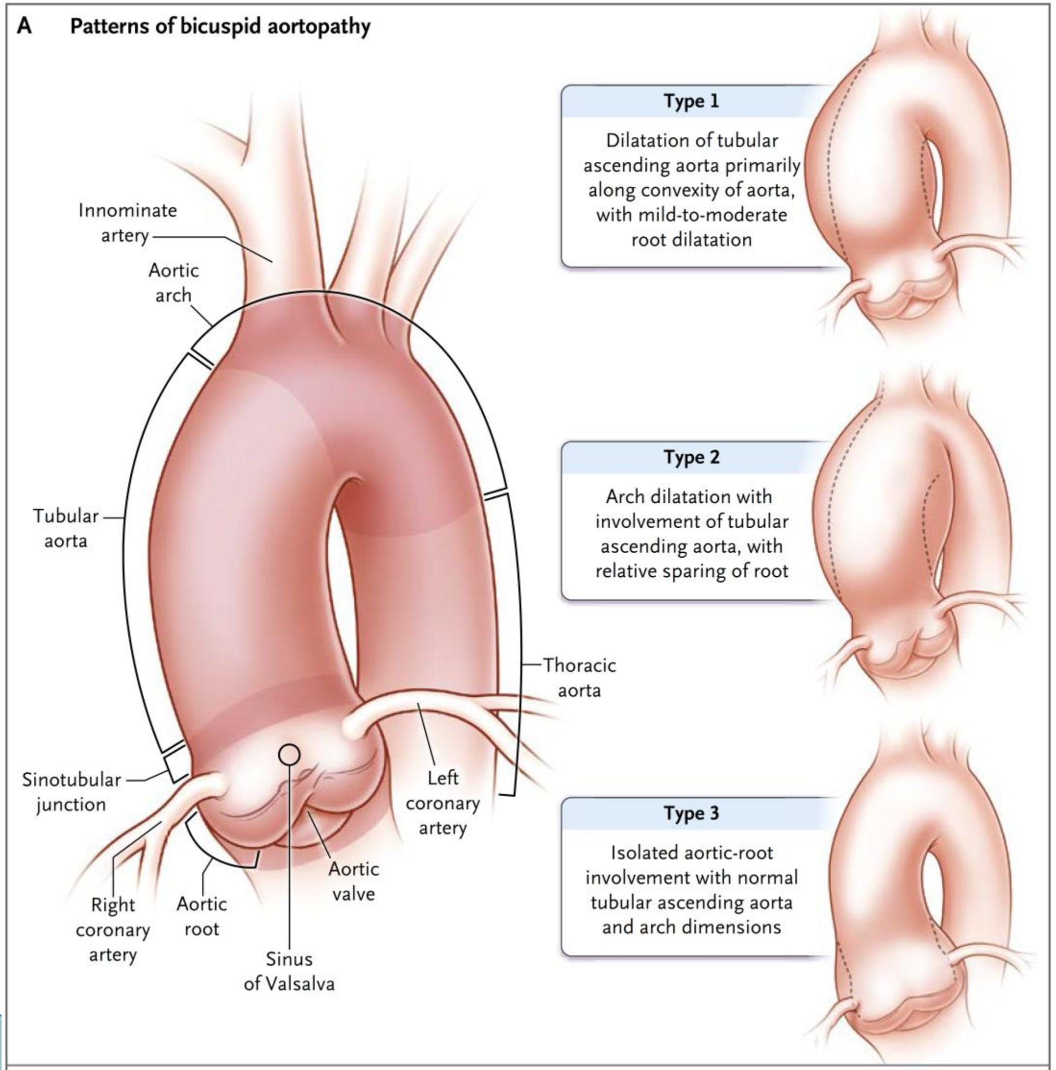
Differential Diagnosis of Aortic Dilatation

- Marfan Syndrome
- Bicuspid aortic valve with BAV aortopathy
- Heritable BAV Aortopathy without BAV
- Familial thoracic aortic aneurysm
- Thoracic aortic aneurysm + PDA
- Coarctation with aortopathy
- MASS phenotype
- Loeys-Dietz syndrome
- Ehlers-Danlos (vascular - Type 4)
- Homocystinuria
- Congenital contractural arachnodactyly

Aortopathy	Defect and Heritability	Mechanism	Region Affected
Marfan syndrome	Fibrillin 1 AD	Defective myofibril binding to TGF-β complex, which upregulates TGF-β signalling and stimulates inflammation and fibrosis	Sinuses of Valsalva with effacement of the STJ
BAV associated Aortopathy	No single gene AD variable penetrance	Upregulation of TGF-β signalling demonstrated but mechanism unclear	Ascending aorta above the STJ
Familial TAA	ACTA2 and TGFBR2 AD variable penetrance	No specific mechanism identified but behaves similarly to BAV aortopathy	Sinuses and STJ, similar to Marfan
TAA + PDA	Smooth muscle myosin heavy chain MYH11 AD	Defective smooth muscle cell contractile protein structure in aortic media and vasa vasorum	Ascending aorta above the STJ

Aortopathy	Defect and Heritability	Mechanism	Region Affected
MASS phenotype (MVP, Ao ULN, skin, skeletal)	No consistent gene, sporadic Dominant negative mutation	No specific mechanism identified	Aortic root and ascending aorta
Loeys-Dietz syndrome	TGFBR1, TGFBR2, SMAD3 AD	Upregulation of TGF-β signalling stimulates aggressive and widespread arterial aneurysm formation	Aortic root, ascending aorta, arch, descending
Ehlers-Danlos (vascular)	COL3A1, COLSA2, COL5A1	Upregulation of TGF-β signalling stimulates aggressive and widespread arterial aneurysm formation	Aortic root, ascending aorta, arch, descending
Congenital contractural arachnodacyly (Beals-Hecht)	Fibrillin 2 AD	No clear mechanism	Aortic root

BAV Associated Aortopathy

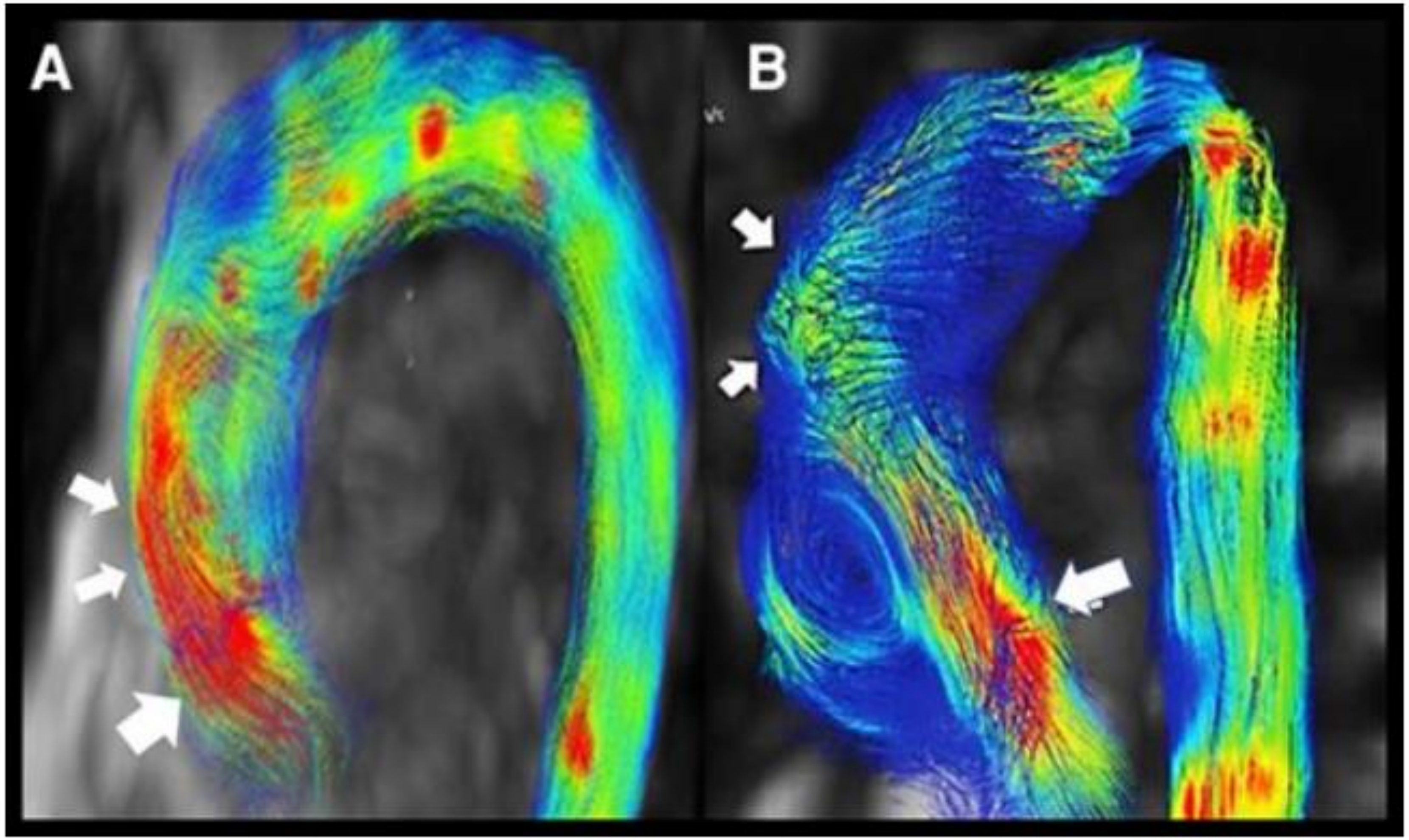


- Age >50 years
- Valvular stenosis
- R-L fusion pattern
- Ascending with varying degrees of root dilatation

- R-N fusion pattern
- Relative root sparing
- Often involves arch

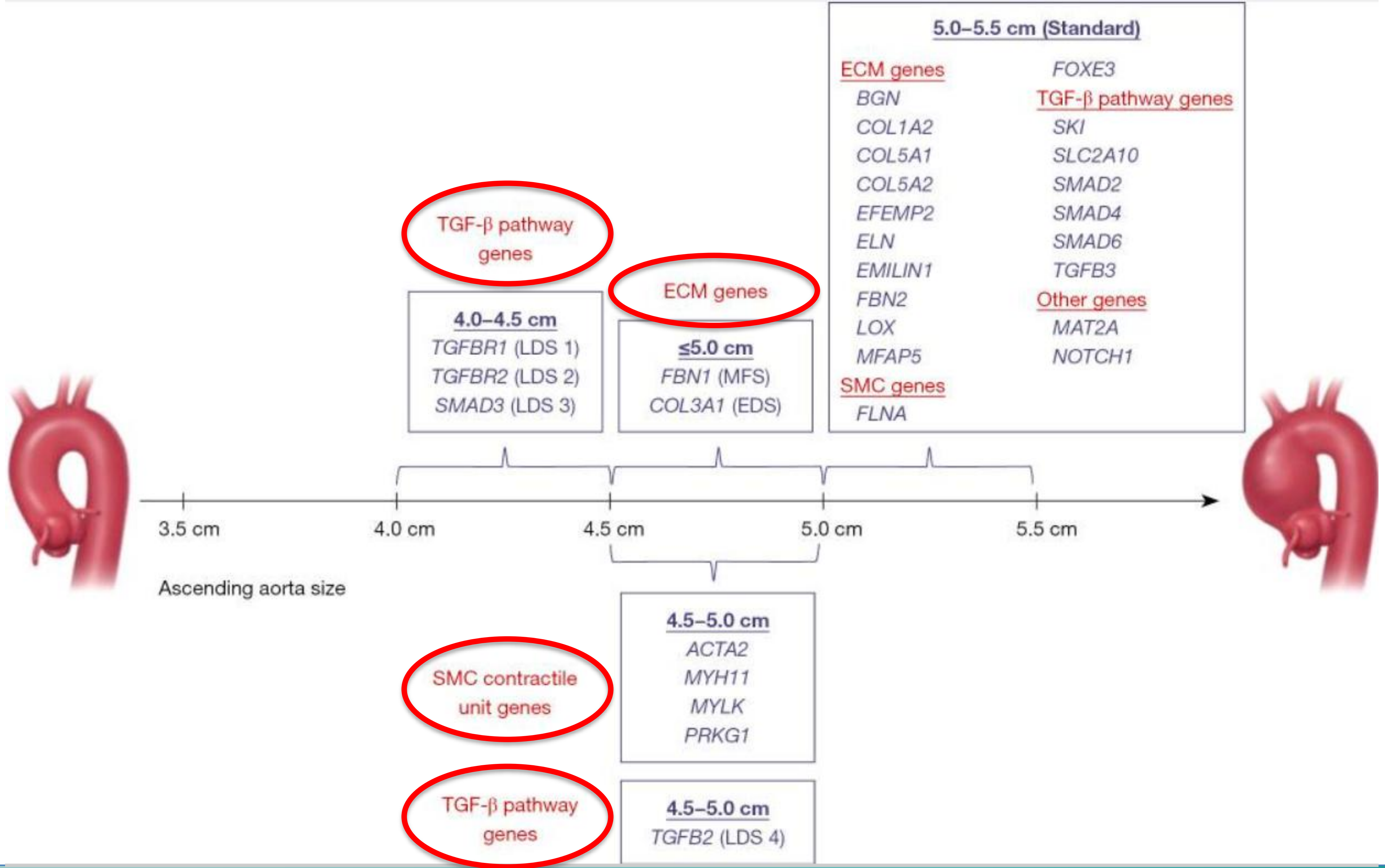
- Root phenotype
- Rare
- Age <40 years
- Male
- AR

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



R – L fusion ***R – N fusion***

Eur Heart J Cardiovasc Imaging, Volume 24, Issue 5, May 2023, Pages e65–e85,



Faggion Vinholo T, Brownstein AJ, Ziganshin BA, et al. *Aorta (Stamford)* 2019;7:99-107

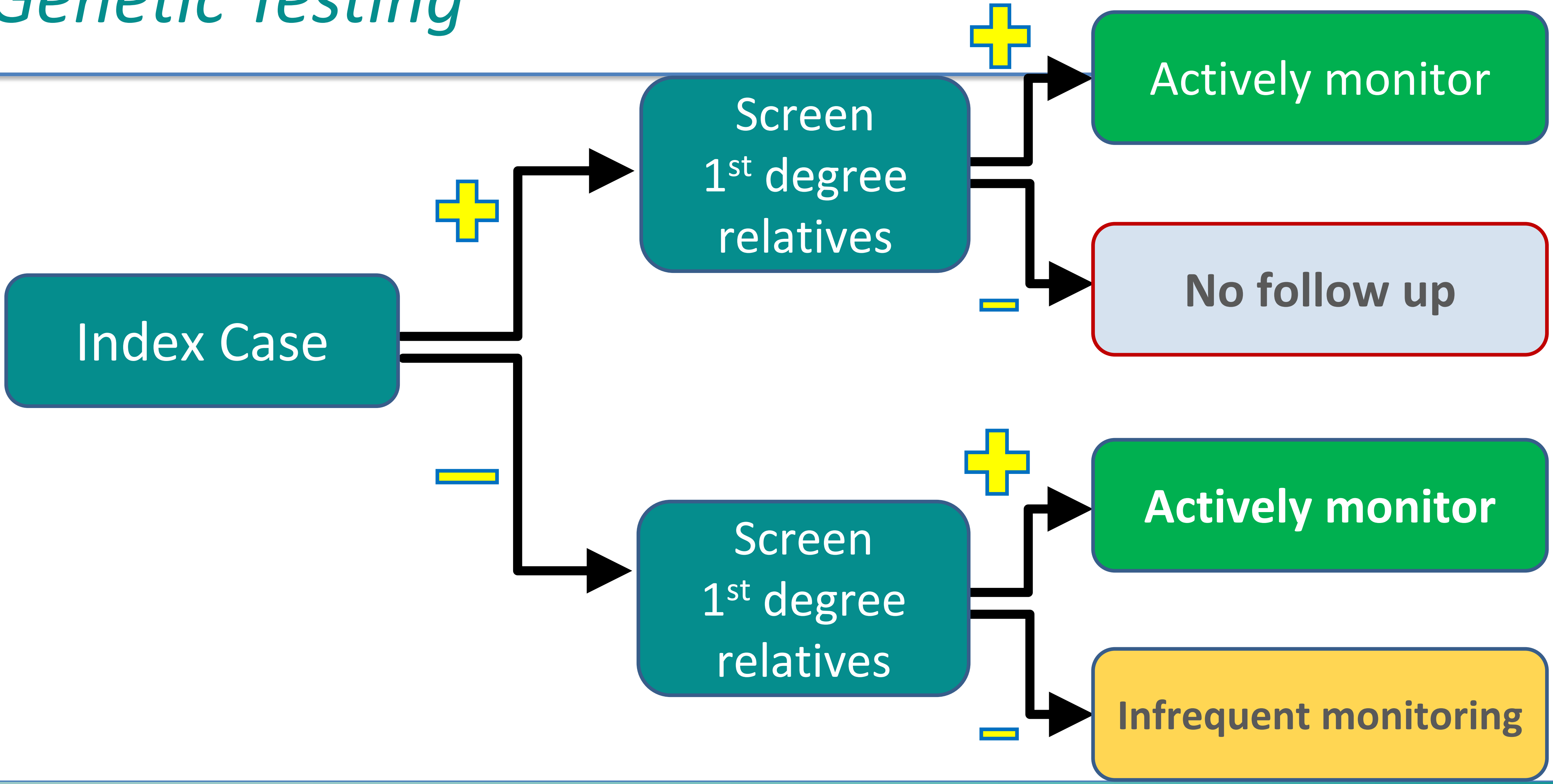
Attributable Gene Profiles

Disorder	Gene	% Disorder Attributed to Gene
Marfan Syndrome	FBN1	>95%
Loeys-Dietz Syndrome	TGFBR2 TGFBR1 SMAD3 TGFB2 TGFB3 SMAD2	55-60% 20-25% 5-10% 5-10% 1-5% 1-5%
EDS Vascular Type (IV)	COL3A1	>95%
Beals-Hecht (CCA)	FBN2	25-75%
EDS Classic Type (I/II)	COL5A1 COL5A2	75-78% 14%
EDS Kyphoscoliotic Type (VI)	PLOD1	High
Arterial Tortuosity Syndrome	SLC2A10	High
Thoracic Aortic Aneurysms	ACTA2 FBN1 LOX, FOXE3, MYH11, MYLK PRKG1, MFAFP5 BGN, EFEMP2	12-21% 3% 1-2% Rare

Genetic Testing

- Helpful in individuals to determine high risk mutations
- Helpful in families/first degree relatives to identify heritability if a genetic mutation is identified
- May trigger earlier intervention at lower aortic dimensions if identified

Genetic Testing



European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2024) **00**, 1–9
https://doi.org/10.1093/ehjci/jeae140

ORIGINAL PAPER

The aortic paradox: a nationwide analysis of 523 994 individual echocardiograms exploring fatal aortic dissection

Elizabeth D. Paratz [1,2,3,4]*, James Nadel [5,6], Julie Humphries [7,8], Stephanie Rowe[1,2,3], Louise Fahy [1,2], Andre La Gerche [1,2,3], David Prior[2,3], David Celermajer [6,9,10], Geoffrey Strange [8,11], and David Playford [11,12]

Aortic Diameter and Risk of Death from Type A Dissection – The Aortic Paradox

NEDA database: 524,994 echocardiograms with events linked to National Death Registry

- **While risk of death from dissection increased significantly >5.5cm, this only represents 2.3% of dissection related deaths**
- **97% of deaths due to dissection occurred at only mild-moderately dilated aortic dimensions**

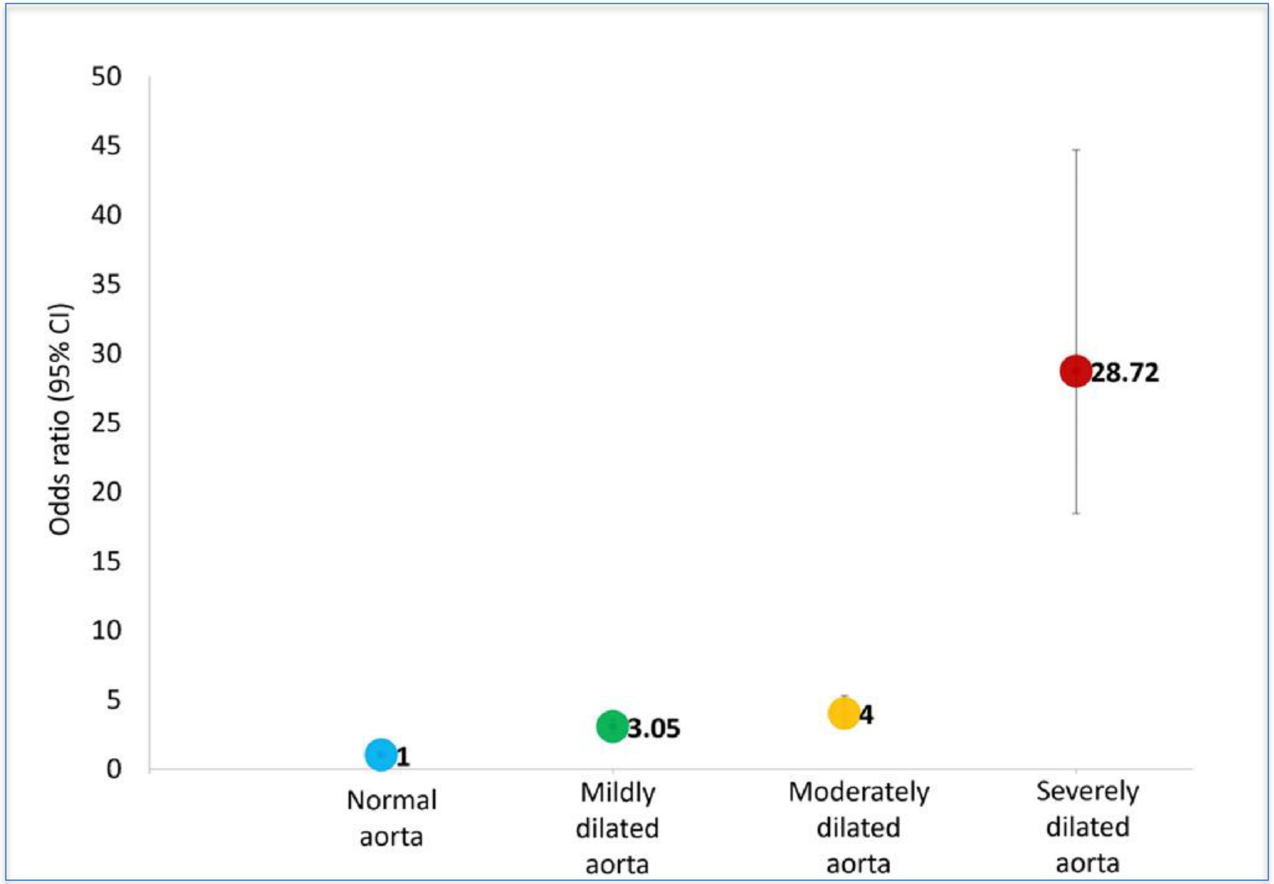
Paratz E, Nadel J, Humphries J et al, EHJCI 2024

Aortic Diameter and Event Rates from Fatal Aortic Dissection – NEDA Database Insights 524,994 pts

Category	Total	Intervention (%)	Dissection (%)	Odds Ratio (95% CI)
Normal <4.0cm	460,992	0 (0.0%)	610 (0.13%)	1.0
Mild 4.0-4.5cm	53,402	0 (0.0%)	215 (0.40%)	**3.05** (2.6-3.5)
Moderate 4.5-5.5cm	10,029	0 (0.0%)	53 (0.53%)	**4.0** (3.0-5.3)
Severe >5.5cm	572	89 (15.6%)	21 (3.6%)	**28.72** (18.4-44.7)

Paratz E, Nadel J, Humphries J et al, EHJCI 2024

Aortic Diameter and Event Rates from Fatal Aortic Dissection – NEDA Database Insights 524,994 pts

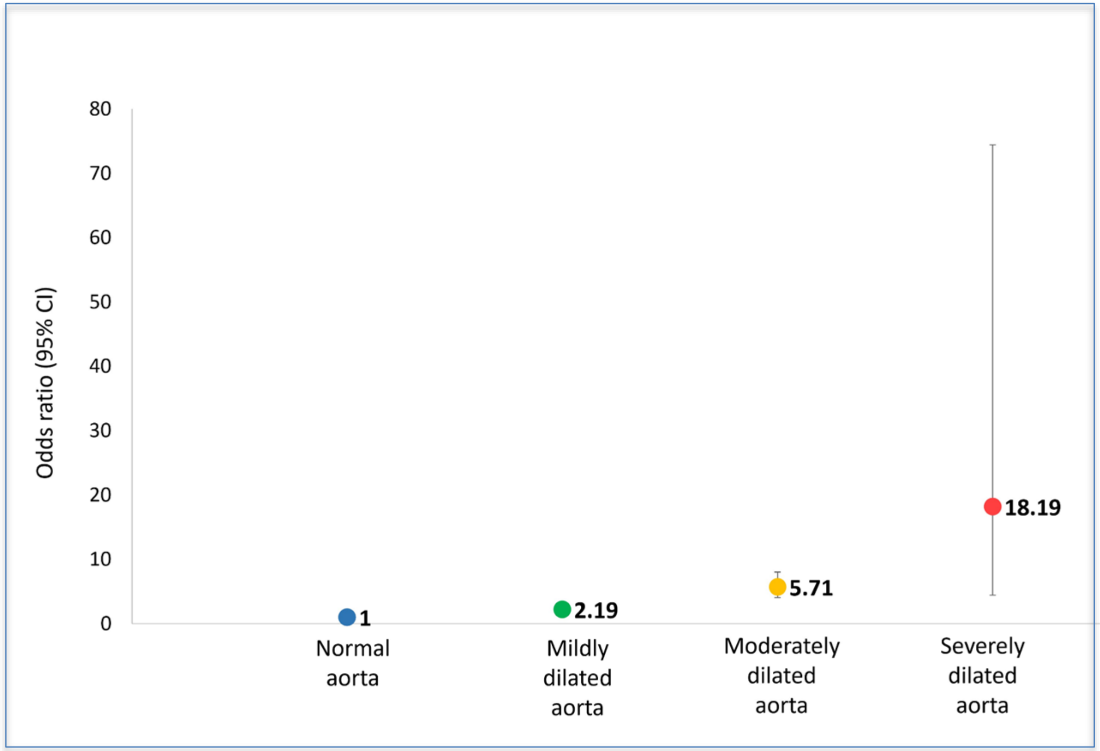


Normal	**<4.0cm**
Mild	**4.0-4.5cm**
Moderate	**4.5-5.5cm**
Severe	**>5.5cm**

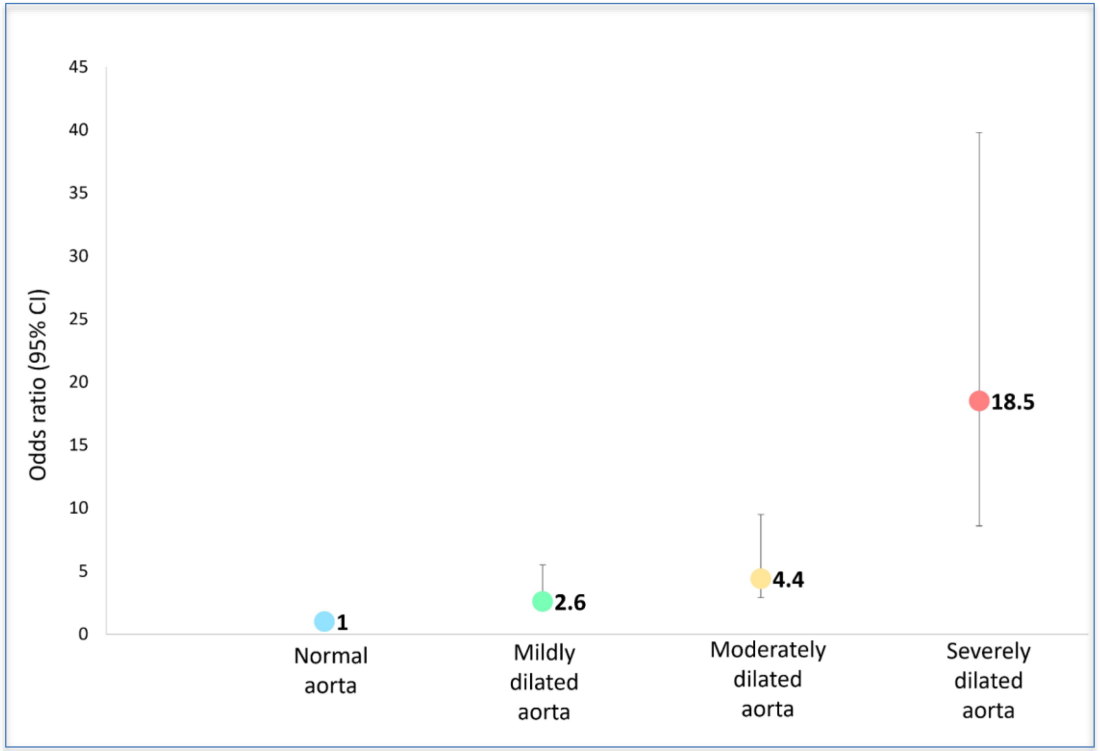
Odds ratios and 95% confidence intervals for fatal aortic dissection according to the degree of aortic dilation, using normally sized aortas as the reference category, where the odds ratio = 1.0.

Paratz E, Nadel J, Humphries J et al, EHJCI 2024

Aortic Diameter and Event Rates from Fatal Aortic Dissection – NEDA Database Insights 524,994 pts



Odds ratios and 95% confidence intervals for fatal aortic dissection according to degree of HEIGHT INDEXED aortic dilation



Odds ratios and 95% confidence intervals for fatal aortic dissection according to degree of BSA INDEXED aortic dilation

Paratz E, Nadel J, Humphries J et al, EHJCI 2024

Aortic Diameter and Event Rates from Fatal Aortic Dissection – NEDA Database Insights 524,994 pts

Group	Dissection <5.5cm (n=879)	Dissection $\geq$ 5.5cm (n=21)	Significance
Male gender n (%)	525 (59.7%)	13 (61.9%)	NS
Mean age	77 (70-83)	78 (53-84)	NS
BMI (kg/m^2)	25.6 (22.9-29.0)	24.6 (21-30)	NS
BSA (m^2)	1.82 (1.68-2.0)	1.78 (1.65-2.0)	NS
BAV	4	1	NS

Paratz E, Nadel J, Humphries J et al, EHJCI 2024

Aortic Diameter and Event Rates from Fatal Aortic Dissection – NEDA Database Insights 524,994 pts

Group	Dissection <5.5cm (n=879)	Dissection $\geq$ 5.5cm (n=21)	Significance
Median Ao Root Diameter (mm)	35 (32-38)	59 (57-61)	P = 0.015
Median Asc Ao Diameter (mm)	37 (32-40)	60 (59-62)	P = 0.03
Time from echo to event (days)	815 (191-1740)	236 (38-1000)	P = 0.02

Paratz E, Nadel J, Humphries J et al, EHJCI 2024

Yale Group

Height (inches)	(m)	Aortic size (cm) 3.5	4.0	4.5	5.0	5.5	6.0	6.5	7.0	7.5	8.0
55	1.40	2.50	2.86	3.21	3.57	3.93	4.29	4.64	5.00	5.36	5.71
57	1.45	2.41	2.76	3.10	3.45	3.79	4.14	4.48	4.83	5.17	5.52
59	1.50	2.33	2.67	3.00	3.33	3.67	4.00	4.33	4.67	5.00	5.33
61	1.55	2.26	2.58	2.90	3.23	3.55	3.87	4.19	4.52	4.84	5.16
63	1.60	2.19	2.50	2.81	3.13	3.44	3.75	4.06	4.38	4.69	5.00
65	1.65	2.12	2.42	2.73	3.03	3.33	3.64	3.94	4.24	4.55	4.85
67	1.70	2.06	2.35	2.65	2.94	3.24	3.53	3.82	4.12	4.41	4.71
69	1.75	2.00	2.29	2.57	2.86	3.14	3.43	3.71	4.00	4.29	4.57
71	1.80	1.94	2.22	2.50	2.78	3.06	3.33	3.61	3.89	4.17	4.44
73	1.85	1.89	2.16	2.43	2.70	2.97	3.24	3.51	3.78	4.05	4.32
75	1.90	1.84	2.11	2.37	2.63	2.89	3.16	3.42	3.68	3.95	4.21
77	1.95	1.79	2.05	2.31	2.56	2.82	3.08	3.33	3.59	3.85	4.10
79	2.00	1.75	2.00	2.25	2.50	2.75	3.00	3.25	3.50	3.75	4.00
81	2.05	1.71	1.95	2.20	2.44	2.68	2.93	3.17	3.41	3.66	3.90

= low risk (~4% per year)

= moderate risk (~7% per year)

= high risk (~12% per year)

= severe risk (~18% per year)

Zafar MA, Li Y, Rizzo JA, et al *J Thorac Cardiovasc Surg* 2018;155:1938-50

Distal Aortic Dilatation portends near 2x greater risk of CV mortality the proximal dilatation.

NEDA database: 121,115 pts (398,905 echocardiograms) with events linked to National Death Registry

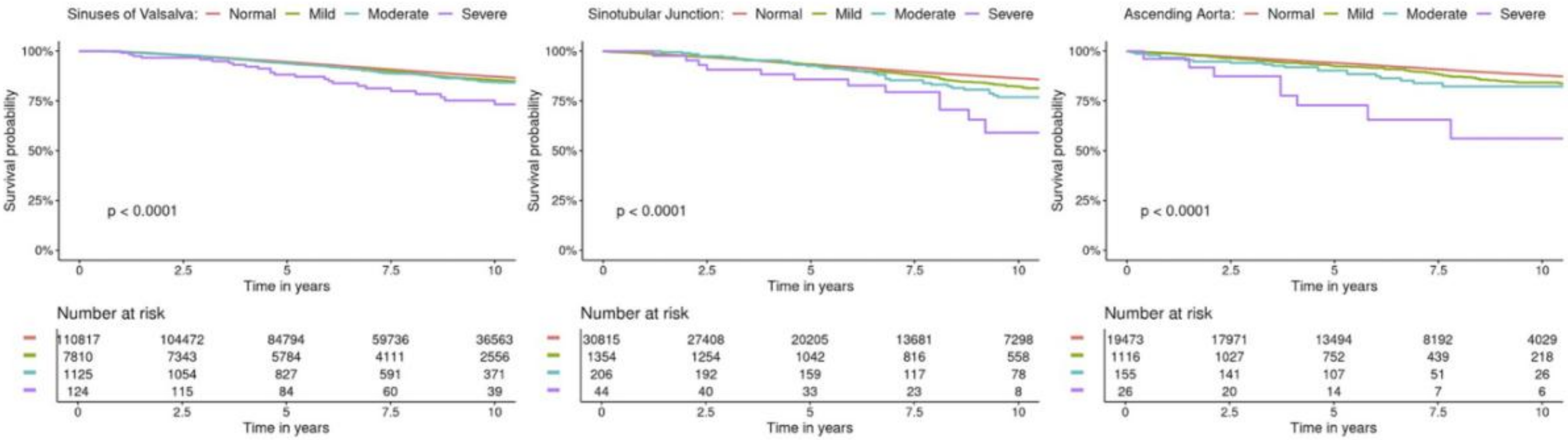
- **SoV, STJ, AscAo measurements in >1 echocardiogram**
- **Categorised as normal (<4.0cm), mild (4.0-4.5cm), moderate (4.5-5cm), severe (>5cm) dilatation and location**
- **Surgical correction vs not**
- **Mortality linked to National Death Index**

Distal Aortic Dilatation portends near 2x greater risk of CV mortality compared to proximal dilatation

- **Mean age 62.6 $\underline{+}$ 16.2**
- **38,681/121,115 (32%) died CVD causes**
- **276 pts (0.007%) died from aortic dissection**
- **Severe dilatation (>5cm) at any site increased 10 year mortality compared with normal p<0.001**
- **Corrective aortic surgery 10 year CVD mortality same as normal aortic dimension pts**

Nadel J, Paratz E, Humphries J et al, EHJ 2024:45(Suppl 1)

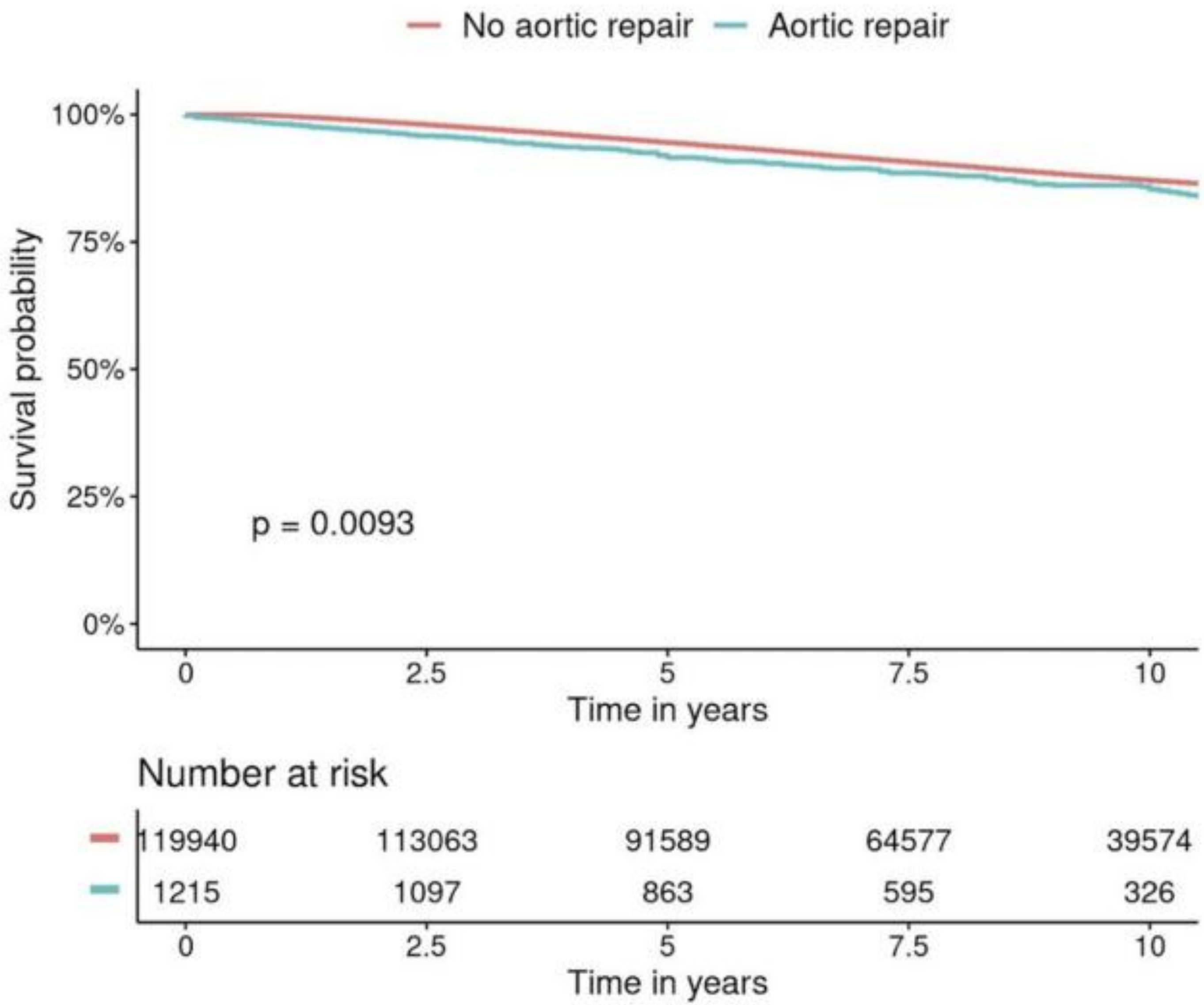
Distal Aortic Dilatation portends near 2x greater risk of CV mortality compared to proximal dilatation



SoV 26% HR 1.93 **STJ 39% HR 2.82** **AscAo 44% HR 4.74**

Nadel J, Paratz E, Humphries J et al, EHJ 2024:45(Suppl 1)

Corrective aortic surgery group 10 year CVD mortality *same as normal aortic dimension pts*



Nadel J, Paratz E, Humphries J et al, EHJ 2024:45(Suppl 1)

Very Long Term Follow Up (>3000 Days) of Aortopathy Patients - Surgical Intervention/Dissection Is Predicted By Accelerated Annualised Aortic Growth Rate

R Aslannif, A Challa, G Scalia, J Humphries

THE PRINCE CHARLES HOSPITAL, BRISBANE, QUEENSLAND, AUSTRALIA

Very Long Term Follow Up (>3000 Days) of Aortopathy Patients

98 patients

8.0 ± 3.1 yrs (range 4-15yrs)

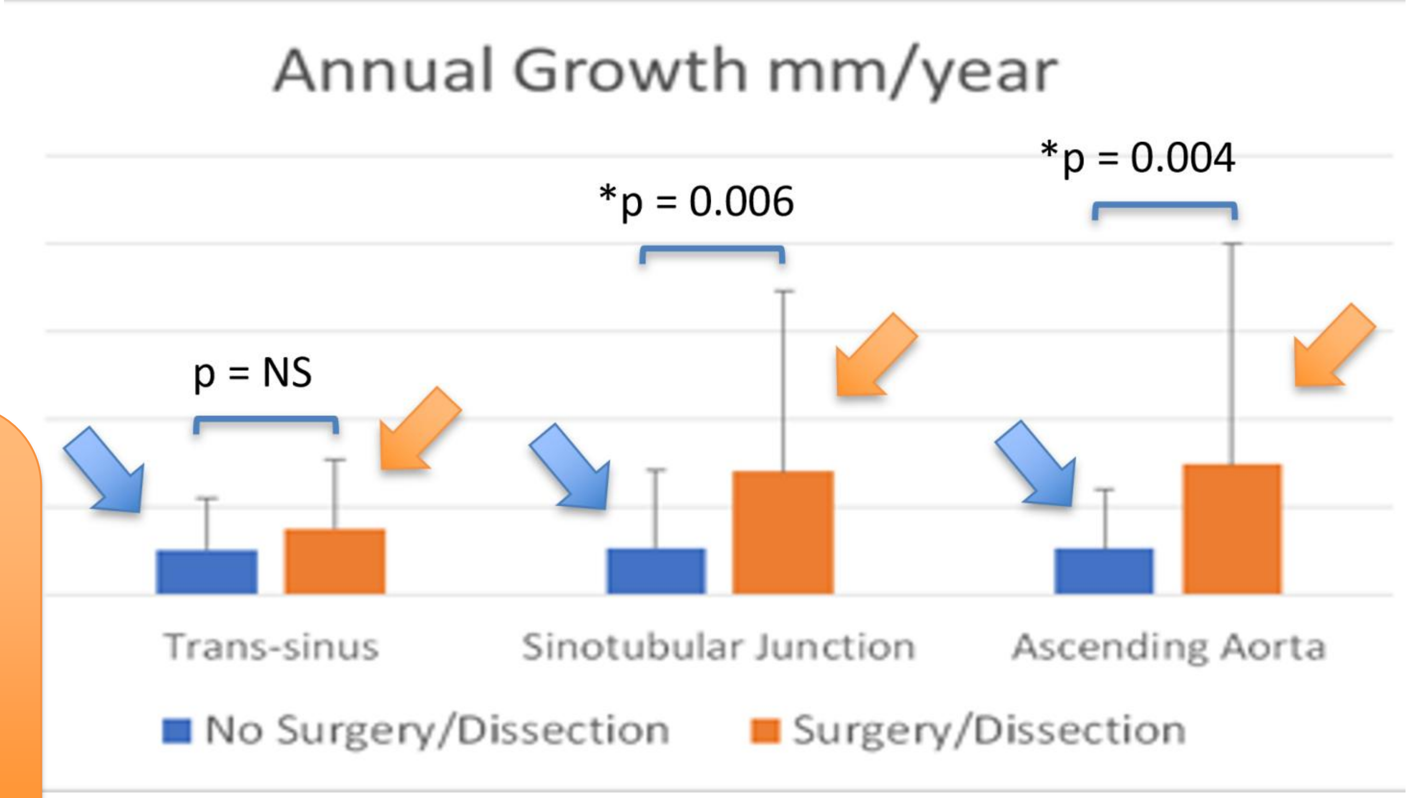
53.5 ± 19.8yrs; 71% male

No Events (80)

55 ± 20yrs (p = 0.01)
STJ 0.3 ± 0.4mm/yr
Asc Ao 0.3 ± 0.3mm/yr
TS 39 ± 4mm

Events (18)

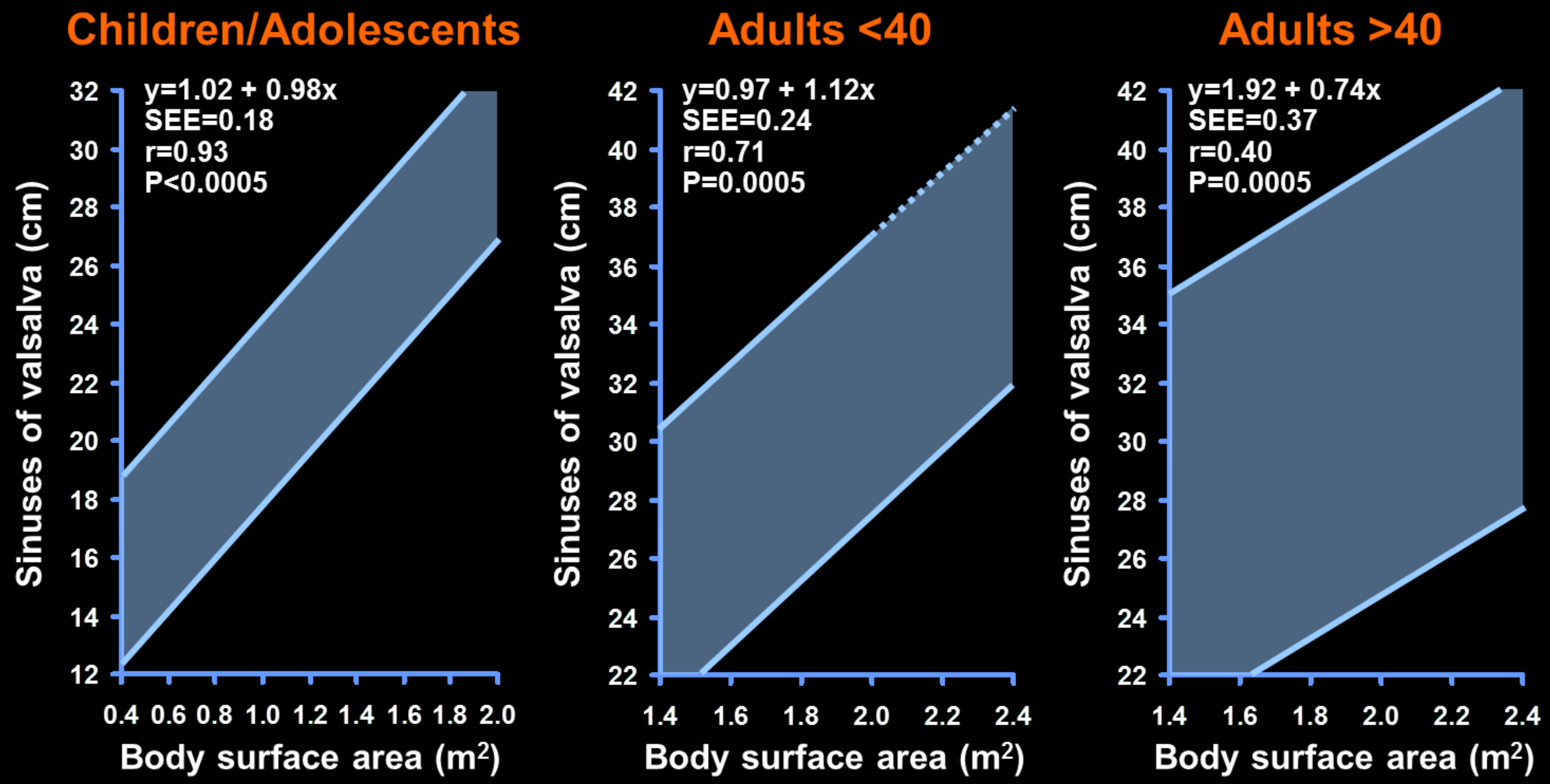
43 ± 15yrs
STJ 0.7 ± 1.0mm/yr *
Asc Ao 0.7 ± 1.2mm/yr*
TS 45 ± 4 mm (p<0.001)



Very Long Term Follow Up (>3000 Days) of Aortopathy Patients

- Patients with events
  - younger (43±15y vs 55±20y $p<0.01$)
  - more accelerated growth during follow up
  - larger TS dimension at diagnosis (45±mm vs 39±4mm)
  - No pattern of accelerated growth
- Patients with no events
  - older and slow/minimal growth

Age-Related Normative Values for Aortic Root Size in Children and Adults



Ascending Aortic Dimensions From A Large Australian Adult Cohort. Should We Be Indexing By Height Not BSA?

Dr Julie Humphries*, Dr Gregory Scalia

Imaging - Mini Oral Session
Friday, Aug 2, 2024

innovation and collaboration

Queensland Government

Faculty disclosure - The presenter has advised that the following presentation will NOT include discussion on any commercial products or service and that there are NO financial interests or relationships with any of the Commercial Supporters of this years ASM.

Aortic Dimensions in a Large Australian Cohort. New Normal Range?

Humphries, JA and Scalia, GM

The Prince Charles Hospital, Brisbane, Australia

Background: There is little published data worldwide about the normal range of aortic dimensions in adults. Guidelines for dilated aortic dimensions and recommendations for surgery are based on small population cohorts and absolute values. Adjustment for BSA and height are becoming more accepted, however the normal range of aortic dimensions for a large population has not been previously published. We present the distribution of aortic dimensions in a large Australian population, with indexation for BSA and height as well as centiles of age.

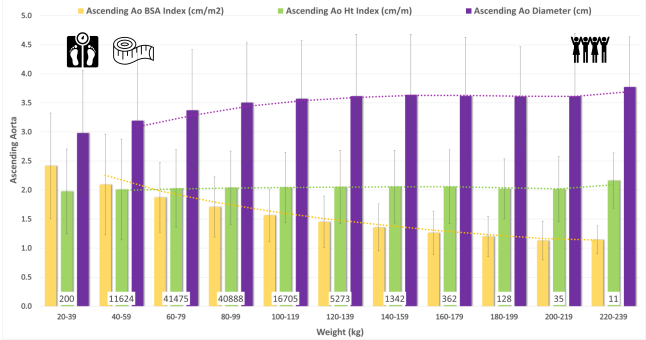
Methods: All patients >18 years of age attending for routine echocardiography at our institution from 2007-2022 were included in the database. Measurements of aortic root, sinotubular junction and ascending aorta using ASE criteria were collated. Dimensions were adjusted for BSA and height. Data was analysed for centiles of weight and height and across decades of age.

117,912	62.8+17.6y	59%	83.7+21.1kg	169.8+10.3cm

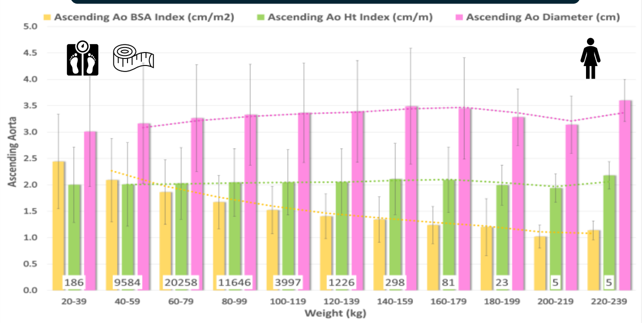
Results: Ascending aortic dimensions are presented in absolute values (average + 2SD cm), and height adjusted (average + 2SD cm/m) and BSA adjusted (average + 2SD cm/m²) values for all patients (Upper Left panel), and separated into females (Middle Left panel), and males (Lower Left panel). Two standard deviations were used to include 95% of patient population and represent "normal range".

Whilst there was a small progressive increase in aortic dimensions for increasing body weight, when absolute dimensions (purple bars) were indexed according to height (green bars) at all centiles of body weight, **a robust ratio was identified at 2.0 + 0.7cm/m for all patients regardless of gender**. In contrast, when adjusted for BSA (yellow bars), the aortic dimensions were progressively and predictably under-reported in patients over 80kg for assessment for normal vs dilated. This relationship was observed for both males and females alike (Left middle and lower panels).

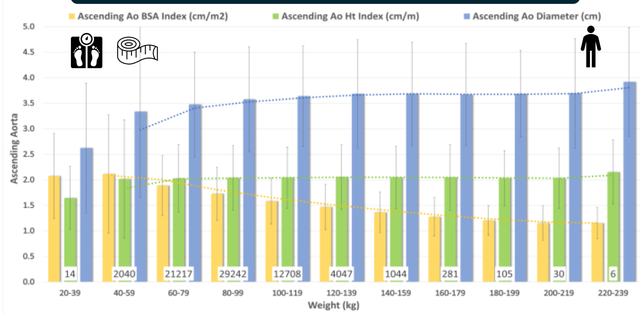
Ascending Ao BSA Indexed v Ht Indexed v Absolute + 2SD (ALL)



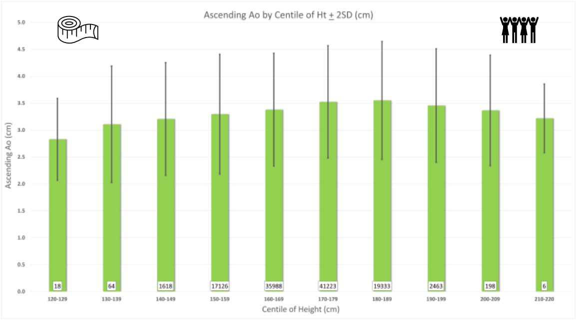
Ascending Ao BSA Indexed v Ht Indexed v Absolute + 2SD (FEMALE)



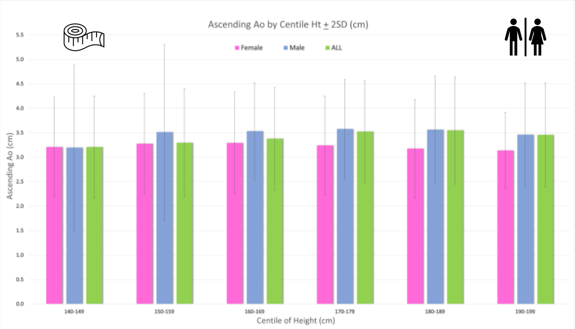
Ascending Ao BSA Indexed v Ht Indexed v Absolute + 2SD (MALE)



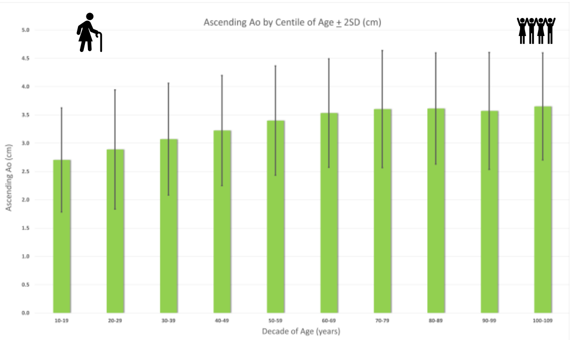
Ascending Ao by Centile of Height + 2SD (ALL)



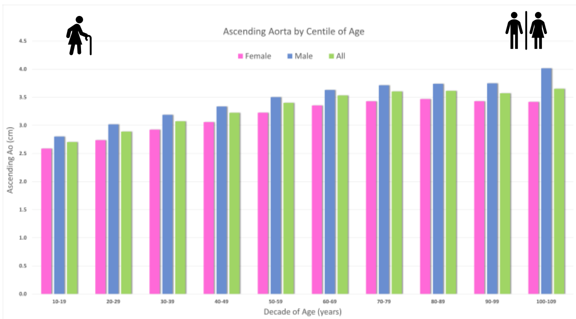
Ascending Ao by Centile of Height (Female, Male, ALL)



Ascending Ao by Decade of Age + 2SD (ALL)



Ascending Ao by Decade of Age (Female, Male, ALL)



Results: Data was also expressed per centile of height (Centre panel) and age (Right panel). There was a small progressive increase in aortic dimensions as expected for increasing height (Upper Centre panel). When separated into females and males, females had slightly smaller than average values compared to males for the same centile of height. When analysed for centiles of age, a small progressive increase in dimension was observed with age (Upper Right panel). When separated into females and males, a similar pattern is observed, although women had slightly smaller than average values compared to men of similar age (Lower Right panel). As there is generally no increase in height as people age, this likely represents normal biological aging with respect to aortic dimensions. For the majority of patients, the upper limit of the 95% confidence interval for ascending aortic dimension was 4.5cm regardless of height, weight or age.

Conclusion:

Aortic dimensions are consistently 2.0+0.7 cm/m when adjusted for patient height across all body weight centiles for men and women. BSA indexing in patients over 80kg tends to under-represent aortic dimensions when assessing for dilatation. Dimensions tend to increase gently with increasing age and height. We propose a new height based nomogram for assessment of normal aortic dimensions in adults.

Population Demographics & Ascending Aortic Dimensions Stratified by Weight

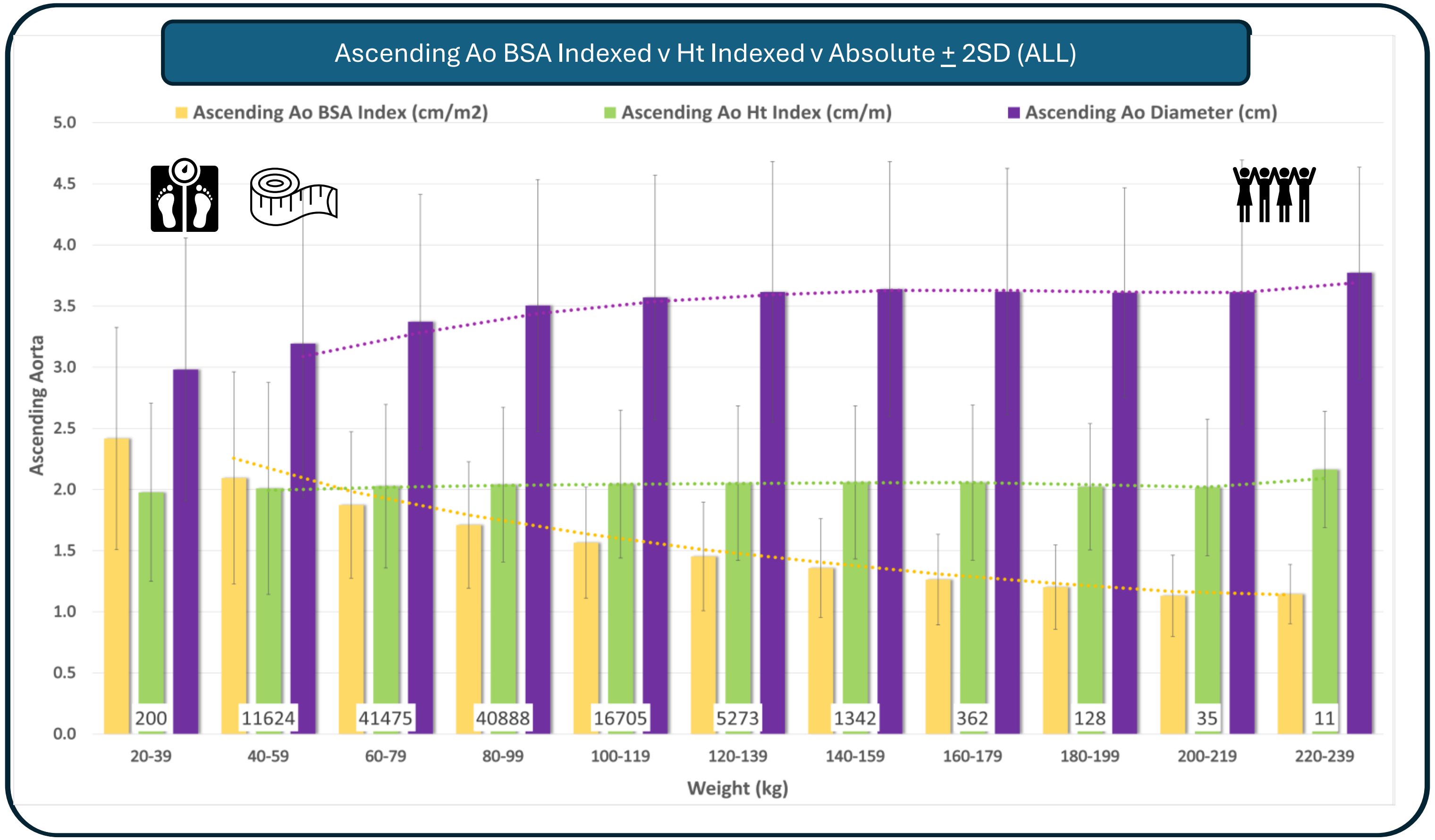
117,912

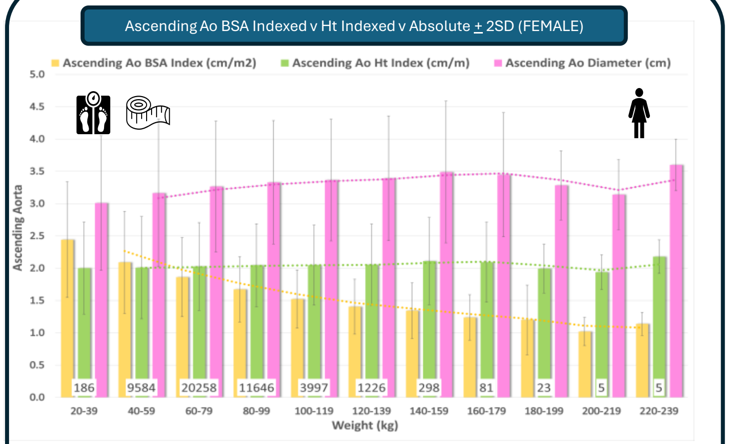
62.8+17.6y

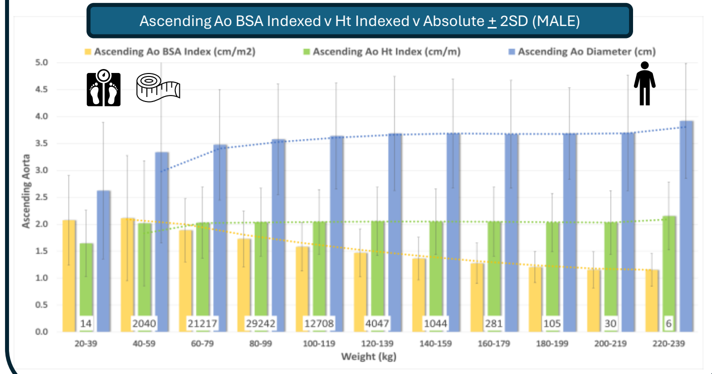
59%

83.7+21.1kg

169.8+10.3cm







When absolute dimensions (purple bars) were indexed according to height (green bars) at all centiles of body weight, a robust ratio was identified at 2.0 + 0.7cm/m for all patients regardless of gender.

In contrast, when adjusted for BSA (yellow bars), the normal range for aortic dimensions was progressively and predictably under-reported as weight increased for both females and males.

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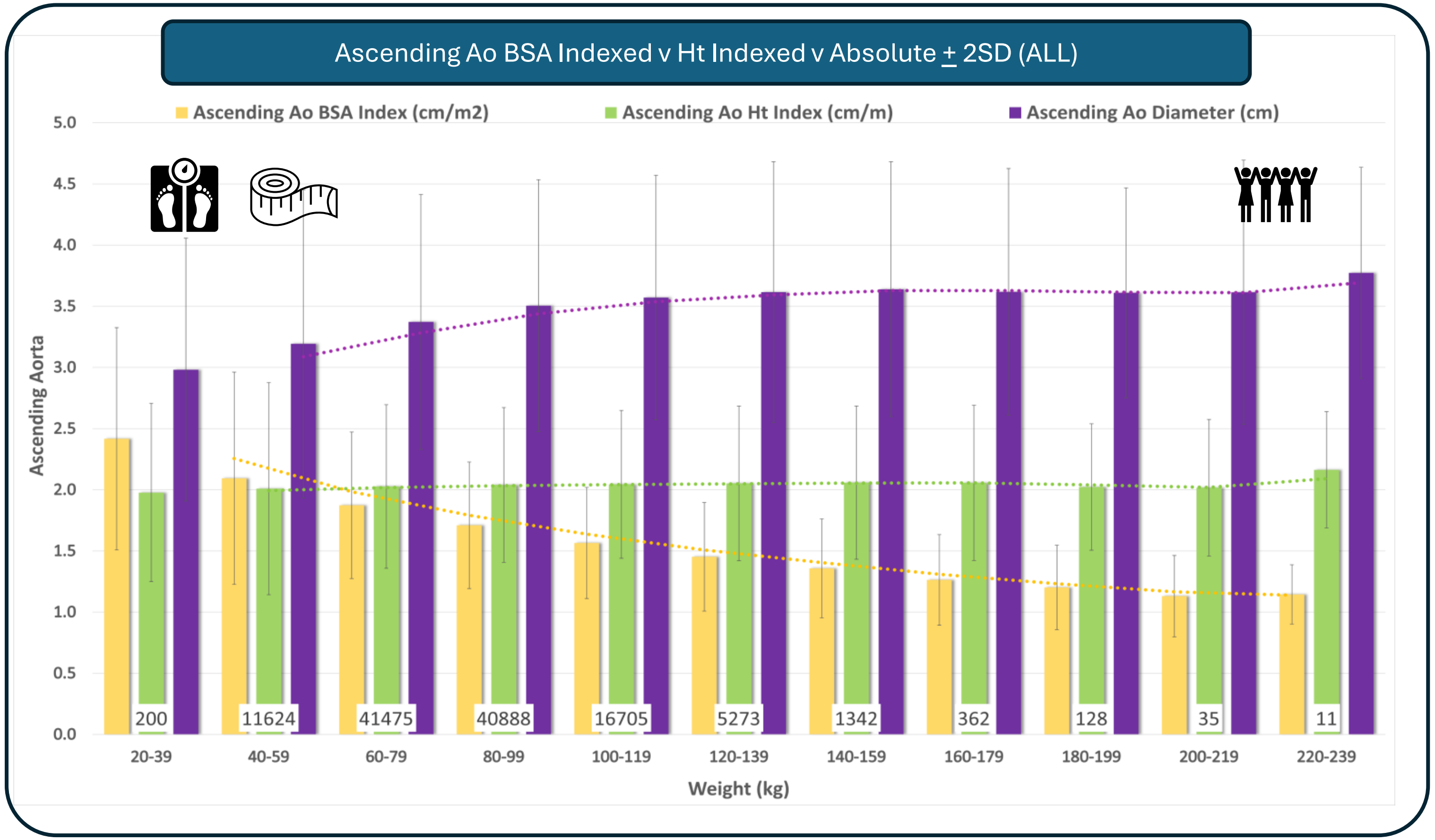

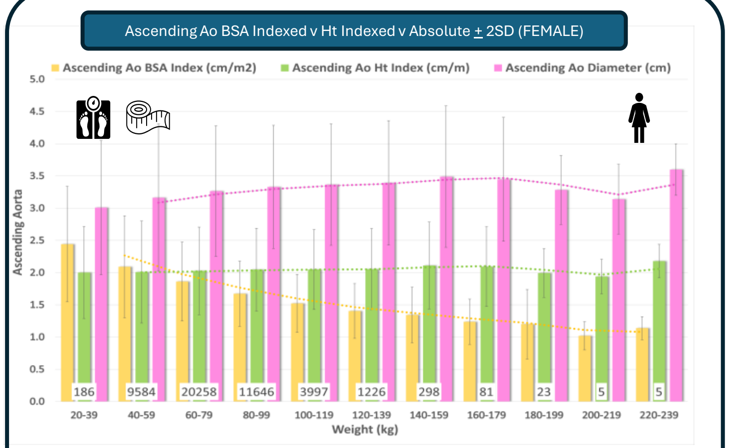

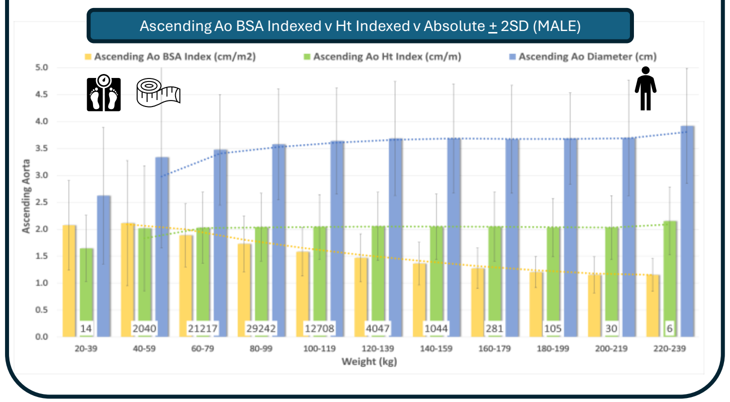

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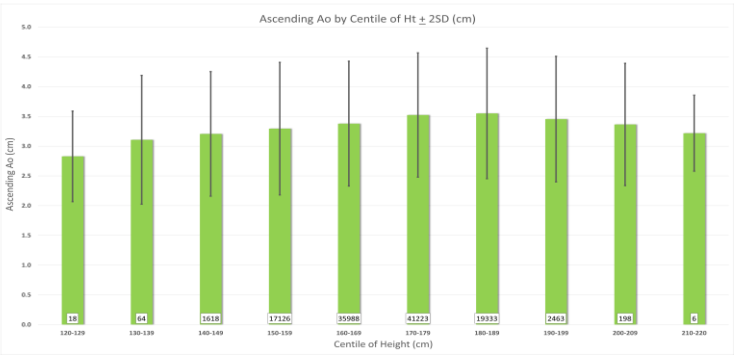
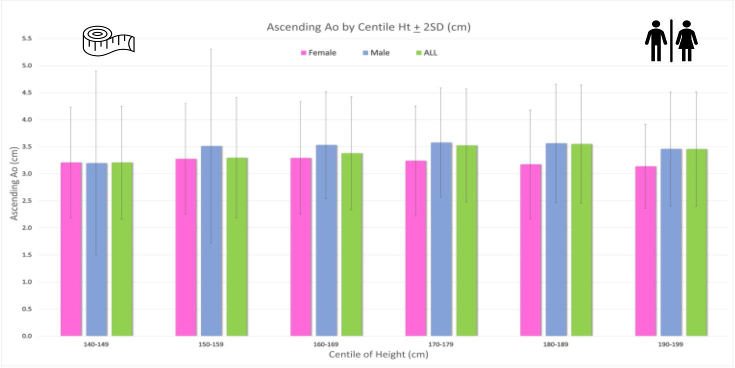
Ascending Aortic Dimensions Stratified by Centile of Height & Decade of Age

Ascending Ao by Centile of Height + 2SD (ALL)

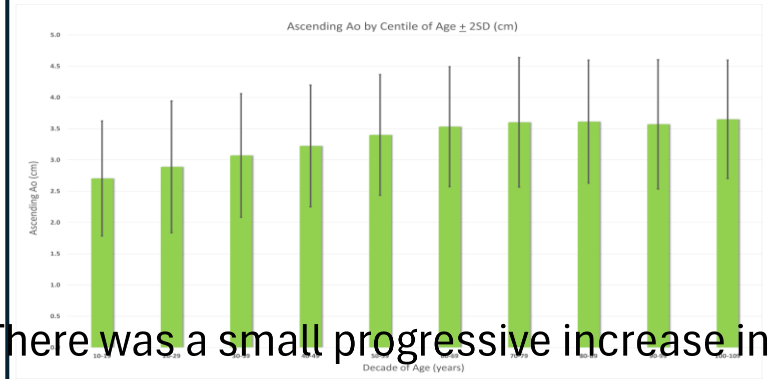


Ascending Ao by Centile of Height (Female, Male, ALL)

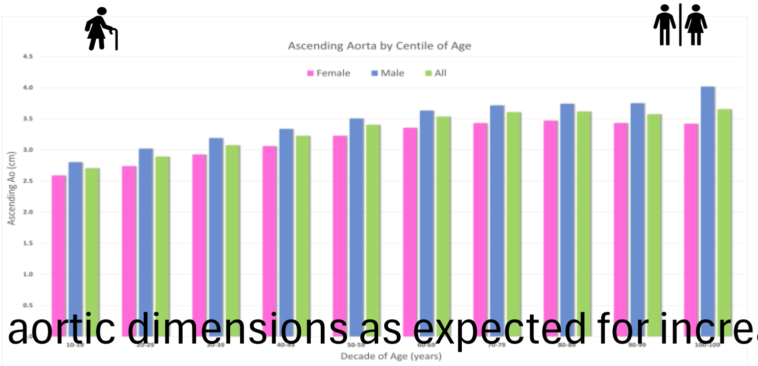


There was a small progressive increase in aortic dimensions as expected for increasing height (green bars), with females on average smaller than males for same height centile (Right panel).

Ascending Ao by Decade of Age + 2SD (ALL)



Ascending Ao by Decade of Age (Female, Male, ALL)

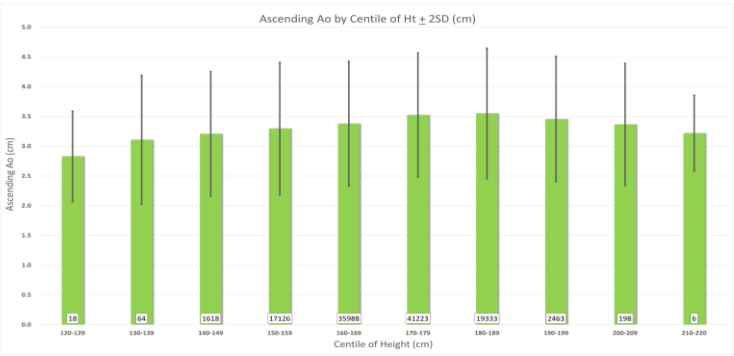


There was a small progressive increase in aortic dimensions observed with increasing age (green bars), with females on average smaller than males at each decade of age (Right panel).

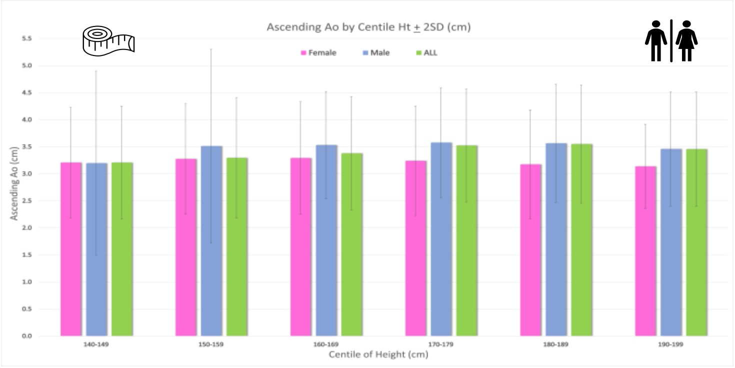
There was a small progressive increase in aortic dimensions as expected for increasing height (green bars), with females on average smaller than males for same height centile (Right panel).

Ascending Aortic Dimensions Stratified by Centile of Height & Decade of Age

Ascending Ao by Centile of Height + 2SD (ALL)

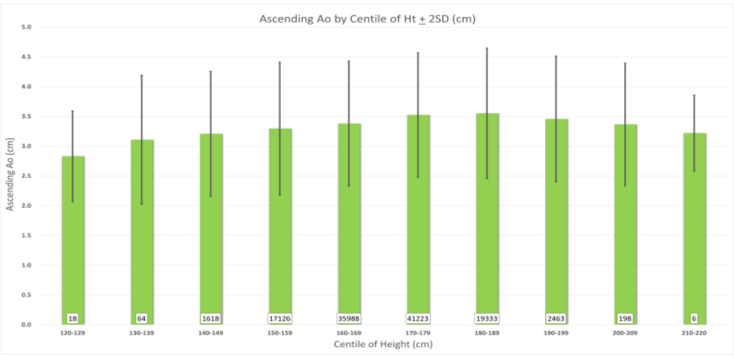


Ascending Ao by Centile of Height (Female, Male, ALL)

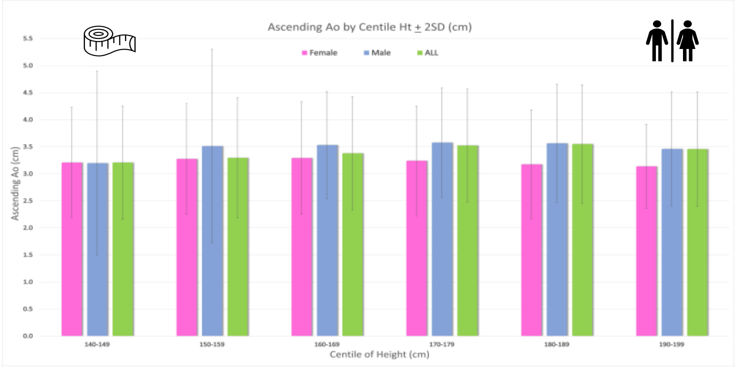


Ascending Aortic Dimensions Stratified by Centile of Height & Decade of Age

Ascending Ao by Centile of Height + 2SD (ALL)

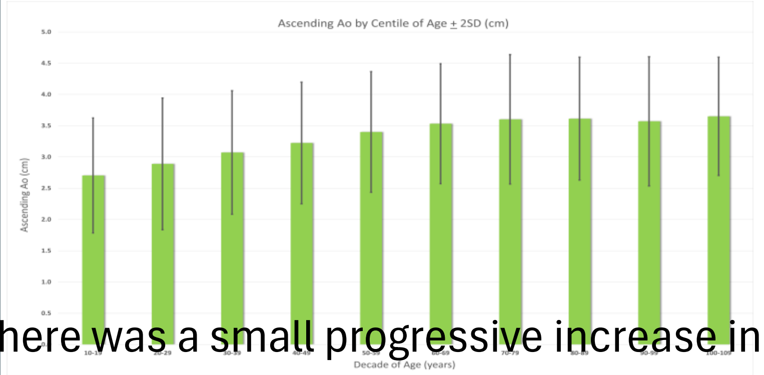


Ascending Ao by Centile of Height (Female, Male, ALL)

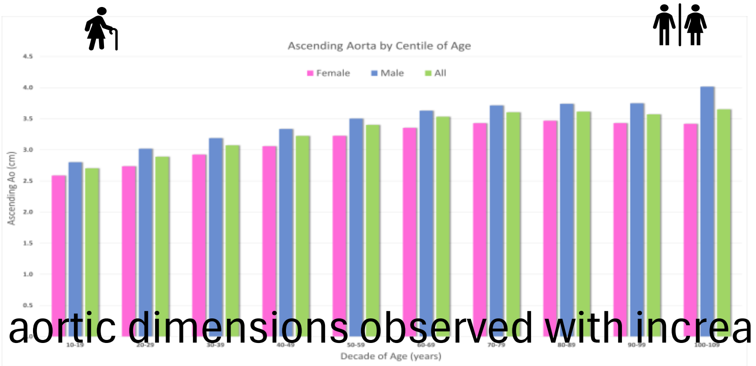


There was a small progressive increase in aortic dimensions as expected for increasing height (green bars), with females on average smaller than males for same height centile (Right panel).

Ascending Ao by Decade of Age + 2SD (ALL)



Ascending Ao by Decade of Age (Female, Male, ALL)



There was a small progressive increase in aortic dimensions observed with increasing age (green bars), with females on average smaller than males at each decade of age (Right panel).

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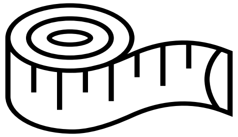
Key Points

In Queensland, there is significant discrepancy for accurate representation of aortic dimensions when adjusted for BSA due to increased rates of obesity, and adjusting for BSA at extremes of weight under-reports degree of dilatation



There is a robust ratio for aortic dimensions when adjusted for height (2.0 ± 0.7 cm/m) regardless of age, gender or weight

Normal ageing demonstrates small but progressive increases in aortic dimensions over time

Conclusions

Aortic dimensions are consistently 2.0$\pm$0.7 cm/m when adjusted for patient height across all body weight centiles for men and women.

BSA indexing in patients over 80kg tends to under-represent aortic dimensions when assessing for dilatation in both females and males.

For the majority of patients, the upper limit of the 95% confidence interval (+2SD) for ascending aortic dimension was 4.5cm regardless of height, weight or age.

We propose a new height based nomogram for assessment of normal aortic dimensions in adults.

Screening and Imaging Protocol in Patients with Suspected or Diagnosed Aortopathy

- Serially measure and record:
  TS, STJ, proximal and distal Asc Ao, arch
  (leading edge to leading edge, RSE)

- Directly compare previous studies (if available)

- Index for BSA and ht to estimate risk (if concordant)

Aortic Dilatation - Diagnosis & Surveillance

Use of absolute vs Ht adjusted vs BSA adjusted values

Method	Absolute	Height	BSA
Normal	<4.0cm	<2.2 cm/m	<2.0 cm/m^2
Mild	4.0-4.5cm	2.2-2.43 cm/m	2.0-2.3 cm/m^2
Moderate	4.5-5.5cm	2.43-3.17 cm/m	2.3-2.8 cm/m^2
Severe	>5.5cm	>3.17 cm/m	>2.8 cm/m^2

Look for any disconnect in values at extremes of height or weight

Screening and Imaging Protocol in Patients with Suspected or Diagnosed Aortopathy

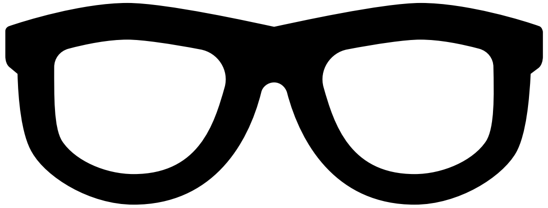
Screening Guidelines

- Screen 1st degree relatives of patients with aortic dilatation or BAV for Ao aneurysm
- Screen 1st degree relatives every 5 years in absence of dilatation at initial screening

Imaging Modality

- Annual TTE in pts with Ao dilatation & in pts with disease known to cause Ao enlargement
- Annual MRI/A if TTE images non-diagnostic or inaccurate
- Compare TTE with CT/MRI at least once to confirm TTE is reliable for f/up

Diagnosis of Aortic Dilatation



- Bicuspid Aortic Valve
- Mitral Valve Prolapse
- Coarctation/PDA

- Family History of TAA
- Family history of BAV
- Family history of coarctation

Predictors of Risk

Historically

- Size (absolute)
- Associated pathology
- Family history
- Growth rates over time

New Approach

- Different indexing
- Consider genetic testing
- Personal history
- Screen 1st degree relatives
- Look for growth, effacement

Aortic Size
~~>5.0cm~~

>4.0cm
or Ht adjust
(or BSA adjust)

Rate of Increase
>0.5cm/year

Predictors of Dissection

Manage hypertension

Genetic testing for known aggressive early dissection genotypes

Family History of early Aortic Complications

Aorta and Pericardial Disease

Diseases of the Aorta

Dr Julie Humphries

ECHO AUSTRALIA

17-19 March 2025