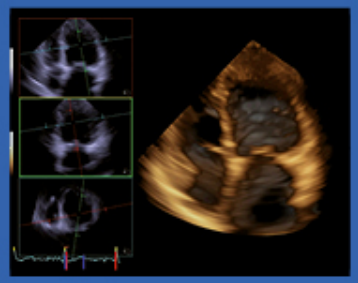

EuroValve
March 27 - 28, 2015

PROPHYLACTIC AORTA SURGERY AT 45-55 mm Which Risk Factors?

Alessandro Della Corte, MD, PhD
II University of Naples – Cardiac Surgery
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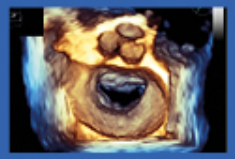
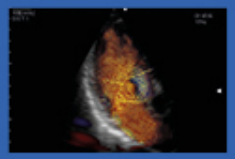
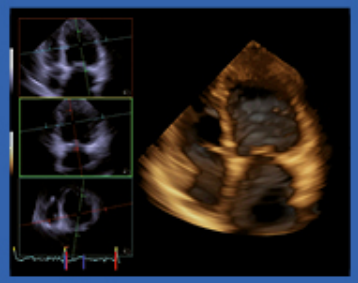
Naples, Italy





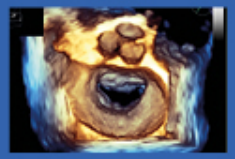
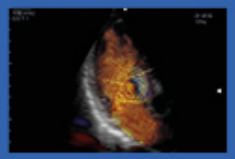
EuroValve
March 27 - 28, 2015

Faculty disclosure

Alessandro Della Corte

I have **no financial relationships** to disclose.



www.eurovalvecongress.com

The New Guidelines

European Heart Journal
doi:10.1093/eurheartj/ehu281

ESC GUIDELINES

2014 ESC Guidelines on the diagnosis and treatment of aortic diseases

Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult

The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC)

Authors/Task Force members: Raimund Erbel* (Chairperson) (Germany), Victor Aboyans* (Chairperson) (France), Catherine Boileau (France), Eduardo Bossone (Italy), Roberto Di Bartolomeo (Italy), Holger Eggebrecht (Germany), Arturo Evangelista (Spain), Volkmar Falk (Switzerland), Herbert Frank (Austria), Oliver Gaemperli (Switzerland), Martin Grabenwöger (Austria), Axel Haverich (Germany), Bernard Iung (France), Athanasios John Manolis (Greece), Folkert Meijboom (Netherlands), Christoph A. Nienaber (Germany), Marco Roffi (Switzerland), Hervé Rousseau (France), Udo Sechtem (Germany), Per Anton Sirnes (Norway), Regula S. von Allmen (Switzerland), Christiaan J.M. Vrints (Belgium).

Eur Heart J 2014;35:2873-926

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

Threshold Diameters

Non-Syndromic and BAV w/o r.f.: 55 mm

Marfan w/o r.f.: 50 mm

BAV+ r.f.: 50 mm

Marfan + r.f.: 45 mm

LDS or VT4-EDS: 43 mm ?

Concomitant AVR: 45 mm

"Which Risk Factors?"

Marfan

BAV

[c]Decision should also take into account the shape of the different parts of the aorta. Lower thresholds can be used for combining surgery on the ascending aorta for patients who have an indication for surgery on the aortic valve.

[d]Family history of AD and/or aortic size increase >3 mm/year (on repeated measurements using the same imaging technique, at the same aorta level, with side-by-side comparison and confirmed by another technique), severe aortic or mitral regurgitation, or desire for pregnancy.

[e]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 aorta level, with side-by-side comparison and confirmed by another technique).

[f]Pending comorbidities in the elderly.

[g]See text in section 8.

…"including but limited to"?

ACCF/AHA guidelines 2010 for Thoracic Aortic Disease

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association
Learn and Live

2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine

Class I

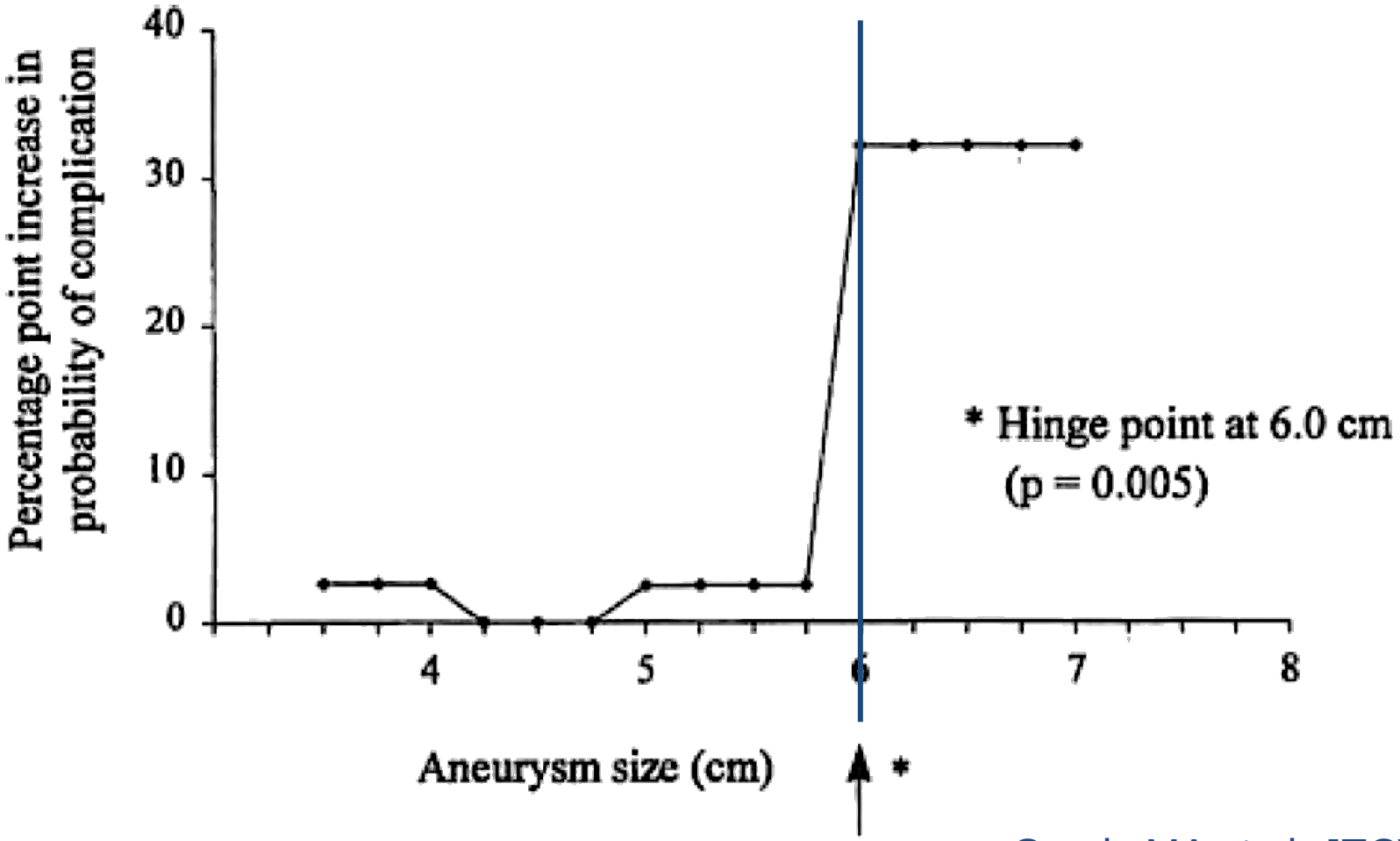
1. Asymptomatic patients with degenerative thoracic aneurysm, chronic aortic dissection, intramural hematoma, penetrating atherosclerotic ulcer, mycotic aneurysm, or pseudoaneurysm, who are otherwise suitable candidates and for whom the ascending aorta or aortic sinus diameter is 5.5 cm or greater, should be evaluated for surgical repair.[371] (*Level of Evidence: C*)
2. Patients with Marfan syndrome or other genetically mediated disorders (vascular Ehlers-Danlos syndrome, Turner syndrome, bicuspid aortic valve, or familial thoracic aortic aneurysm and dissection) should undergo elective operation at smaller diameters (4.0 to 5.0 cm depending on the condition; see Section 5) to avoid acute dissection or rupture.[81,114,143,371,436–439] (*Level of Evidence: C*)
3. Patients with a growth rate of more than 0.5 cm/y in an aorta that is less than 5.5 cm in diameter should be considered for operation. (*Level of Evidence: C*)
4. Patients undergoing aortic valve repair or replacement and who have an ascending aorta or aortic root of greater than 4.5 cm should be considered for concomitant repair of the aortic root or replacement of the ascending aorta. (*Level of Evidence: C*)

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*)

The Available Evidence

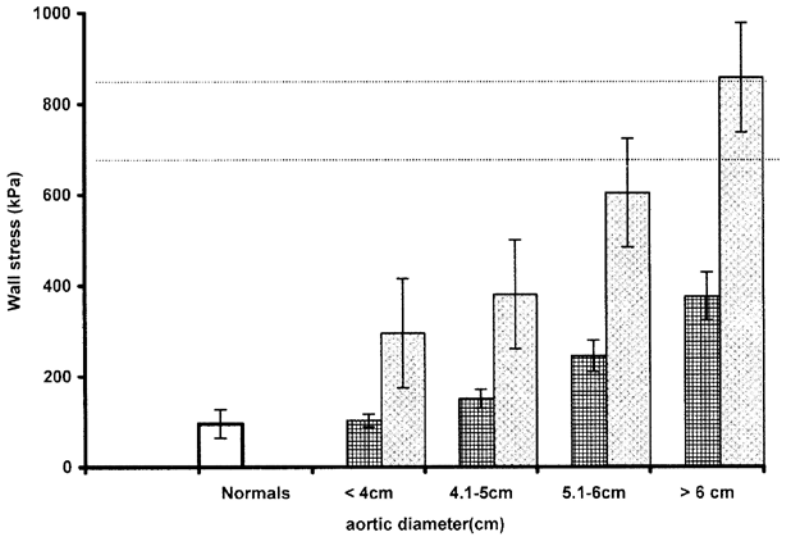
Average risk of acute aortic events as a function of the diameter



Coady MA et al. JTCVS 1997

Mechanical deterioration underlies malignant behavior of aneurysmal human ascending aorta

George Koullias, MD,[a] Raj Modak MD,[b] Maryann Tranquilli, RN,[a] Dimitris P. Korkolis, MD,[a] Paul Barash, MD,[a] and John A. Elefteriades, MD[a]



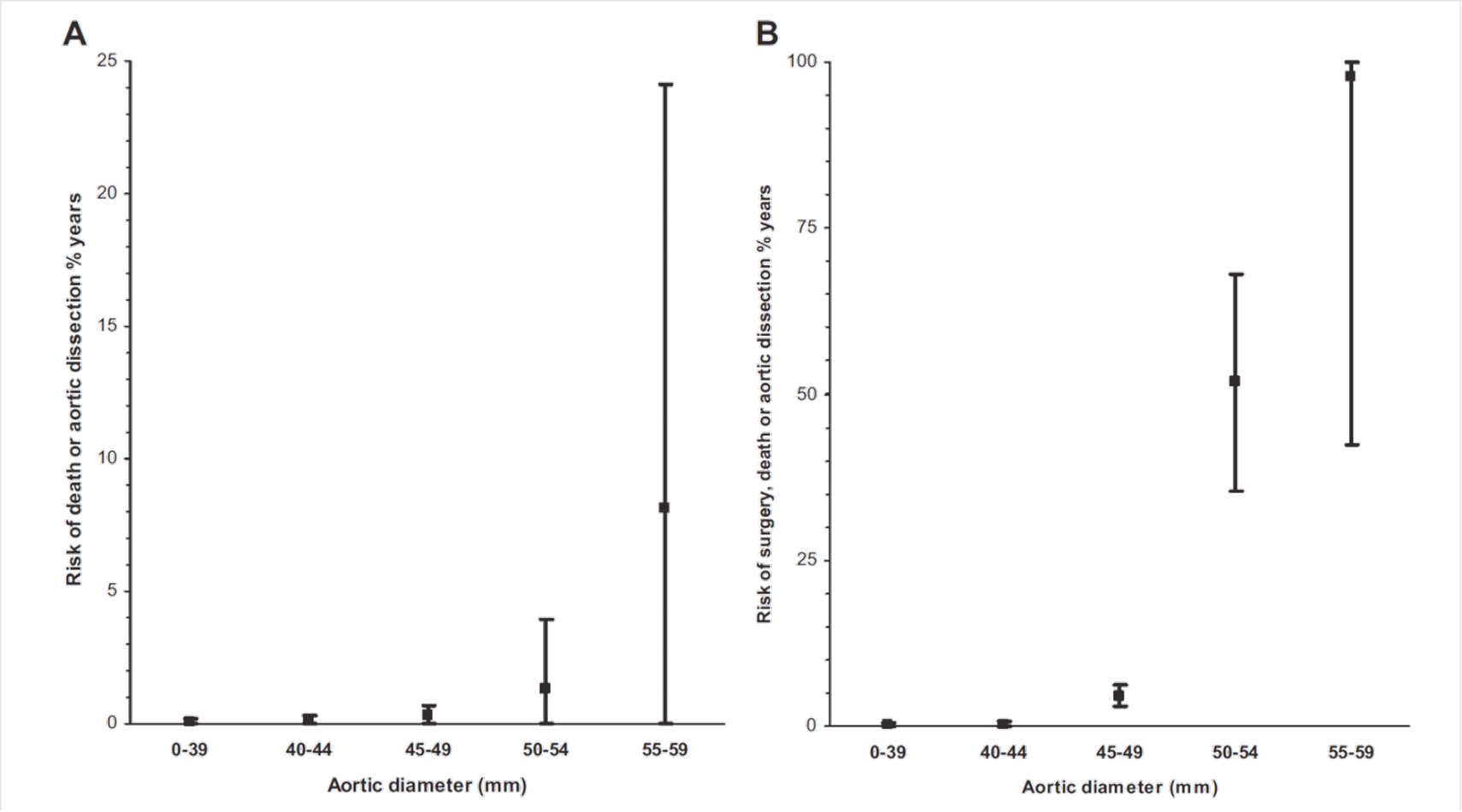
We were intrigued to discover a striking correlation between this study of the mechanical properties of the aneurysmal human ascending aorta and our previous studies on the natural behavior of aortic aneurysms on different diameters. Specifically, our previous clinical studies had shown that when the aortic diameter reaches 6 cm, the risk of catastrophic acute events (rupture or dissection) increases dramatically. It is for this reason that we have previously recommended a diameter criterion of 5.5 cm for preventive surgical extirpation of the aneurysmal ascending aorta.

In this study of the mechanics of ascending aortic aneurysm, we found that the mechanical properties of the human aorta deteriorated dramatically at precisely the same diameter of 6 cm. At this size, the aorta became essentially a nondistensible tube (Figures 1 and E1.) As a correlate, at

Koullias G et al. JTCVS 2005

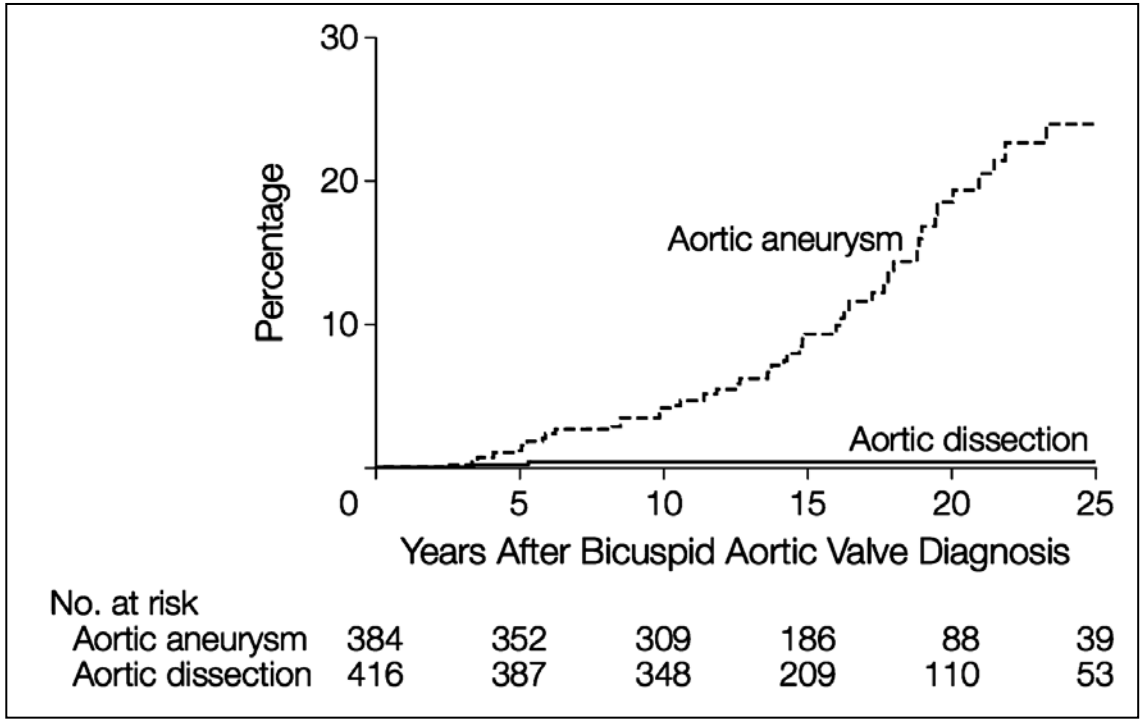
Aortic Event Rate in the Marfan Population:

"Natural history" or "Clinical history" ?



Jondeau G et al. Circulation 2012

Aortic Dissection is a rare event in the BAV Population



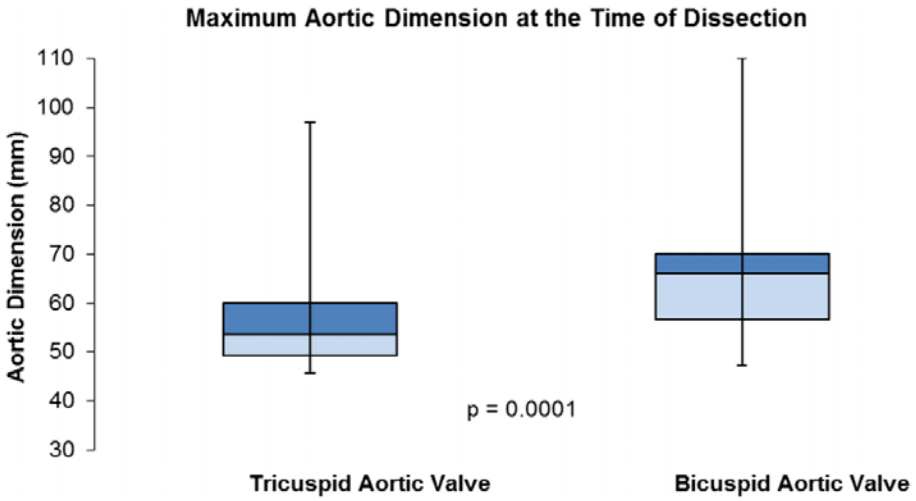
Risk of ac ao ev in the BAV population: 0.3%/pt-year

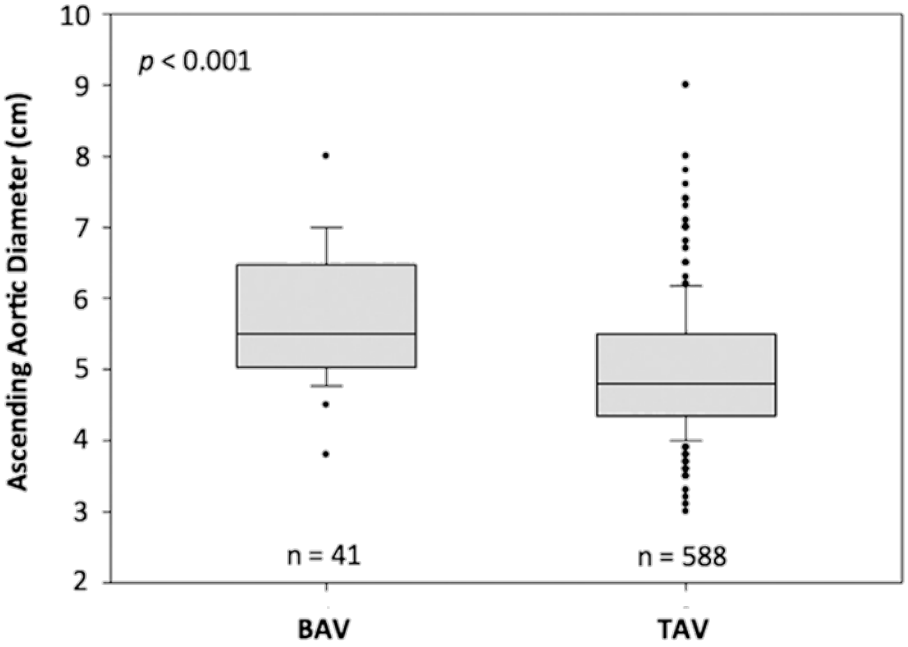
Michelena HI et al. JAMA 2011

Hardikar AA et al. JACC Img 2013

"The conundrum of BAV aortopathy"

Aortic Dissection occurs at greater diameter with BAV





Eleid MF et al. Heart 2013

Rylski B et al. Ann Thorac Surg 2014

Della Corte A, EJCTS 2015

The Principle on which prophylactic surgery of the ascending aorta is based

---

Indications for aortic aneurysmectomy: Too many variables and not enough equati

Aortic Di

Observati

Linda A. Pape
Patrick T. O'Gara,
Santi Trimarchi
James B. Froehlich,
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K. Oh, MD;
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Cooper, MS;
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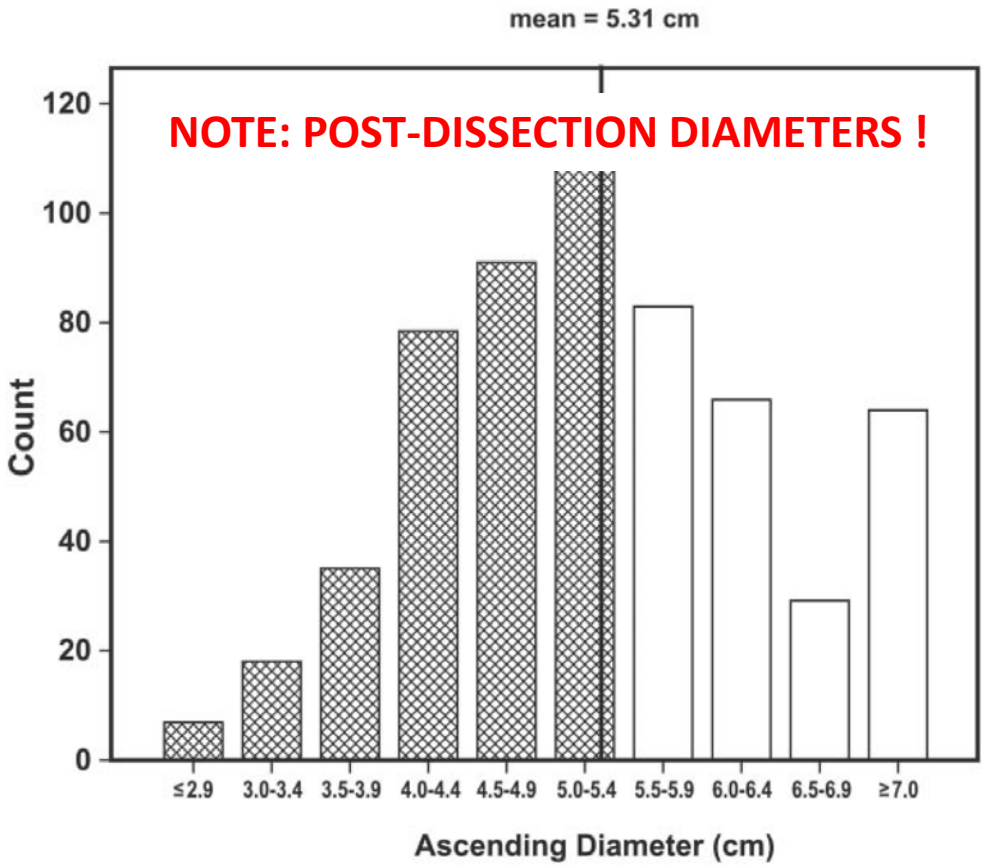
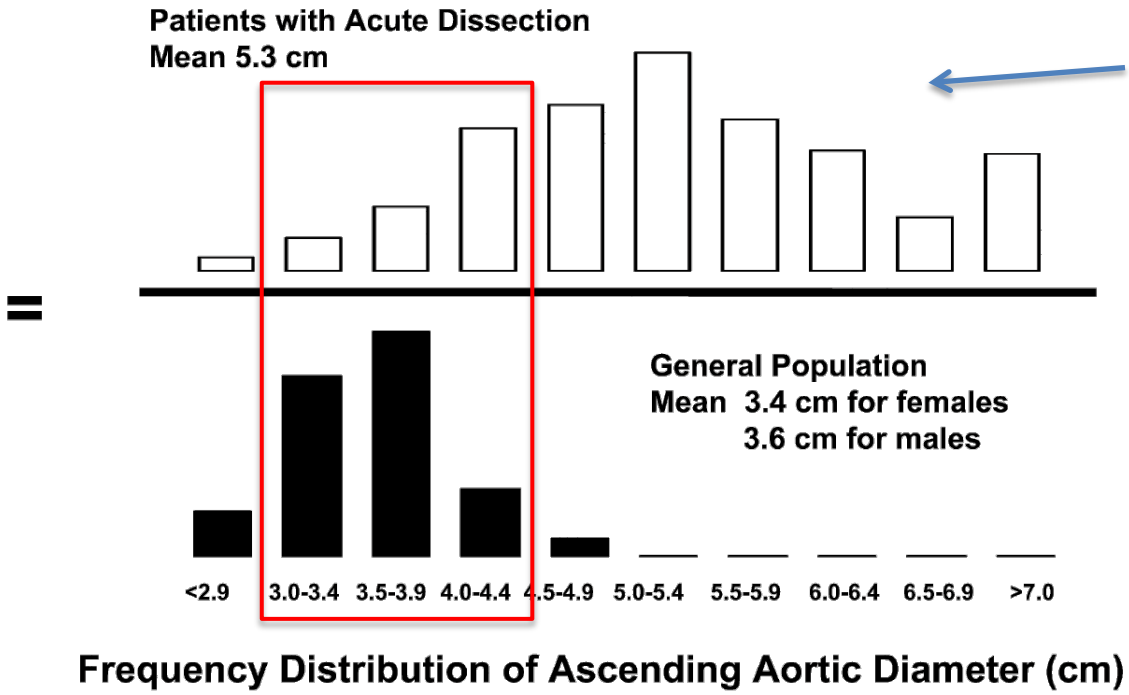


Risk of Dissection at a Given Diameter



Hospital referral

FIGURE 1. Calculating the risk of dissection requires knowledge of both the numerator and denominator.

Sundt TM - JTCVS 2010
Elefteriades JA – JTCVS 2014

Lack of Evidence

Which indexing method for the aortic diameter?

European Heart Journal
doi:10.1093/eurheartj/ehu281

ESC GUIDELINES

2014 ESC Guidelines on the diagnosis and treatment of aortic diseases

In borderline cases, the individual and family history, patient age, and the anticipated risk of the procedure should be taken into consideration. In patients with small body size, in particular in patients with Turner syndrome, an indexed aortic diameter of 27.5 mm/m^2 body surface area should be considered.[323] Lower thresholds of aortic dia-

American Heart Association

2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine

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 (π r^2) in cm^2 divided by the patient's height in meters exceeds 10.[16,143] (*Level of Evidence: C*)**

Davies RR et al. ATS 2006;81:169-77 → diameter/BSA

Svensson LG et al. JTCS 2003;126:892-3 → CS-area/height

A simulation of usage of different indexing methods in 640 pts

- 4 different criteria:
  - absolute diameter
  - Aortic Ratio
  - Aortic Size Index (diameter/BSA)
  - CSA/h ratio
- 15 to 47% patients reached indications according to the absolute diameter threshold, but not by indexing methods
- 7-16% patients did not reach surgical indication by absolute size, but should have been operated on according to an indexing method

Della Corte A, et al. *unpublished*

	Concordance with diameter	Concordance with ASI	Concordance with CSA/h	Concordance with AR
Indication by diameter	100%	80%	86%	85%
Indication by ASI	80%	100%	84%	83%
Indication by CSA/h	86%	84%	100%	93%
Indication by AR	85%	83%	93%	100%

- Overall, only in 72% of patients indications were consistent by all methods

Della Corte A, et al. *unpublished*

Former studies on the risk of aortic events considered rupture & dissection together

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ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2013.12.028

How Does the Ascending Aorta Geometry Change When It Dissects?

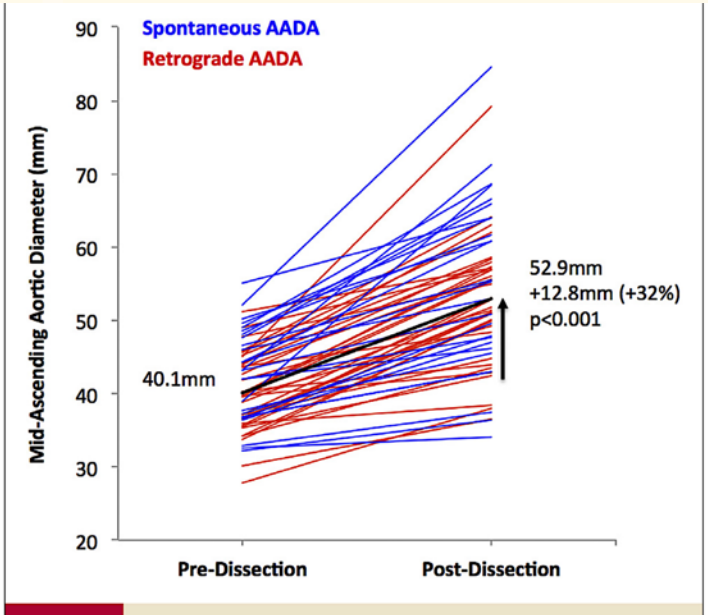
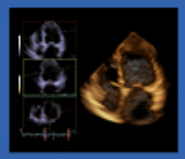


Figure 6 Ascending Aortic Diameter Change After AADA Onset

Rylski B et al., JACC 2014



EuroValve

Modeling of predissection aortic size in acute type A dissection: More than 90% fail to meet the guidelines for elective ascending replacement

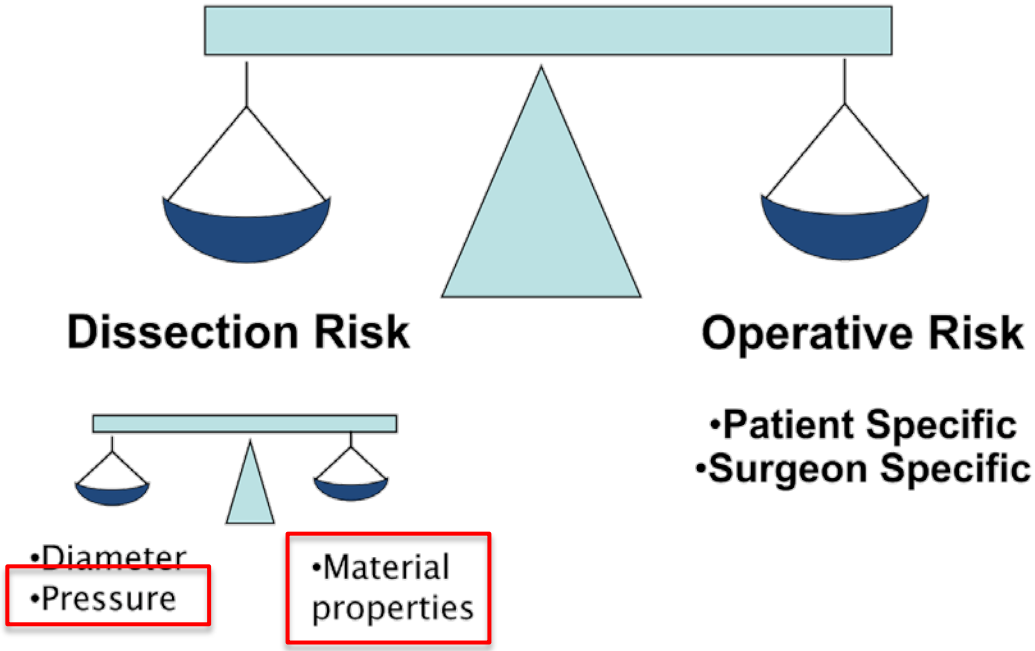
Bartosz Rylski, MD,[a,b] Emanuela Branchetti, PhD,[a] Joseph E. Bavaria, MD,[a]
Prashanth Vallabhajosyula, MD,[a] Wilson Y. Szeto, MD,[a]
Rita K. Milewski, MD, PhD,[a] and Nimesh D. Desai, MD, PhD[a]

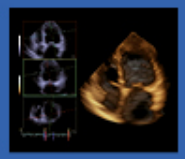
CONCLUSIONS

Modeling of the predissection ascending aortic geometry enabled us to predict the incidence of aortic dilatation in patients with acute type A dissection. More than 60% of patients with spontaneous, non-Marfan, nonbicuspid type A dissection had a nondilated ascending aorta before dissection onset. Only 3% would have met the criteria for elective ascending replacement to prevent aortic dissection. Additional research on the genetic, biochemical, and imaging predictors of aortic dissection is essential.

The Principle Revisited

Need for non-dimensional criteria of risk stratification!





Genetics

↓

Aortic Wall Remodelling

↓

Mechanical Response

to

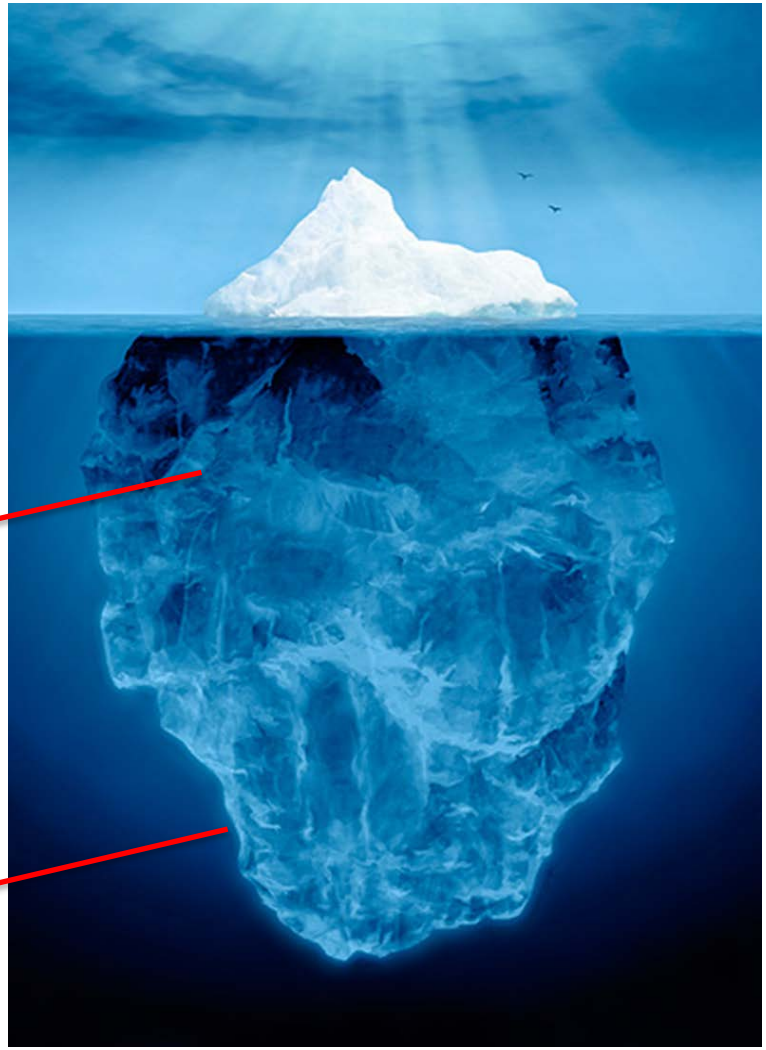
Hemodynamic Forces

↑

→ **Mechanical Failure**

Distinguish between
rutpure and dissection!

"Which Risk Markers?"



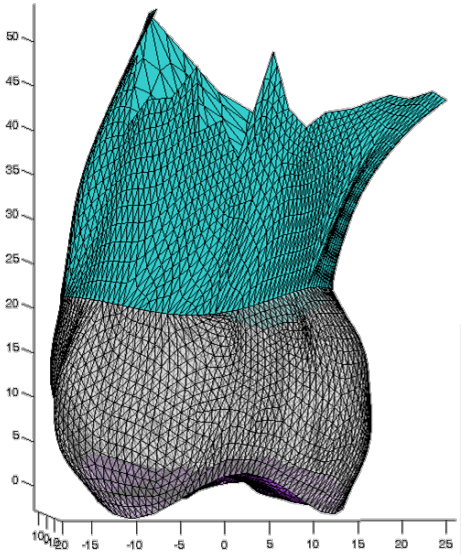
Functional and Biological Markers

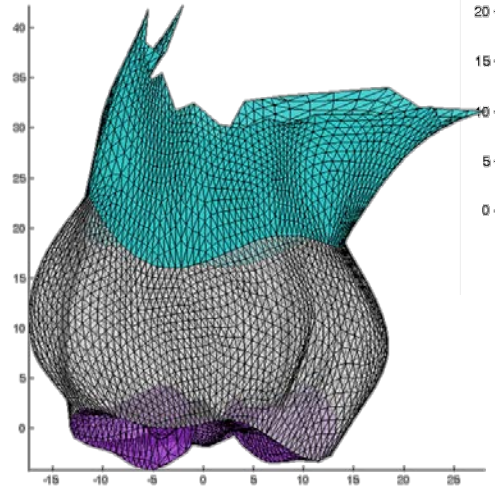
- Wall stresses
- Aortic wall biomech properties
- Circulating biomarkers?

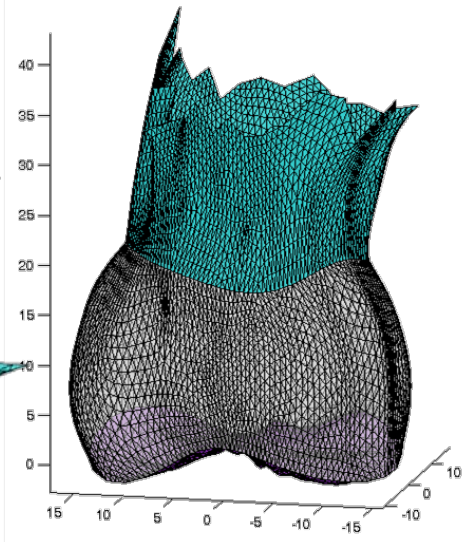
Genotypic Markers

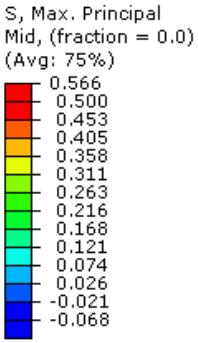
- Sequencing of known genes
- Unknown genes?

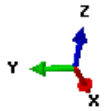
Examples of **patient-specific** finite element modelling of the aortic root: computation of wall stress

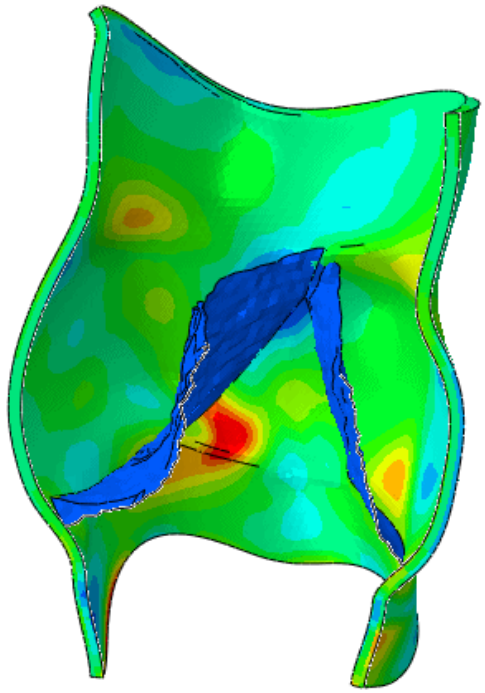












Novel Imaging Predictors of Aortopathy Progression

Journal of the American College of Cardiology Vol. 60, No. 4, 2012
© 2012 by the American College of Cardiology Foundation ISSN 0735-1097/$36.00
Published by Elsevier Inc.

Restricted cusp motion in right-left type of bicuspid aortic valves:

CORRESPONDENCE

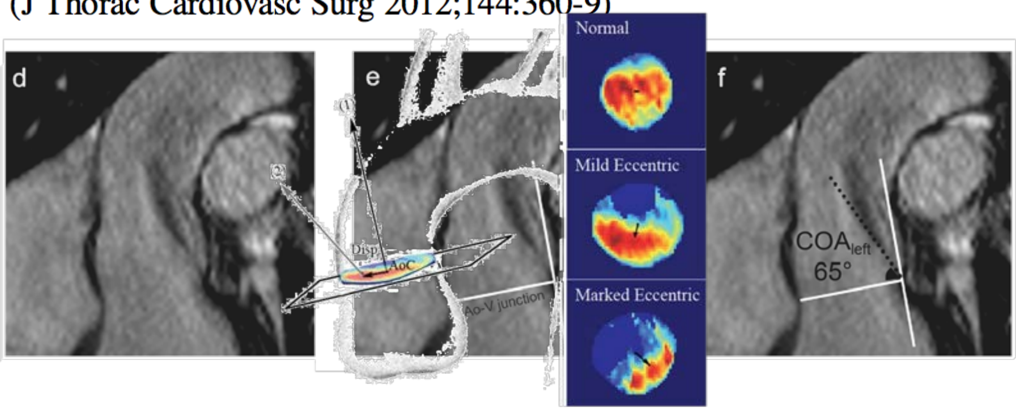
Research Correspondence

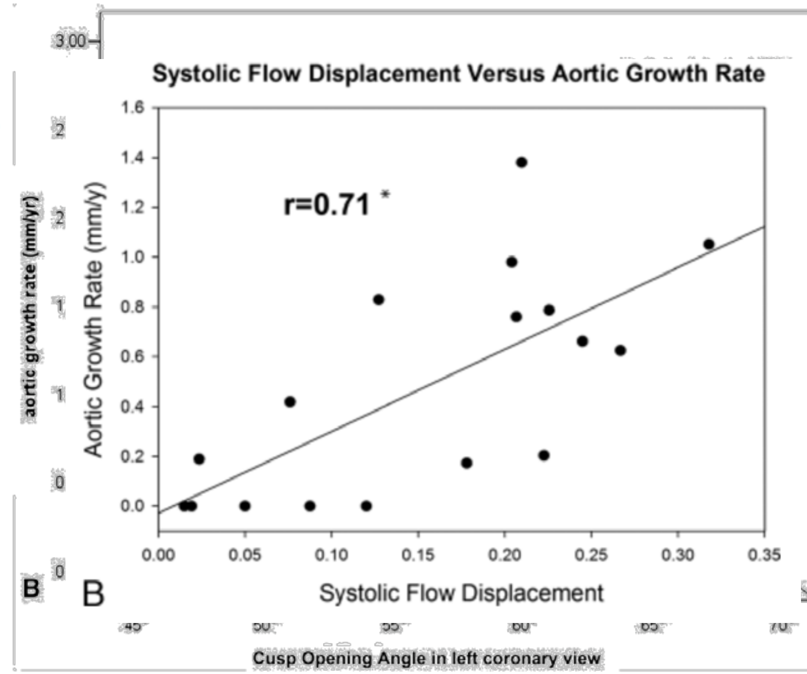
Imaging Biomarkers of Aortic Disease

Increased Growth Rates With Eccentric Systolic Flow

Al… Corte, MD, PhD,[a] Ciro Bancone, MD,[a] Carlo A. Conti, PhD,[b] Emiliano Votta, PhD,[b]
Al… hD,[b] Luca Del Viscovo, MD,[c] and Maurizio Cotrufo, MD[d]

(J Thorac Cardiovasc Surg 2012;144:360-9)





Phenotypic Markers

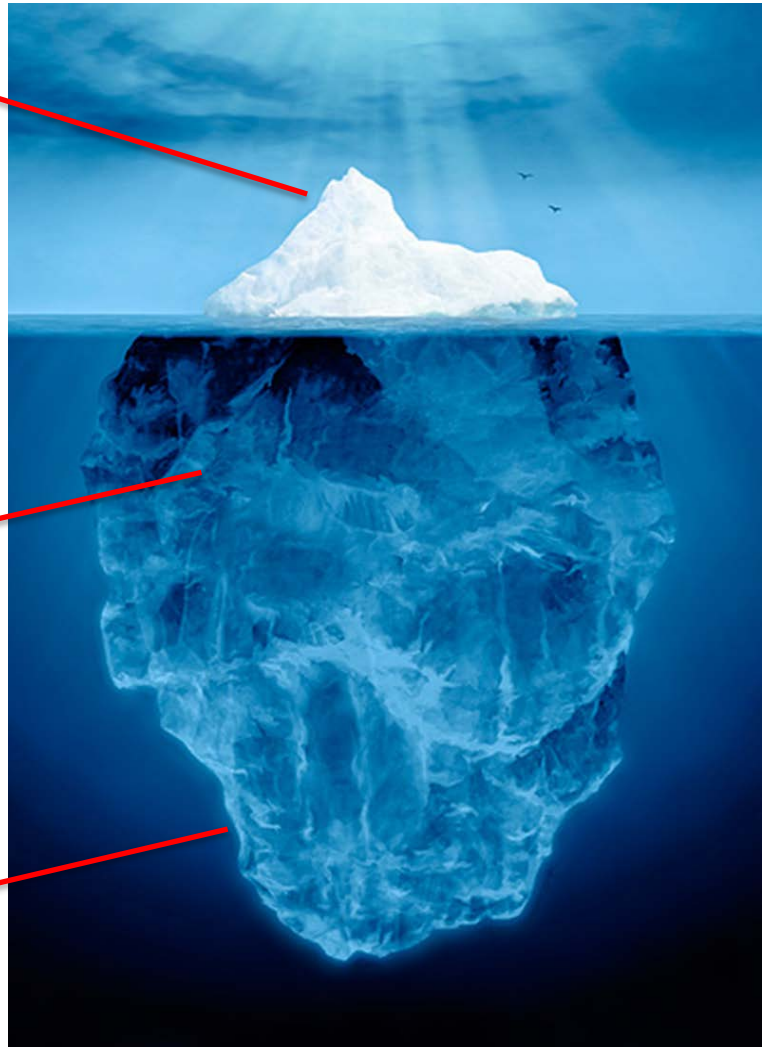
- Valve type (BAV, TAV) and function
- Aortic shape
- Anatomic variants (bovine arch)
- Wall thickness
- Aorta elongation

Functional and Biological Markers

- Wall stresses
- Aortic wall biomech properties
- Circulating biomarkers?

Genotypic Markers

- Sequencing of known genes
- Unknown genes?



Examples of **anatomic risk markers**

Predicting the Risk for Acute Type B Aortic Dissection in Hypertensive Patients Using Anatomic Variables

Aditya S. Shirali, BS,* Moritz S. Bischoff, MD,* Hung-Mo Lin, PHD,* Irina Oyfe, MS,†
Robert Lookstein, MD,† Randall B. Griepp, MD,* Gabriele Di Luozzo, MD*
New York, New York

Multivariable Model and Model Validation for Pr(AAD) Prediction

Predictor	β-Coefficient	Standard Error	Odds Ratio	95% Confidence Interval	p Value	Predictability (Area Under ROC)
Intercept	−31.9842	7.6473			<0.0001	0.974
Diameter: aortic arch	0.1264	0.0322	1.135	1.065, 1.209	<0.0001	
Length: AR to iliac BF	0.2000	0.0606	1.211	1.085,1.375	0.001	
HVA: brachiocephalic	−0.0646	0.0241	0.937	0.894, 0.983	0.0072	

The “Aortic Phenotype”

European Heart Journal
doi:10.1093/eurheartj/ehu281

ESC GUIDELINES

2014 ESC Guidelines on the diagnosis and treatment of aortic diseases

Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult

[c]Decision should also take into account the shape of the different parts of the aorta. Lower thresholds can be used for combining surgery on the ascending aorta for patients who have an indication for surgery on the aortic valve.

?

Geometric factors may include elongation of the ascending, asymmetric dilatation, arch curvature, “loss” of STJ etc.

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

Recommendations	Class[a]	Level[b]
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.	I	C
Beta-blockers may be considered in patients with BAV and dilated aortic root >40 mm.	IIb	C
Because of familial occurrence, screening of first-degree relatives should be considered.	IIa	C
In patients with any elastopathy or BAV with dilated aortic root (>40 mm), isometric exercise with a high static load (e.g. weightlifting) is not indicated and should be discouraged.	III	C

Valvulo-aortic Phenotype in BAV aortopathy

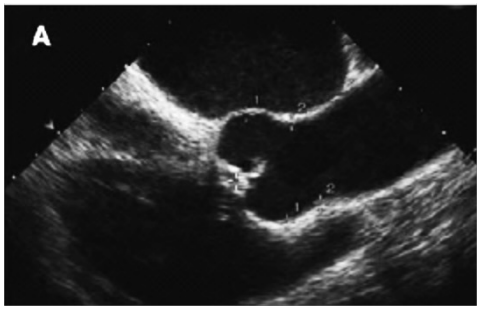
Does a 50 mm root dilatation imply similar risk of dissection as a 50 mm ascending dilatation?
(may apply to both BAV and TAV)

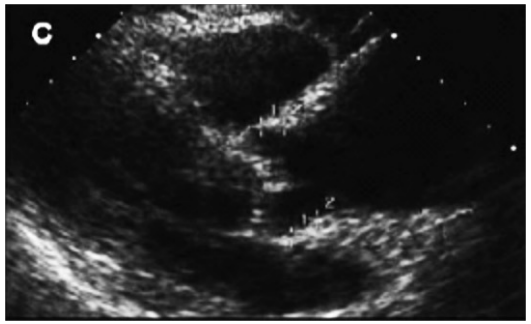
Valvulo-aortic Phenotype in BAV aortopathy

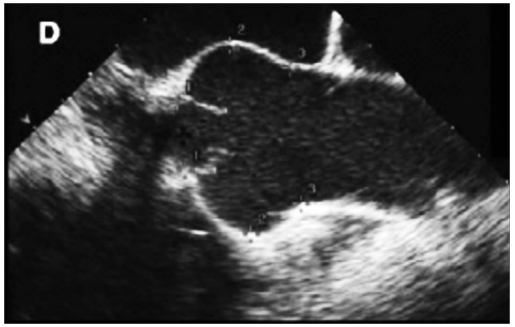
Predictors of ascending aortic dilatation with bicuspid aortic valve: a wide spectrum of disease expression☆

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

Non-dilated Aorta	Ascending phenotype (dilated, asc>root)	Root phenotype (dilated, root>asc)



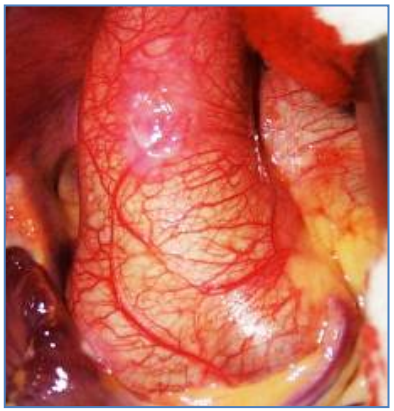




Della Corte A, et al. **EJCTS** 2007;31:397-405

- Aortic stenosis
- Older age
- Hypertension
- RN type

Ascending phenotype



Root phenotype

- Aortic regurgitation
- Younger age
- Male sex
- Taller stature
- RL type

80% dilatations

20% dilatations

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Pattern of Ascending Aortic Dimensions Predicts the Growth Rate of the Aorta in Patients With Bicuspid Aortic Valve

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Table 4. Multivariate Predictors of Fast Growth of the Aortic Diameter

	Predictor	OR	95% CI	p Value
Dependent variable: ascending tract growth rate >0.9 mm/year				
All patients	Root phenotype	14.0	3.2–62	*0.001*
RL type	Root phenotype	7.0	2.0–24	*0.002*
RN type	Aortic regurgitation (any degree)	20.0	1.3–76	*0.03*

Della Corte A, et al. **JACC Img** 2013

Root phenotype: may account for about 80% of aortic dissections in BAV pts

Aortic Valve Morphology Determines the Presentation and Surgical Approach to Acute Type A Aortic Dissection

Bartosz Rylski, MD, Nimesh D. Desai, MD, PhD, Joseph E. Bavaria, MD, Prashanth Vallabhajosyula, MD, William Moser, CRNP, Alberto Pochettino, MD, Wilson Y. Szeto, MD, and Rita K. Milewski, MD, PhD

Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, and Heart Center Freiburg University, Freiburg, Germany

(Ann Thorac Surg 2014;97:1991–7)

the application of Teflon felt "neomedia" or a Wheat procedure were performed in 85% of TAV patients and in fewer than 20% of BAV patients. Aortic root replacement was necessary in BAV patients, usually because of root aneurysm frequently accompanied by severe dissection propagating to the aortic annulus involving one or both coronary arteries. Patients whose sinus

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

Recommendations	Class[a]	Level[b]
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.	I	C
Beta-blockers may be considered in patients with BAV and dilated aortic root >40 mm.	IIb	C
Because of familial occurrence, screening of first-degree relatives should be considered.	IIa	C
In patients with any elastopathy or BAV with dilated aortic root (>40 mm), isometric exercise with a high static load (e.g. weightlifting) is not indicated and should be discouraged.	III	C

Valvulo-aortic Phenotype in BAV aortopathy

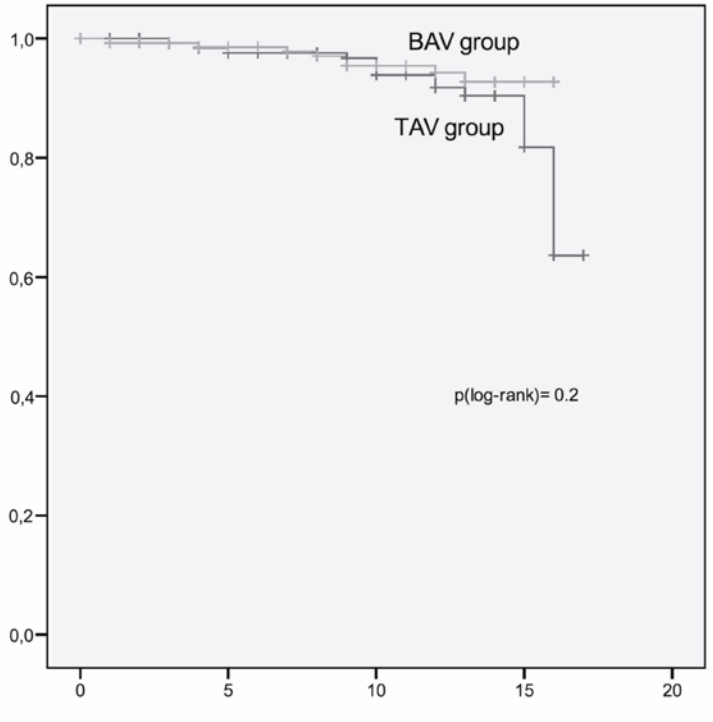
Does a 45 mm dilatation with severe AV stenosis imply similar risk of dissection as a 45 mm dilatation associated with severe AV regurgitation?

(may apply to both BAV and TAV)

Long-term prognosis of ascending aortic aneurysm after aortic valve replacement for bicuspid versus tricuspid aortic valve stenosis

Evaldas Girdauskas, MD,[a] Kushtrim Disha, MD,[a] Michael A. Borger, MD, PhD,[b] and Thomas Kuntze, MD[a]

- Aortic diameter 40-50 mm
- Only AVR
- Mean f-up time: 10 yrs



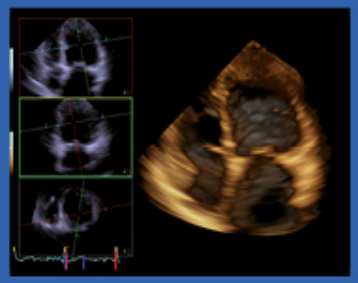
	0	5	10	15
BAV	153	133	113	22
TAV	172	120	102	20

FIGURE 2. Freedom from adverse aortic events (Kaplan-Meier).

JTCVS 2012

CONCLUSIONS

- ✓ The current practice of *prophylactic surgery for ascending aorta* dilatation yields good results in terms of safety, but is inspired by principles and criteria that appear not so robust today as in the past
- ✓ The important new aspect, in the ESC 2014 guidelines was the adjunct of risk criteria *beside the diameter* (a call for better stratification)
- ✓ Further non-dimensional criteria for *prediction* of the *individual* risk of dissection should be developed and validated in the near future
- ✓ We need to *expand our knowledge* about the biomolecular and biomechanical determinants of acute aortic events
- ✓ In BAV aortopathy, surgery may be considered between 45 and 55 in the presence of the *"root phenotype"* (more severe form – risk of dissection – chance of sparing the valve?), while probably some BAV stenosis patients (AVR) should not be treated at 45 mm



EuroValve

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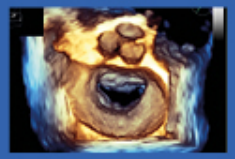
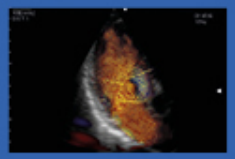
Thank you



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