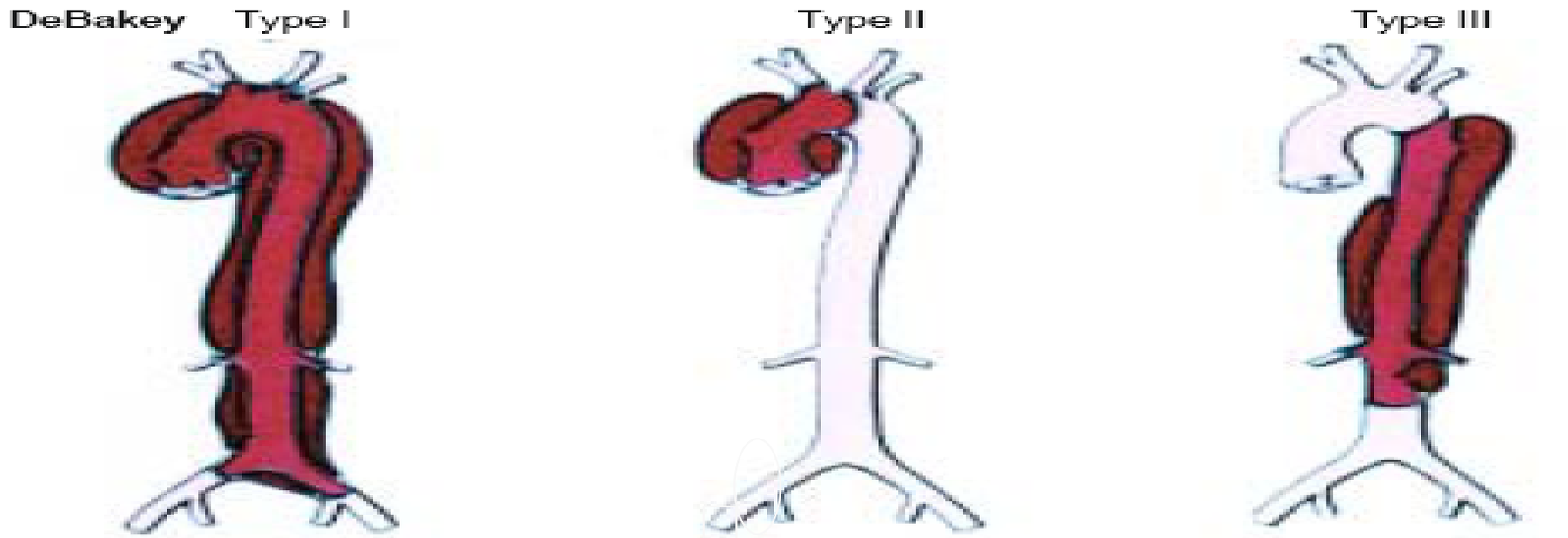
Diseases of The Aorta 2017 - 2018
Understanding & Approach

TAA, TAD, AAA, AAR

ACC New York, Dec 9, 2017 - No Disclosures

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

VS **Ramanath et. al. *Mayo Clin Proc*. 2009;84:465.**

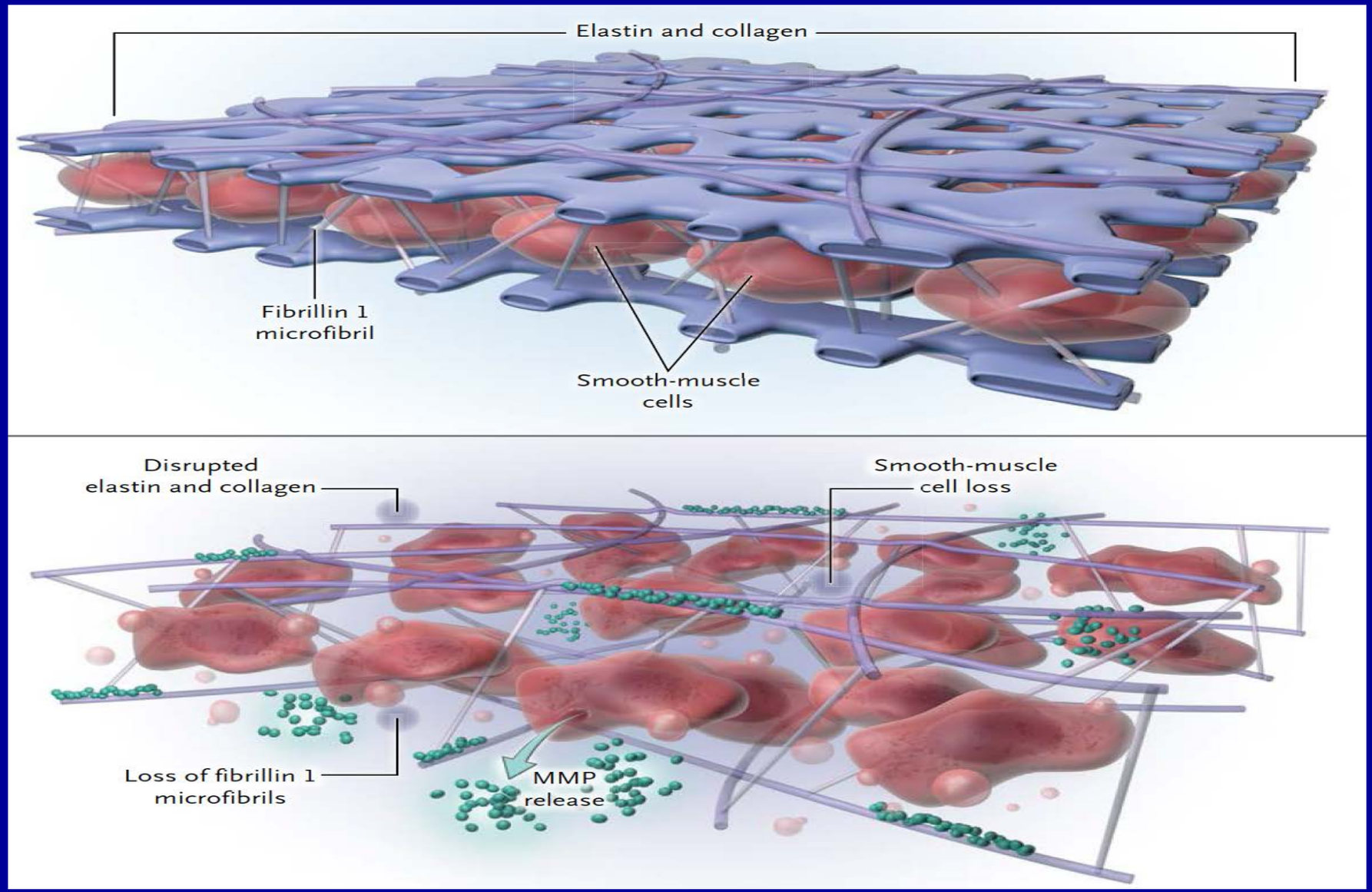
CA Nienaber et. al. *Circulation* 2003;108:628.

2) 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

3). Pathophysiological Features of Marfan's & Bicuspid Aortopathy



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

The Aorta - TAA, TAD, AAA, AAR – 2017 - 2018

- *Area & Types (TAA,TAD,AAA,AAR)*
- *Pathogenesis (Marfan's, BHA, AAA)*
  - *Dysfunctional Structure*
  - *Hemodynamics*
  - *Approach to Hemodynamics*
  - *Approach to Dysfunctional Structure*
- *Interventional (TAA,TAD,AAA,AAR)*

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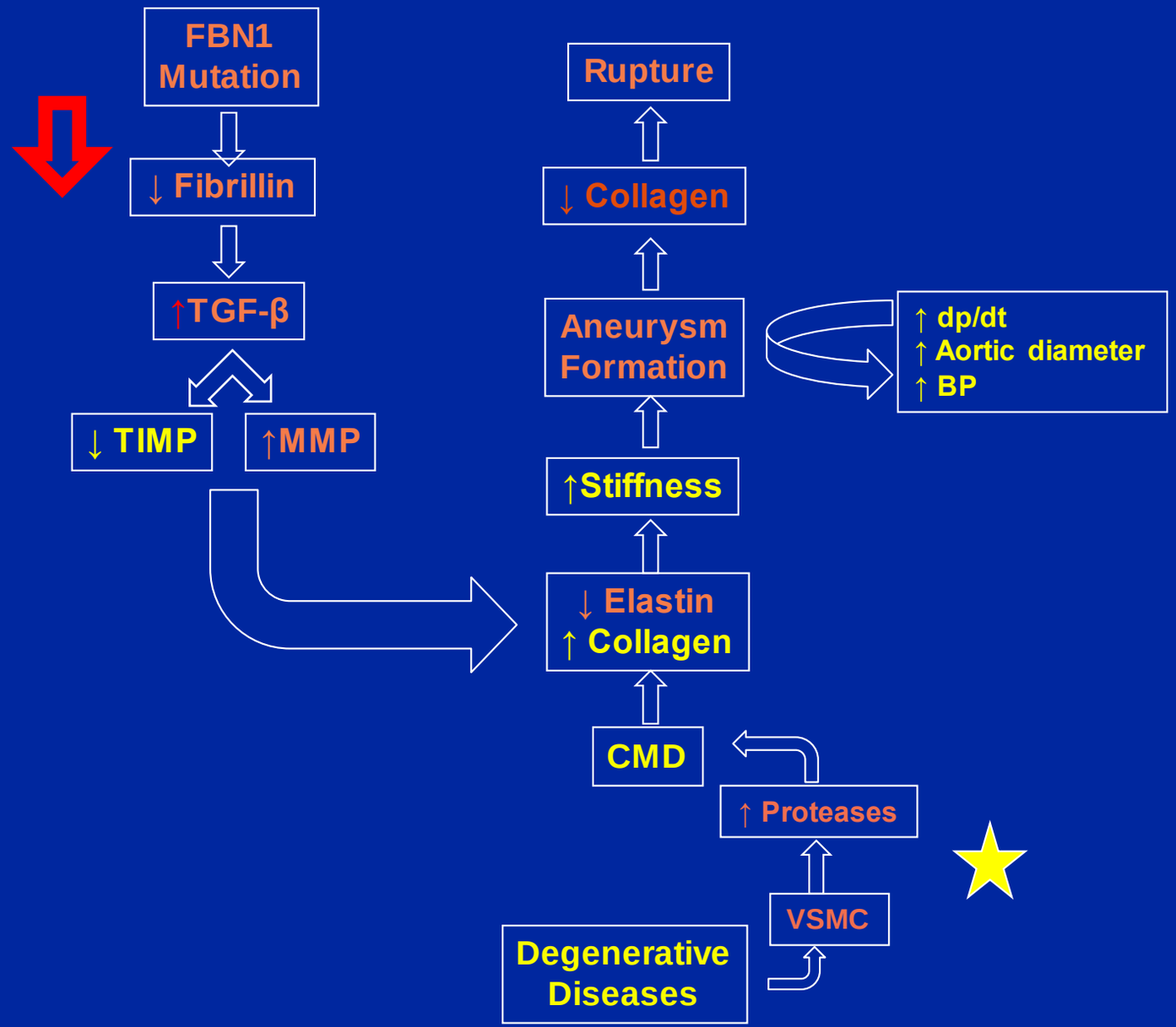
JZ Goldfinger, V Fuster et al., JACC 2014;64:1725

1. MARFAN'S / NSTAA & 2. BHA

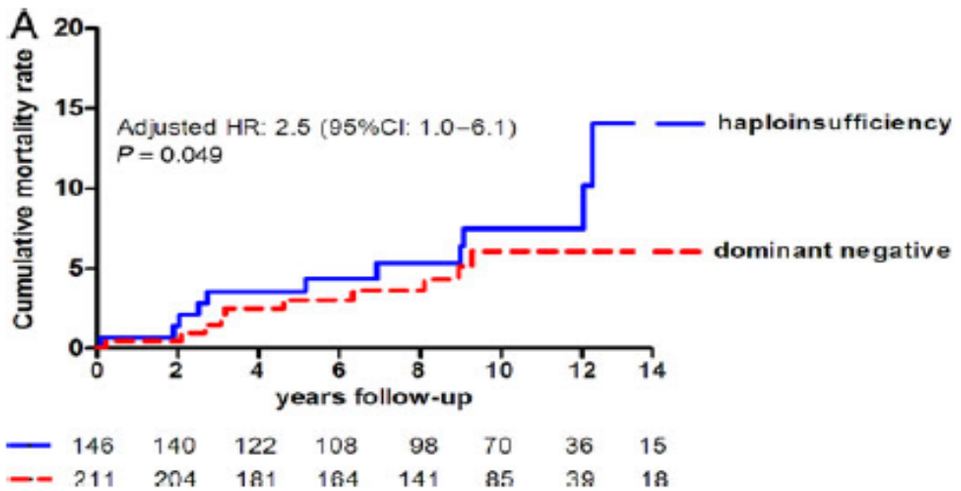


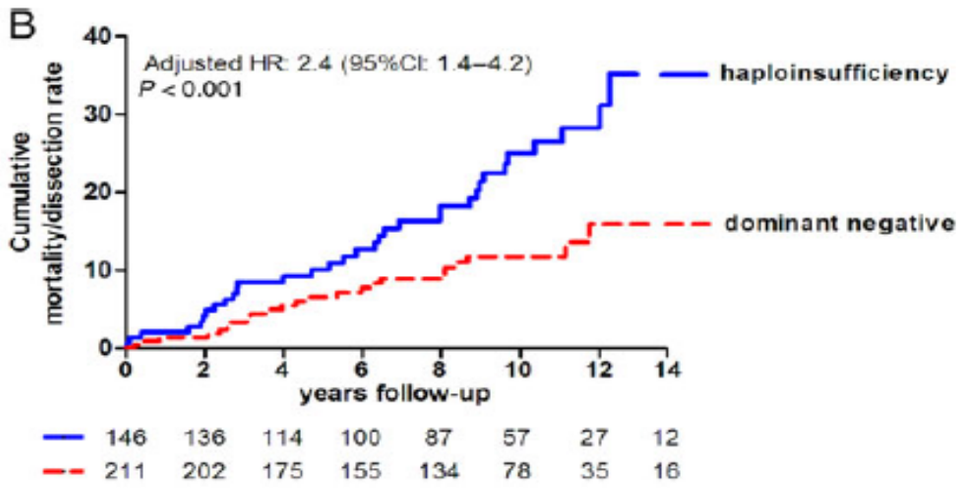
JZ Goldfinger, V Fuster et al., JACC 2014;64:1725

1a. Genotype Impacts Survival In Marfan's

	Haploinsuffciency, $n = 146$	Dominant negative, $n = 211$
Age (Q1–Q3 in years)*	33.3 ± 11.5	37.1 ± 14.0
Sex (male)	74 (50.7%)	110 (52.1%)
Prior aortic surgery	57 (39.0%)	69 (32.7%)
Prior aortic dissection	13 (8.9%)	19 (9.0%)
No aortic complication at inclusion	89 (61.0%)	139 (66.0%)
Follow-up (Q1–Q3 in years)	8.5 ± 3.4	8.3 ± 3.1

*$P = 0.005$.





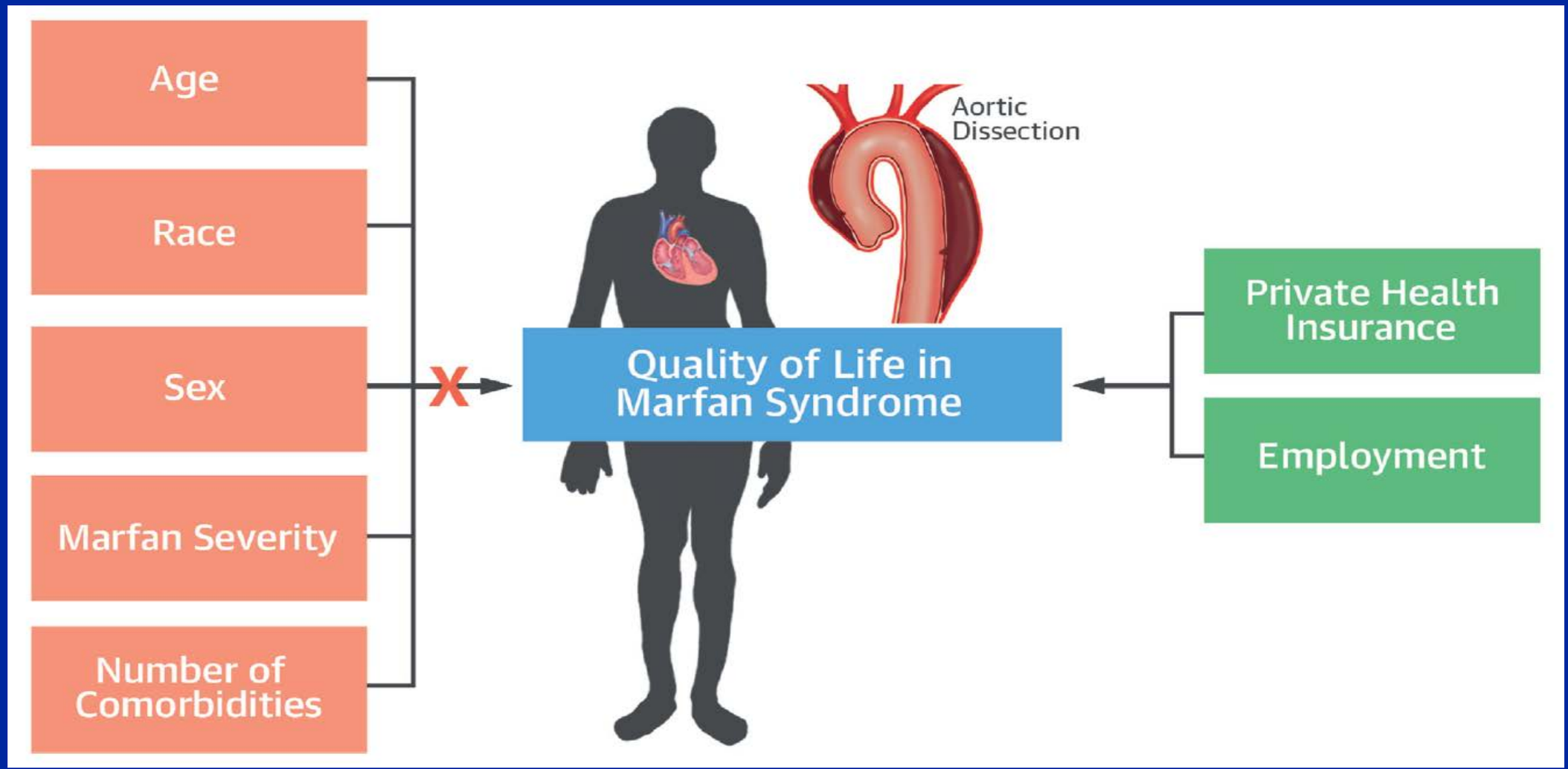
R Franken et. al. Eur Heart J. 2016;37:3285

1b. Marfan Syndrome and Quality of Life in the GenTAC Registry

The national registry of GenTAC is a longitudinal observational cohort study of patients with conditions that predispose to thoracic aortic aneurysms and dissections, including MFS. QOL was assessed using the SF-36 approach. In the GenTAC registry, 389 adults with MFS completed the SF-36. Mean age was 41 years, 51% were men, 92% were white, and 65% were college graduates. Health-related QOL was below the population norm. Better QOL was independently associated with socioeconomic factors, not factors related to health or MFS severity.

JZ Goldfinger et al., J Am Coll Cardiol 2017; 69:2821

Factors That Impact Quality of Life in Marfan Syndrome



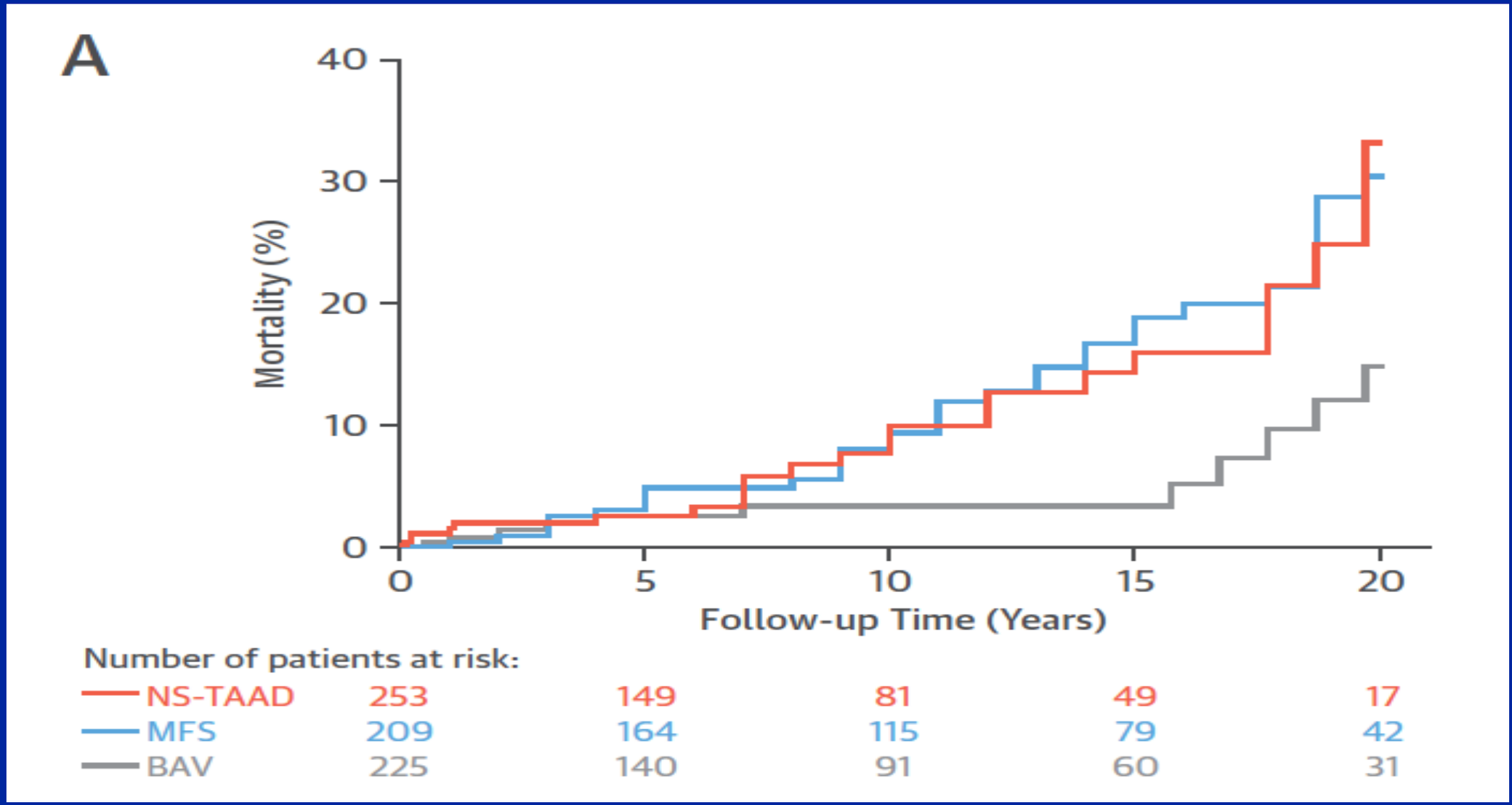
GenTAC Registry (JZ Goldfinger et. al.) J Am Coll Cardiol 2017;69:2821

1c. Nonsyndromic Thoracic Aortic Aneurysm Dissection vs Marfan's vs. Bicuspid Aortic Valve Aneurysm

Genetic aortopathy (GA) underlies thoracic aortic aneurysms (TAA) in younger adults. Diagnosis of GA was made for 760 patients (NS-TAA, n=311; MFS, n=221; BAV, n=228). The 687 patients surviving > 30 days after presentation were followed for a median of 7 years. Clinical outcomes for MFS and NS-TAA are similar buy worse than BAV. Independent predictors of mortality, including family history of aortic dissection and age. Management of NS-TAA, including surgical intervention, should be similar to that of MFS.

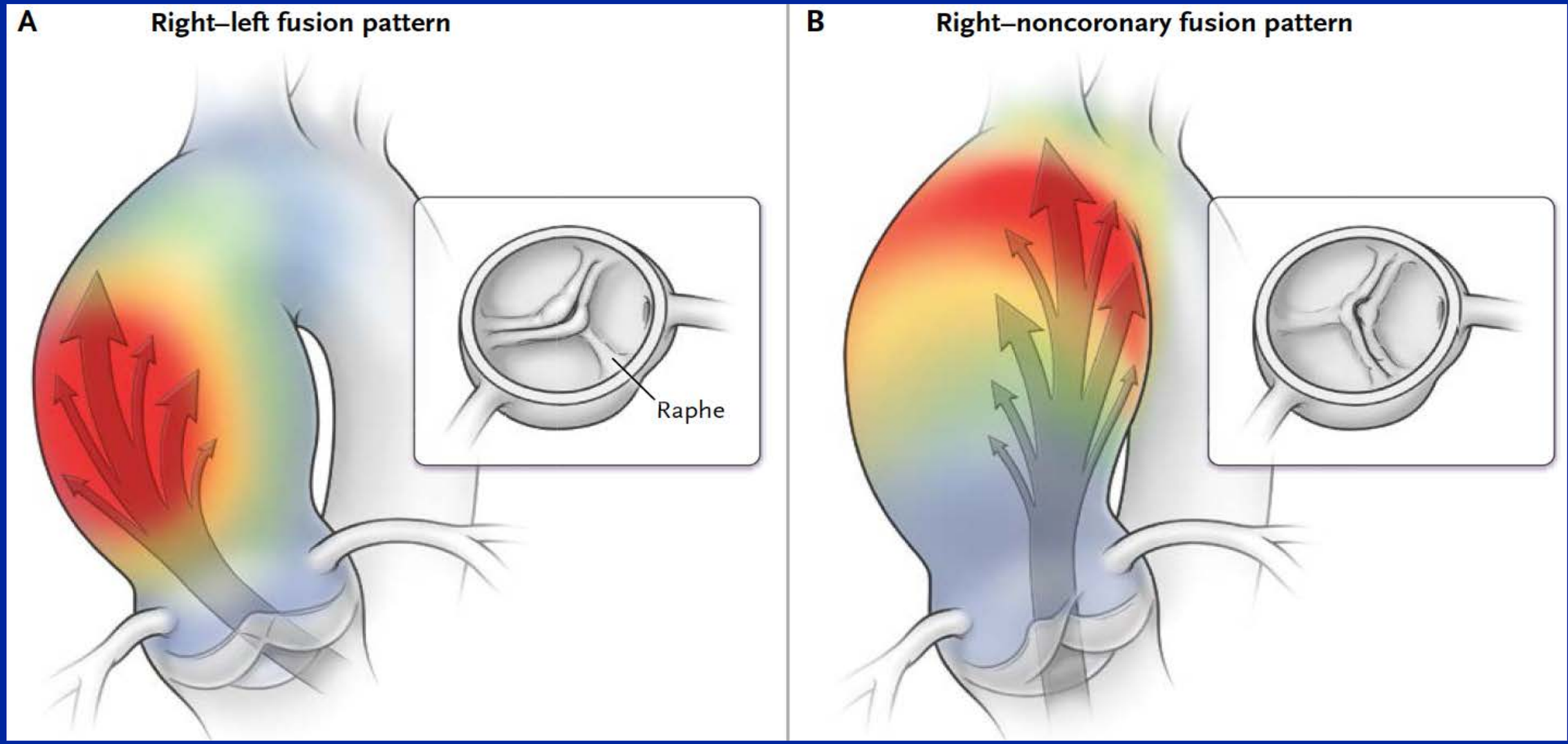
AG Sherrah et al., J Am Coll Cardiol 2016; 67:618 (Sydney)

Nonsyndromic Thoracic Aortic Aneurysm and Dissection Outcomes vs Marfan Syndrome vs Bicuspid Aortic Valve



AG Sherrah et. al. J Am Coll Cardiol 2016;67:618

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

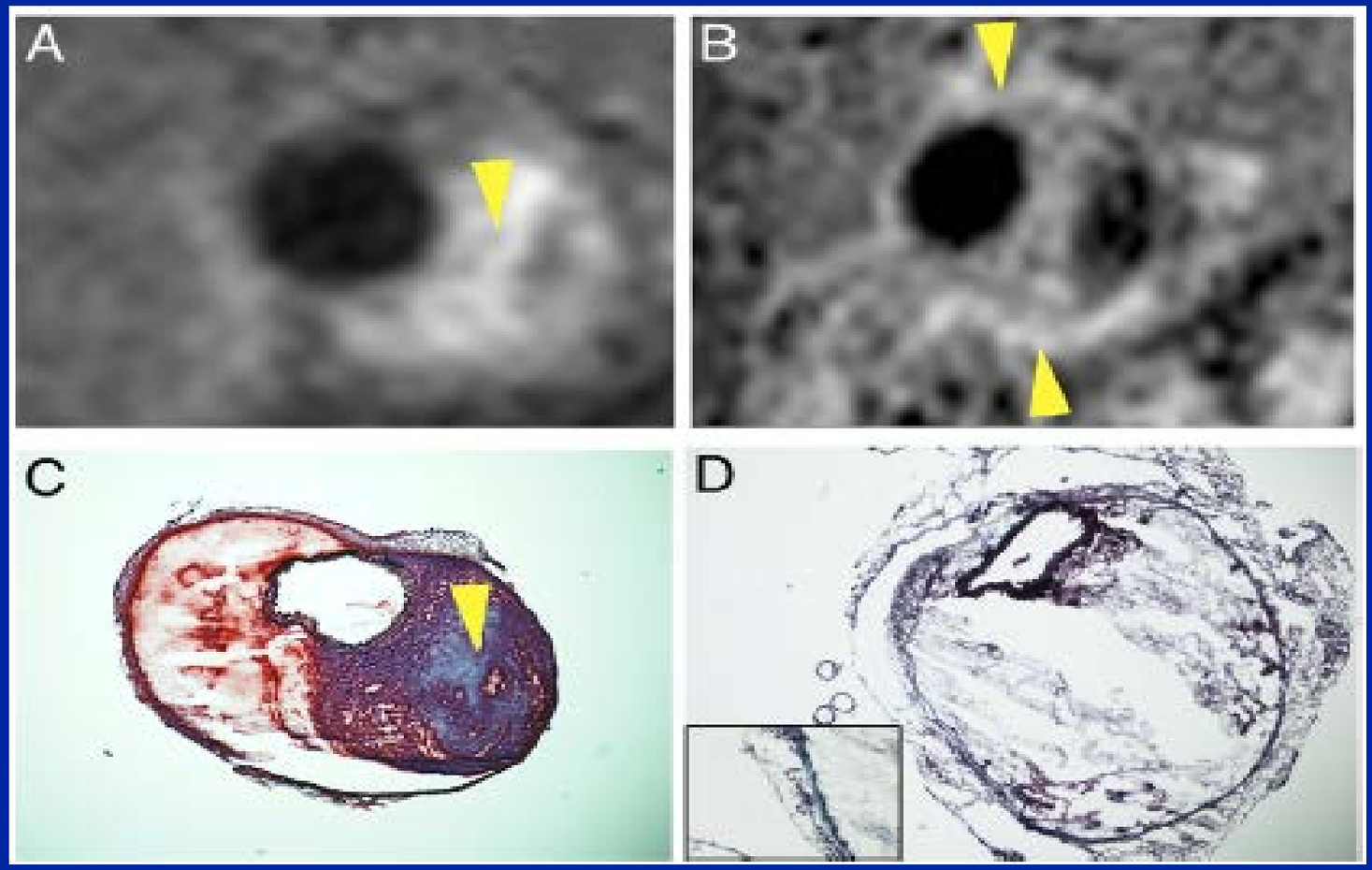


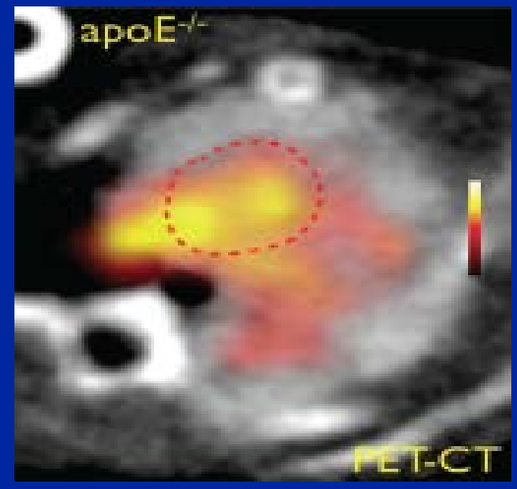
S Verma et. al. N Engl J Med 2014;370:1920 – Types 1,2,3

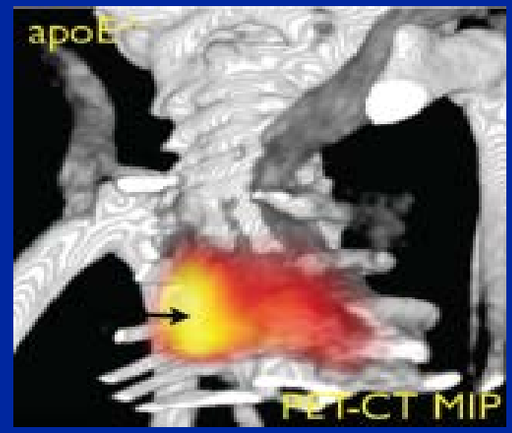
R Mahadevia et. al. Circulation. 2014;129:673 - Detail

3. 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) – MMP9

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

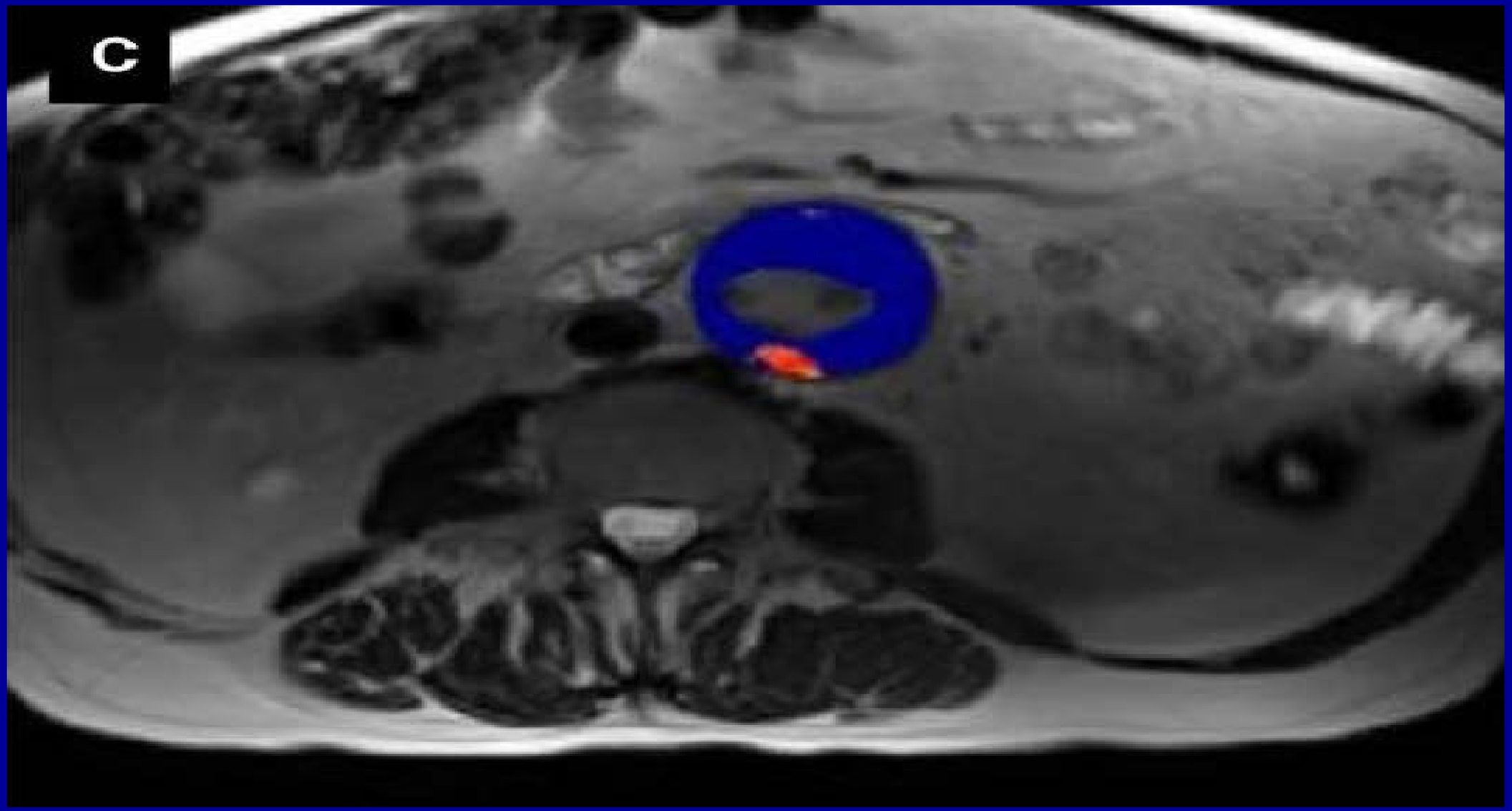
A Klink, V Fuster, ZA Fayad et. al. J Am Coll Cardiol 2011;58:2522

Aortic Wall Inflammation Predicts AAA Expansion, Rupture, and Need for Surgical Repair

Ultrasmall superparamagnetic particles of iron oxide (USPIO) detect cellular inflammation (macrophages) on MRI. In a prospective multicenter open-label cohort study, 342 patients with AAA (diameter ≥40 mm) were classified by the presence of USPIO enhancement and were monitored with serial ultrasound and clinical follow-up for ≥2 years. The primary end point was the composite of aneurysm rupture or repair. USPIO-enhanced MRI predicts the rate of aneurysm growth and clinical outcome. However, it does not provide further information recognized by clinical risk factors.

MA³RS Study Investigators (D Newby et. al) Circulation. 2017;136:787

T2 Map (Blue) Demonstrating Enhancement Of The Posterior Aneurysm Wall With USPIO (Red) By MRI*



MA³RS Study Investigators** (D Newby et. al) Circulation. **2017;136:787

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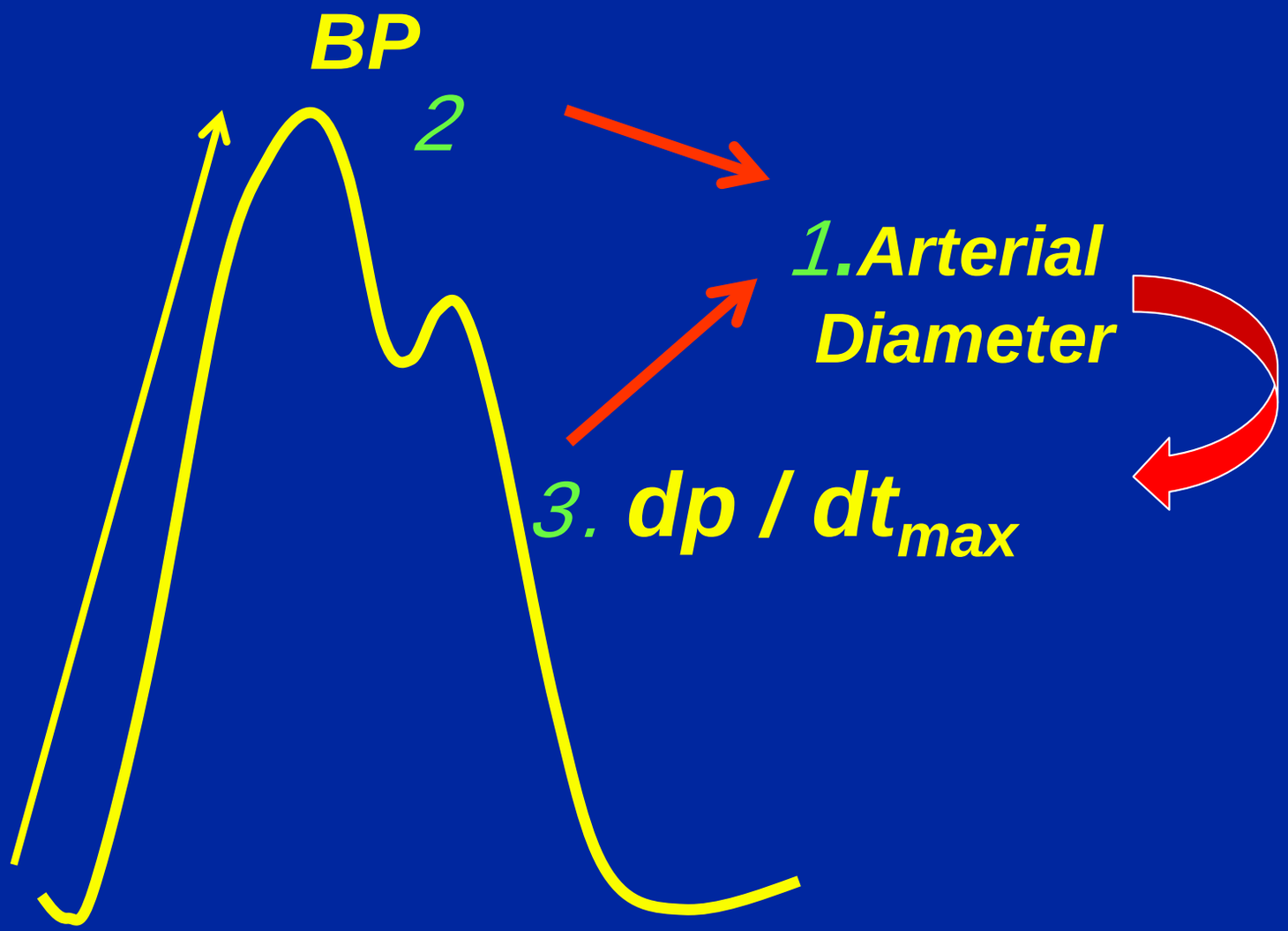
JZ Goldfinger, V Fuster et al., JACC 2014;64:1725

Hemodynamic Frs - Dilatation To Dissection



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

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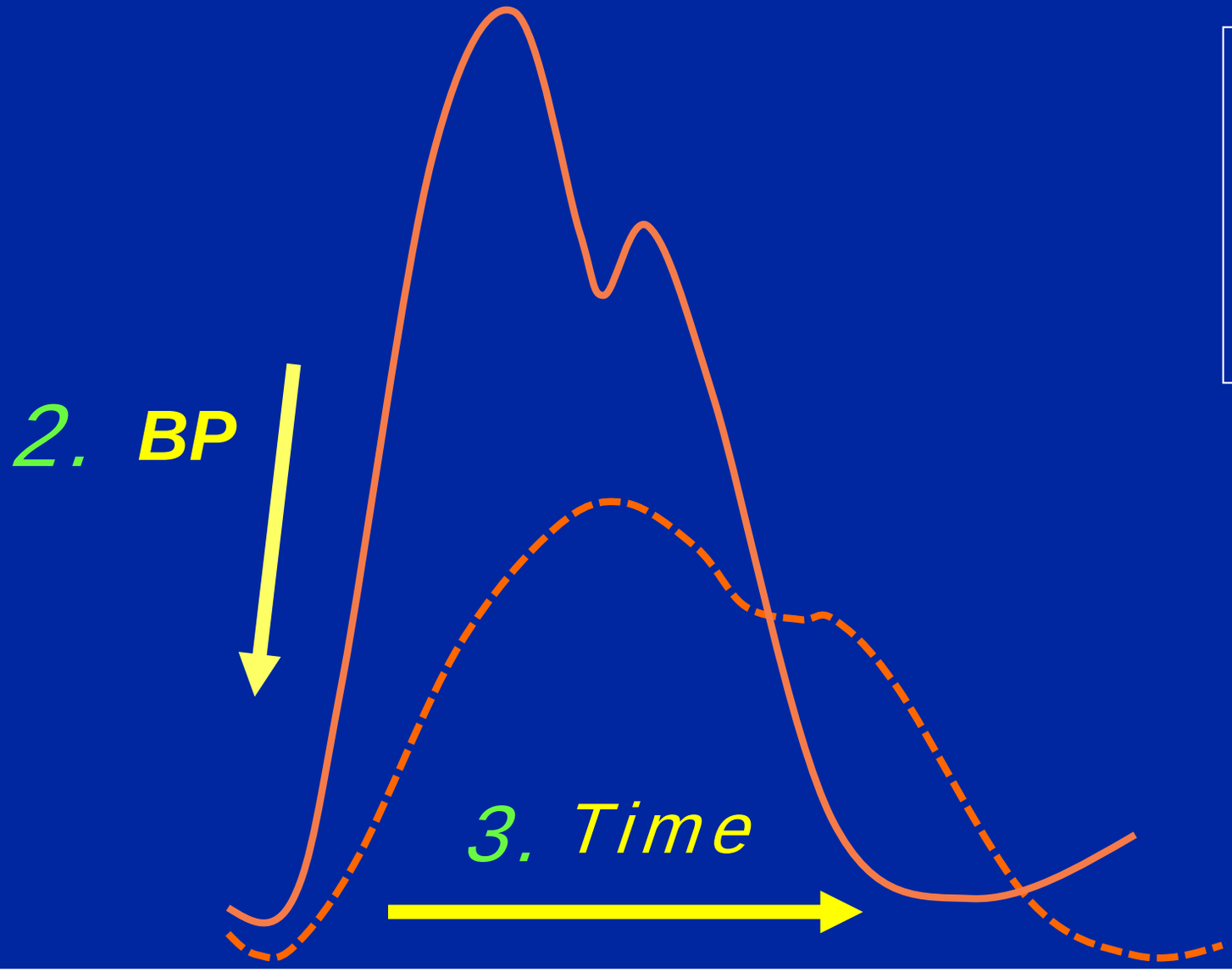
JZ Goldfinger, V Fuster et al., JACC 2014;64:1725

TAD – Hemodynamic Approach



Baseline

1) Vasodilator
(i.e., Nitroprusside)
(2) Beta blockade

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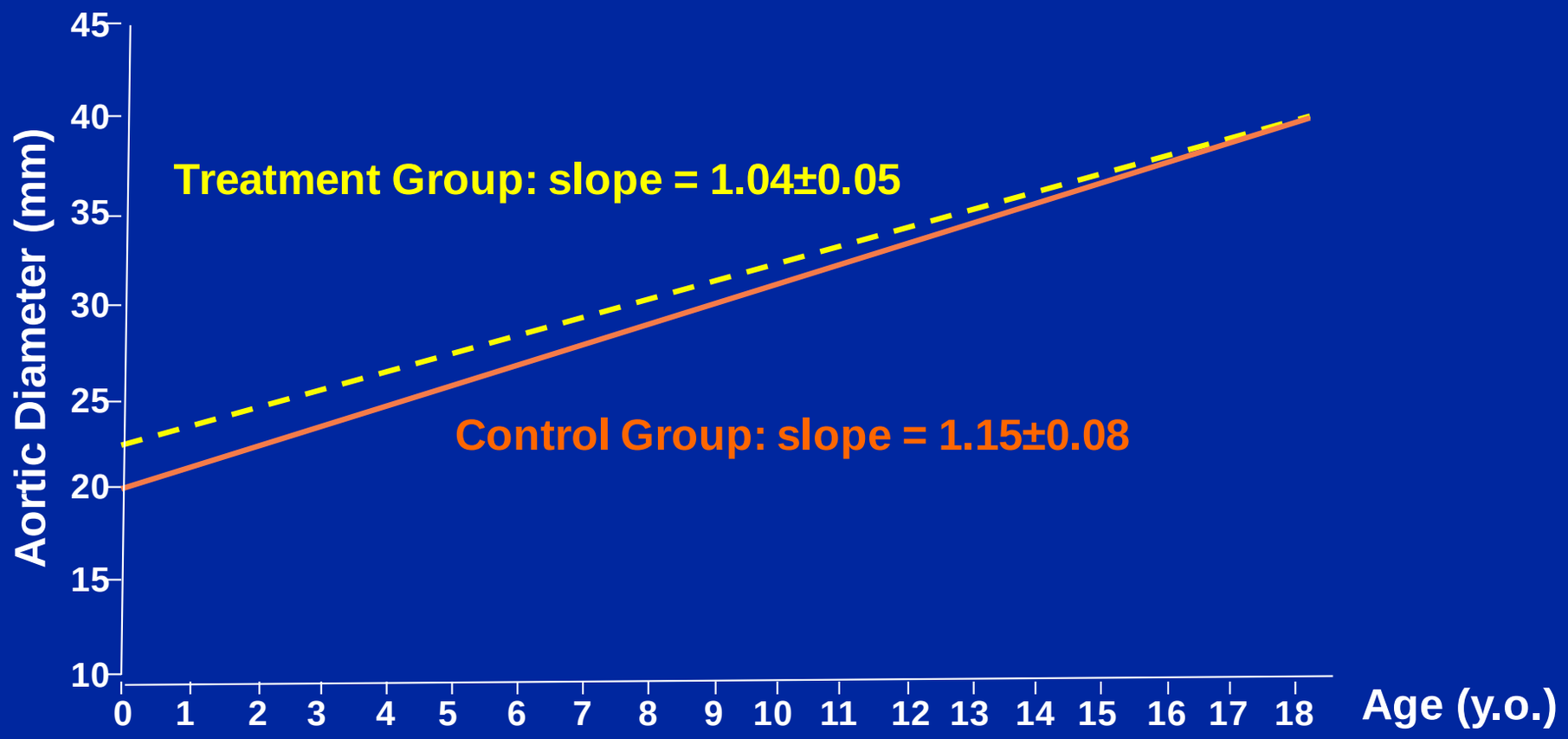
1) MFS - IMPACT OF β BLOCKERS ON AORTIC ROOT DIAMETER



2). M Groenink et al., EHJ 2013; Aug 21 – Netherlands - ARB ?
RV Lacro et al., NEJM 2014; 371:2061 – American Study – ARB Negative
O Milleron et al., Eur Heart J 2015; 36:2160 – French Study – ARB Negative

Regulation of membrane type-1 matrix metalloproteinase activity and intracellular localization in clinical thoracic aortic aneurysms

John S. Ikonomidis, MD, PhD,[a] Elizabeth K. Nadeau, BS,[a] Adam W. Akerman, MS,[a] Robert E. Stroud, MS,[a] Rupak Mukherjee, PhD,[a,b] and Jeffrey A. Jones, PhD[a,b]

3). Targeted inhibition of MT1-MMP may have therapeutic relevance as an approach to attenuating the TAA development.

J Thorac Cardiovasc Surg 2017;153:537

Understanding - TAA, TAD, AAA, AAR - 2017

- ***Definition, Mortality, Imaging, ECM (4)***
- ***Area & Types (TAA,TAD,AAA,AAR) (4)***
- ***Pathogenesis (Marfan's, BHA, AAA) (4)***
  - ***Dysfunctional Structure (3)***
  - ***Hemodynamics (4)***
  - ***Approach to Hemodynamics (2)***
  - ***Approach to Dysfunctional Structure (2)***
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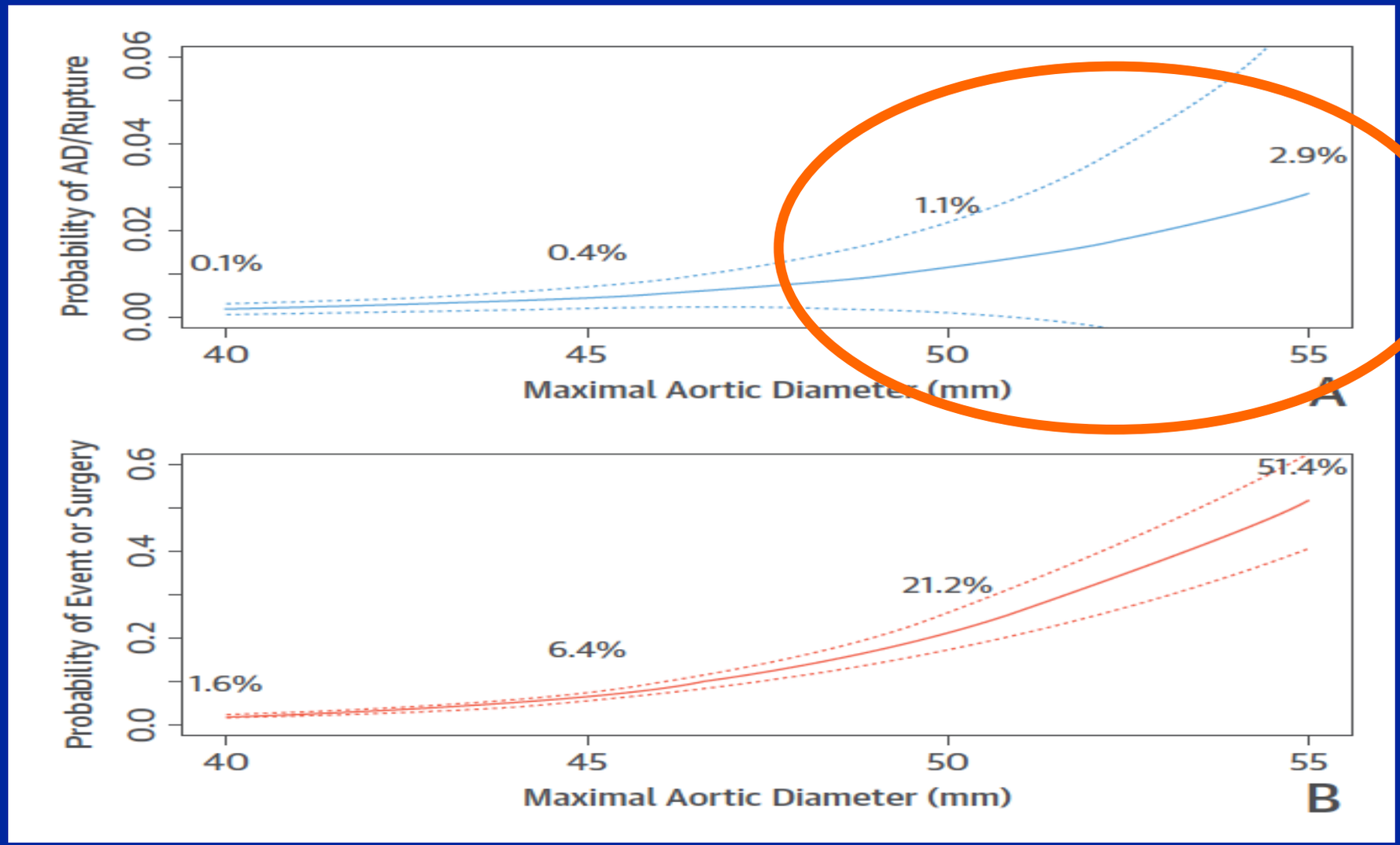
- ≥ 40 mm with indication for elective AVR (BAV)
- ≥ 45 mm in MFS, NSTAA (?)
- ≥ 50 mm in BAV (?)
- ≥ 55 mm for an ascending aortic aneurysm (?)
- ≥ 60 mm for a descending aortic aneurysm;
- ≥ 70 mm in high-risk comorbidities;
- Growth rate ≥ 10 mm per year in <55 mm diameter
- Recurrent symptoms, Evidence of proximal dissect.

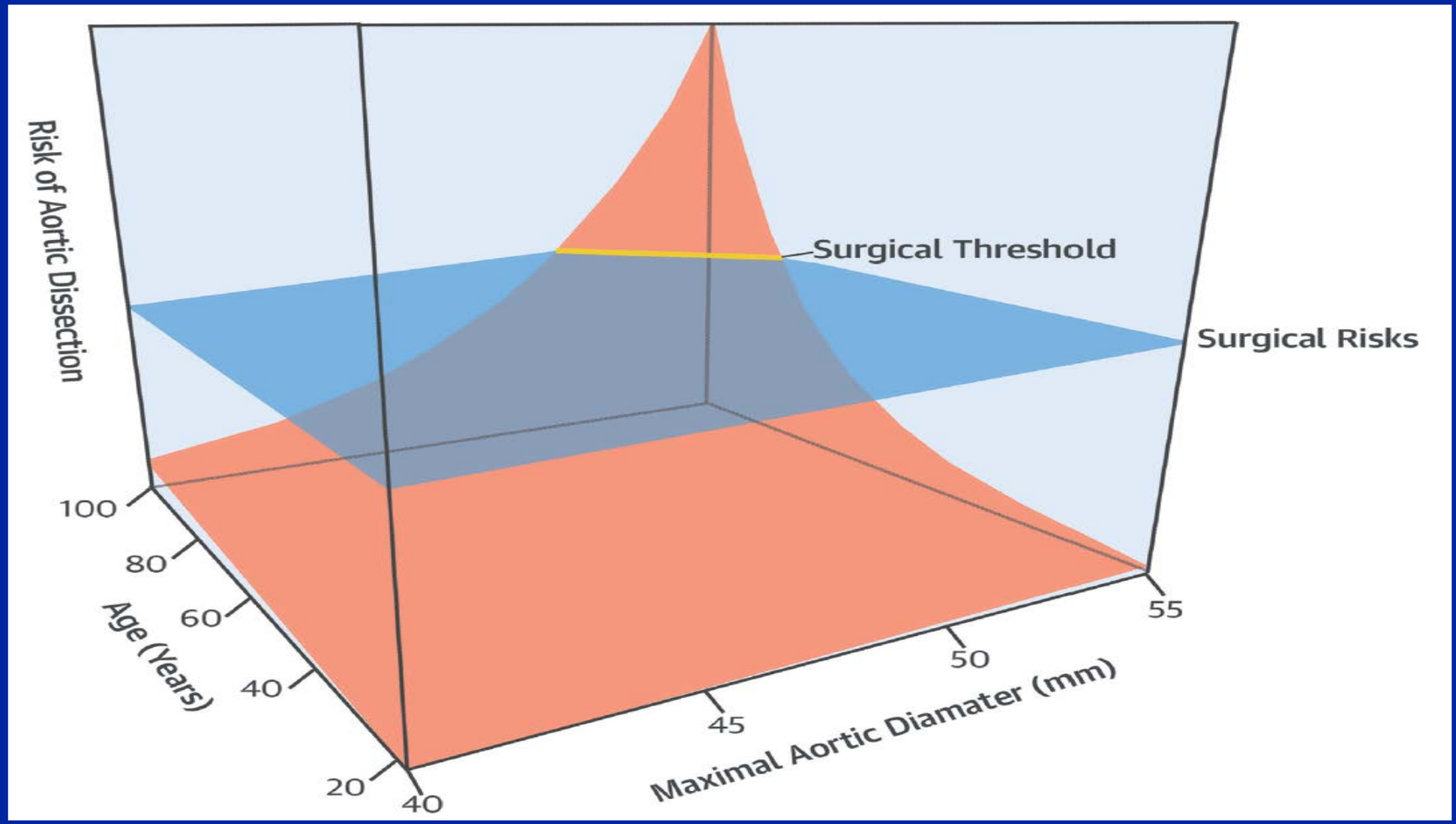
L Cozijnsen et al., Circ 2011; 123:924
ACC/AHA Circulation. 2016;133:680

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



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

3. Dissection in Ascending Aortic Aneurysms: Risk Threshold - Age



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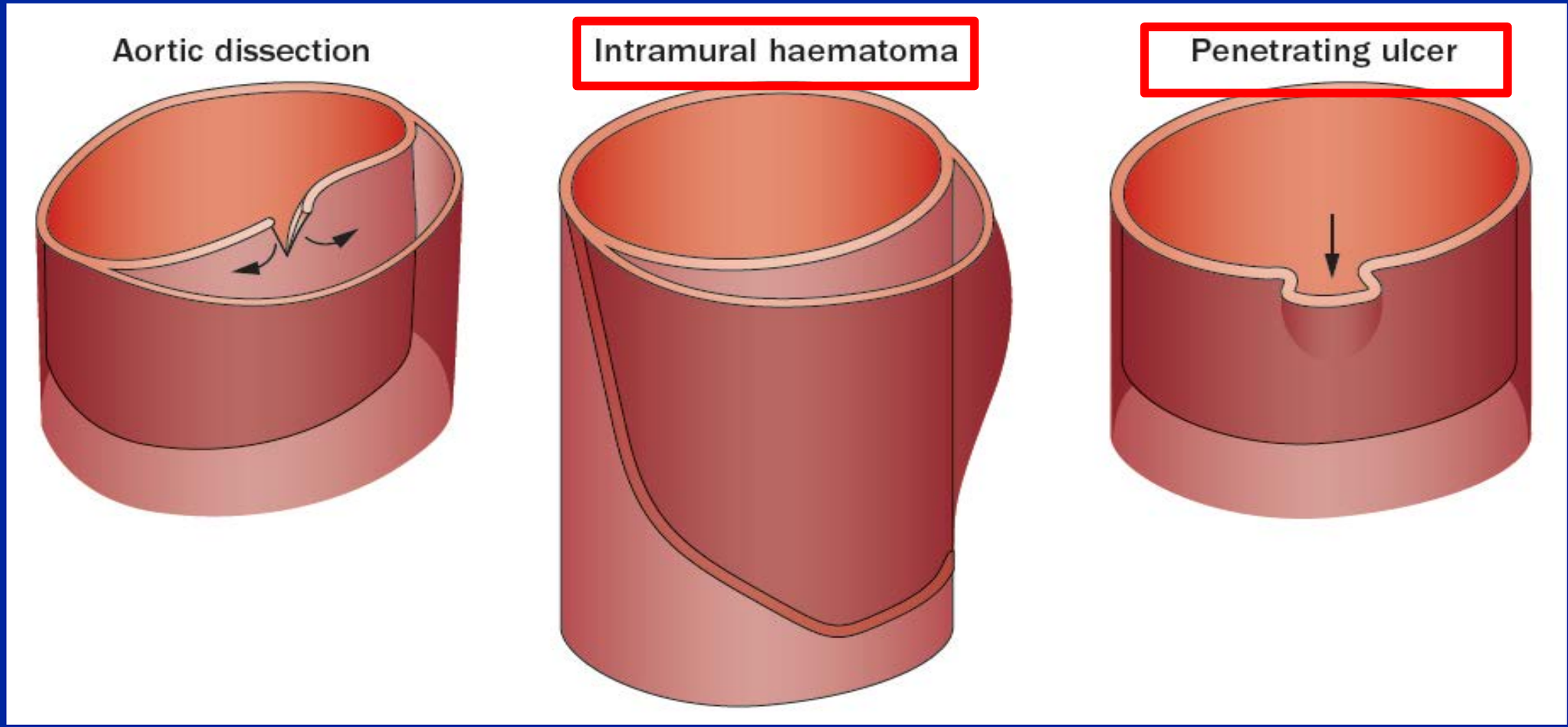
1. Contained Acute Aortic Syndrome



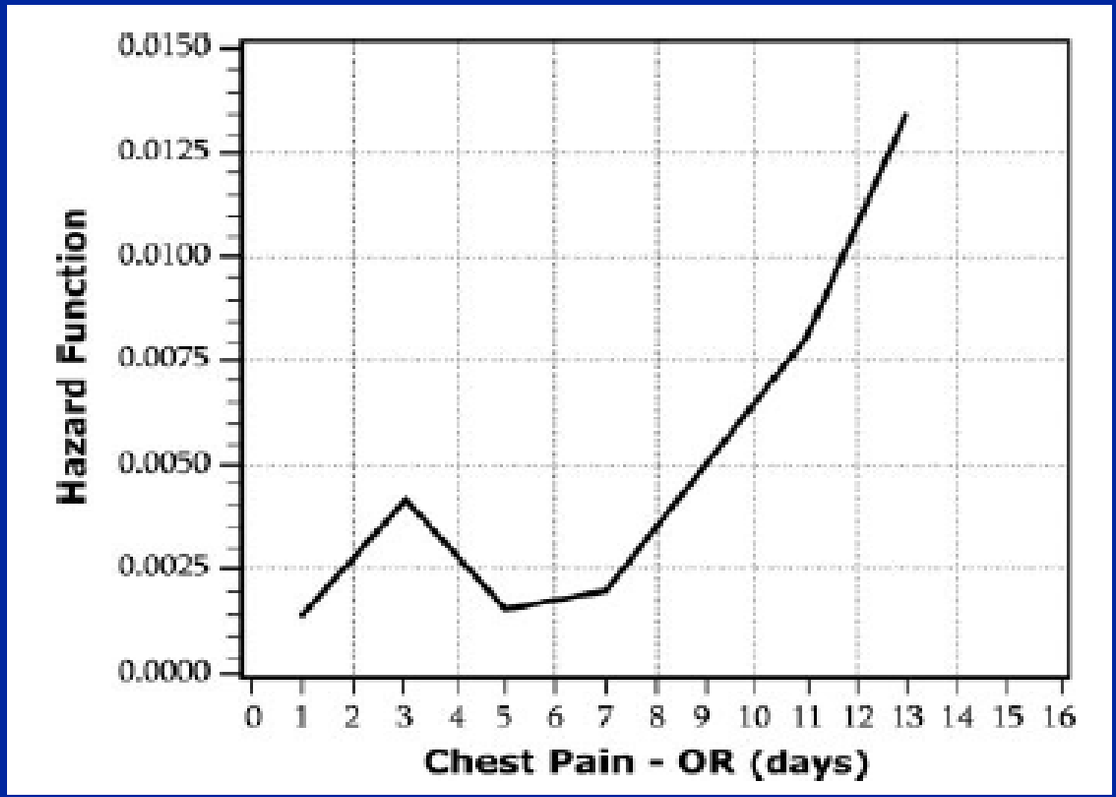
RE Clough et. al. Nat. Rev. Cardiol. 2015;12:103

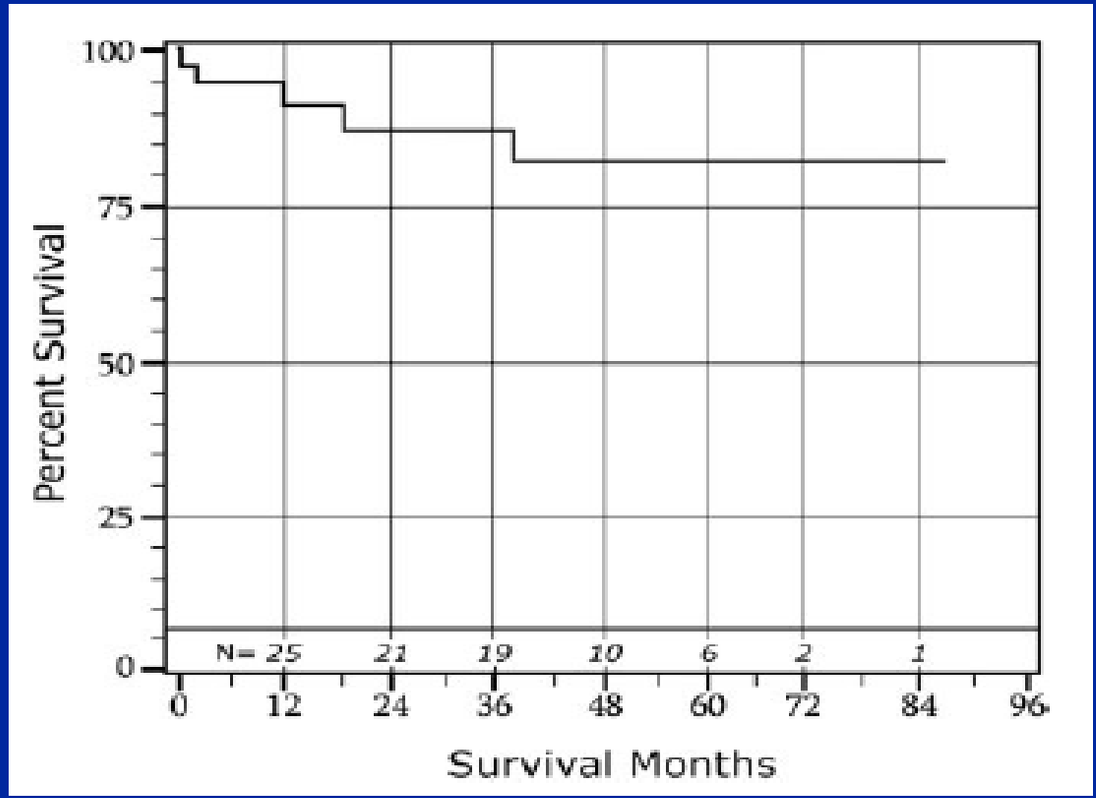
RR Baliga et. al. J Am Coll Cardiol Img 2014;7:406

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

Acute Type A Intramural Hematoma

Analysis of Current Management Strategy



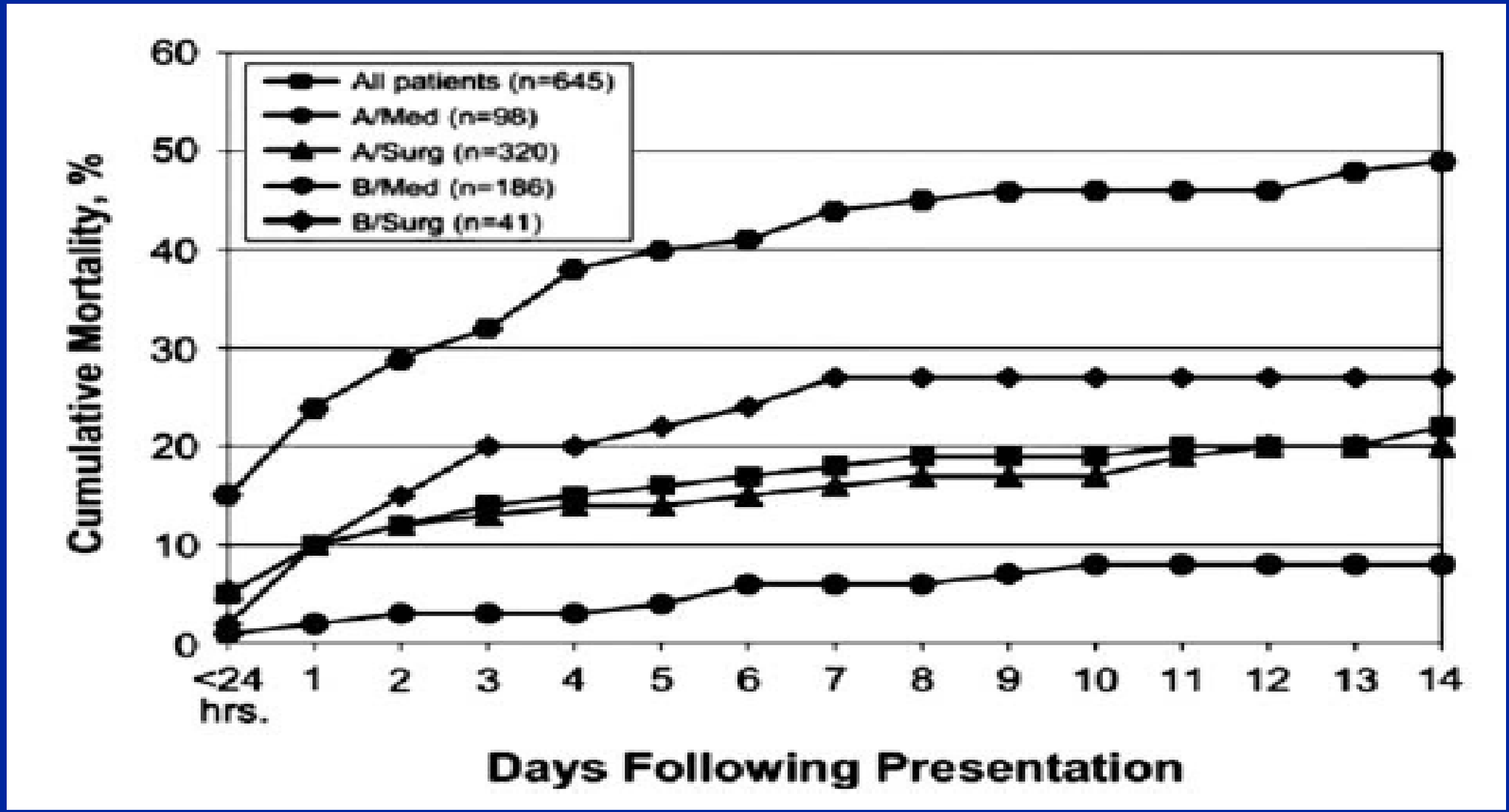


Best cutoff to Predict Events: 16 mm (Hematoma) - Often Type A

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%).

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

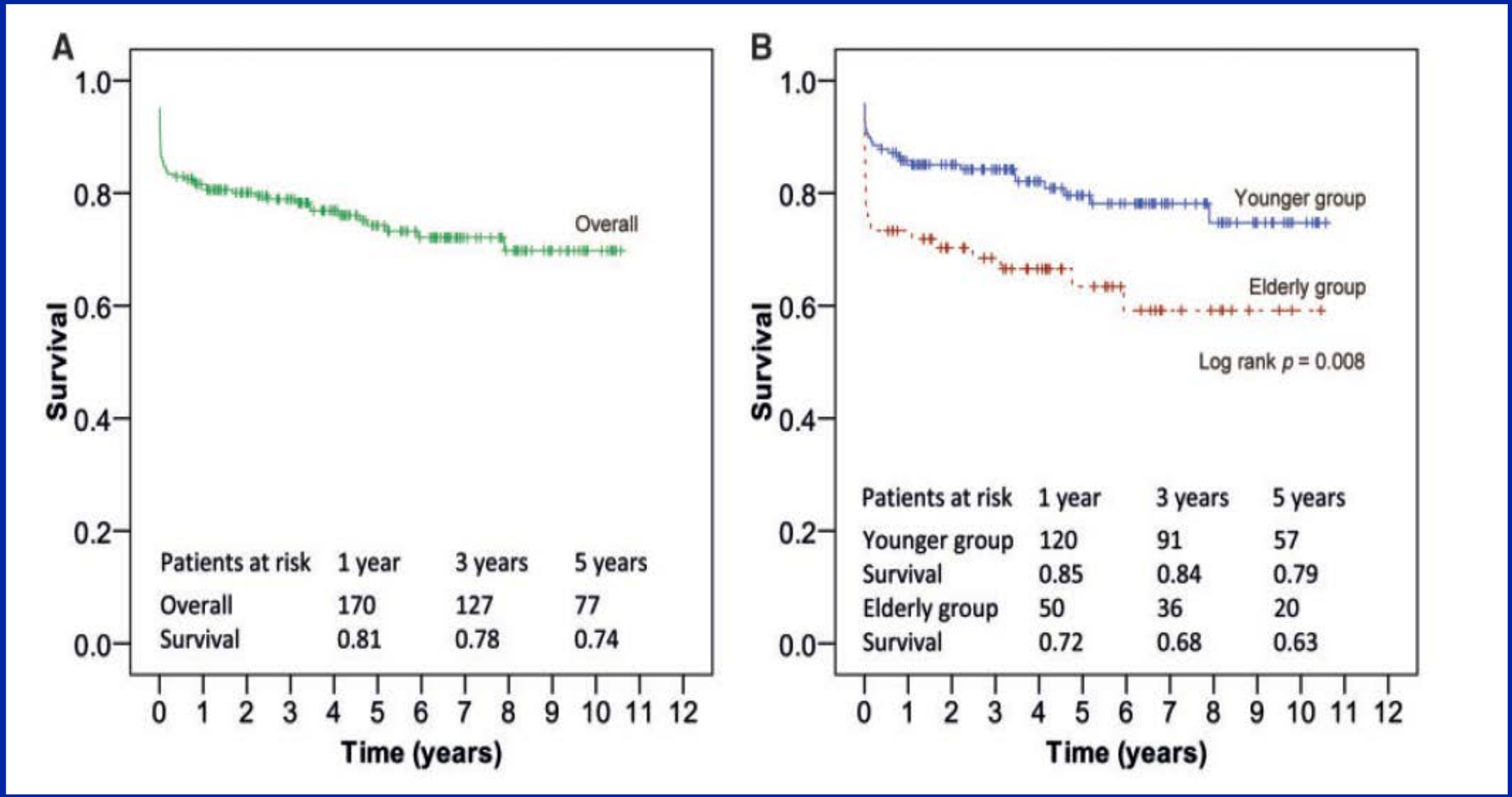
TA. S

TB. M

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

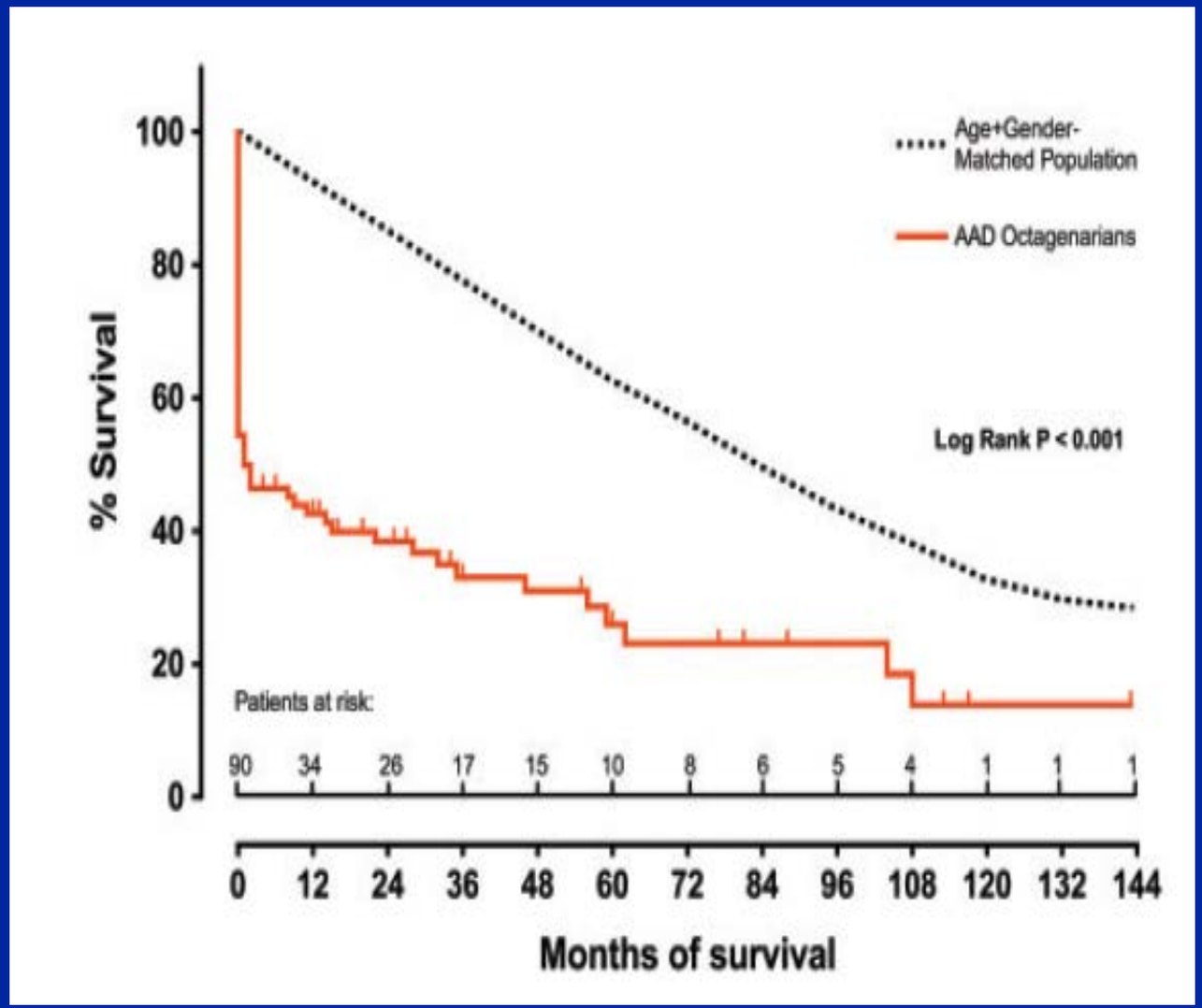
PG Hagan et. al. JAMA 2000;283:897

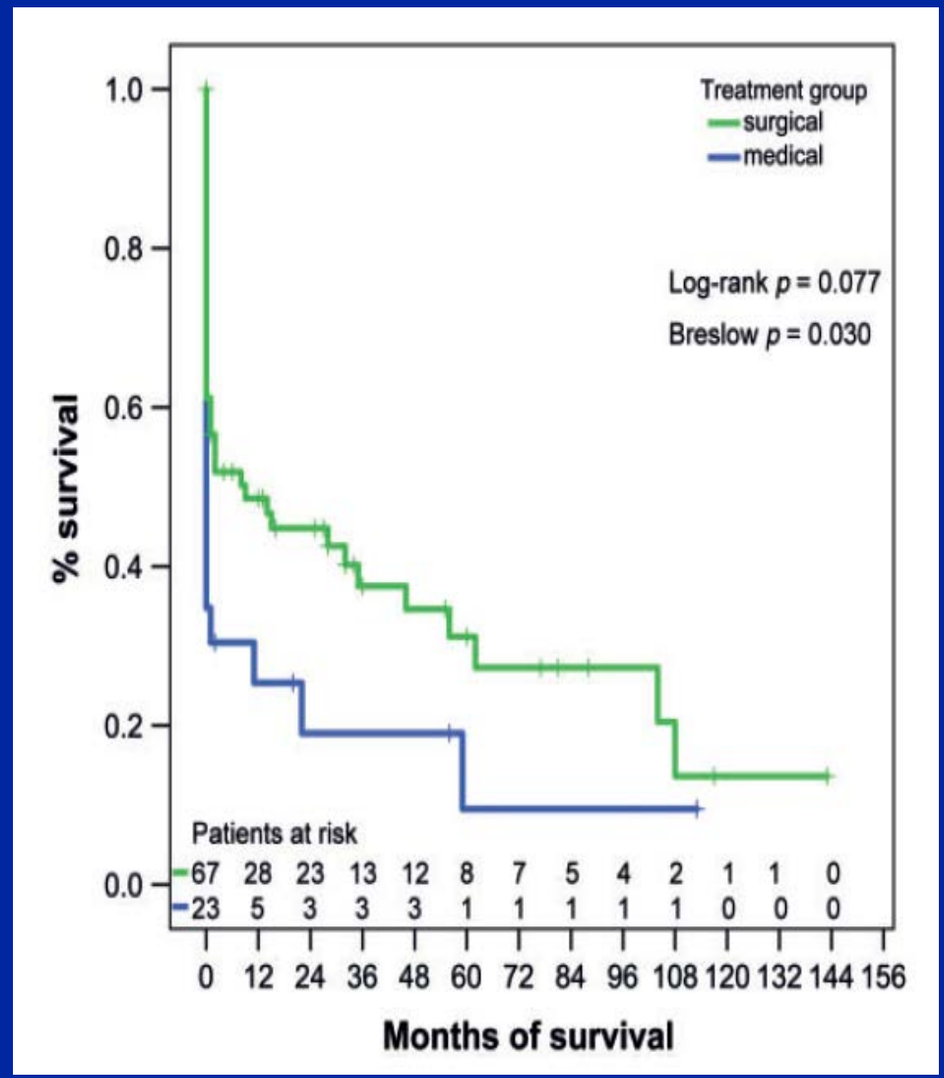
2a. Long-term Outcome & Quality of Life Post Surgery For AAD Type A, in Young & Elderly Adults



J Jussli-Melchers et. al. Eur J Cardiothorac Surg 2017;51:465

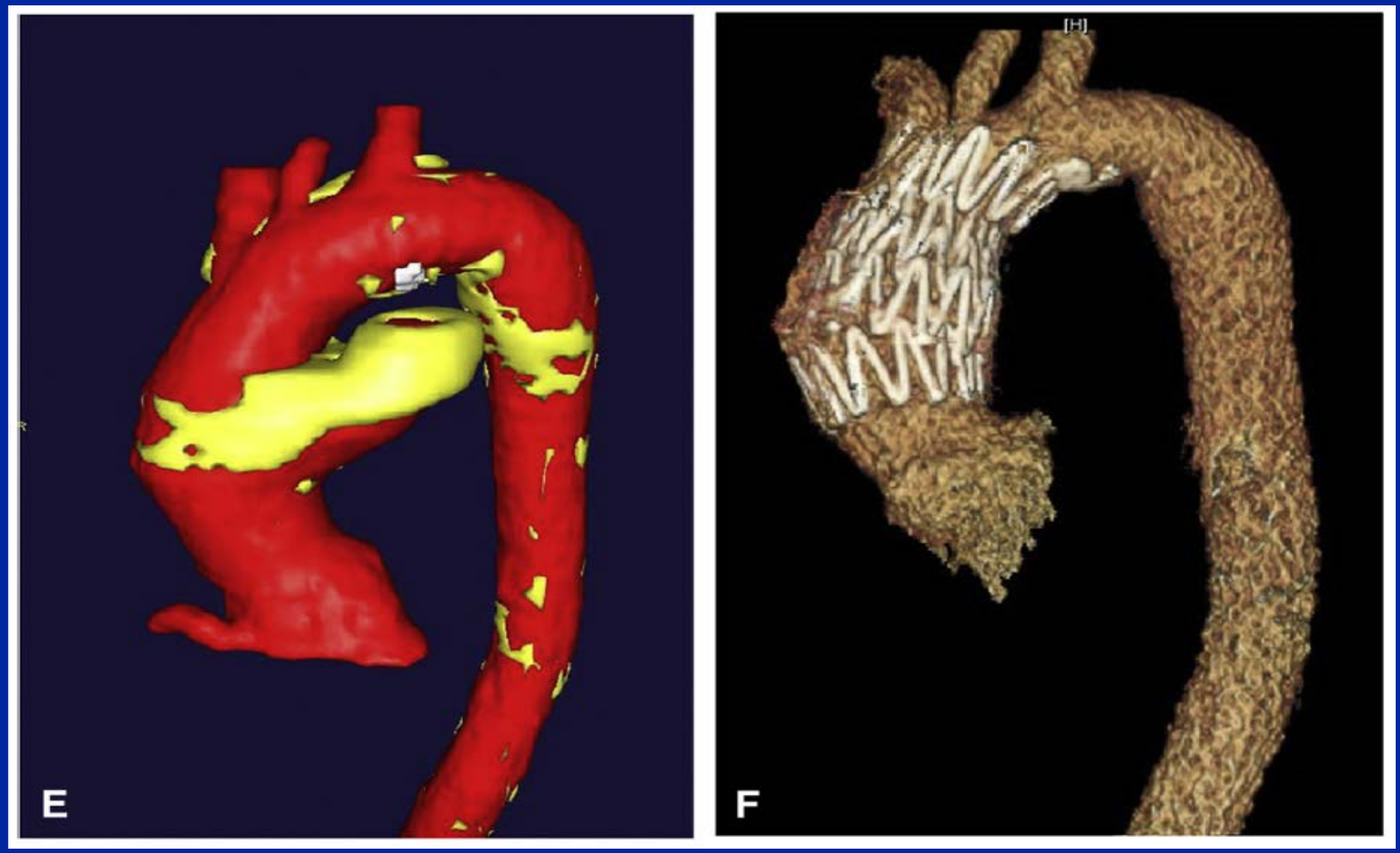
2b. Acute Type A Dissection In Octogenarians
In-hospital Outcome & Long-term Survival





J Dumfarth et. al. Eur J Cardiothorac Surg 2017;51:472

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



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

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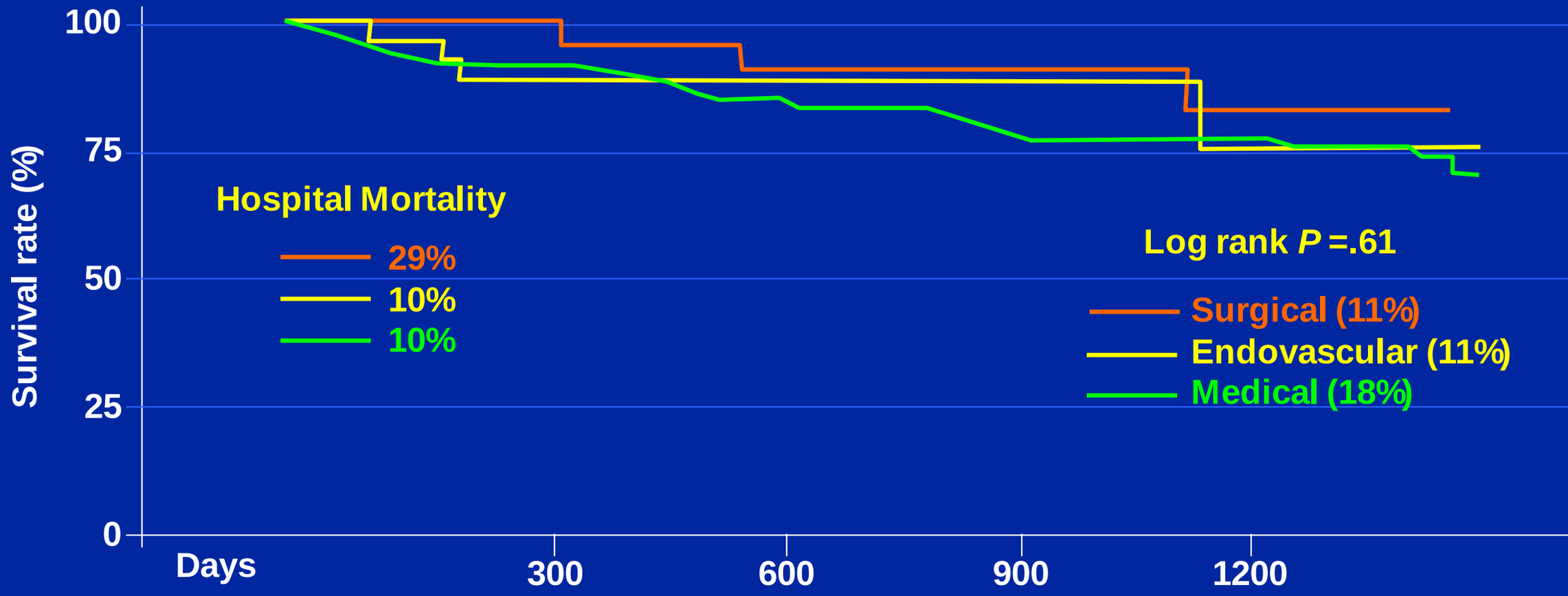
- ≥ 55 mm for an ascending aortic aneurysm,
- ≥ 60 mm for a descending aortic aneurysm;
- ≥ 70 mm in high-risk comorbidities;
- Growth rate ≥ 10 mm per year in <60 mm diameter
- Recurrent symptoms, Evidence of proximal dissect.

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

4a). Type B Dissection – Survival Curve (N=300)



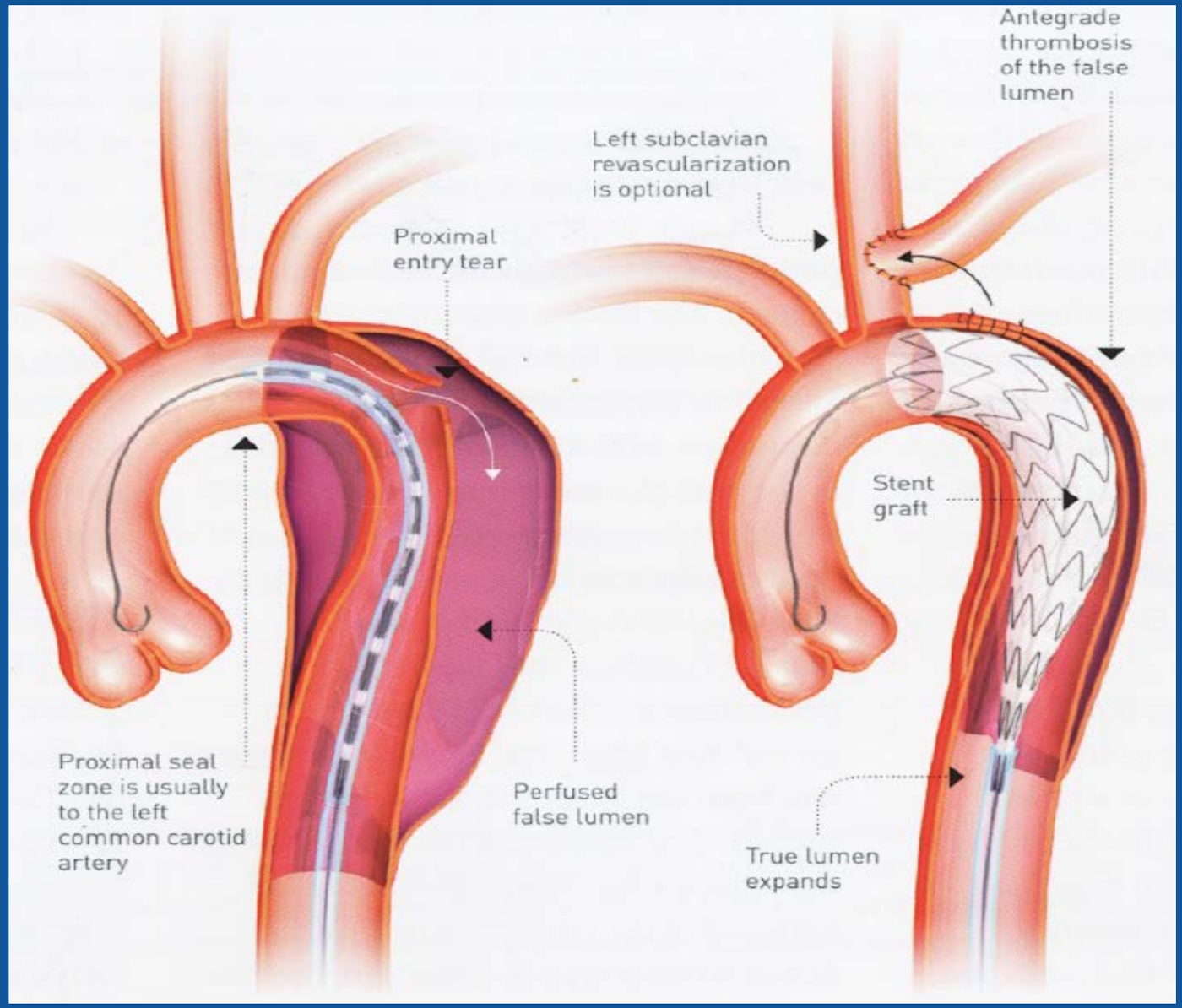
Worst Prognosis: Hypotension, Pleural Effusion, Renal Failure

Refractory Pain & Hypertension

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

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

4b). Site of TEVAR Implementation



RP Cambria. Advances at Mass General. 2015

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  - ***Hemodynamics***
  - ***Approach to Hemodynamics***
  - ***Approach to Dysfunctional Structure***
- ***Interventional (TAA,TAD,AAA,AAR)***

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. 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

Population Screen and Intervention for Vascular Disease in Danish Men (VIVA): A Randomised Controlled Trial

In this randomized controlled trial, we randomly allocated (1:1) all men aged 65-74 years living in the Central Denmark Region to screening for AAA, PAD, and hypertension, or to no screening. We invited participants who were found to have AAA, PAD or hypertension to the most appropriate treatment. The primary outcome was all-cause mortality, assessed 5 years after randomisation. Between Oct 8, 2008, and Jan 11, 2011, we randomly allocated 50,156 participants, with 25,078 (50%) each in the screening and non-screening groups. AAA was detected in 3.3% of patients, PAD in 10.9%, and unknown potential hypertension in 10.5%. There was a reduction of mortality risk from AAA, PAD and hypertension that can be linked to therapy. The number needed to invite to save one life was 169 people.

JS Lindholt, R Søgaard. Lancet 2017; 390:2256 – AAA no Difference

2. 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

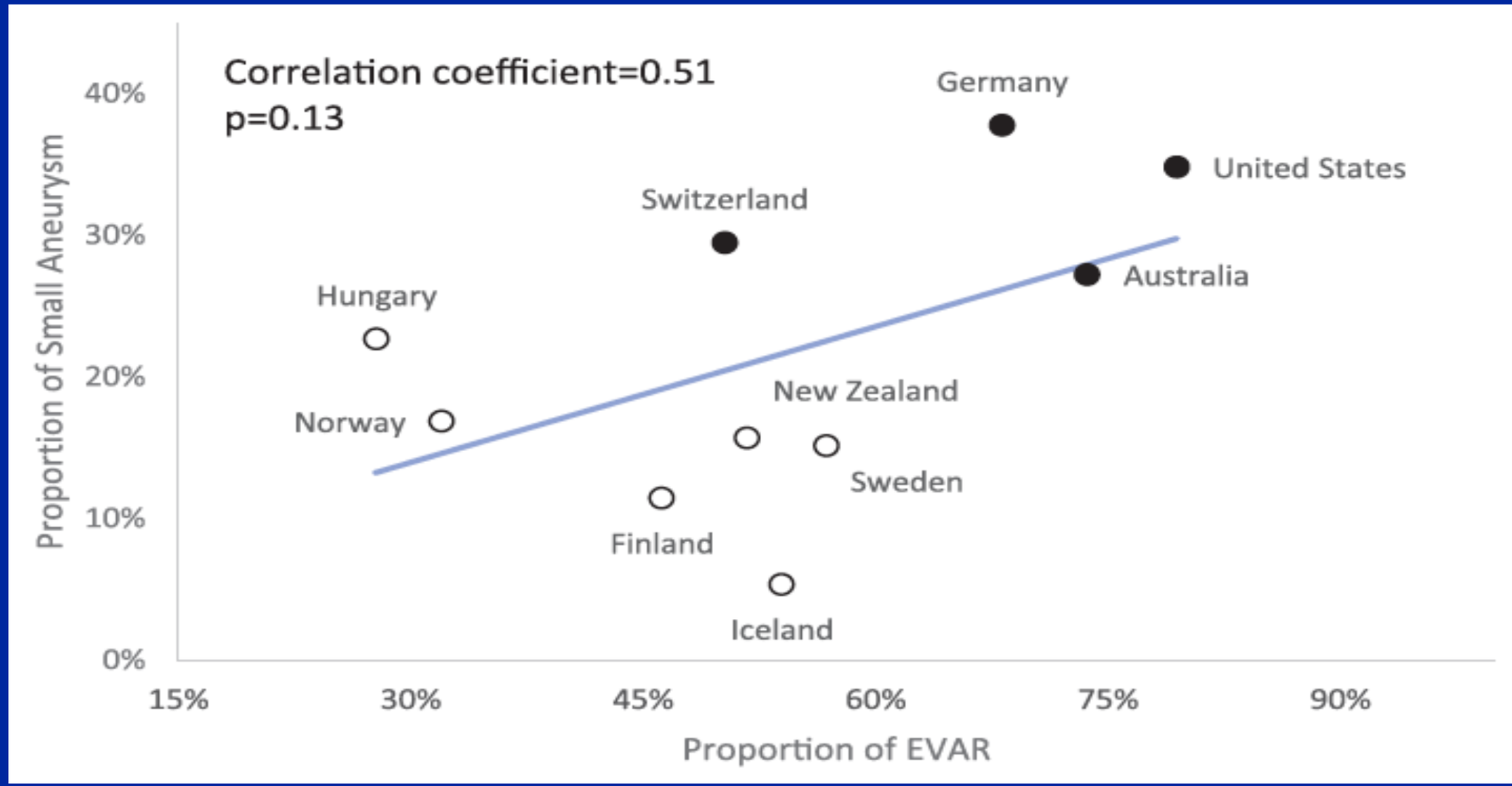
JM Guirguis-Blake et al., Ann Intern Med 2014; 160:321 – Validated Prospectively

3. 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

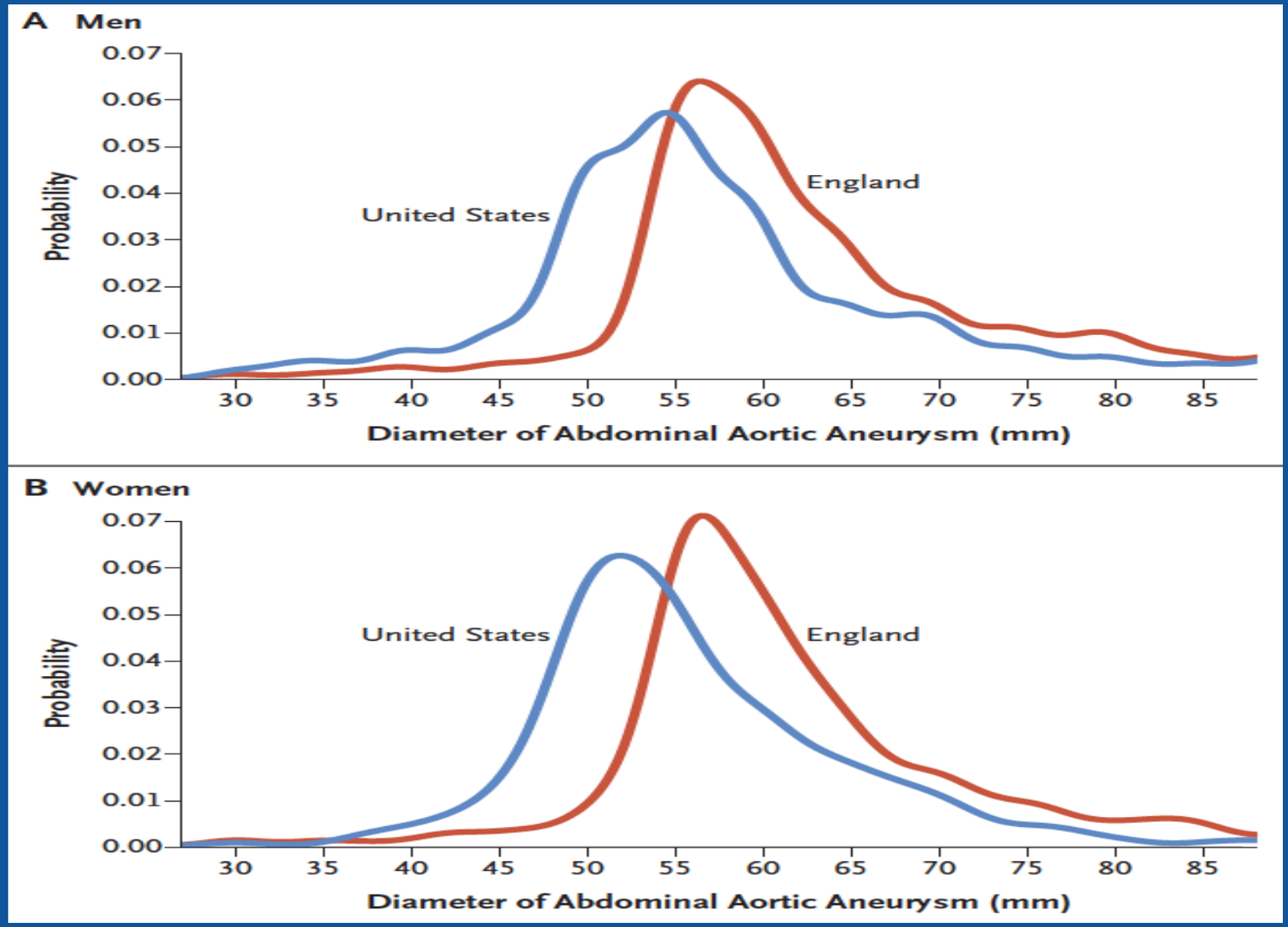
K Craig Kent. N Engl J Med 2014;371:2101

Aneurysm Diameter Related To EVAR And Healthcare Reimbursement Model



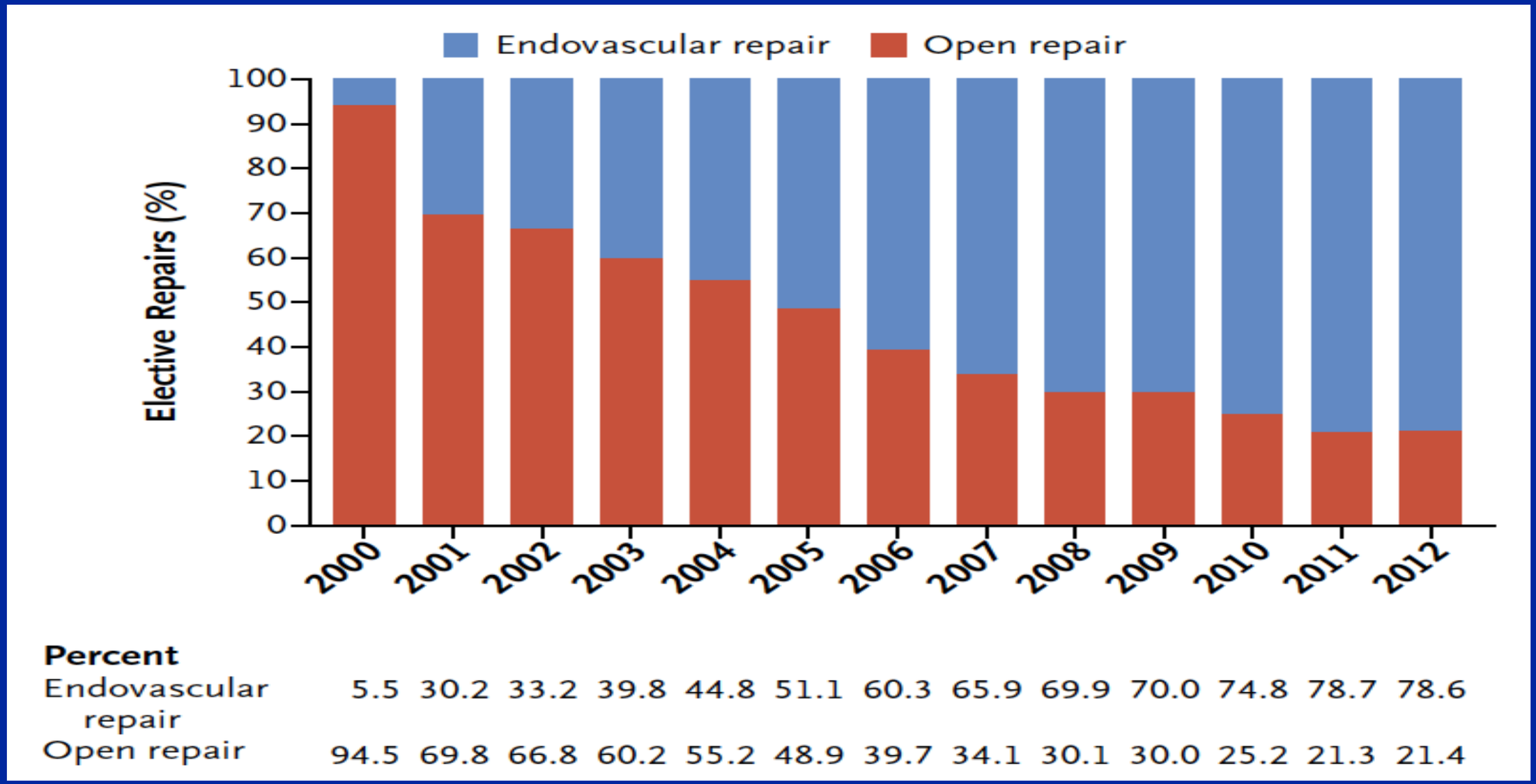
AW Beck et. al. Circulation. 2016;134:1948

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 - > Death

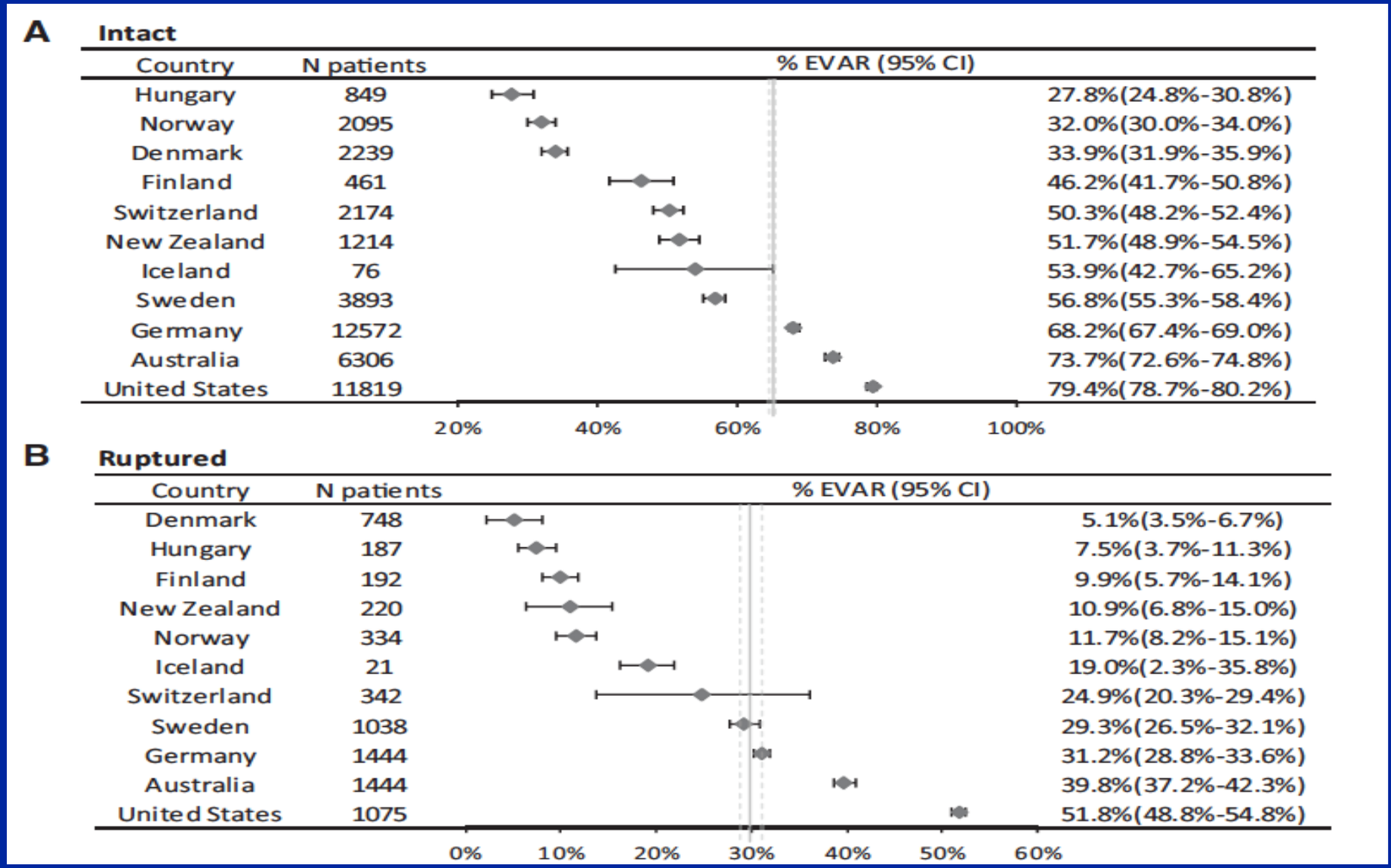
4. Annual Proportion of Elective Endovascular & Open Repairs for AAA in the US



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

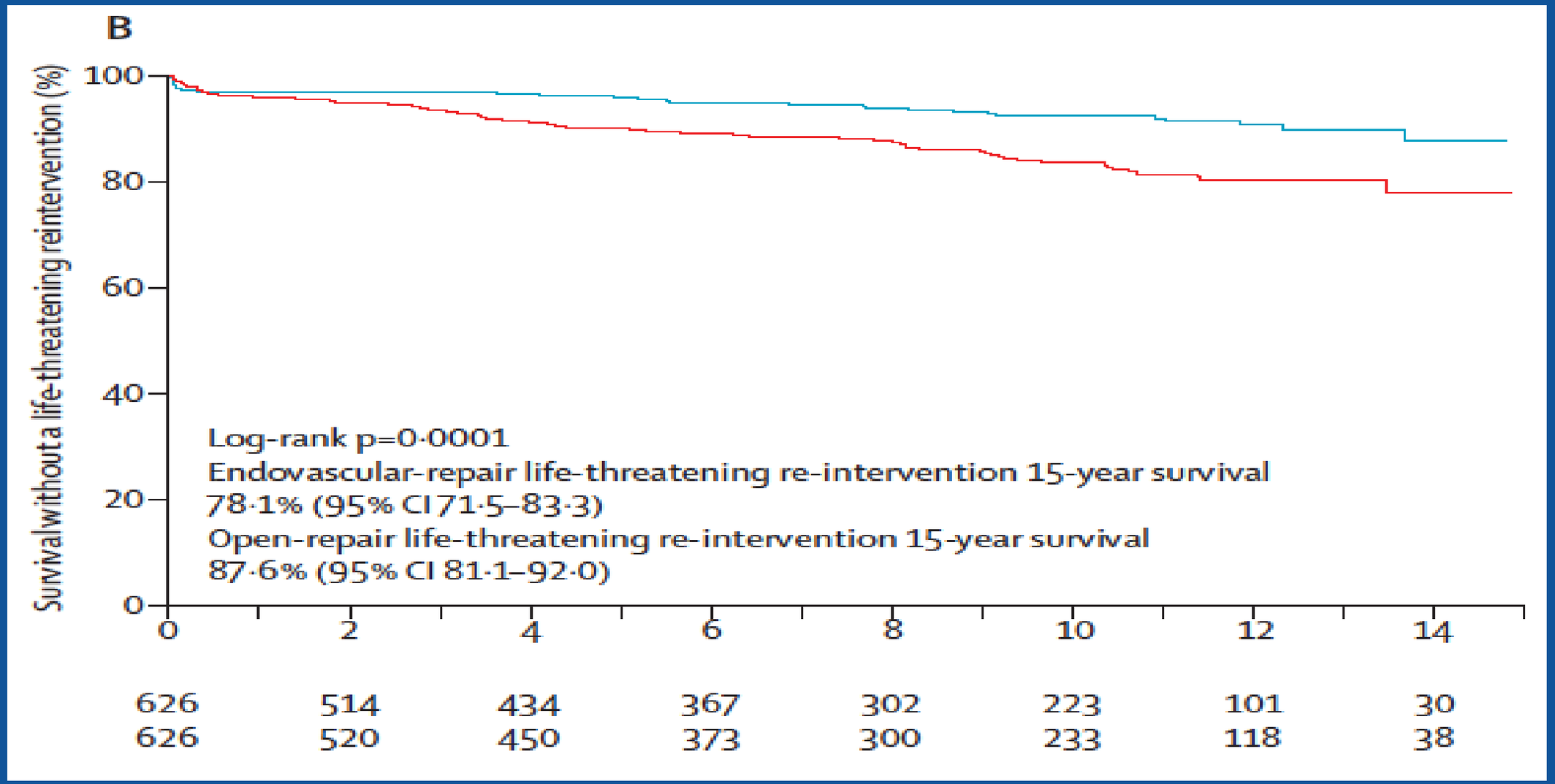
K Craig Kent. N Engl J Med 2014;371:2101

Pts (%) EVAR For Intact (A) & Ruptured (B) AAA.



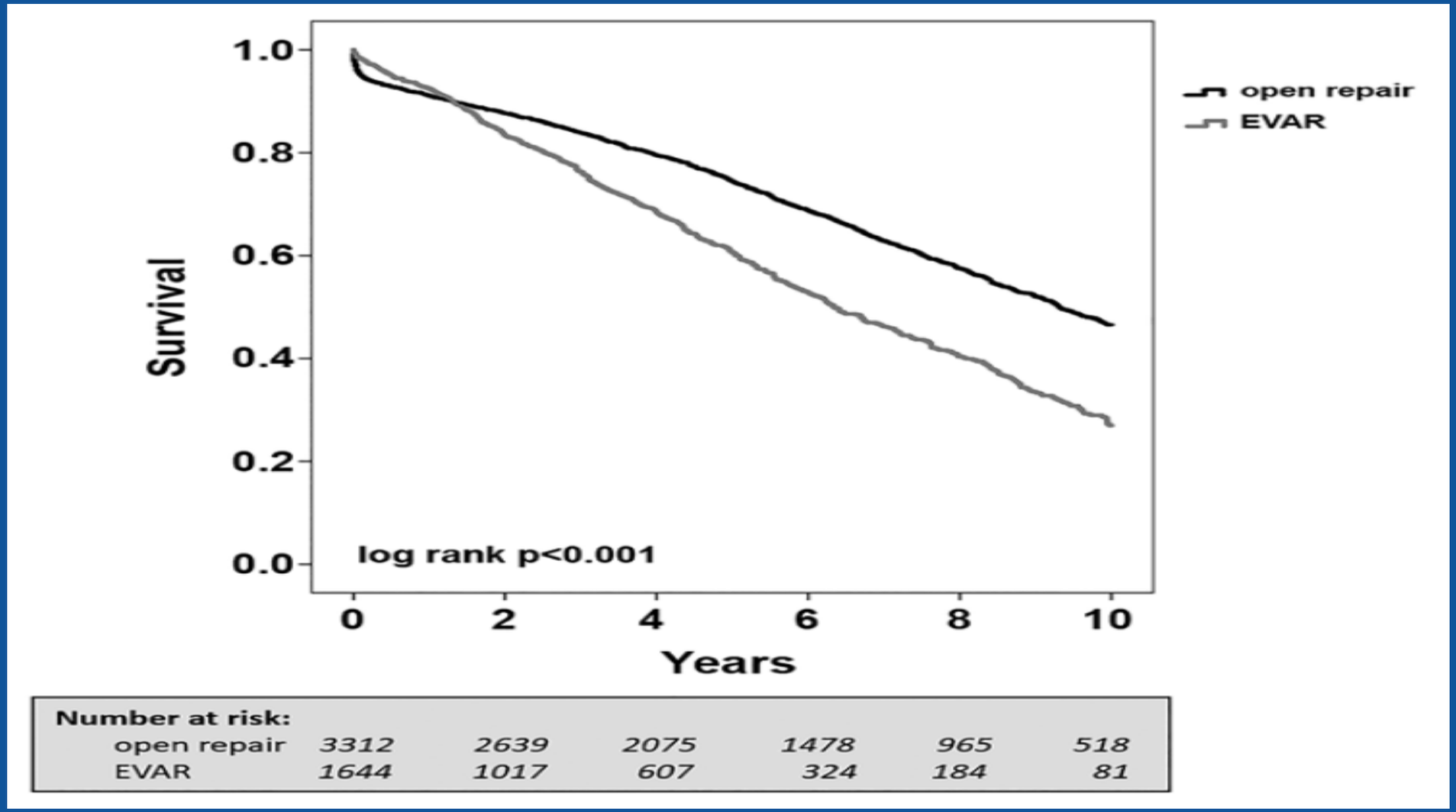
AW Beck et. al. Circulation 2016;134:1948

4a. Time To First Re-intervention In The EVAR Open Repair Groups During 15 Years (5.5 cm)



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

4b. Open And Endovascular Repair Showing Survival After Intact AAA Repair



Number at risk:						
open repair	3312	2639	2075	1478	965	518
EVAR	1644	1017	607	324	184	81

MT Laine et. al. Circulation. 2017;136:1726

A Population-Based Study of AAA Treatment in Finland 2000 to 2014

Ruptured AAA incidence for men >65 years has declined by nearly 30% in Finland, likely because of the decrease in AAA prevalence. The treatment results have improved as well for both elective and emergency repair. Increased use of EVAR has resulted in a decrease of mortality after elective AAA repair, but results of open repair have improved as well. However, late mortality from elective EVAR is surprisingly high in comparison with open repair, which may have been exaggerated by patient selection.

MT Laine et al., Circulation 2017; 136:1726

The Aorta - TAA, TAD, AAA, AAR – 2017 - 2018

- ***Area & Types (TAA,TAD,AAA,AAR)***
- ***Pathogenesis (Marfan's, BHA, AAA)***
  - ***Dysfunctional Structure***
  - ***Hemodynamics***
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JZ Goldfinger, V Fuster et al., JACC 2014;64:1725

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

Diseases of The Aorta 2017
Understanding & Approach

TAA, TAD, AAA, AAR

ACC New York, Dec 9, 2017 - No Disclosures