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

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Faculty disclosure

Alessandro Della Corte

I have no financial relationships to disclose.
The New 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\textsuperscript{e} (Chairperson) (Germany), Victor Aboyans\textsuperscript{e} (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 Jung (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
### Threshold Diameters

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery is indicated in patients who have aortic root aneurysm, with maximal aortic diameter ≥50 mm for patients with Marfan syndrome.</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>
| 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.  
  - ≥50 mm for patients with bicuspid valve with risk factors.  
  - ≥55 mm for other patients with no elastopathy. | 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 |

- **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?”

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.

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.

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).

Pending comorbidities in the elderly.

See text in section 8.

…“including but limited to”? 
ACCF/AHA guidelines 2010 for Thoracic Aortic Disease

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 (\(\pi r^2\)) 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 TGFB1 or TGFB2 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)
Average risk of acute aortic events as a function of the diameter

The Available Evidence

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

Hinge point at 6.0 cm (p = 0.005)

Coady MA et al. JTCVS 1997
Mechanical deterioration underlies malignant behavior of aneurysmal human ascending aorta

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

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
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 aortic events 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


Della Corte A, EJCTS 2015
Indications for aortic aneurysmectomy: Too many variables and not enough equations?*

NOTE: POST-DISSECTION DIAMETERS!
Risk of Dissection at a Given Diameter

Frequency Distribution of Ascending Aortic Diameter (cm)

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?

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
<table>
<thead>
<tr>
<th>Indication by diameter</th>
<th>Concordance with diameter</th>
<th>Concordance with ASI</th>
<th>Concordance with CSA/h</th>
<th>Concordance with AR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication by diameter</td>
<td>100%</td>
<td>80%</td>
<td>86%</td>
<td>85%</td>
</tr>
<tr>
<td>Indication by ASI</td>
<td>80%</td>
<td>100%</td>
<td>84%</td>
<td>83%</td>
</tr>
<tr>
<td>Indication by CSA/h</td>
<td>86%</td>
<td>84%</td>
<td>100%</td>
<td>93%</td>
</tr>
<tr>
<td>Indication by AR</td>
<td>85%</td>
<td>83%</td>
<td>93%</td>
<td>100%</td>
</tr>
</tbody>
</table>

- 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

Rylski B et al., JACC 2014

Diseases of the Aorta

How Does the Ascending Aorta Geometry Change When It Dissects?

![Graph showing changes in ascending aortic diameter before and after AADA onset.](image-url)

Rylski B et al., JACC 2014
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!

Dissection Risk

Operative Risk

- Patient Specific
- Surgeon Specific

- Diameter
- Pressure
- Material properties
Genetics

Aortic Wall Remodelling

Mechanical Response to Hemodynamic Forces

Mechanical Failure

Distinguish between rupture 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?
Novel Imaging Predictors of Aortopathy Progression

Acquired Cardiovascular Disease

Della Corte et al

Restricted cusp motion in right-left type of bicuspid aortic valves:
A novel imaging biopsy marker (J Thorac Cardiovasc Surg 2012;144:360-9)

Research Correspondence

Increased Growth Rates With Eccentric Systolic Flow

Correspondence

Cusp Opening Angle in left coronary view
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

<table>
<thead>
<tr>
<th>Predictor</th>
<th>β-Coefficient</th>
<th>Standard Error</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p Value</th>
<th>Predictability (Area Under ROC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>−31.9842</td>
<td>7.6473</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
<td>0.974</td>
</tr>
<tr>
<td>Diameter: aortic arch</td>
<td>0.1264</td>
<td>0.0322</td>
<td>1.135</td>
<td>1.065, 1.209</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Length: AR to iliac BF</td>
<td>0.2000</td>
<td>0.0606</td>
<td>1.211</td>
<td>1.085, 1.375</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>HVA: brachiocephalic</td>
<td>−0.0646</td>
<td>0.0241</td>
<td>0.937</td>
<td>0.894, 0.983</td>
<td>0.0072</td>
<td></td>
</tr>
</tbody>
</table>
The “Aortic Phenotype”

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

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.
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

Della Corte A, et al. EJCTS 2007;31:397-405
- Aortic stenosis
- Older age
- Hypertension
- RN type

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

80% dilatations

20% dilatations

Ascending phenotype

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

Alessandro Della Corte, MD, Ph.D., Ciro Bancone, MD, Ph.D., Marianna Buonocore, MD, Giovanni Dialetto, MD, Franco E. Covino, MD, Sabrina Mandra, MD, Giancarlo Scognamiglio, MD, Veronica D’Oria, MD, Marisa De Feo, MD, Ph.D.

Naples, Italy

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

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>14.0</td>
<td>3.2–62</td>
<td>0.001</td>
</tr>
<tr>
<td>Root phenotype</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RL type</td>
<td>7.0</td>
<td>2.0–24</td>
<td>0.002</td>
</tr>
<tr>
<td>Root phenotype</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RN type</td>
<td>20.0</td>
<td>1.3–76</td>
<td>0.03</td>
</tr>
<tr>
<td>Aortic regurgitation (any degree)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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


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
Valvulo-aortic Phenotype in BAV aortopathy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>In cases of BAV, surgery of the ascending aorta is indicated in case of:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• aortic root or ascending aortic diameter &gt;55 mm.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>• aortic root or ascending aortic diameter &gt;50 mm in the presence of other risk factors.</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>• aortic root or ascending aortic diameter &gt;45 mm when surgical aortic valve replacement is scheduled.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Beta-blockers may be considered in patients with BAV and dilated aortic root &gt;40 mm.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Because of familial occurrence, screening of first-degree relatives should be considered.</td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>In patients with any elastopathy or BAV with dilated aortic root (&gt;40 mm), isometric exercise with a high static load (e.g. weightlifting) is not indicated and should be discouraged.</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

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

*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
Thank you