Diseases of The Aorta 2016
Understanding & Approach

TAA, TAD, AAA, AAR

New York, Dec 10, 12016

No Disclosures

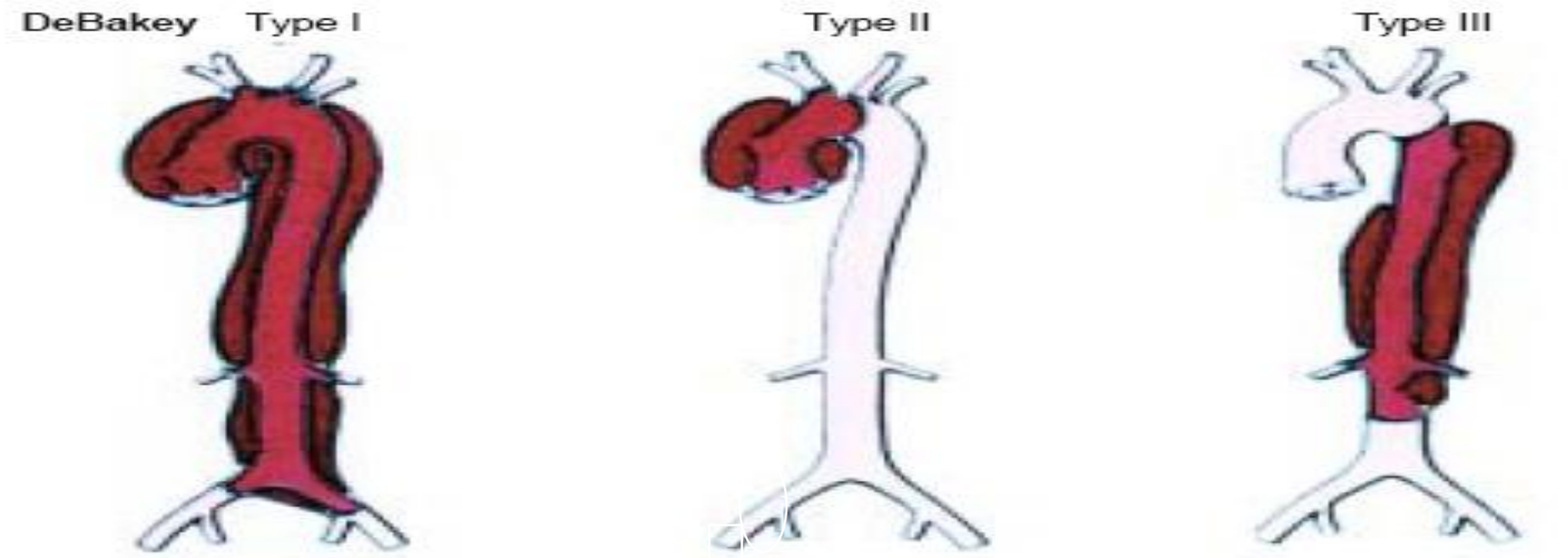
Understanding - TAA, TAD, AAA, AAR - 2016

- *Definition, Mortality, Imaging, ECM* *(4)*
- *Types, Demographics (TAA,TAD,AAA,AAR)* *(4)*
- *Pathogenesis (Marfan's a,b,c, BHA, AAA)* *(3)*
  - *Dysfunctional Structure* *(3)*
  - *Hemodynamics* *(4)*
  - *Approach to Hemodynamics* *(2)*
  - *Approach to Dysfunctional Structure* *(1)*
- *Interventional (TAA,TAD,AAA,AAR)* *(4)*

TAA: Th.Ao.An. –TAD: Th.Ao.Dis. – AAA: Abd.Ao.An – AAR: Abd,Ao.Rupt.

JZ Goldfinger, V Fuster et al., JACC 2014;64:1725

1). Classification of Thoracic Aortic Dissection (6 people per 100.000 per year)



DeBakey

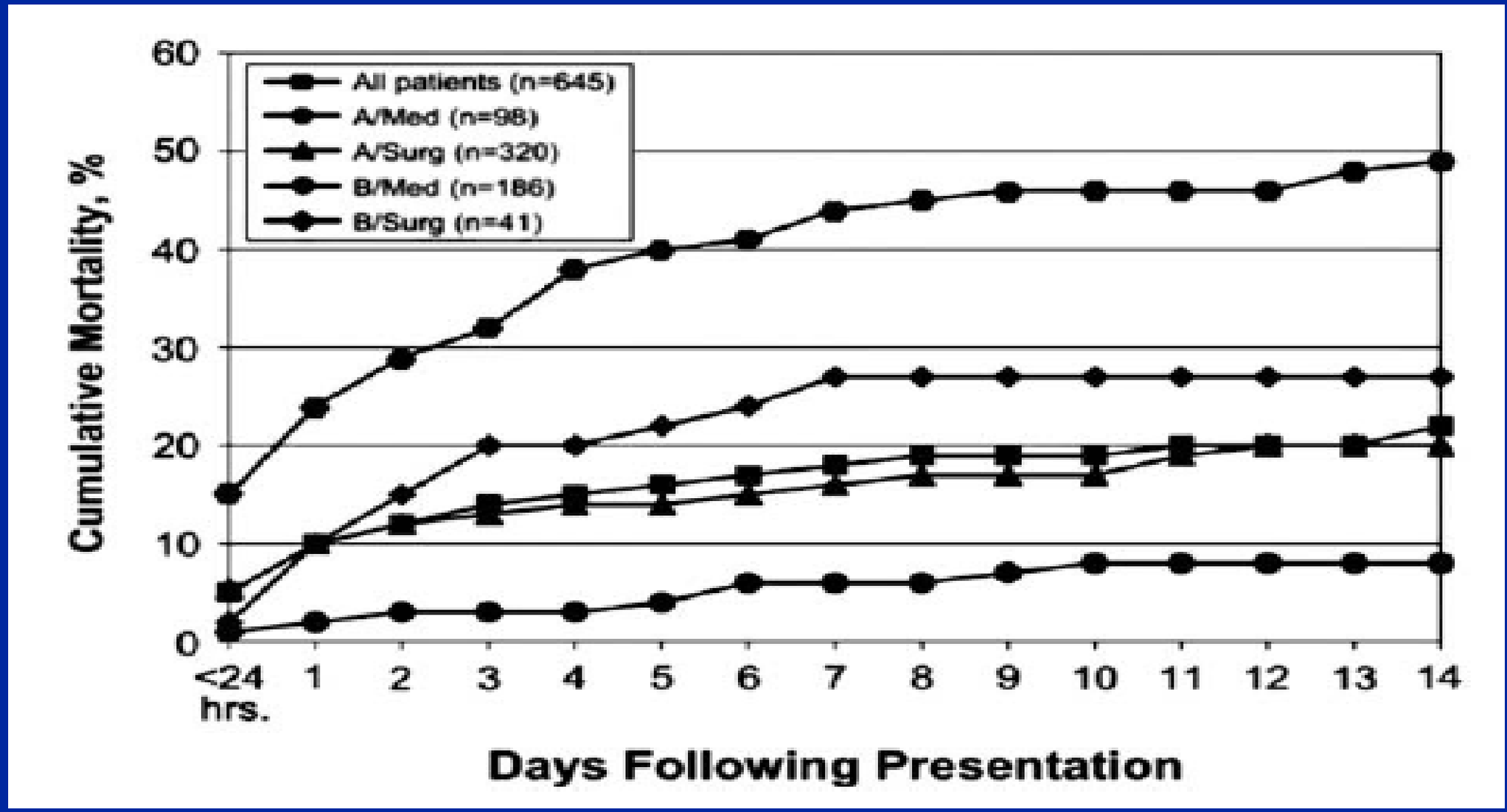
Type I	Originates in the ascending aorta, propagates at least to the aortic arch and often beyond it distally
Type II	Originates in and is confined to the ascending aorta
Type III	Originates in the descending aorta and extends distally down the aorta or rarely retrograde into the aortic arch and ascending aorta

Stanford

Type A	All dissections involving the ascending aorta, regardless of the site of origin
Type B	All dissections not involving the ascending aorta

Ramanath et. al. *Mayo Clin Proc*. 2009;84:465.
CA Nienaber et. al. *Circulation* 2003;108:628.

2) A 14-day Mortality In 645 Pts From IRAD Stratified By Medical And Surgical Treatment In TAD Type A & B



TA Mort
1% q.2h
4 Days

TB. S

TA. S

TB. M

IRAD (TT Tsai et. al.) Eur J Vasc Endov Surg 2009;37:149-Av 9h to Surgery

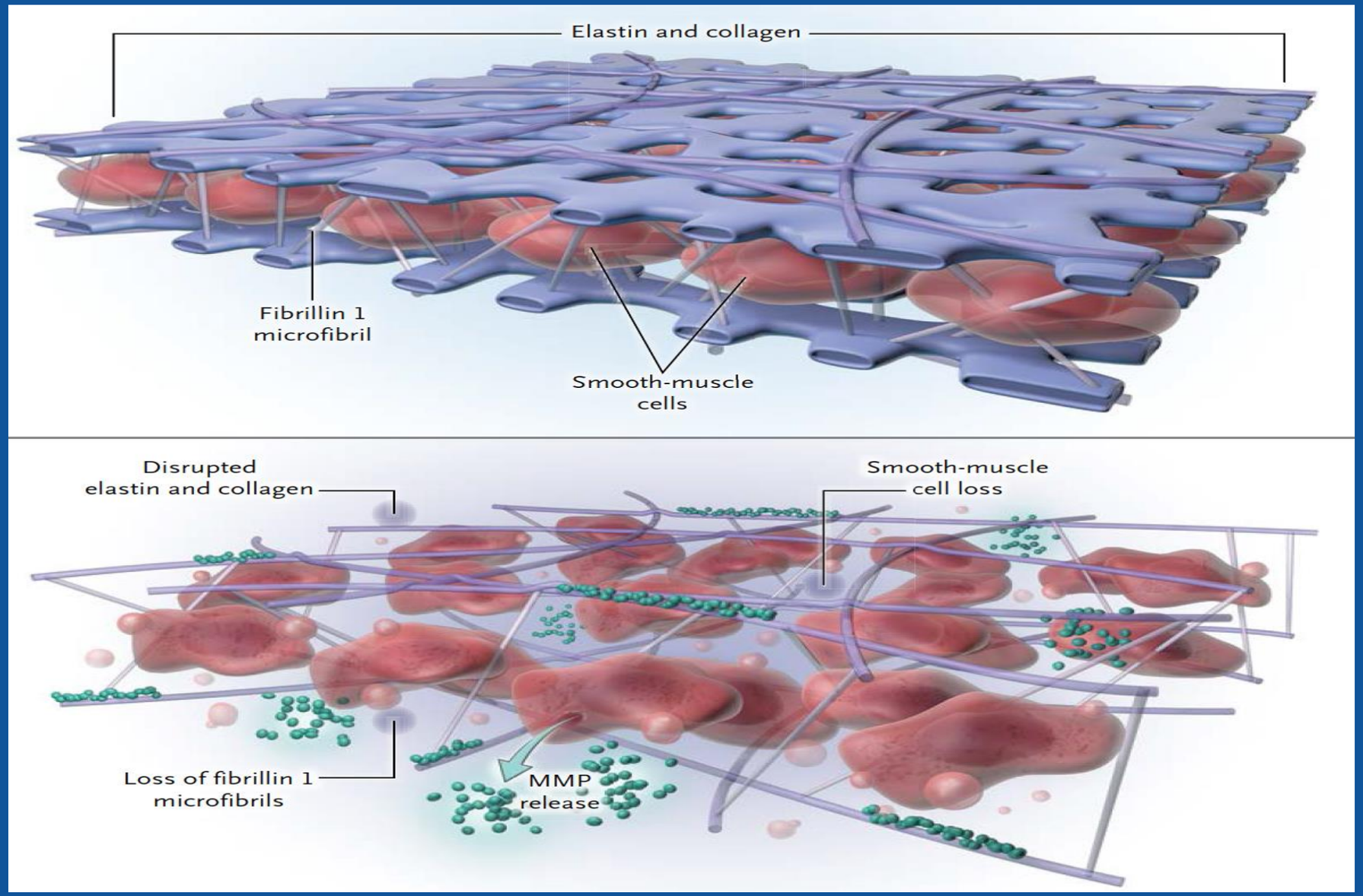
PG Hagan et. al. JAMA 2000;283:897

3) Imaging Modalities In The Diagnosis Of AAS

Feature of imaging modality	Angio	CT	MRI	TEE	TTE
Advantages					
Readily available	+	+++	+	+	+++
Quickly performed	+	+++	+	++	+++
Performed at bedside	–	–	–	+++	+++
Noninvasive	–	+++	+++	+	+++
No iodinated contrast	–	–	+++	+++	+++
No ionizing radiation	–	–	+++	+++	+++
Low cost	+	++	++	++	+++
Diagnostic performance					
Sensitivity	++	+++	+++	+++	+
Specificity	+++	+++	+++	+++	++
Detection of intramural haematoma	–	+++	+++	++	–
Detection of site of intimal tear	++	+++	+++	++	+
Detection of aortic regurgitation	+++	–/+*	++	+++	+++
Detection of coronary artery involvement	+++	+/+++*	+	++	–
Detection of pericardial effusion	–	++	++	+++	+++
Detection of branch vessel involvement	+++	+++	++	+	+
Detection of periaortic haemorrhage	–	+++	+++	+	–

A Evangelista et. al. Nat. Rev. Cardiol. 2013;10:477 – End Doing Both

Pathophysiological Features of Marfan's & Bicuspid Aortopathy



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

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	1).TAA,	2).TAD,	3). AAA,	4). AAR
		2. TAA	1. TAA-Marfan's a,b,c	3. AAA,
Prevalence		1.25%	1 in 10,000	5%
Pathogenesis		Genetic Predisposition Bicuspid Valve Hypertension Atherosclerosis	Genetic Predisposition	Genetic Predisposition Male Hypertension Smoking
Histology		Cystic medial Necrosis	Cystic medial Necrosis Apoptosis	Inflammatory Infiltrate, VSMC
Rupt./ Disect.		+	+++	++

SL Liao, V Fuster et al. Nat. Rev. Card. 2012

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JZ Goldfinger, V Fuster et al., JACC 2014;64:1725

NORMAL AORTA

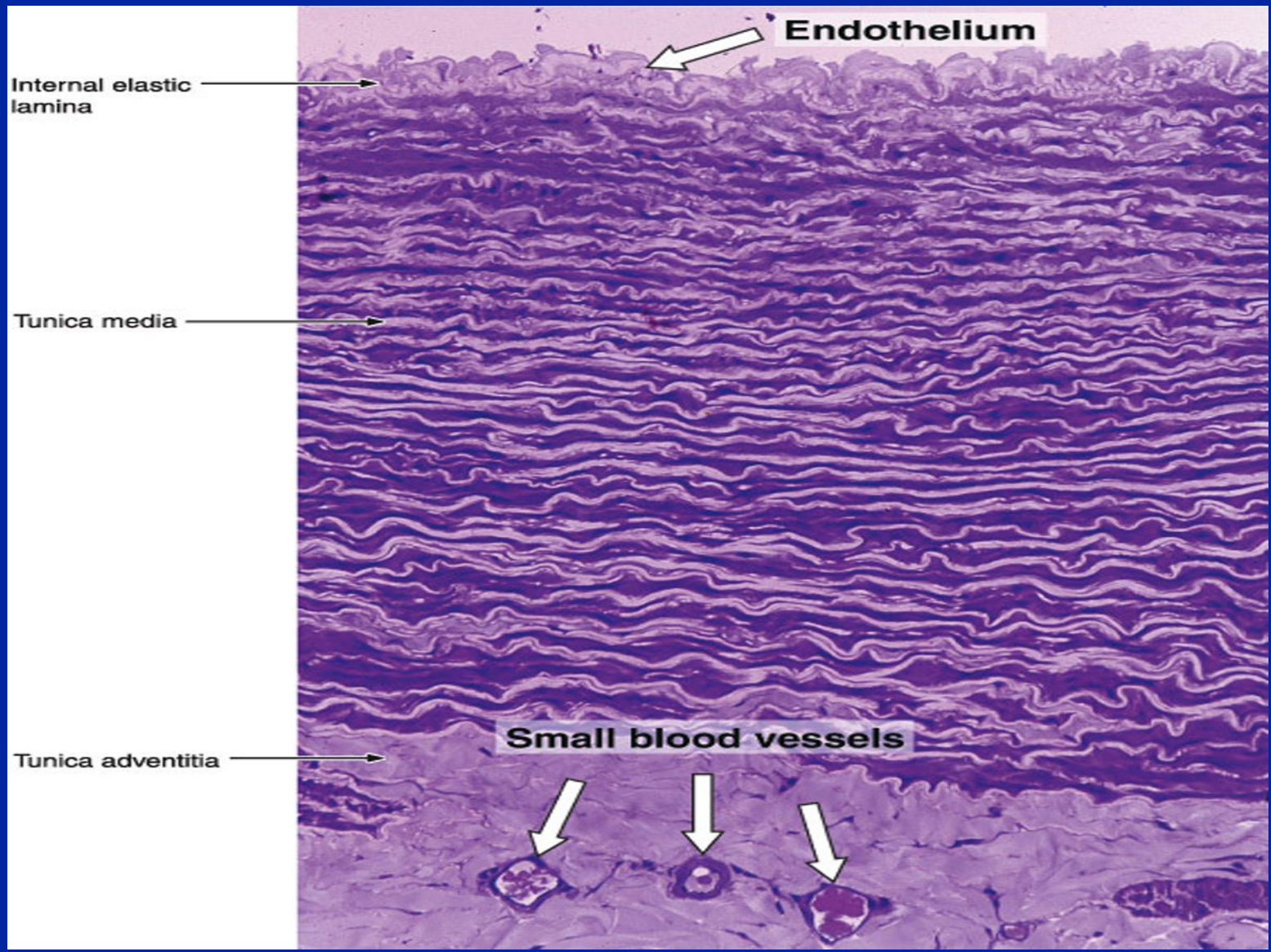
STRUCTURE

ELASTIN
Fibrillin
TGF-b
MMPs

SMC

COLLAGEN

VASA VASORUM



FUNCTION

DISTENSION

ACTIVITY
> Mucoid

RESISTANCE

NUTRITION

Junquiera LC, Carneiro J:
Basic Histology Text and Atlas, 11th ed. McGraw-Hill Access Medicine. 2005.

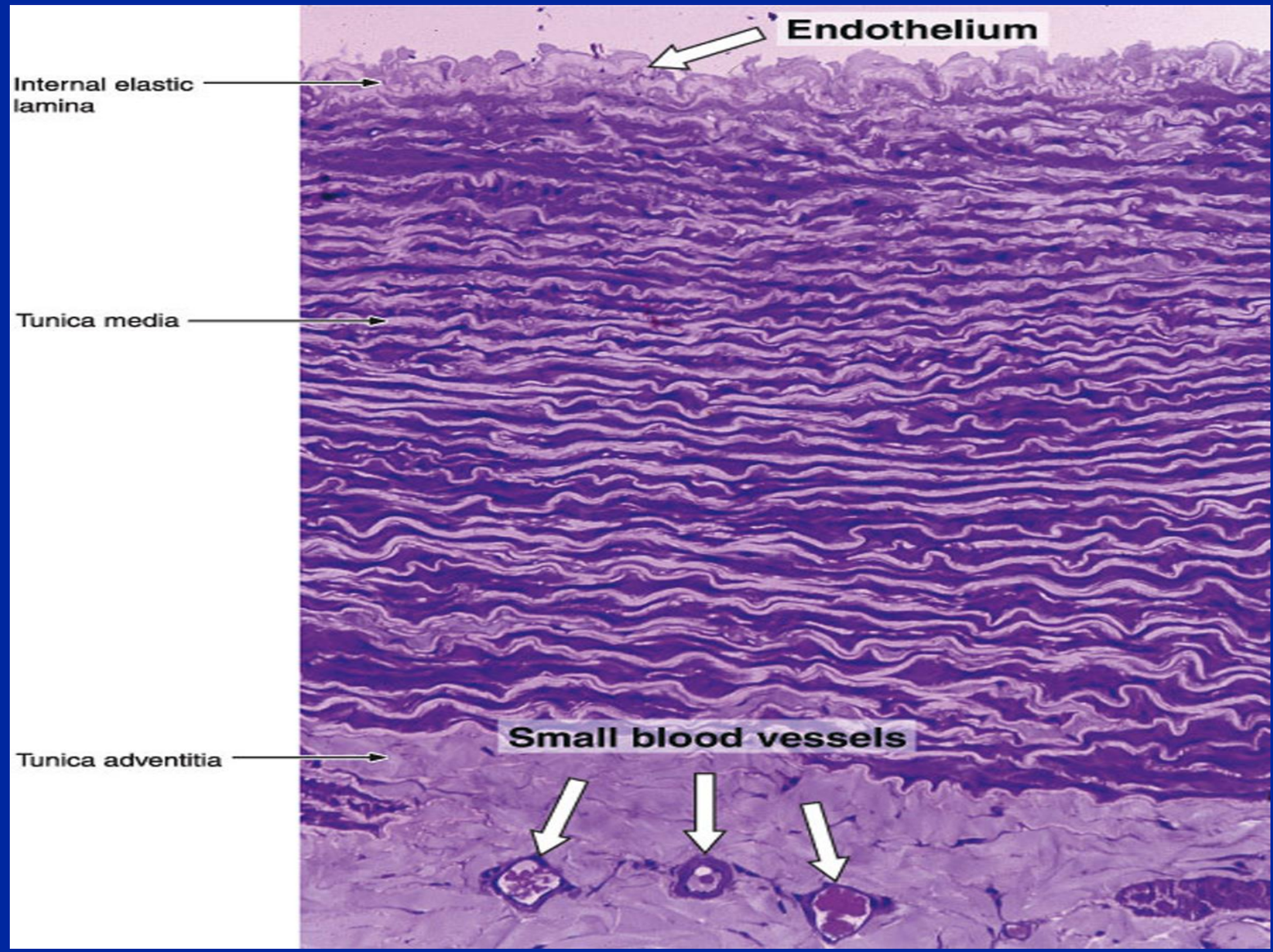
STRUCTURE — AORTIC ANEURYSM - MFS — DYSFUNCTION

< Fibrillin
> TGF
> MMPs
< ELASTIN

>SMC
< SMC

< COLLAGEN

< VASA VASORUM



< DISTENSION

> ACTIVITY
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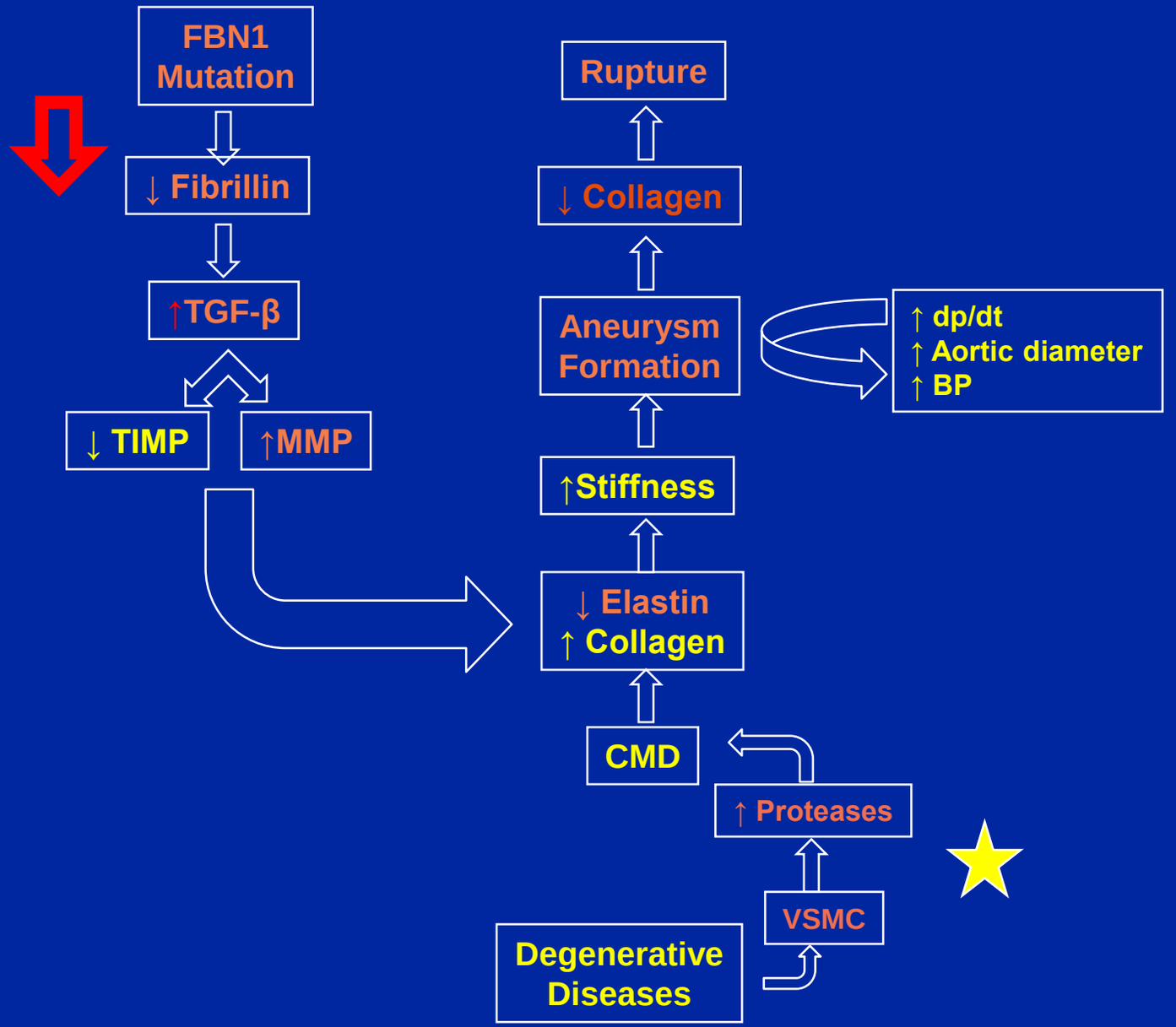
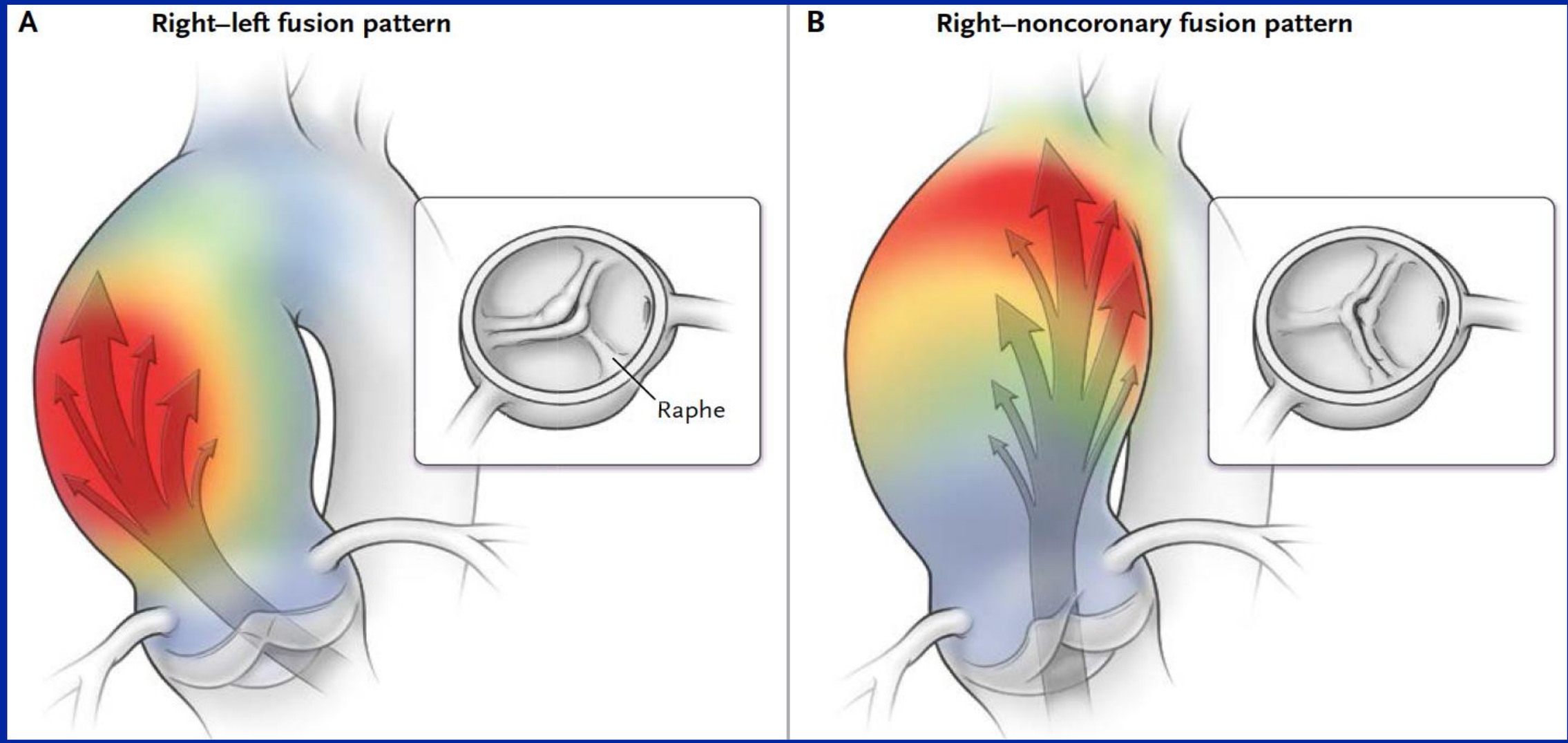
Basic Histology Text and Atlas, 11th ed. McGraw-Hill Access Medicine. 2005.

TAA/TAD – MARFAN'S a,b,c & 2BHA ★



JZ Goldfinger, V Fuster et al., JACC 2014;64:1725

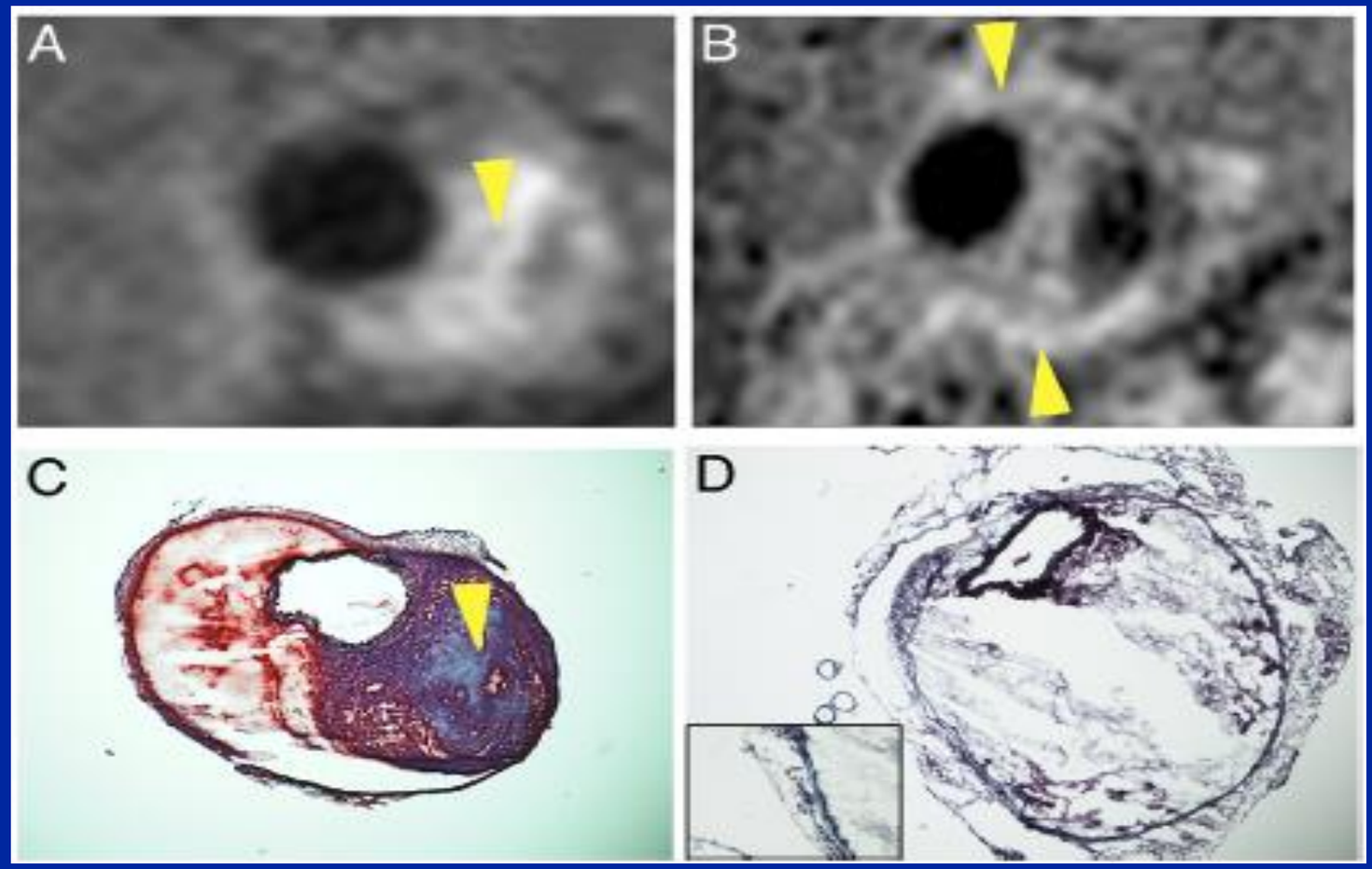
Bicuspid Aortic Valve - Morphology Features That Influence the Pattern of Aortopathy

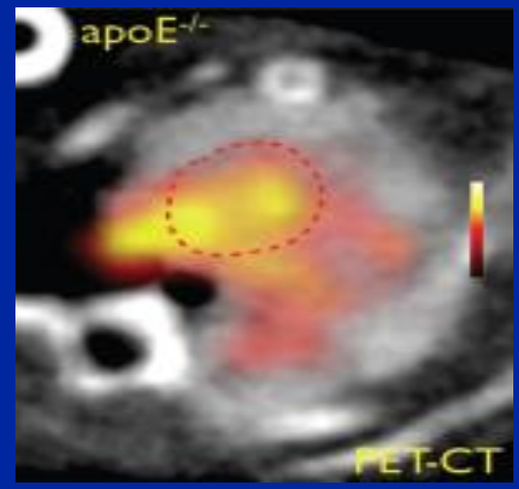


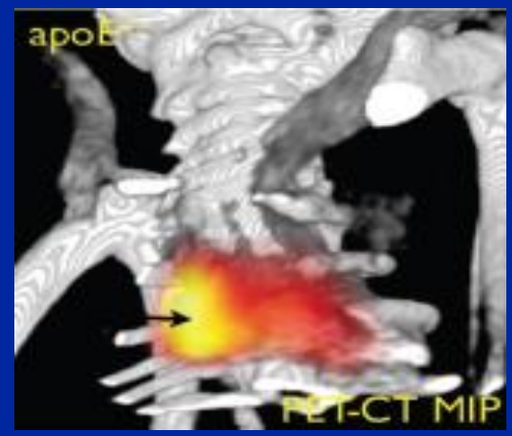
S Verma et. al. N Engl J Med 2014;370:1920 – Types 1,2,3

R Mahadevia et. al. Circulation. 2014;129:673 - Detail

Abdominal Aortic Aneurysm - MRI Imaging
Mouse Model and Nanoparticle PET-CT







J Swedenborg et. al. Arterioscler Thromb Vasc Biol. 2011;31:73

T Duellman et al. Circ Cardiov. Genet 2012; 5:529 (Marshfield, WI) – MMP 9

M Nahrendorf, Rweissleder et. al. ATVB. 2011;31:750

A Klink, V Fuster, ZA Fayad et. al. J Am Coll Cardiol 2011;58:2522

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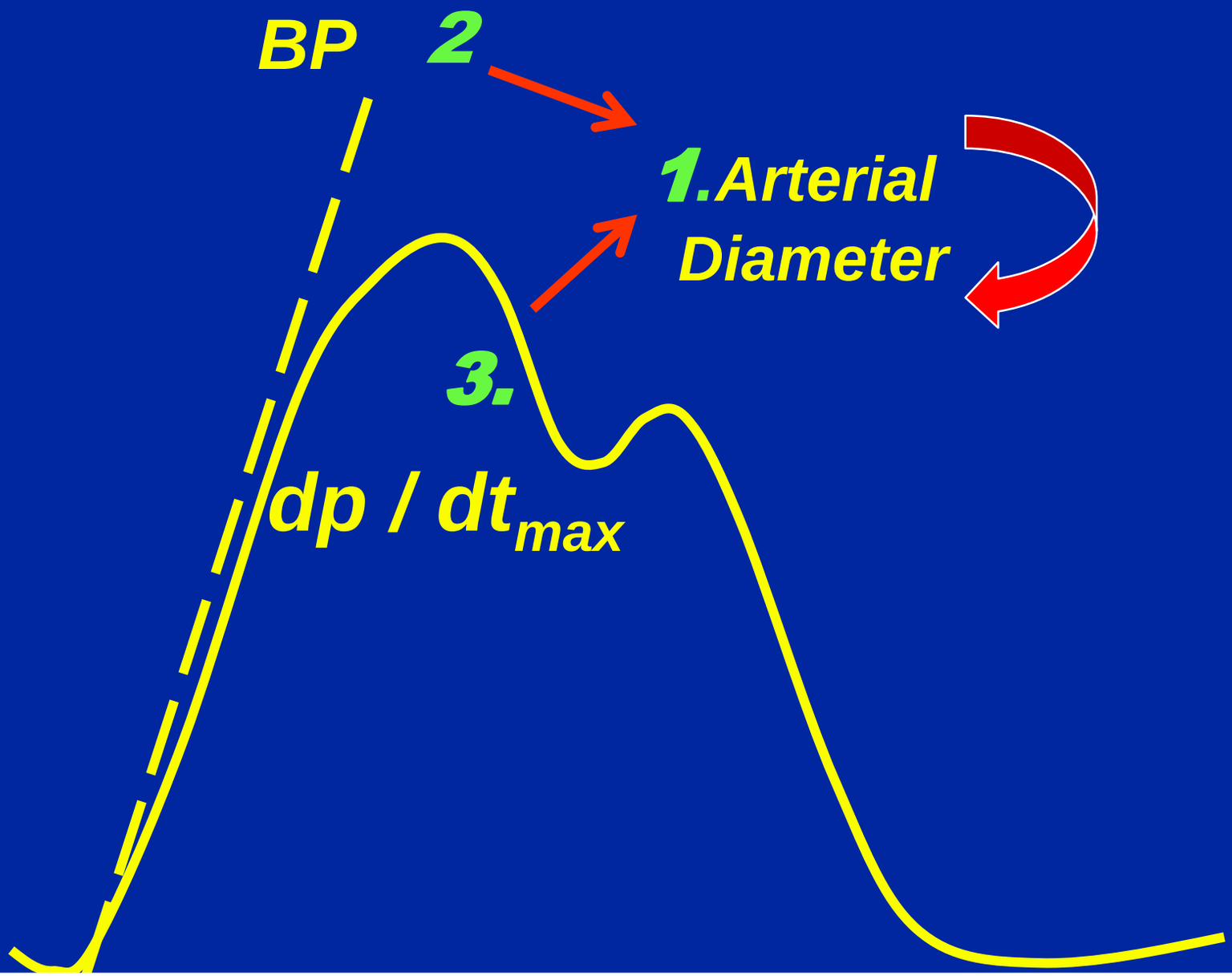
Hemodynamic Frs - Dilatation To Dissection



1-EK Prokop, RF Palmer, MW Wheat. Circ Res 1970; 27:121 – TURKEY DISSECTION

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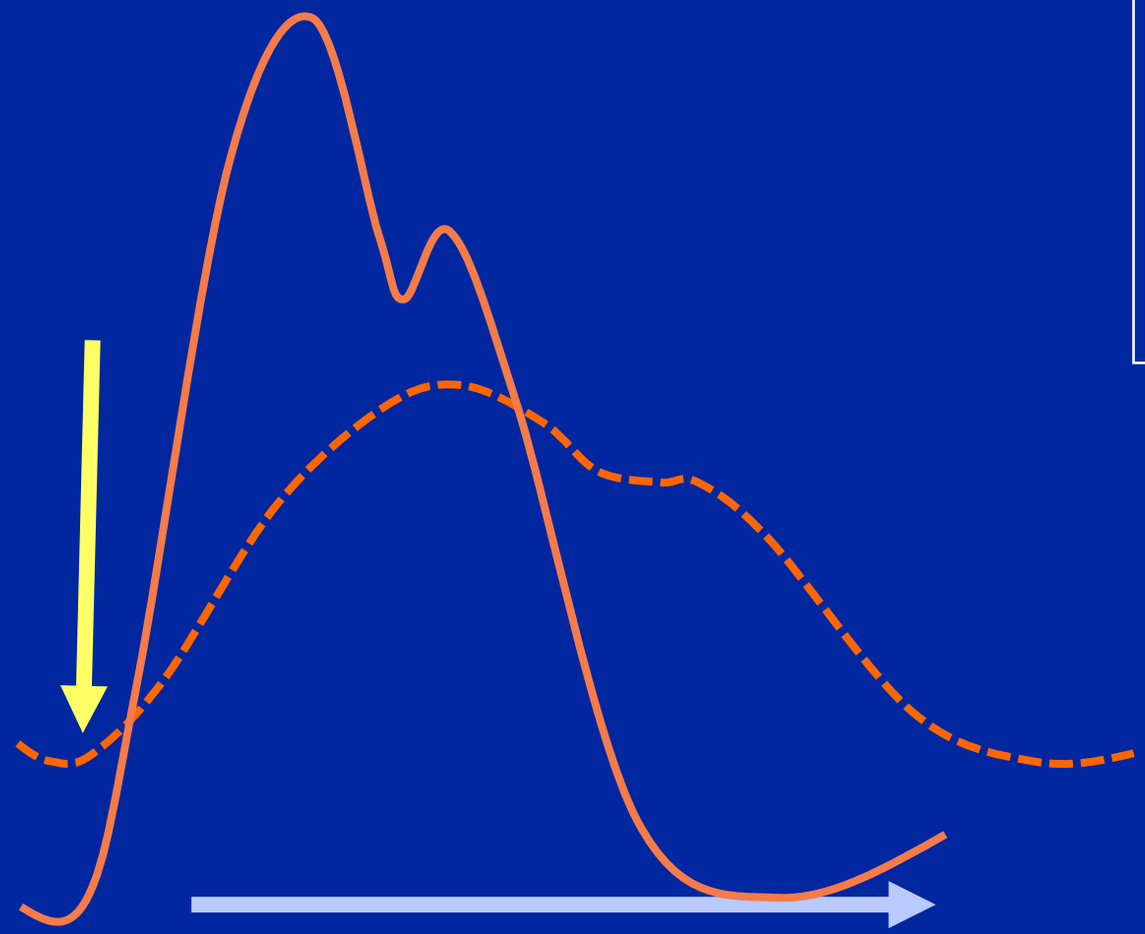
TAD – Hemodynamic Approach



Baseline

1) Vasodilator
(i.e., Nitroprusside)

(2) Beta blockade

Time

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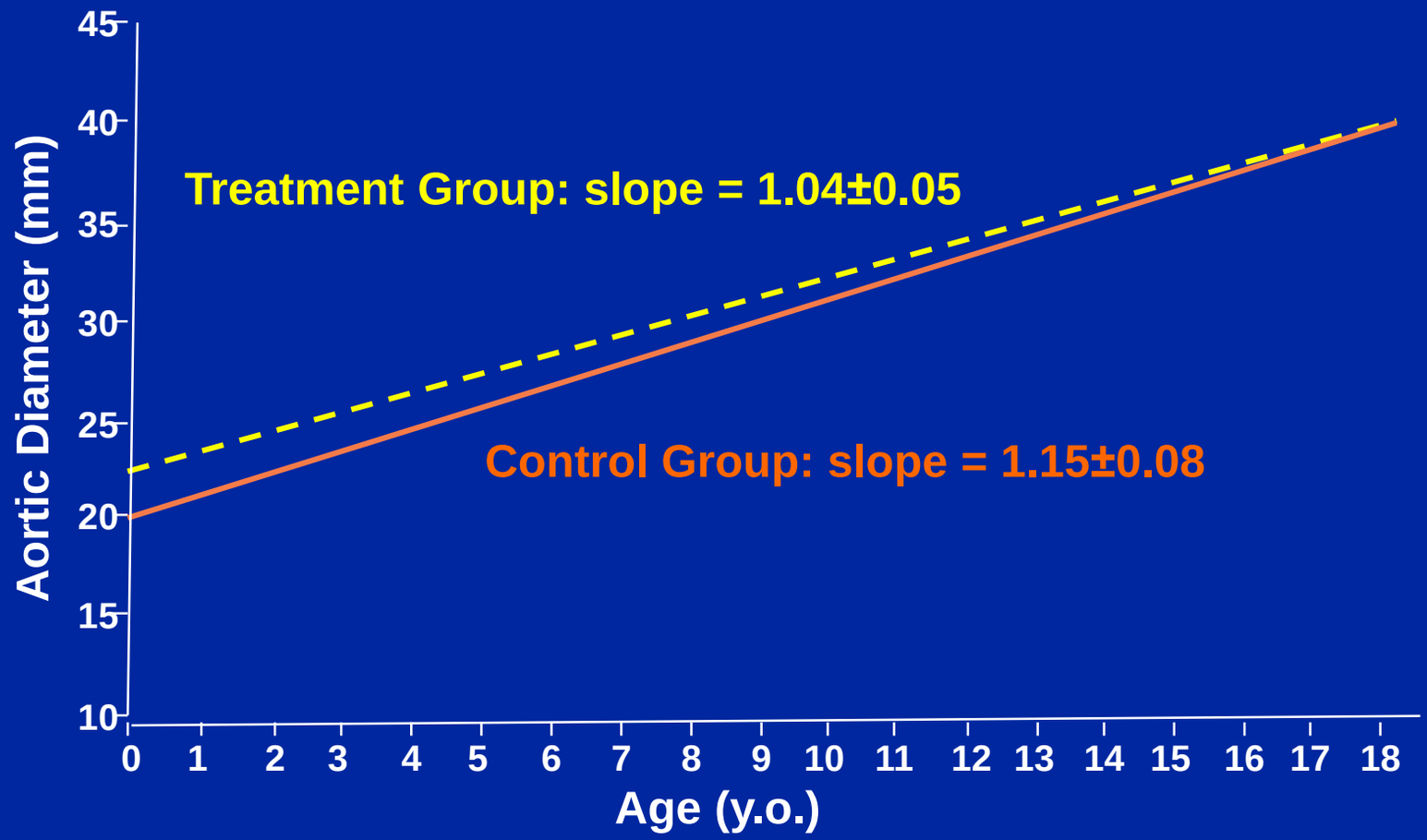
MFS - IMPACT OF β BLOCKERS ON AORTIC ROOT DIAMETER



M Ladouceur et al., AJC 2007; 99:406 (Paris)

1a) TAA in Marfan's (and Other?) - ARBs Look Promising

COMPARE: evaluated the effect of losartan on aortic dilatation rate in adults with Marfan syndrome (MFS). Patients with MFS have an increased risk of life-threatening aortic complications, mostly preceded by aortic dilatation. A total of 233 patients (47% female) underwent randomization to losartan 50-100mg/d (n=116) or no additional treatment (n=117). Follow-up was 3.1 ± 0.4 years.

End Points	Losartan	Control	p
1. Aortic-root enlargement (mm)	0.77	1.35	0.014
No aortic-root growth (%)	50	31	0.022

2. Previous root replacem.: significant lower aortic arch expansion

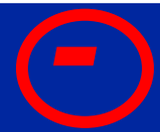
MARFAN SARTAN: 300 patients, 1ary EP-root diameter, 2ary EP-clinical

M Groenink et al., EHJ 2013; Aug 21 – Netherlands

1b) Atenolol vs Losartan in Children and Young Adults with Marfan's Syndrome

We conducted a randomized trial comparing losartan with atenolol in children and young adults with Marfan's syndrome. The primary outcome was the rate of aortic-root enlargement, over a 3-year period. Secondary outcomes included the rate of change in the absolute diameter of the aortic root; the rate of change in aortic regurgitation; the time to aortic dissection, aortic-root surgery, or death; somatic growth; and the incidence of adverse events. A total of 21 clinical centers enrolled 608 participants, 6 months to 25 years of age (mean [±SD] 11.5±6 years. We found no significant difference in the rate of aortic-root dilatation between the two treatment groups over a 3-year period.

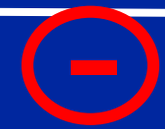
RV Lacro et al., NEJM 2014; 371:2061 – American Study



1c). Marfan Sartan: A Randomized, Double-Blind, Placebo-Controlled Trial

A double-blind, randomized, multi-centre, placebo-controlled, add on trial comparing Losartan (50 mg when < 50 kg, 100 mg otherwise) vs. placebo in patients with MFS according to Ghent criteria, age > 10 years old, and receiving standard therapy. 303 patients, mean age 29.9 years old, were randomized. The two groups were similar at baseline, 86% receiving β-blocker therapy. The median follow-up was 3.5 years. Losartan was able to decrease blood pressure in patients with MFS but not to limit aortic dilatation during a 3-year period in patients > 10 years old. β-blocker therapy alone should therefore remain the standard first line therapy in these patients.

O Milleron et al., Eur Heart J 2015; 36:2160 – French Study



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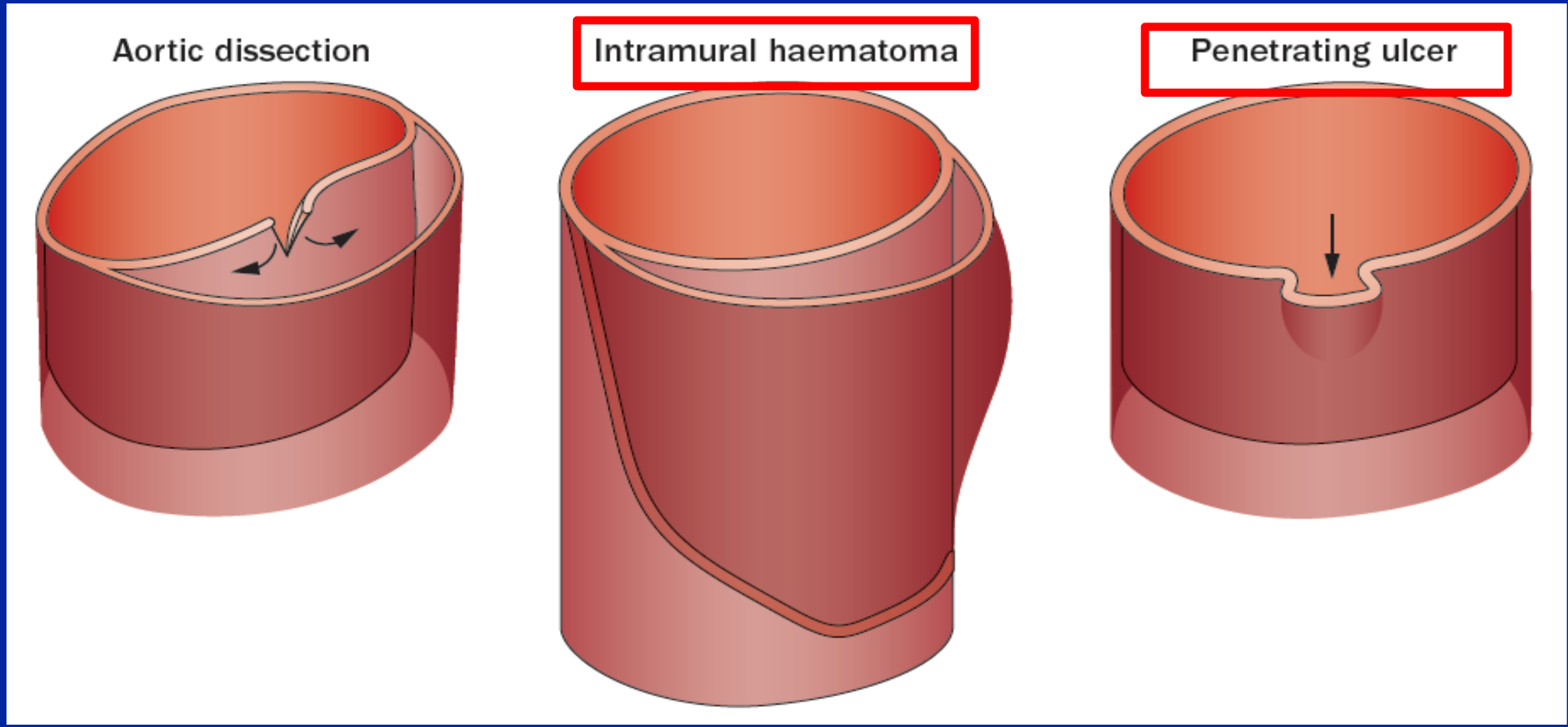
1) TAA - Indications For Surgery

- ≥ 40 mm with indication for elective AVR (BAV?)
- ≥ 45 mm in MFS, NSTAA?
- ≥ 50 mm in BAV (?)
- ≥ 55 mm for an ascending aortic aneurysm,
- ≥ 60 mm for a descending aortic aneurysm;
- ≥ 70 mm in high-risk comorbidities;
- Growth rate ≥ 10 mm per year in <55 mm diameter
- Recurrent symptoms, Evidence of proximal dissect.

L Cozijnsen et al., Circ 2011; 123:924
ACC/AHA Circulation. 2016;133:680

2) Contained Acute Aortic Syndrome



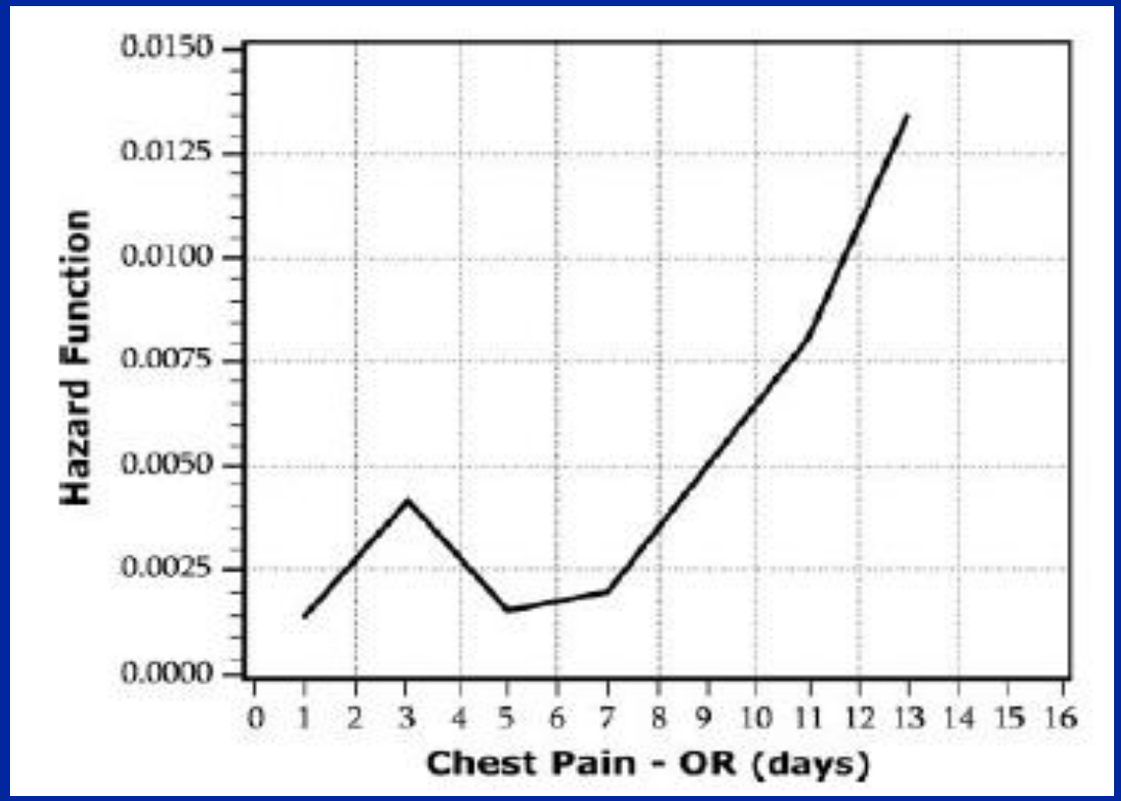
RE Clough et. al. Nat. Rev. Cardiol. 2015;12:103

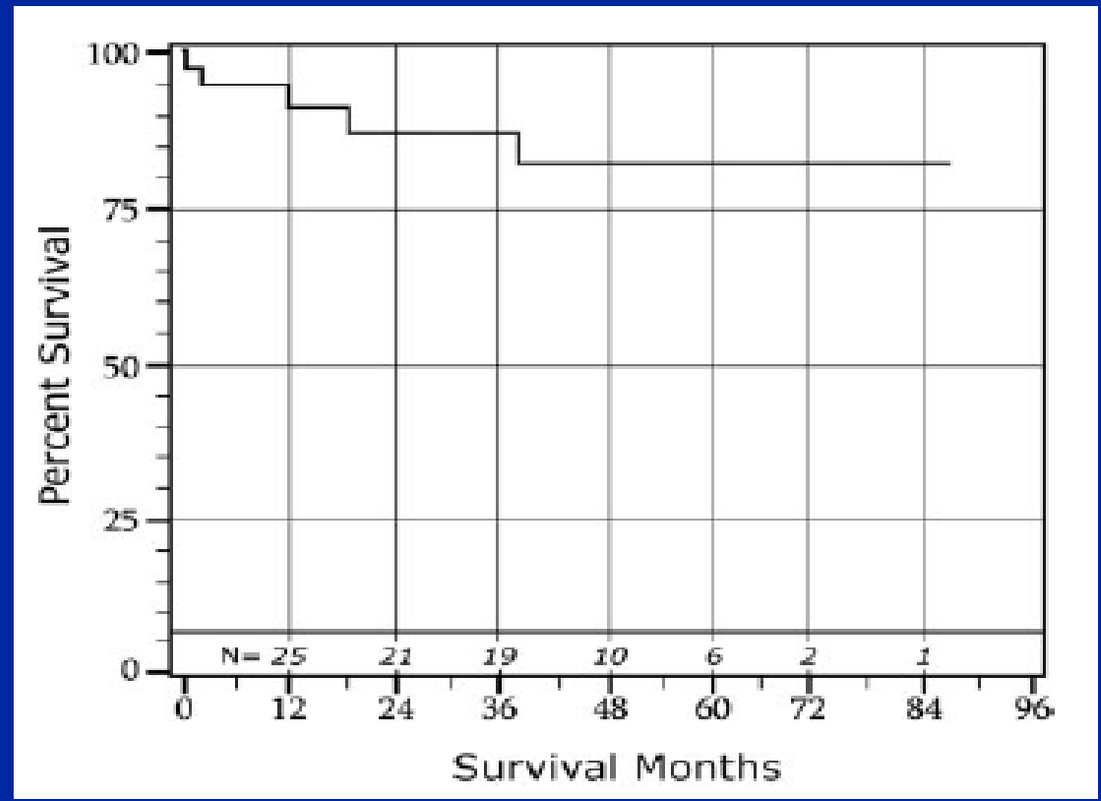
RR Baliga et. al. J Am Coll Cardiol Img 2014;7:406

6-15% - CT / MR Diameter 16 mm, Rupture within 10 days

Acute Type A Intramural Hematoma

Analysis of Current Management Strategy



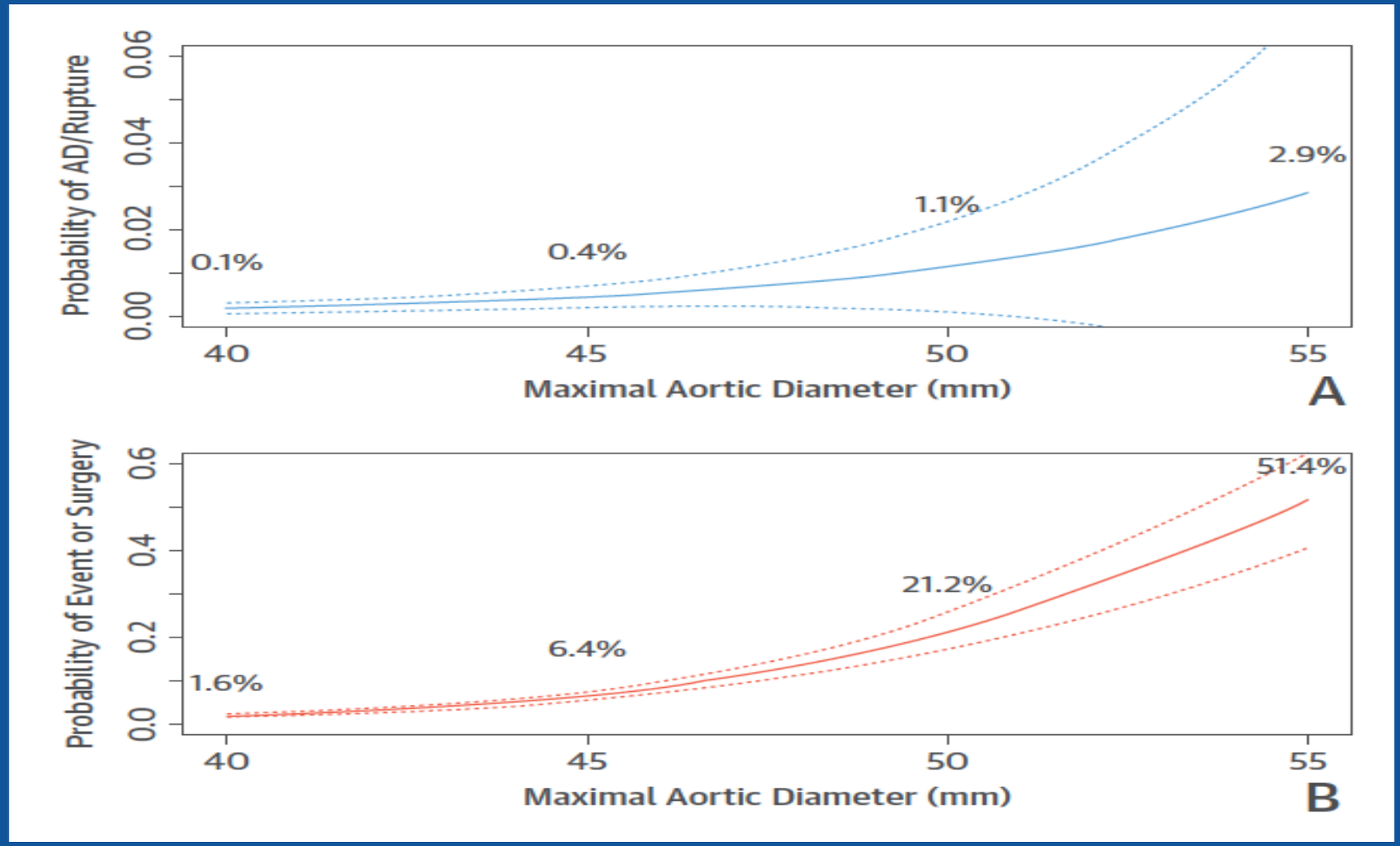


Best cutoff to Predict Events: 16 mm (Hematoma) - Often Type A

AL Estrera et al., J Thorac Cardiovasc Surg 2015; 149:137 (Houston)

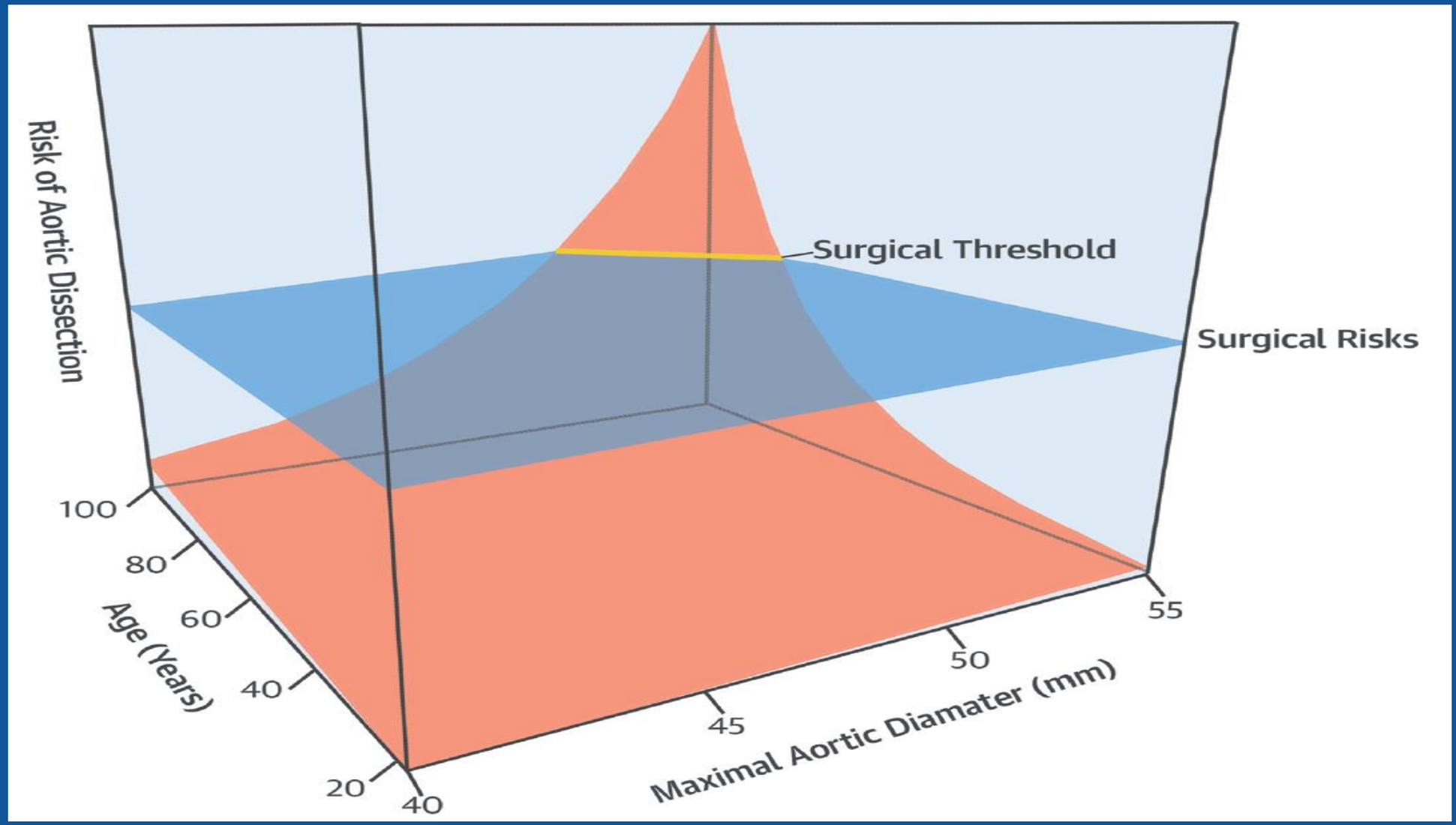
No mortality occurred within 3 days of presentation. Mortality with IMH did not differ from typical dissection (10.9% vs 14.7%).

3a). Aortic Dissection and/or Rupture, and Composite of Event & Surgery Within 5 Years



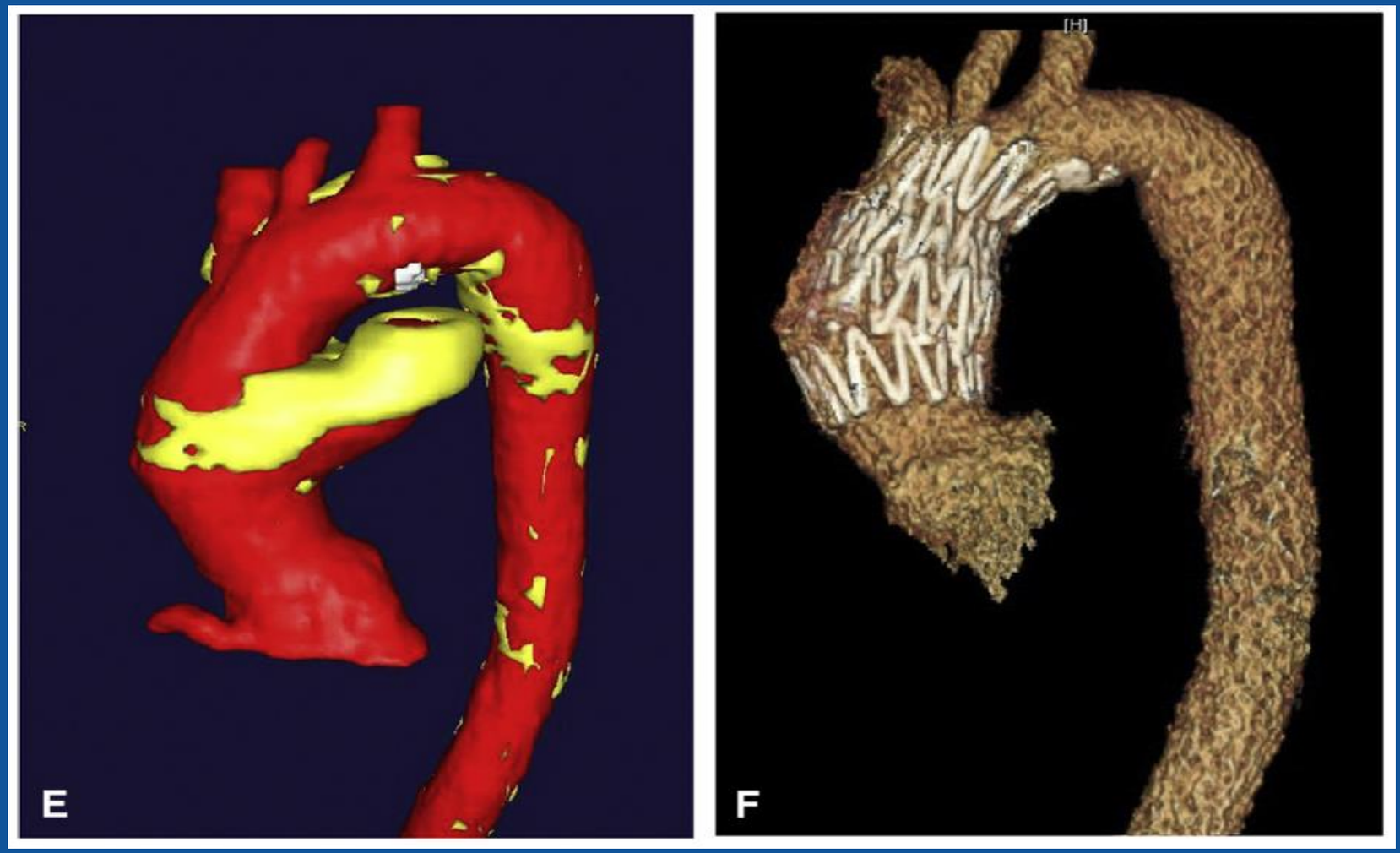
JB Kim et. al. J Am Coll Cardiol 2016;68:1209

Dissection in Ascending Aortic Aneurysms: Risk Threshold



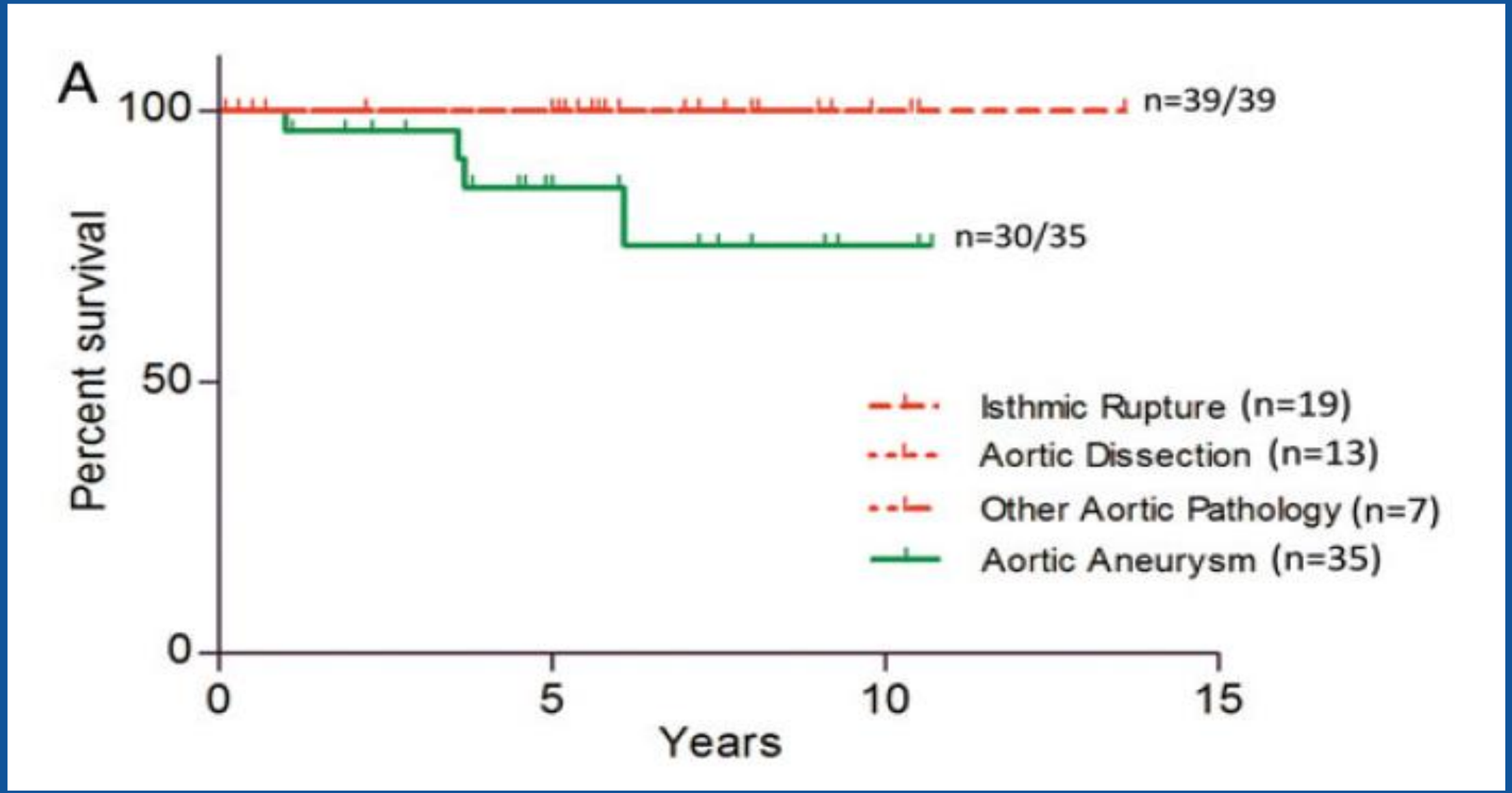
JB Kim et. al. J Am Coll Cardiol 2016;68:1209

3b) Endovascular Repair Of The Asc Aorta In Pts At High Risk For Open Repair



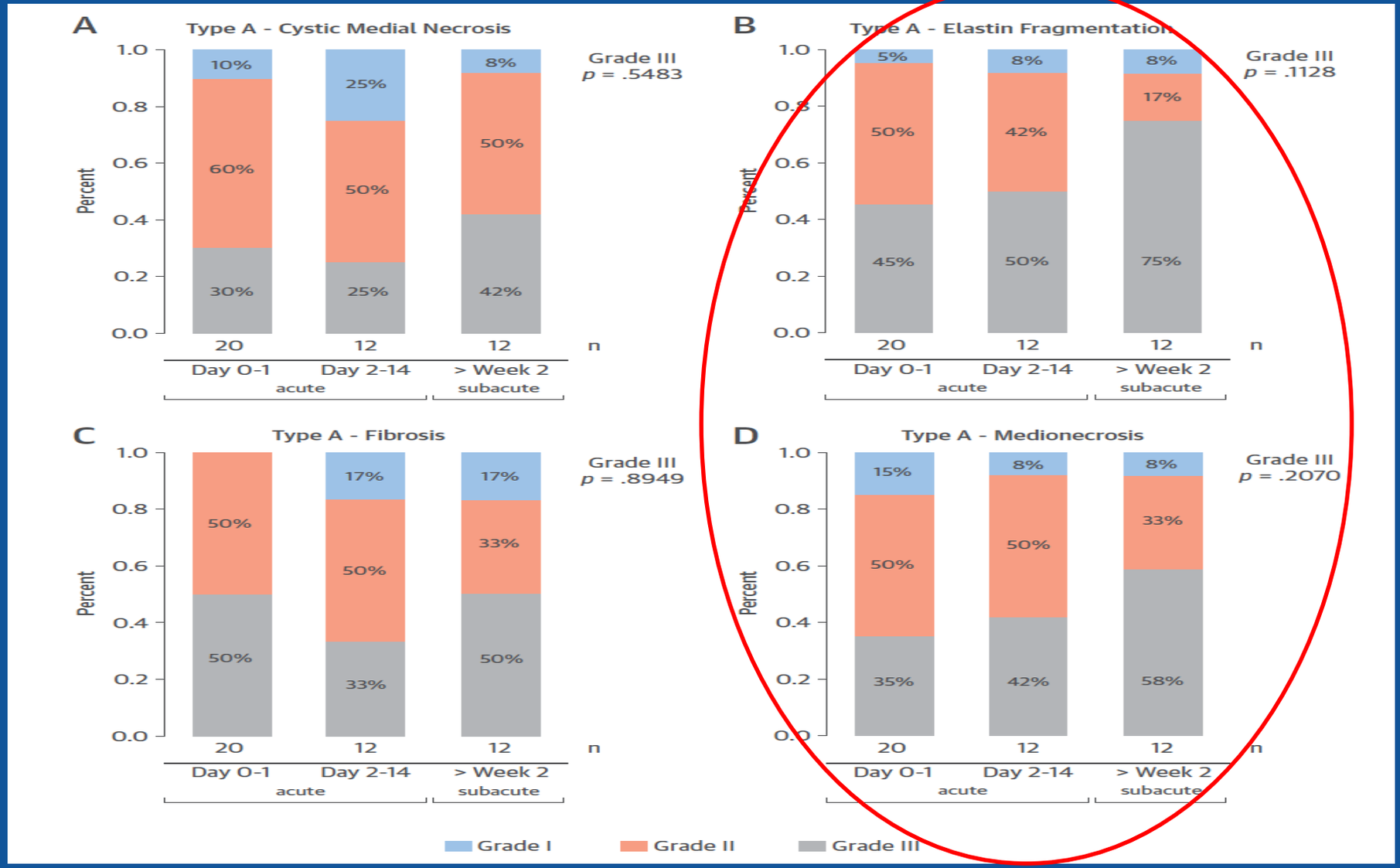
P Vallabhajosyula et. al. JTCS 2015;149:S144

Survival & Different Indications For TEVAR



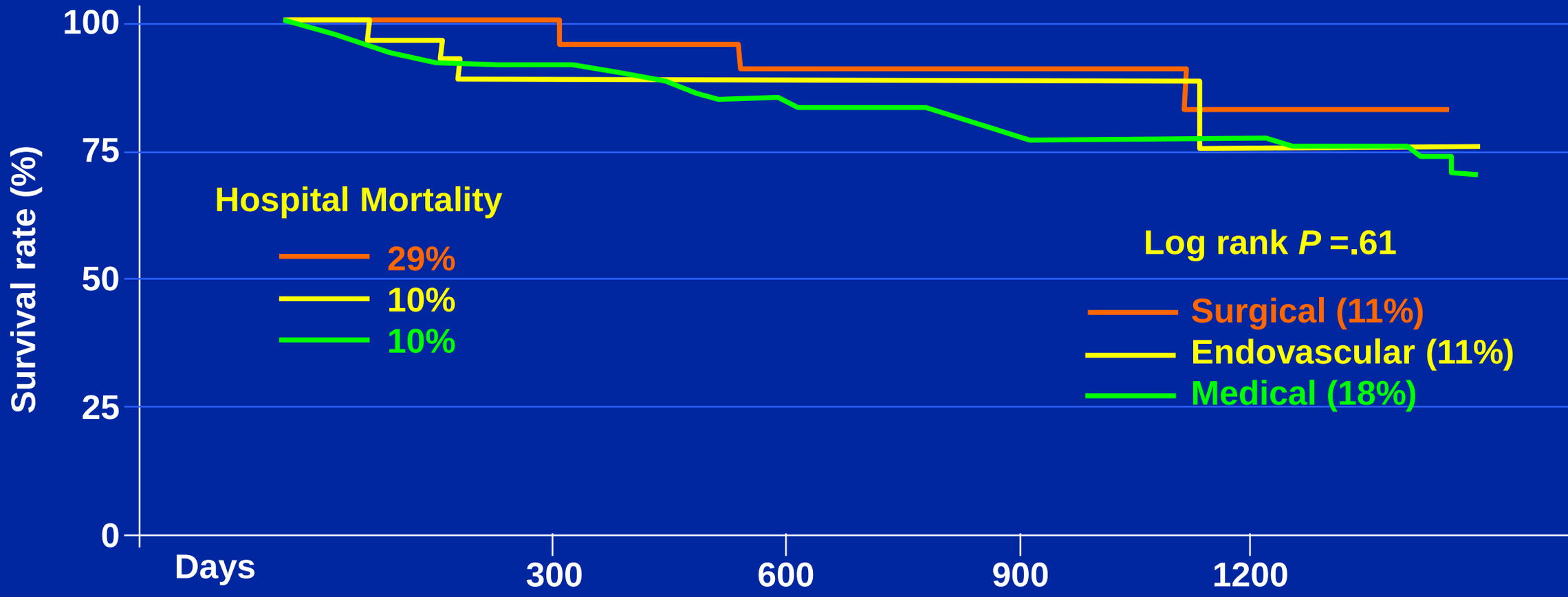
C Dufour et. al. Eur J Cardio-Thoracic Surgery. 2015;48:923

4). Histopathology Changes in Type A Dissection Over Time



S Peterss et. al. J Am Coll Cardiol 2016;68:1054

1). Type B Dissection – Survival Curve (N=300)



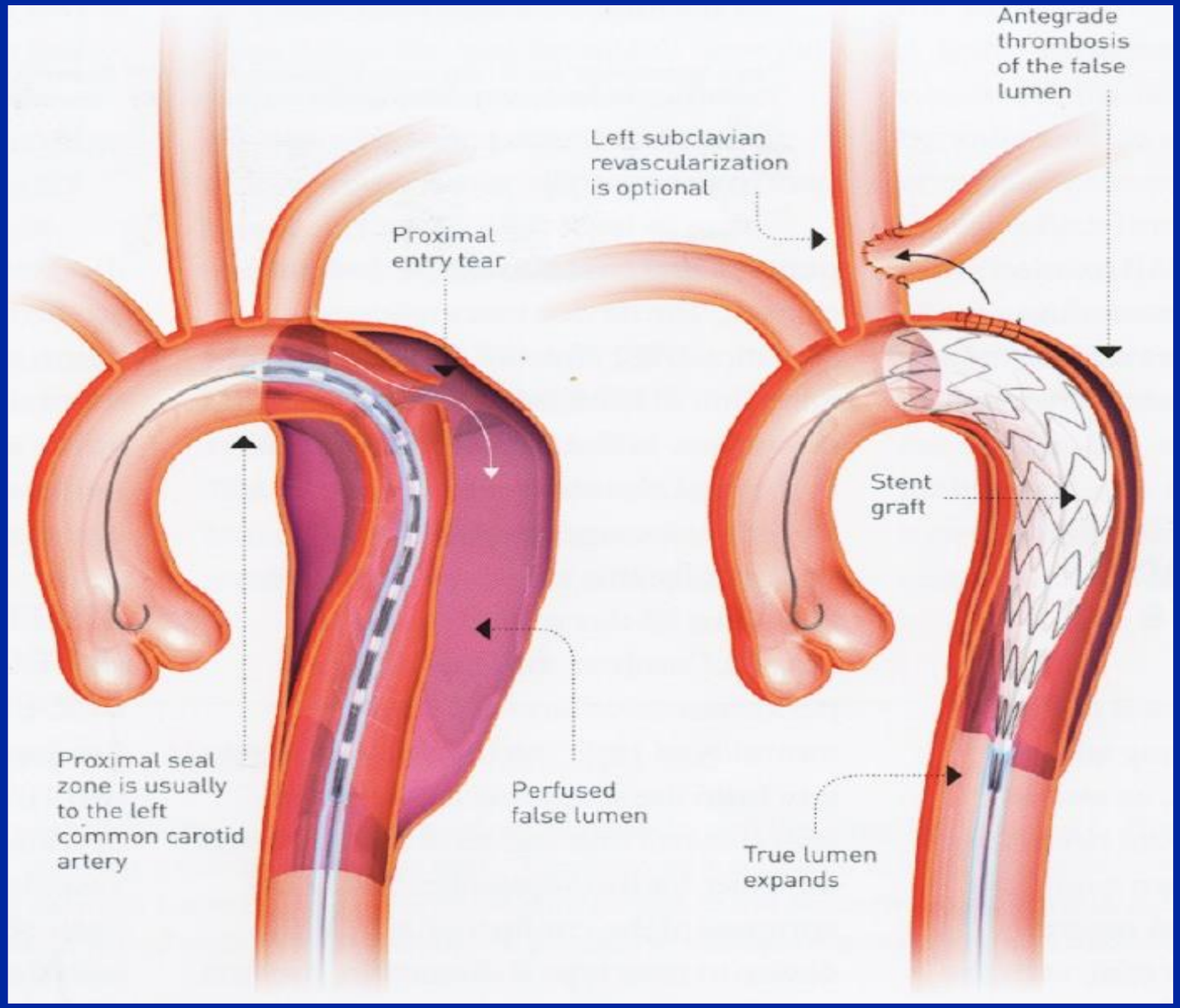
Worst Prognosis: Hypotension, Pleural Effusion, Renal Failure

Refractory Pain & Hypertension

IRAD (Tsai TT et al.) Circulation 2006; 114:2226

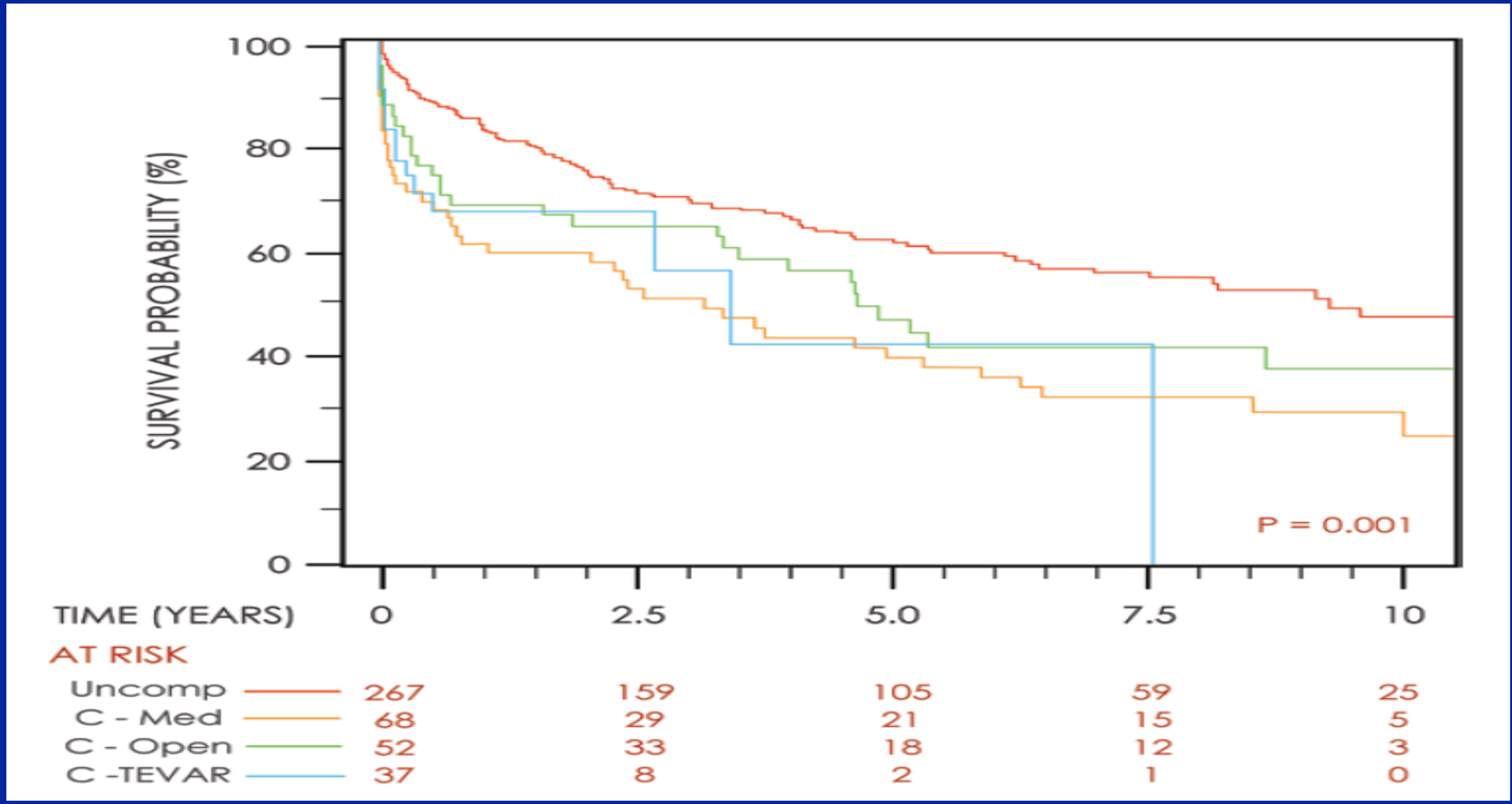
IRAD (S Trimarchi et al.) Circulation 2010; 122:1283

2). Site of TEVAR Implementation



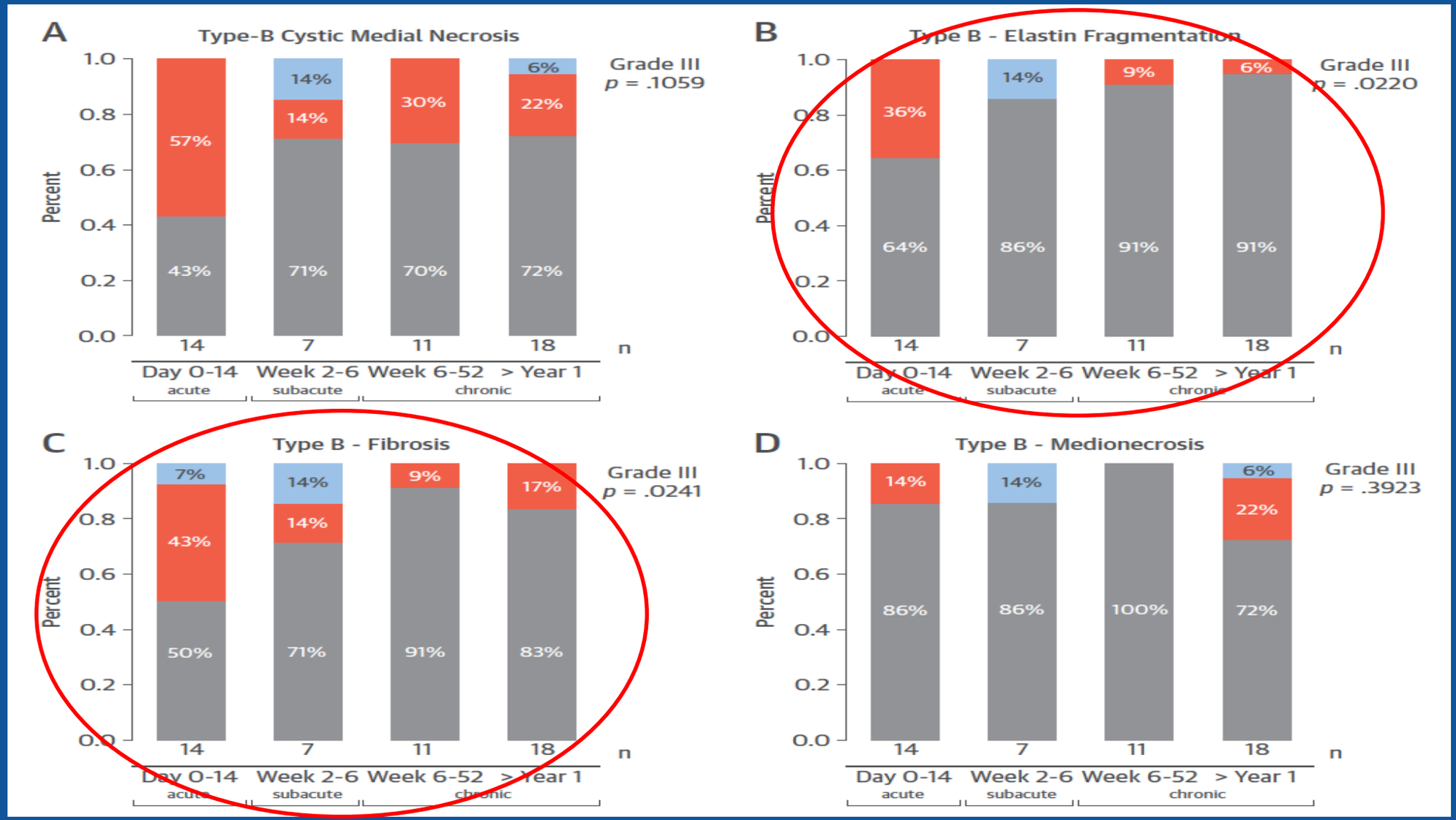
RP Cambria. Advances at Mass General. 2015

Outcomes of Patients With Acute Type B Aortic Dissection



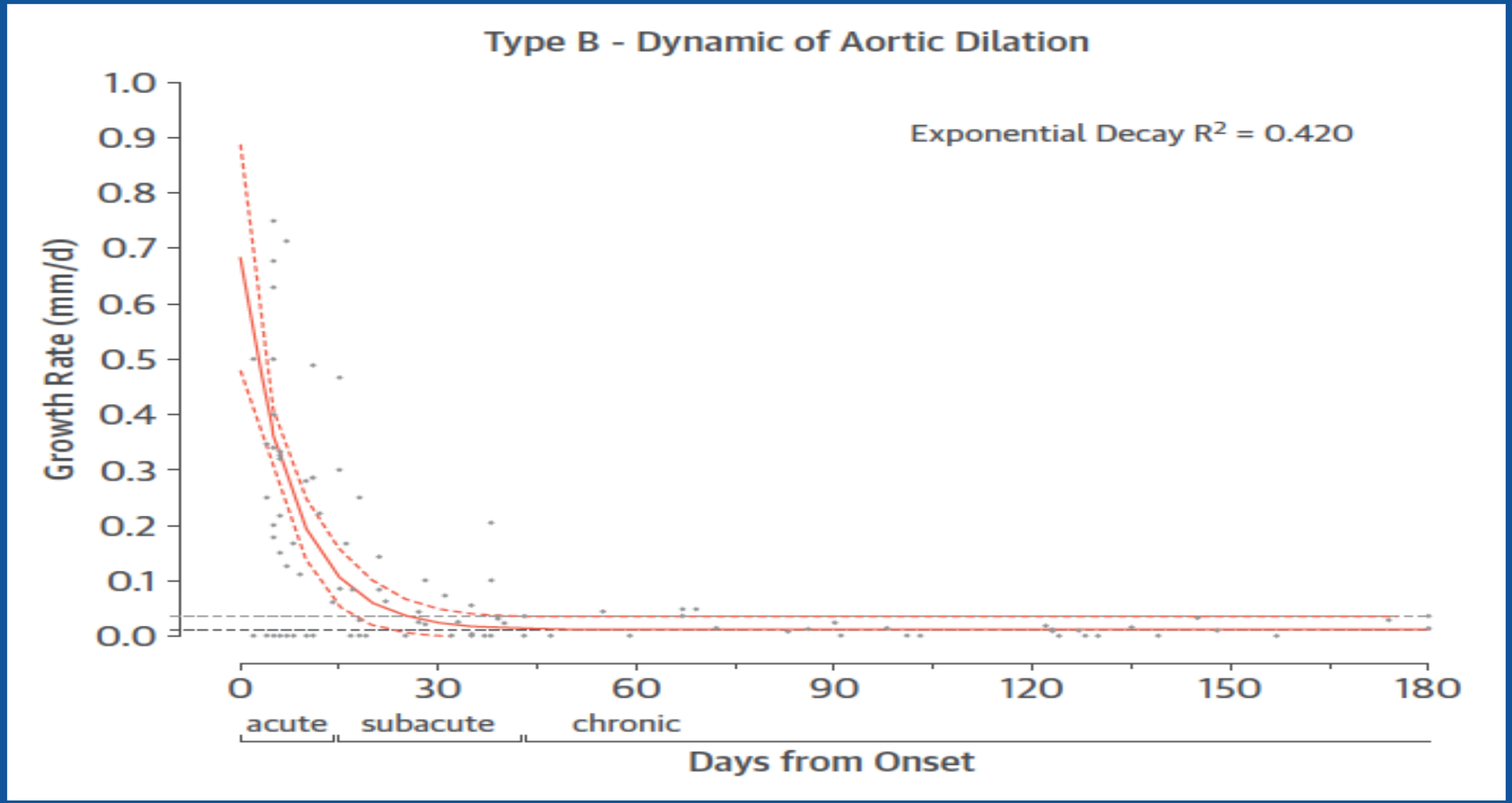
RO Afifi et. al. Circulation 2015;132:748

3a). Histopathology Changes in Type B Dissection Over Time



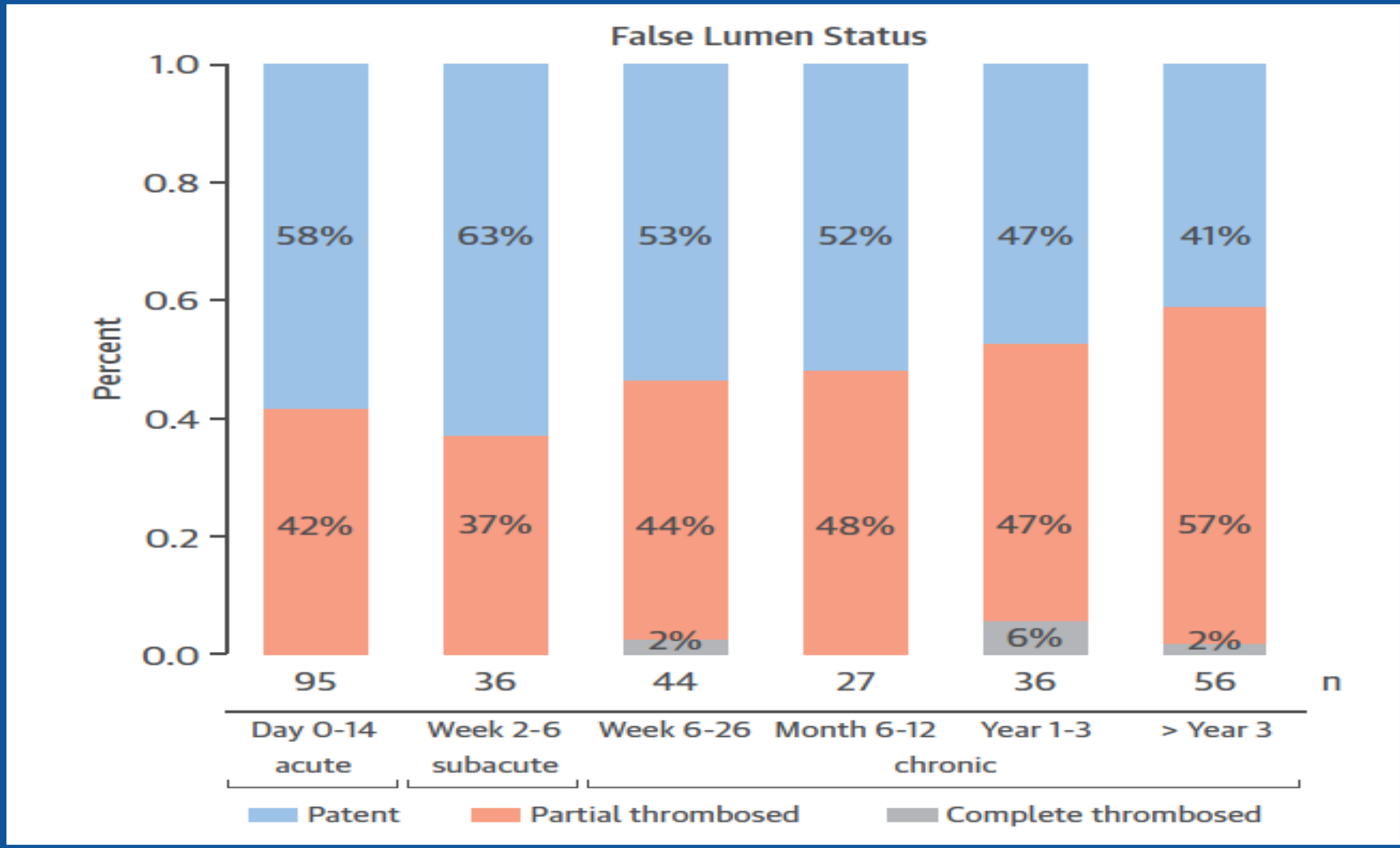
S Peterss et. al. J Am Coll Cardiol 2016;68:1054

Temporal Dynamic Of Aortic Dilation In Type B Dissection Over Time



S Peterss et. al. J Am Coll Cardiol 2016;68:1054

3b). False Lumen Status in Type B Dissection



S Peterss et. al. J Am Coll Cardiol 2016;68:1054

1). Annual Risk of Rupture of AAA

Aneurysm Size	1-yr Incidence of Rupture
	%
<5.5 cm	≤1.0
5.5–5.9 cm	9.4
6.0–6.9 cm	10.2
≥7.0 cm	32.5

K Craig Kent. N Engl J Med 2014;371:2101

2a). Screening for AAA: U.S. Preventive Services Task Force Recommendation Statement

- *The USPSTF recommends 1-time screening for AAA with ultrasonography in men aged 65 to 75 years who have ever smoked. (B recommendation)*
- *The USPSTF recommends that clinicians selectively offer screening for AAA in men aged 65 to 75 years who have never smoked (C recommendation)*
- *The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for AAA in women aged 65 to 75 years who have ever smoked. (1 statement)*
- *The USPSTF recommends against routine screening for AAA in women who have never smoked. (D recommendation)*

ML LeFevre et al., Ann Intern Med 2014; 161:281

2b). Growth Rate for Small AAA – Meta-Analysis

Small AAAs of 3.0 cm – 5.4 cm in diameter are monitored by ultrasound surveillance. The intervals between surveillance scans should be chosen to **detect an expanding aneurysm prior to rupture.** Studies were identified for inclusion through a systematic literature search through December 2010. Study authors were contacted, which yielded 18 data sets providing repeated ultrasound measurements of AAA diameter over time in **15,471 patients.** Predictions of the **risk of exceeding 5.5-cm diameter and of rupture** within given time intervals were estimated. **Growth rates increased on average by 0.59 mm per year.** In contrast to the commonly adopted surveillance intervals in current AAA screening programs, **surveillance intervals of several years may be clinically acceptable for the majority of patients with small AAA.**

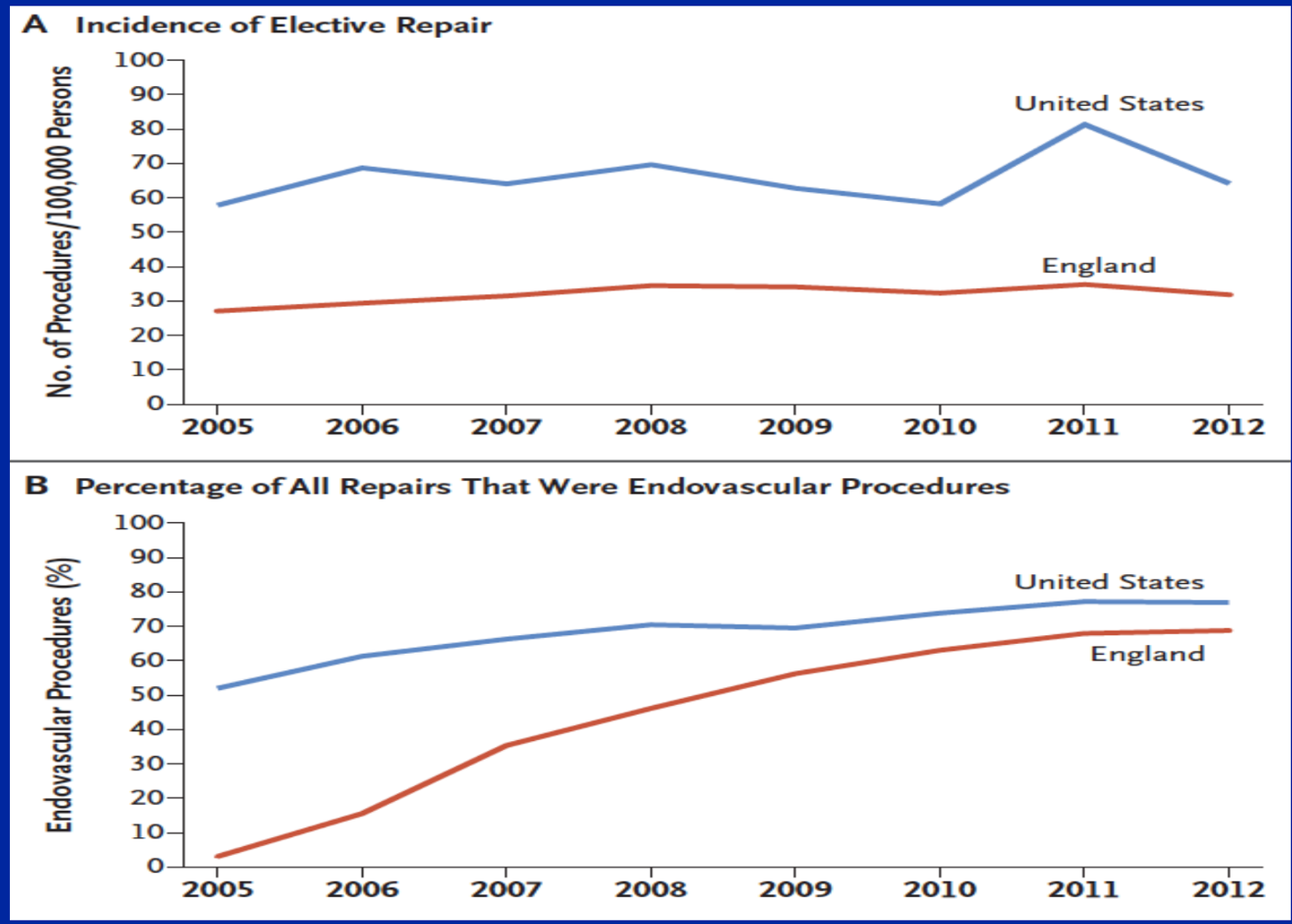
The RESCAN. JAMA 2013; 309:806 – JL Duncan BMJ 2012; 344:e2958 > 25 mm LT Risk
JM Guirguis-Blake et al., Ann Intern Med 2014; 160:321 – Validated Prospectively

3a). Thresholds for Abdominal Aortic Aneurysm Repair in England and the US

During the period from 2005 through 2012, a total of 29,300 patients in England and 278,921 patients in the United States underwent repair of intact abdominal aortic aneurysms. We found a lower rate of repair of abdominal aortic aneurysms and a larger mean aneurysm diameter at the time of repair in England than in the United States and lower rates of aneurysm rupture and aneurysm-related death in the United States than in England.

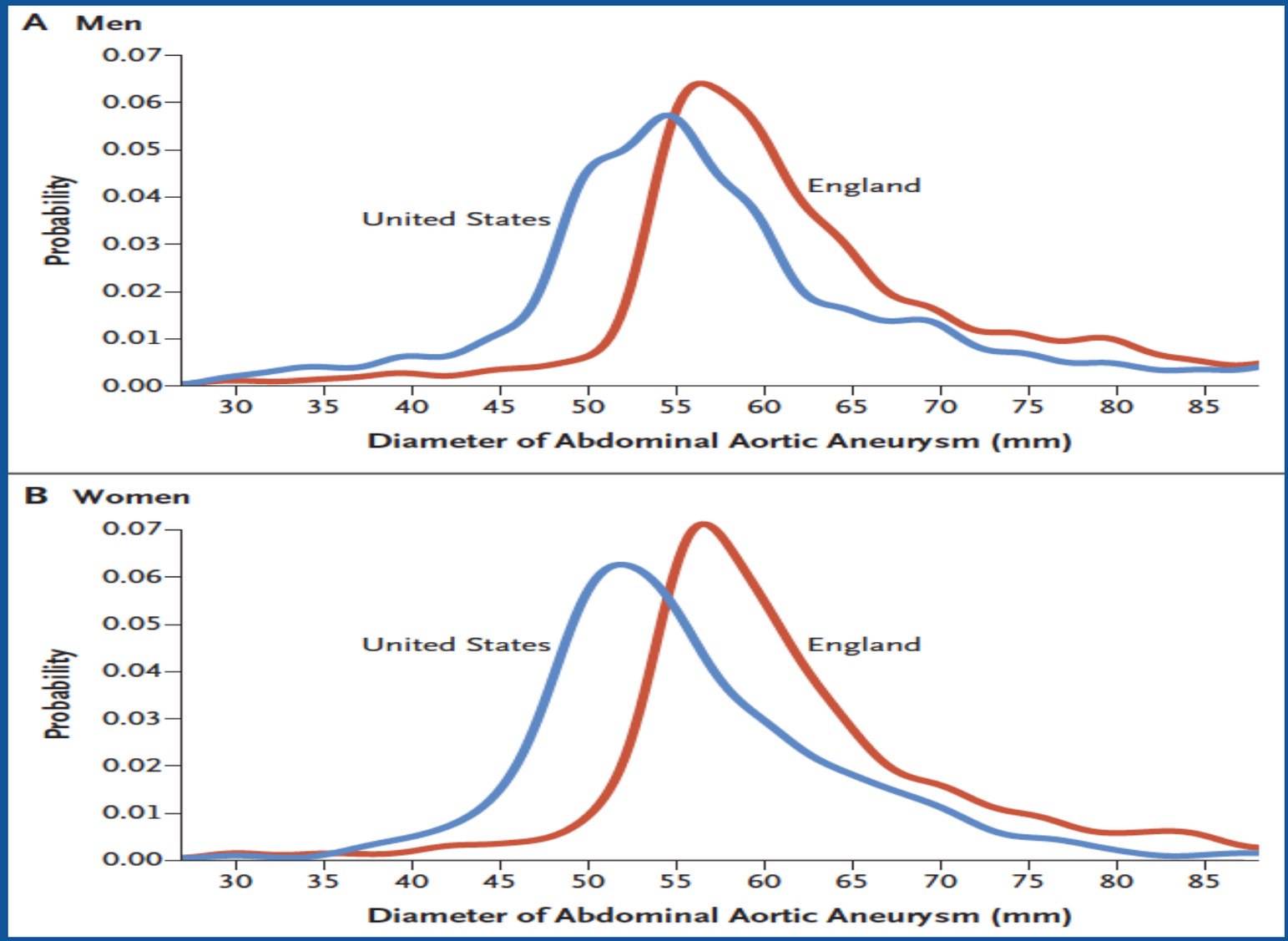
A Karthikesalingam et al., N Engl J Med 2016; 375:2051

Repair of Intact Abdominal Aortic Aneurysms in England and the United States, 2005–2012



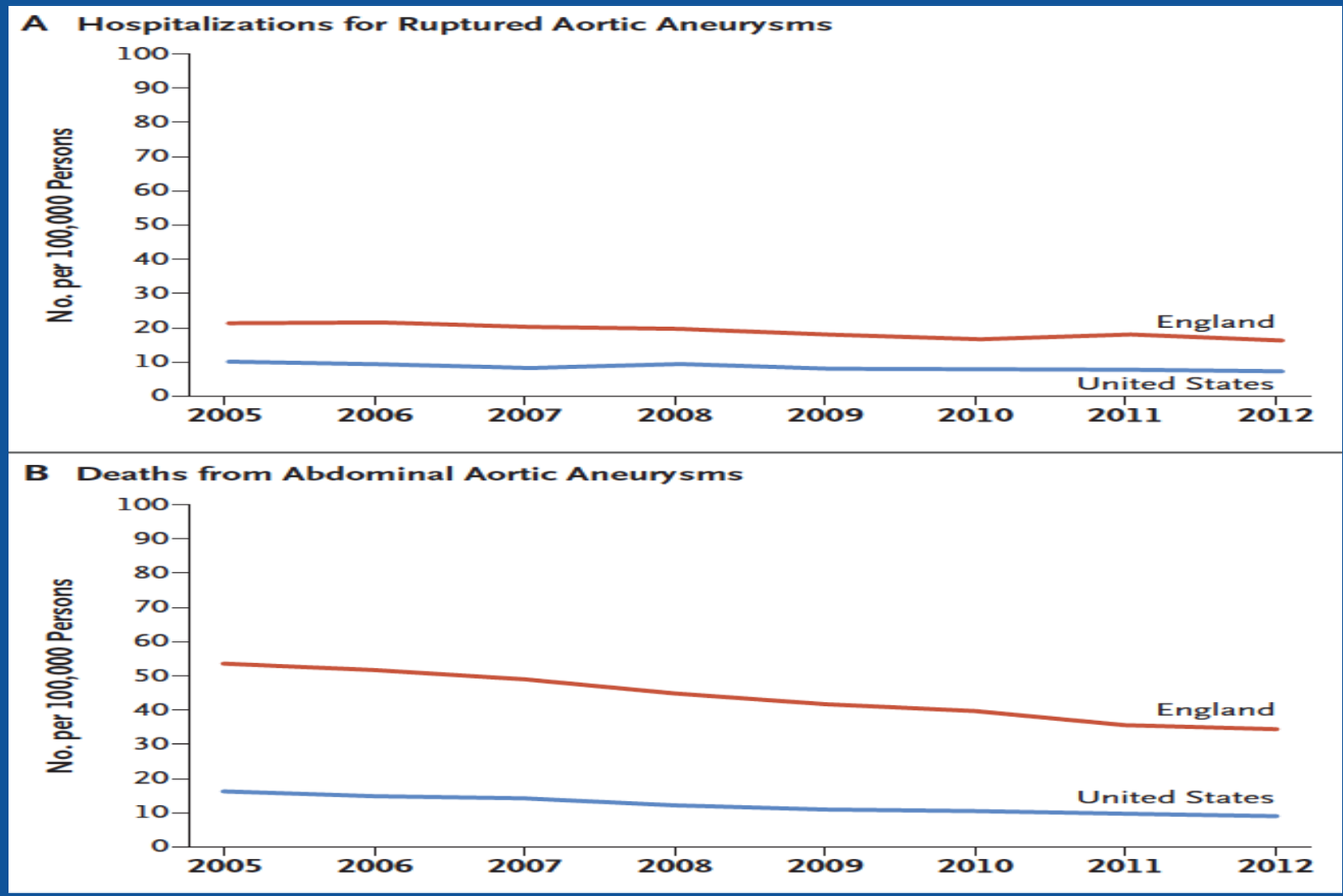
A Karthikesalingam et. al. N Engl J Med 2016;375:2051

Diameter of AAA at the Time of Repair in England in 2014 and in the United States in 2013



A Karthikesalingam et. al. N Engl J Med 2016;375:2051

Hospitalization and Death due to AAA in England and the United States, 2005–2012



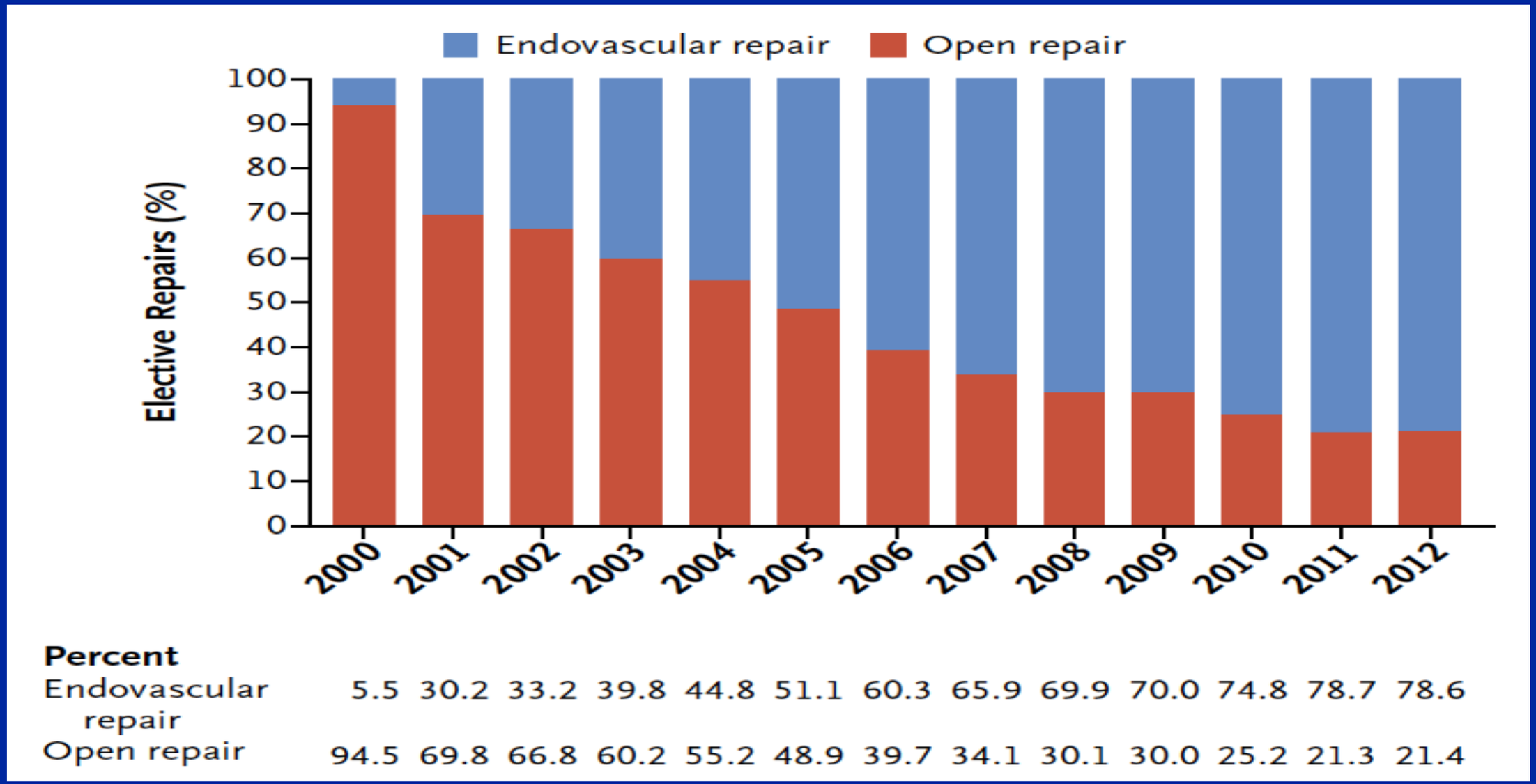
A Karthikesalingam et. al. N Engl J Med 2016;375:2051

3b) Endovascular or Open Repair For Ruptured AAA One-year Outcomes

This pragmatic multicentre (29 UK and 1 Canada) trial randomized 613 patients with a clinical diagnosis of ruptured aneurysm; 316 to an endovascular first strategy and 297 to open repair. The principal 1-year outcome was mortality; secondary outcomes were re-interventions, hospital discharge, health-related quality-of-life (Qol) (EQ-5D), costs. An endovascular first strategy does not offer a survival benefit over 1 year but offers patients faster discharge with better Qol and is cost-effective.

IMPROVE Trial (R Grieve et. al.) Eur Heart J. 2015;36:2061

4) Annual Proportion of Elective Endovascular & Open Repairs for AAA in the US



Percent	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Endovascular repair	5.5	30.2	33.2	39.8	44.8	51.1	60.3	65.9	69.9	70.0	74.8	78.7	78.6
Open repair	94.5	69.8	66.8	60.2	55.2	48.9	39.7	34.1	30.1	30.0	25.2	21.3	21.4

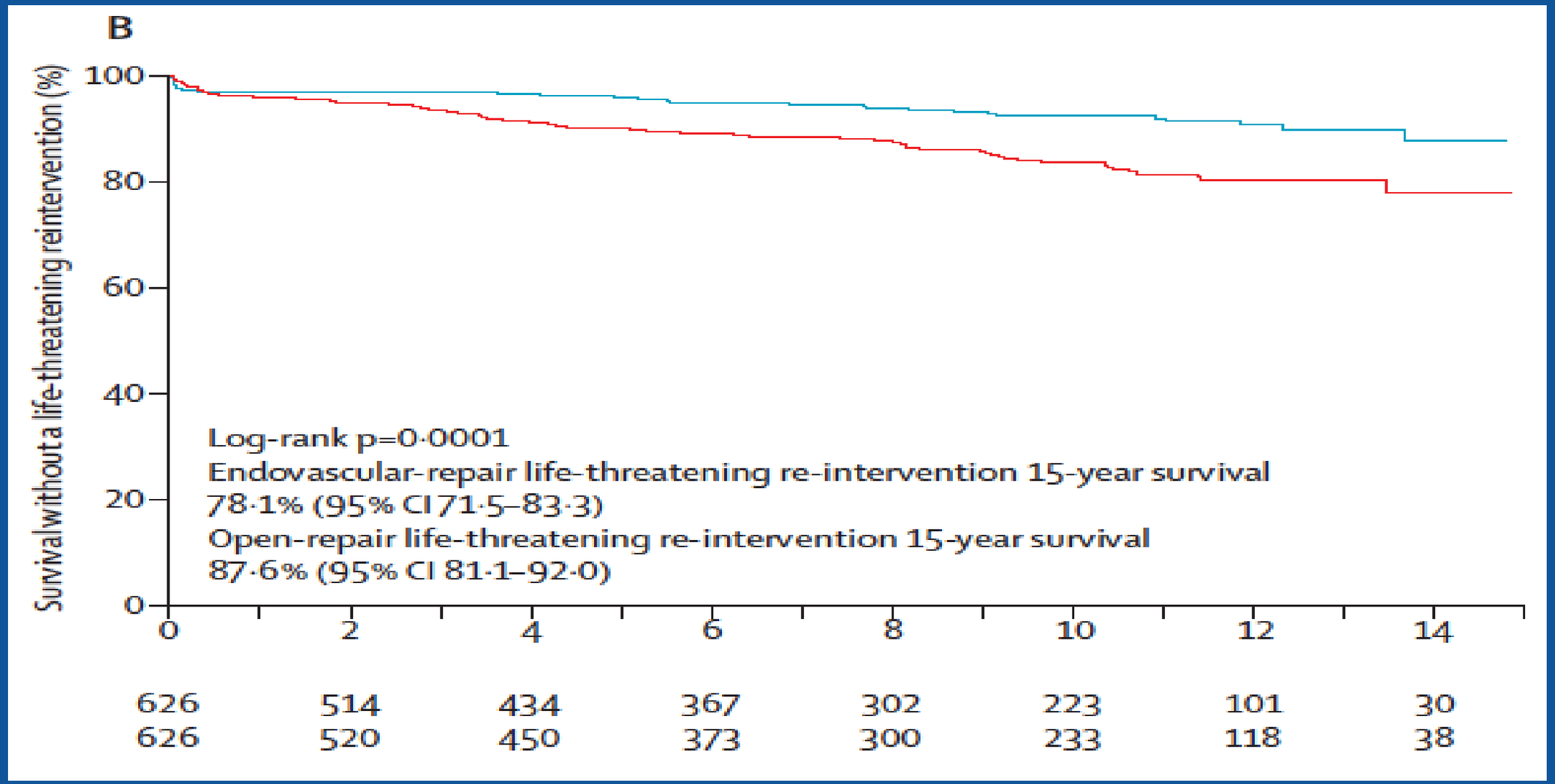
K Craig Kent. N Engl J Med 2014;371:2101

Endovascular vs Open Repair of AAA in 15-Yrs' FU UK Endovascular Aneurysm Repair (EVAR) trial 1)

We used data from the EVAR 1 randomised controlled trial, which enrolled 1252 patients from 37 centres in the UK between Sept 1, 1999, and Aug 31, 2004. Patients had to be aged 60 years or older, have aneurysms of at least 5.5 cm in diameter, and deemed suitable and fit for either EVAR or open repair. Eligible patients were randomly assigned. EVAR has an early survival benefit but an inferior late survival compared with open repair, which needs to be addressed by lifelong surveillance of EVAR and re-intervention if necessary.

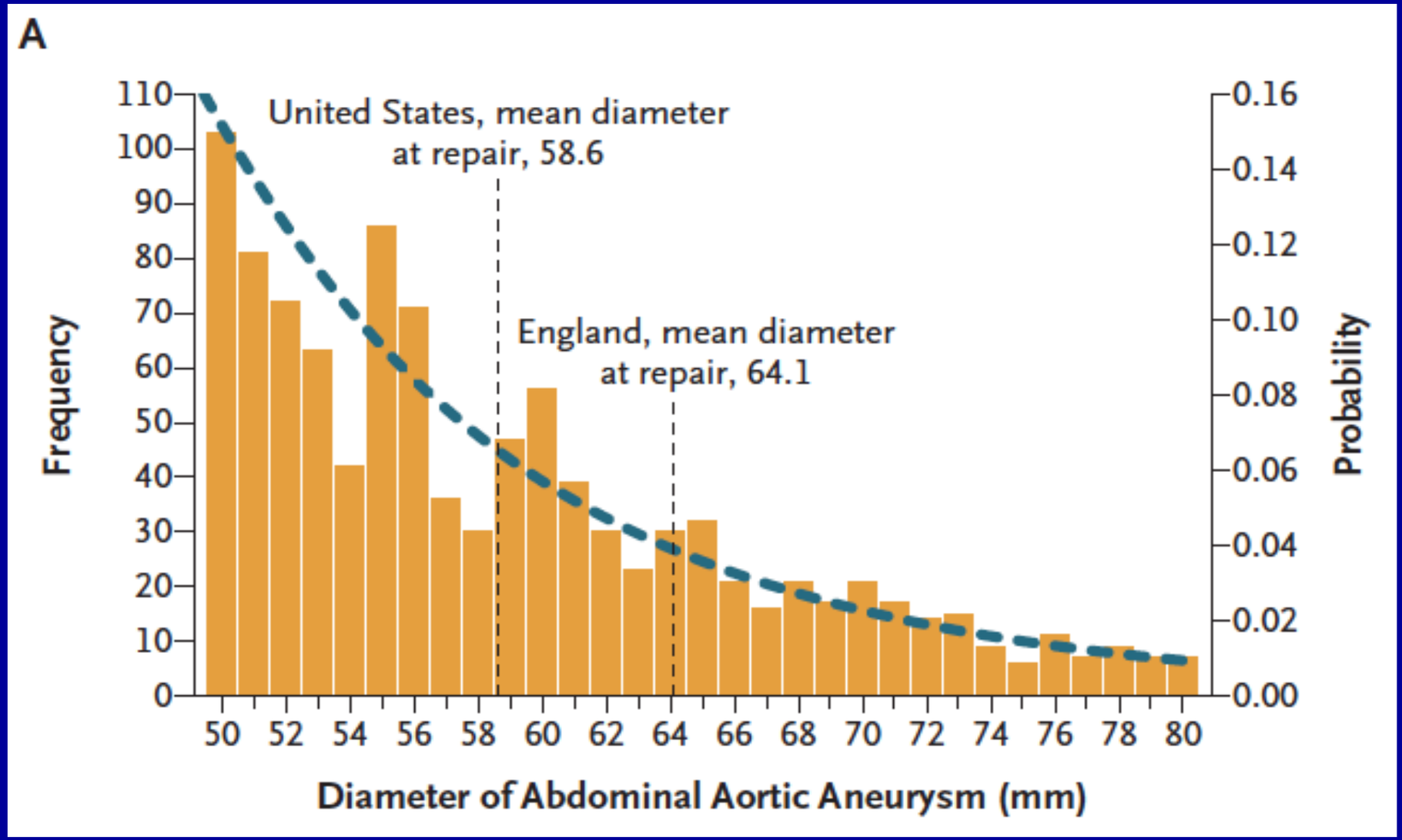
R Patel et al., Lancet 2016; 388:2366

Time To First Re-intervention In The EVAR And Open Repair Groups During 15 Years



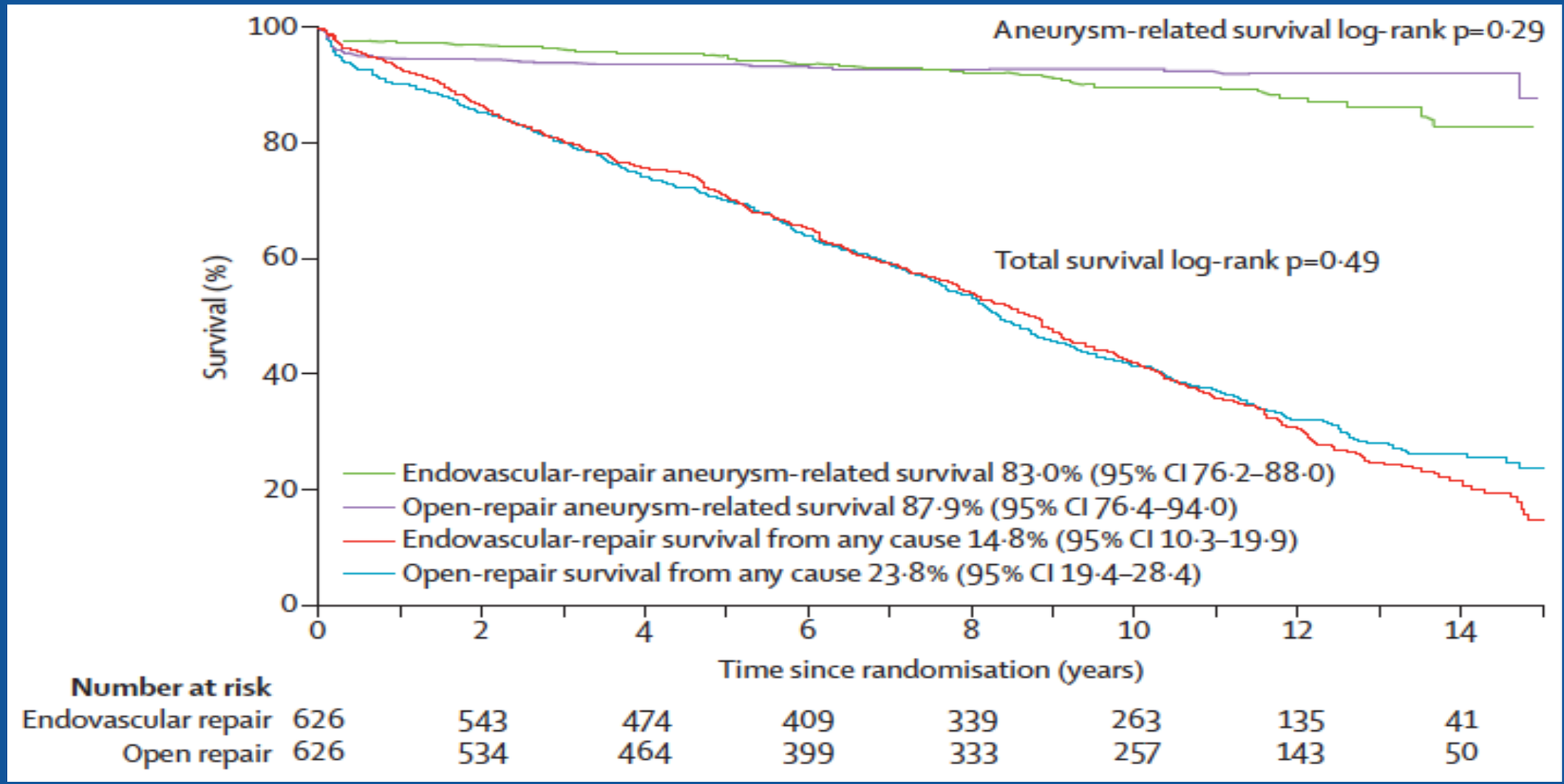
EVAR Trial Investigators (R Patel et. al.) Lancet 2016; 388: 2366

Diameter of Abdominal Aortic Aneurysms in England and the United States



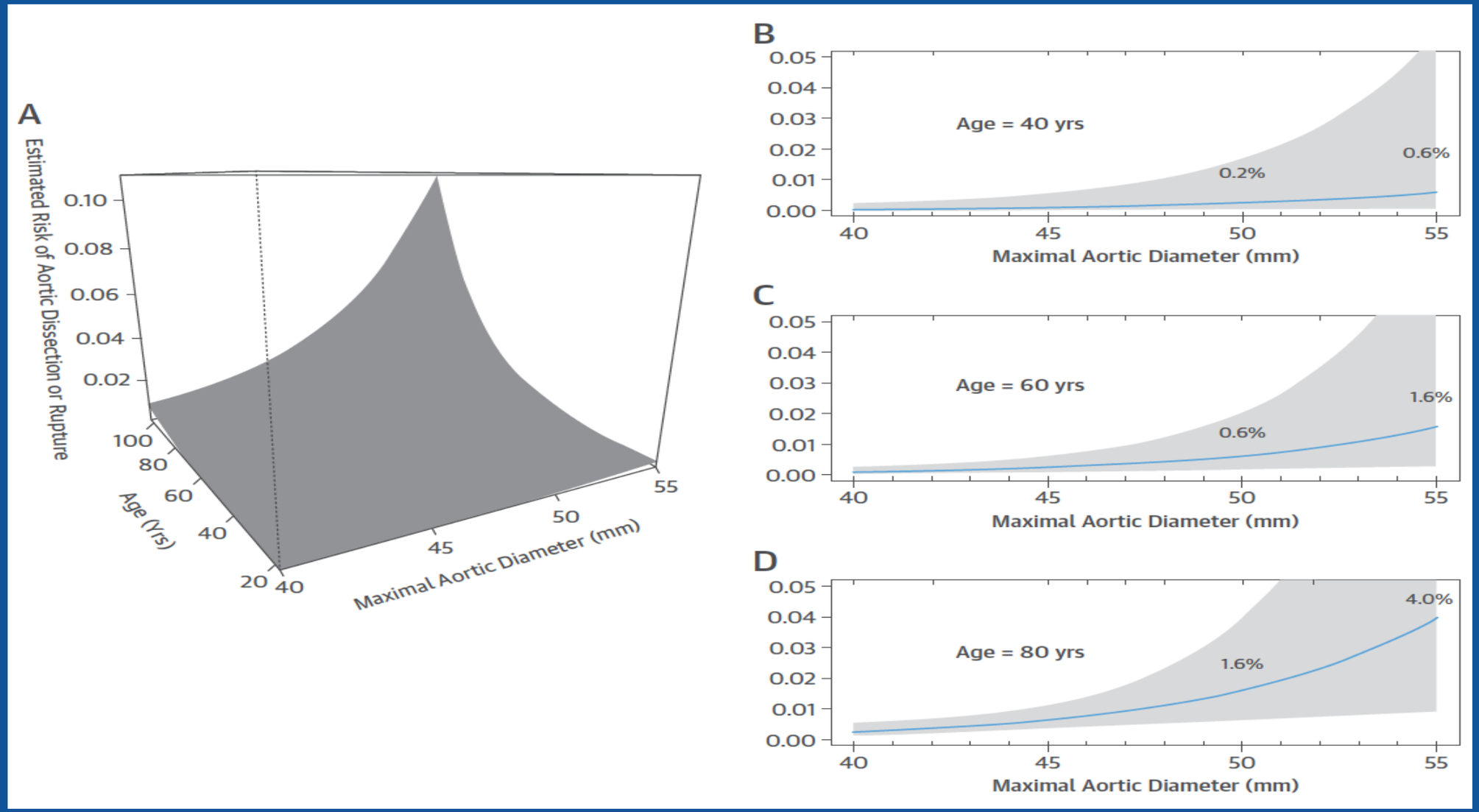
A Karthikesalingam et. al. N Engl J Med 2016;375:2051

Estimates For Total Survival And Aneurysm-related Survival Up To 15 Yrs



EVAR Trial Investigators (R Patel et. al.) Lancet 2016; 388: 2366

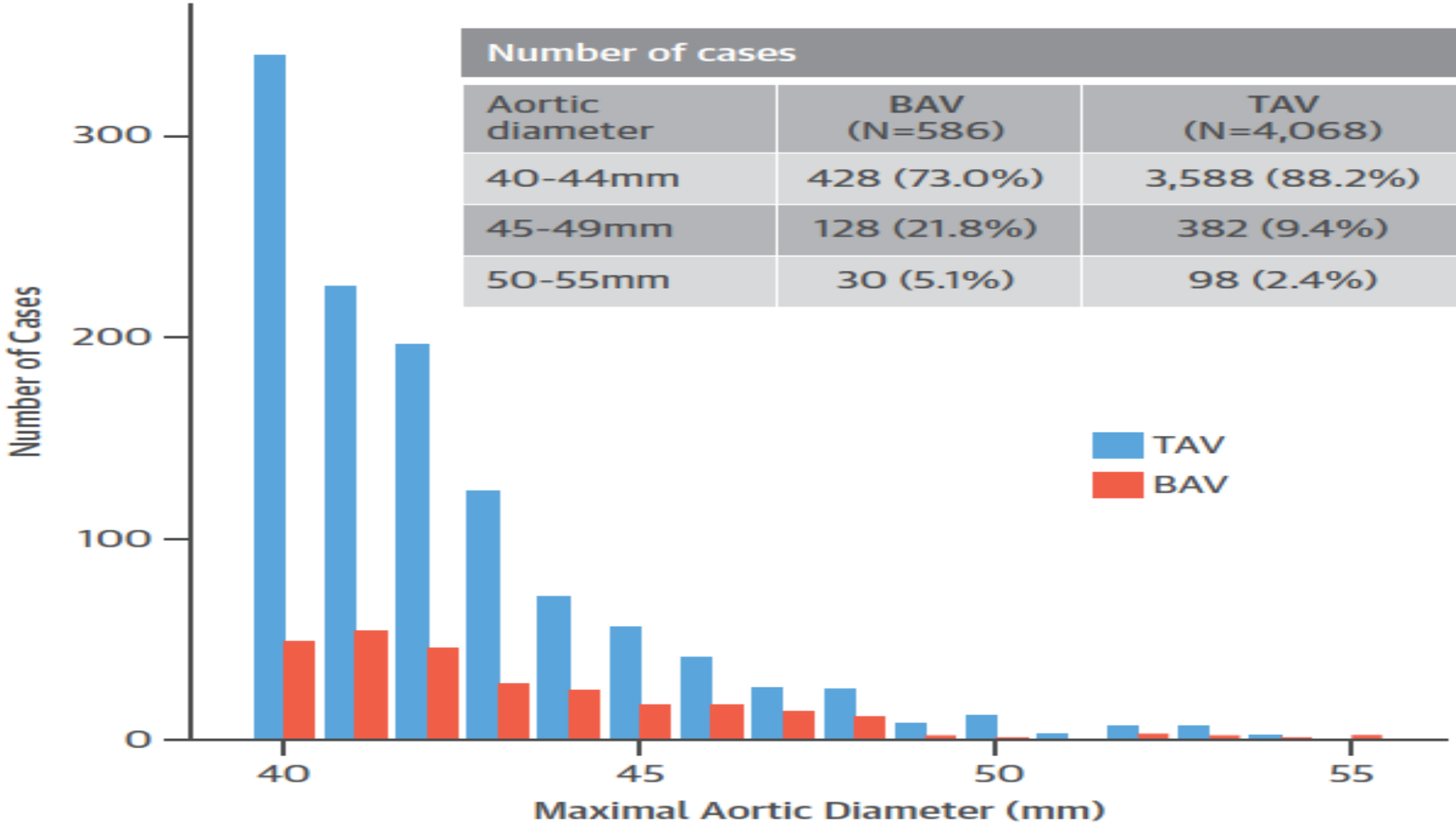
Probability of Aortic Dissection and/or Rupture Within 5 Yrs Based on Aortic Diameter & Age



JB Kim et. al. J Am Coll Cardiol 2016;68:1209

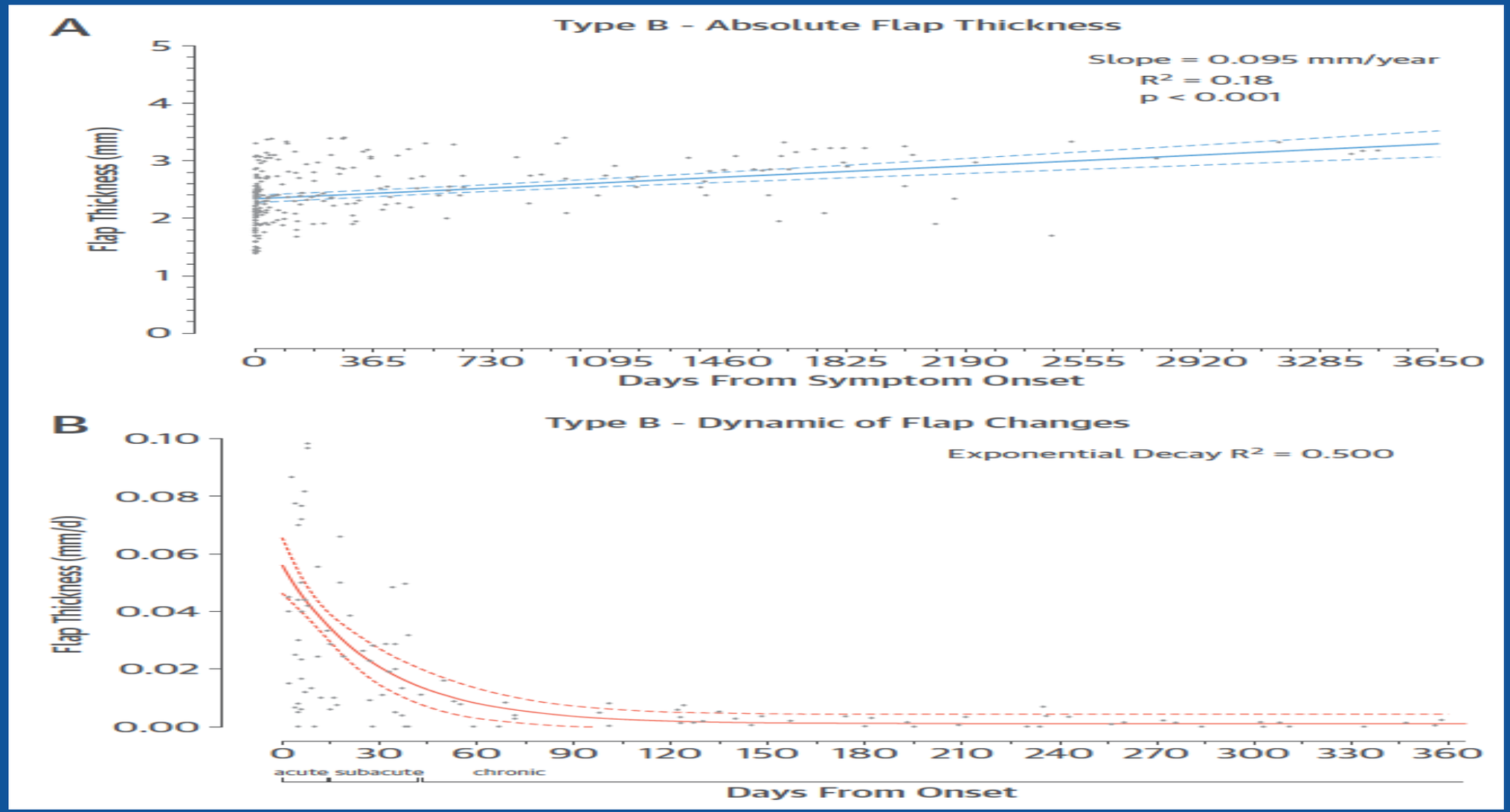
Distribution Plots for Index Asc. Aorta Diameters in BAVs &TAVs

Number of cases		
Aortic diameter	BAV (N=586)	TAV (N=4,068)
40-44mm	428 (73.0%)	3,588 (88.2%)
45-49mm	128 (21.8%)	382 (9.4%)
50-55mm	30 (5.1%)	98 (2.4%)



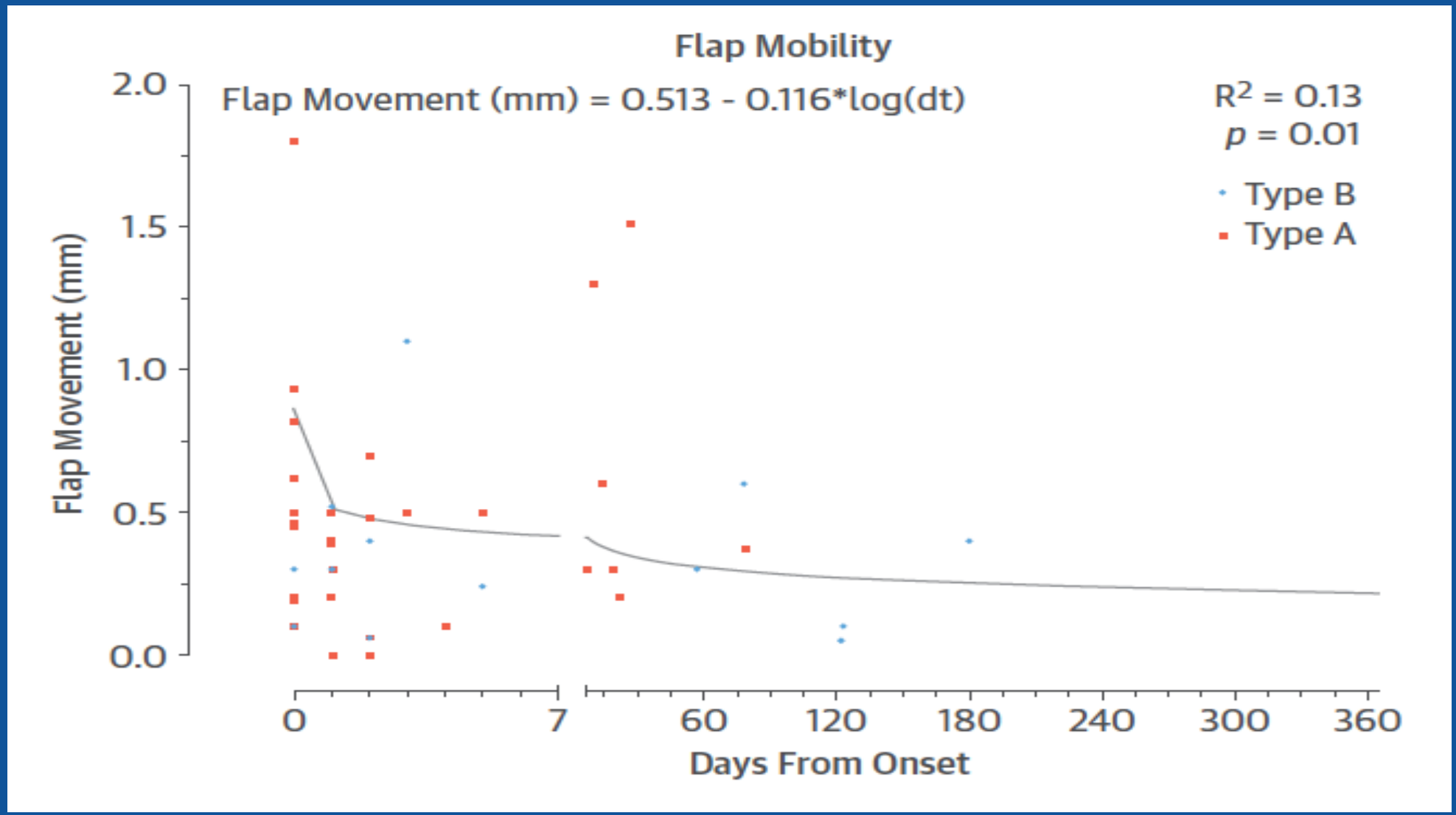
JB Kim et. al. J Am Coll Cardiol 2016;68:1209

Absolute Flap Thickness & Temporal Changes of Architecture Over Time in Type B Dissection



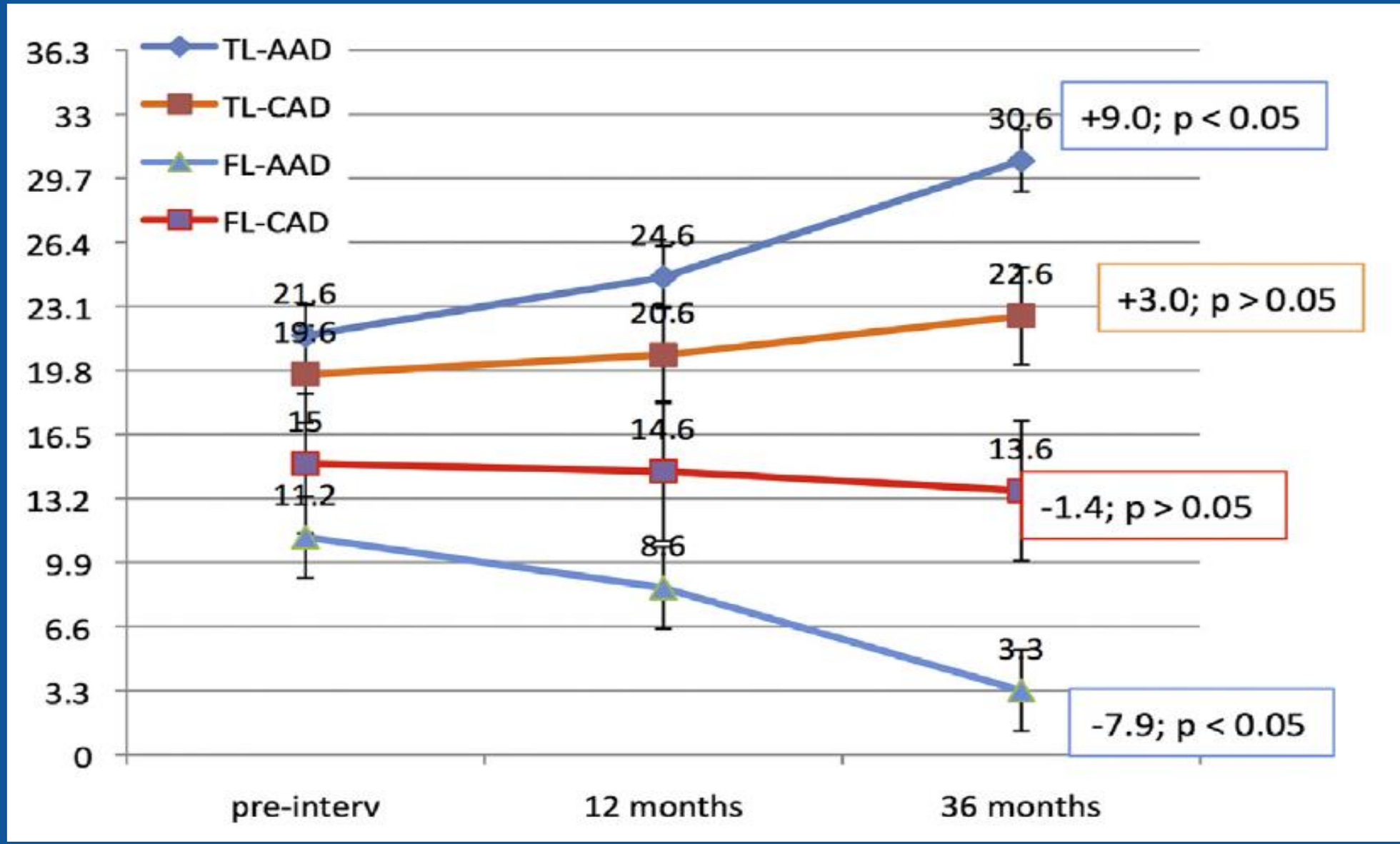
S Peterss et. al. J Am Coll Cardiol 2016;68:1054

Absolute Flap Mobility Over Time in Type B Dissection



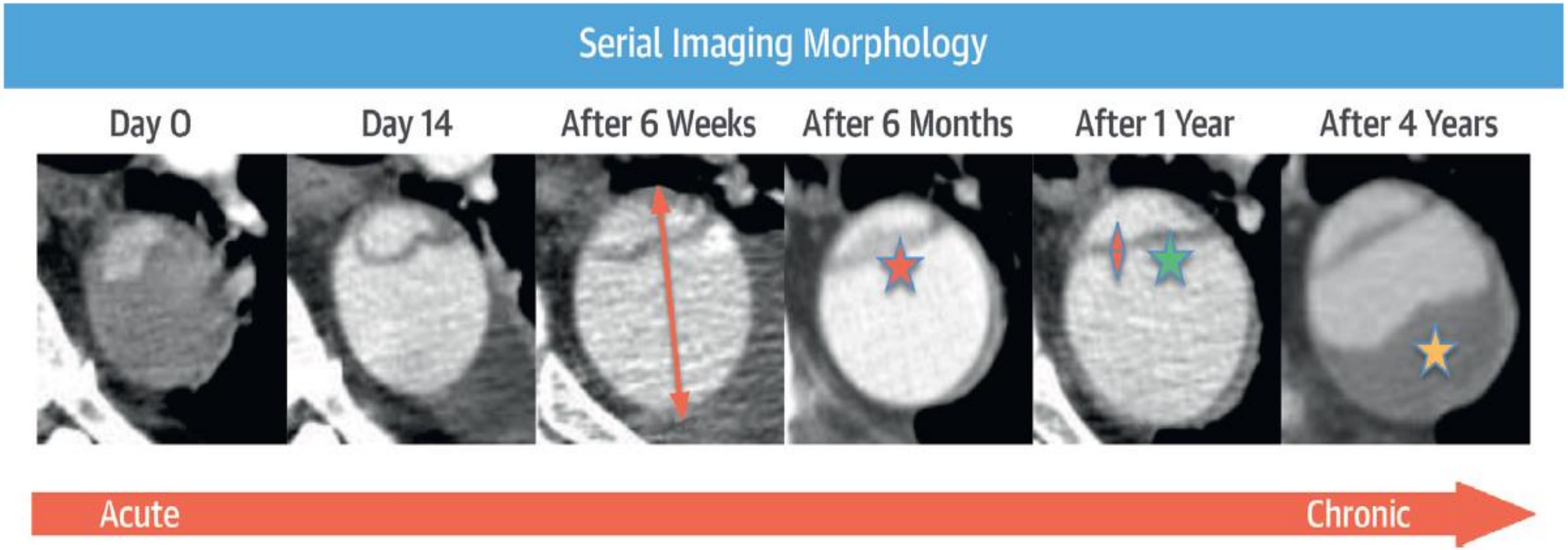
S Peterss et. al. J Am Coll Cardiol 2016;68:1054

Aortic Remodeling at the Level of the Stent-Graft



F Fanelli et. al. J Am Coll Cardiol Intv. 2016;9:183

Changing Pathology of Aortic Dissection



Peterss, S. et al. J Am Coll Cardiol. 2016;68(10):1054-65.

Changing morphology of a type B dissection over time by computed tomography in a single illustrative patient with multiple good quality images at the same aortic level. Please note: 1) marked early increase in aortic diameter **(orange arrow)**; 2) intimal thickening over time **(orange star)**; 3) decreased flap motion over time **(orange triangles)**; 4) flap straightening over time **(green star)**; and 5) increased false lumen thrombosis over time **(yellow star)**.

S Peterss et. al. J Am Coll Cardiol 2016;68:1054

Management of Early Graft Infections in the Asc. Aorta & Aort. Arch: Graft Replacement vs Graft Preservation

Between 1996 and August 2015, 25 patients were treated in our institution for early graft infection after thoracic aortic surgery via sternotomy. *In situ* graft-sparing surgical therapy is safe and effective if diagnosis and treatment of aortic graft infection is initiated promptly and aggressively, ideally < 1 month post-surgery. Our method produces good midterm results (3 years). For aortic graft infections that become clinically apparent > 3-6 months after surgery, replacement of grafts with biological conduits (homografts or pericardial xenografts) most likely remain the best treatment option.

J Umminger et al., EJ Cardio Thorac Surg 2016; 50:660 (Hannover)