Acute Aortic Dissection:
Insights from the IRAD Registry

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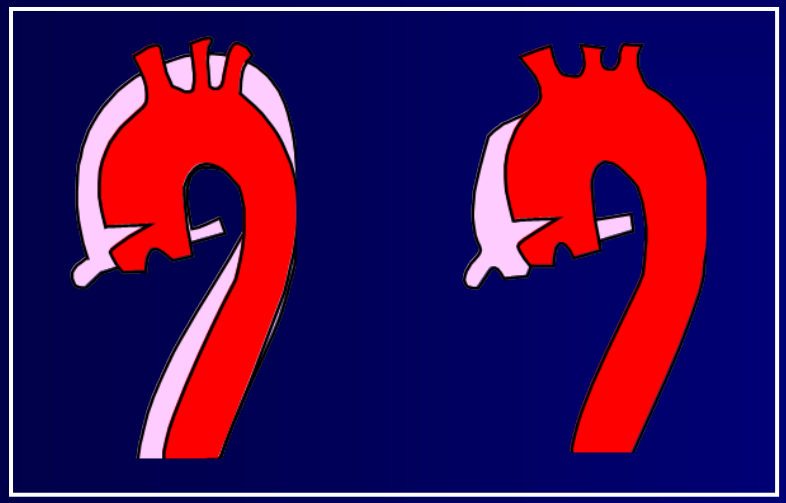
Lecture Outline

- Classification
- Presenting Symptoms/Signs
- Biomarker?
- Imaging
- Treatment
- Follow-up
- Future Directions
- Acknowledgements

Current Classification by Time From Symptom Onset - Outdated

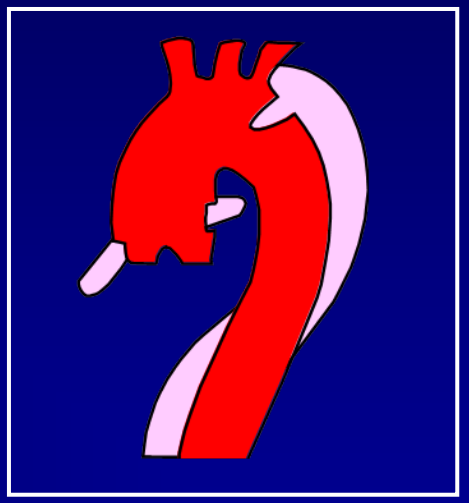
Acute AoD

- Presentation within 14 days of onset



Stanford Type A

Involves the ascending aorta with or without descending aorta

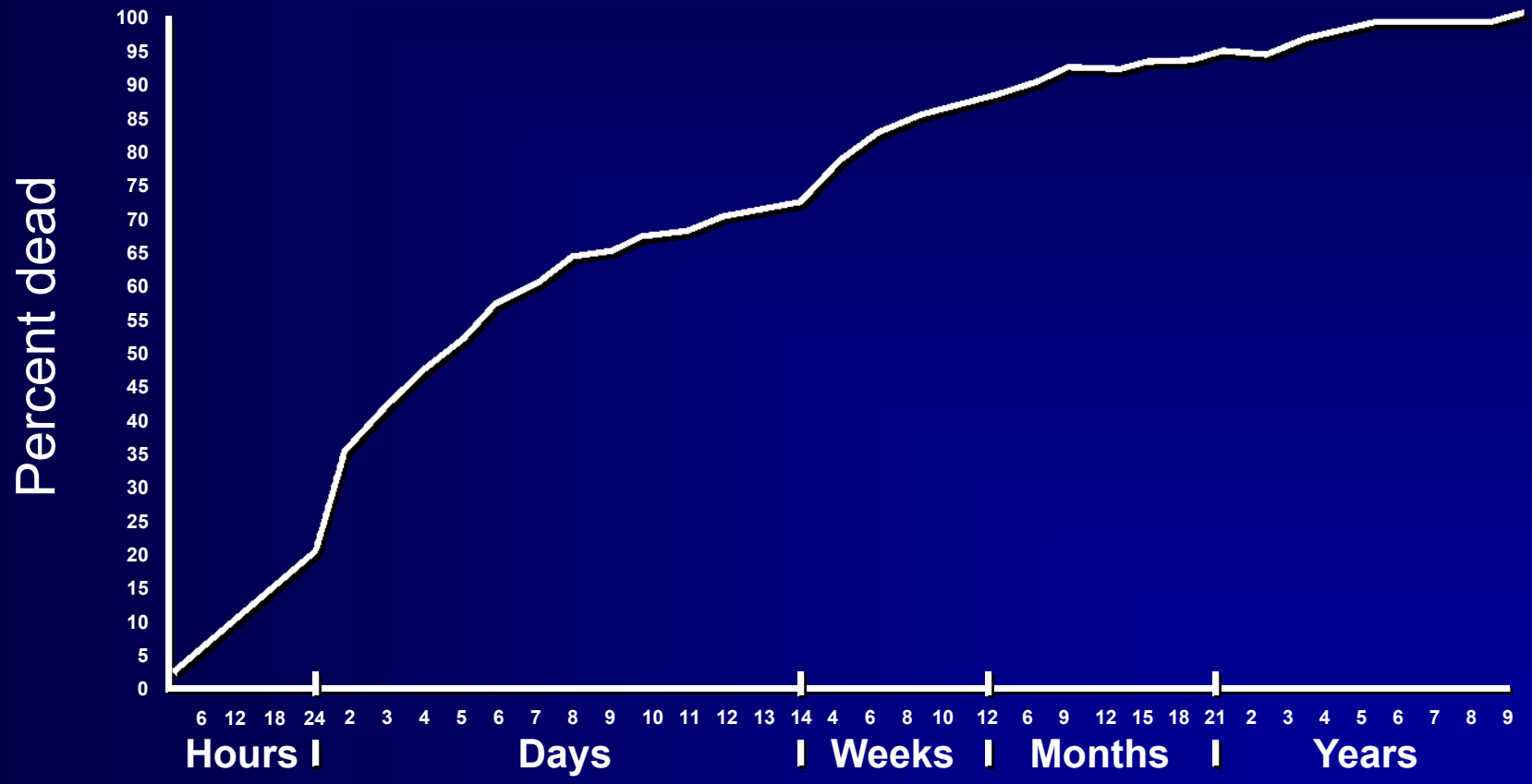


Stanford Type B

Confined to descending aorta

Treasure T, et al. *J Heart Valve Dis* 1996;5:623-29.

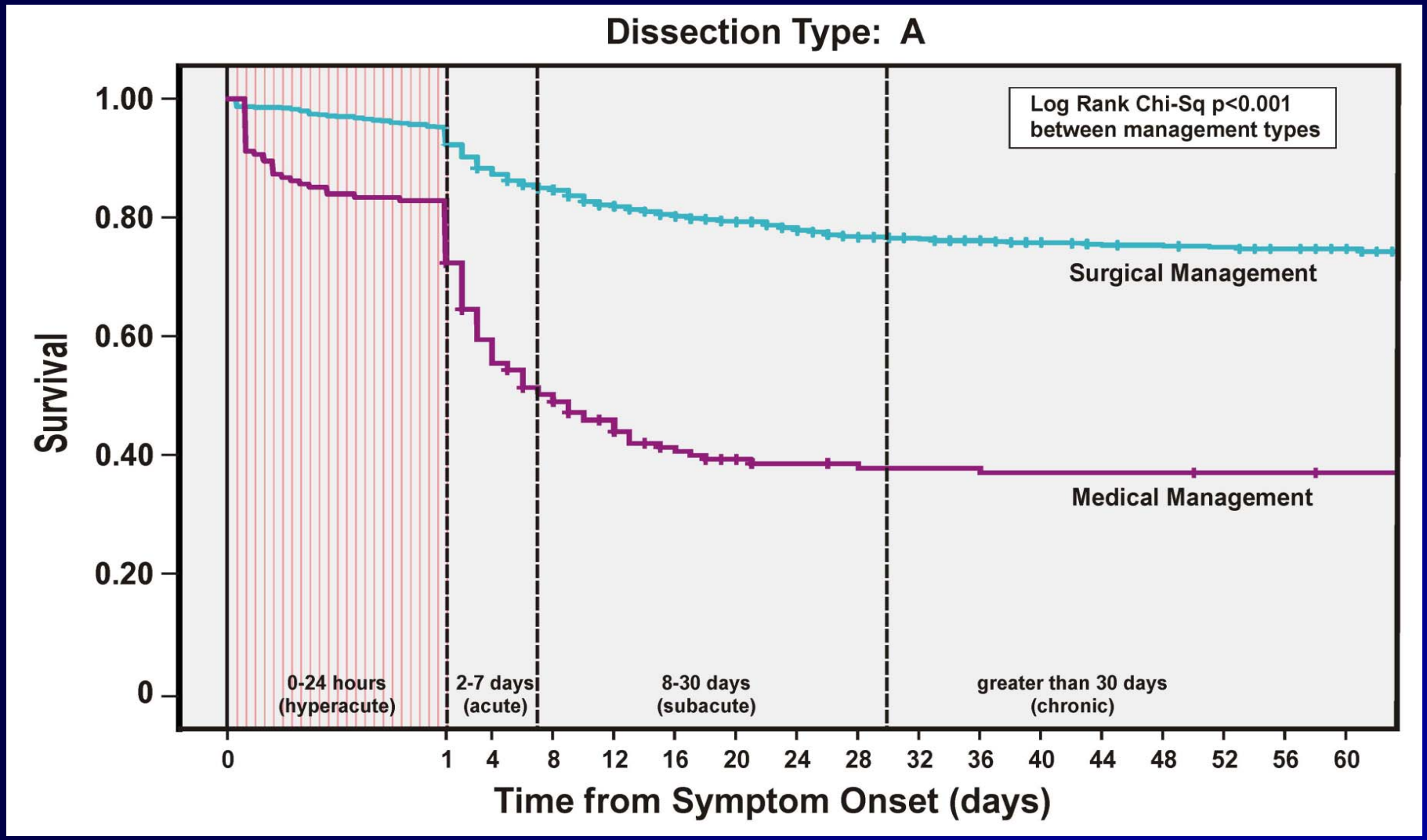
Aortic Dissection:
Mortality vs. Time from Symptom Onset



Mortality rate ….425 Cases

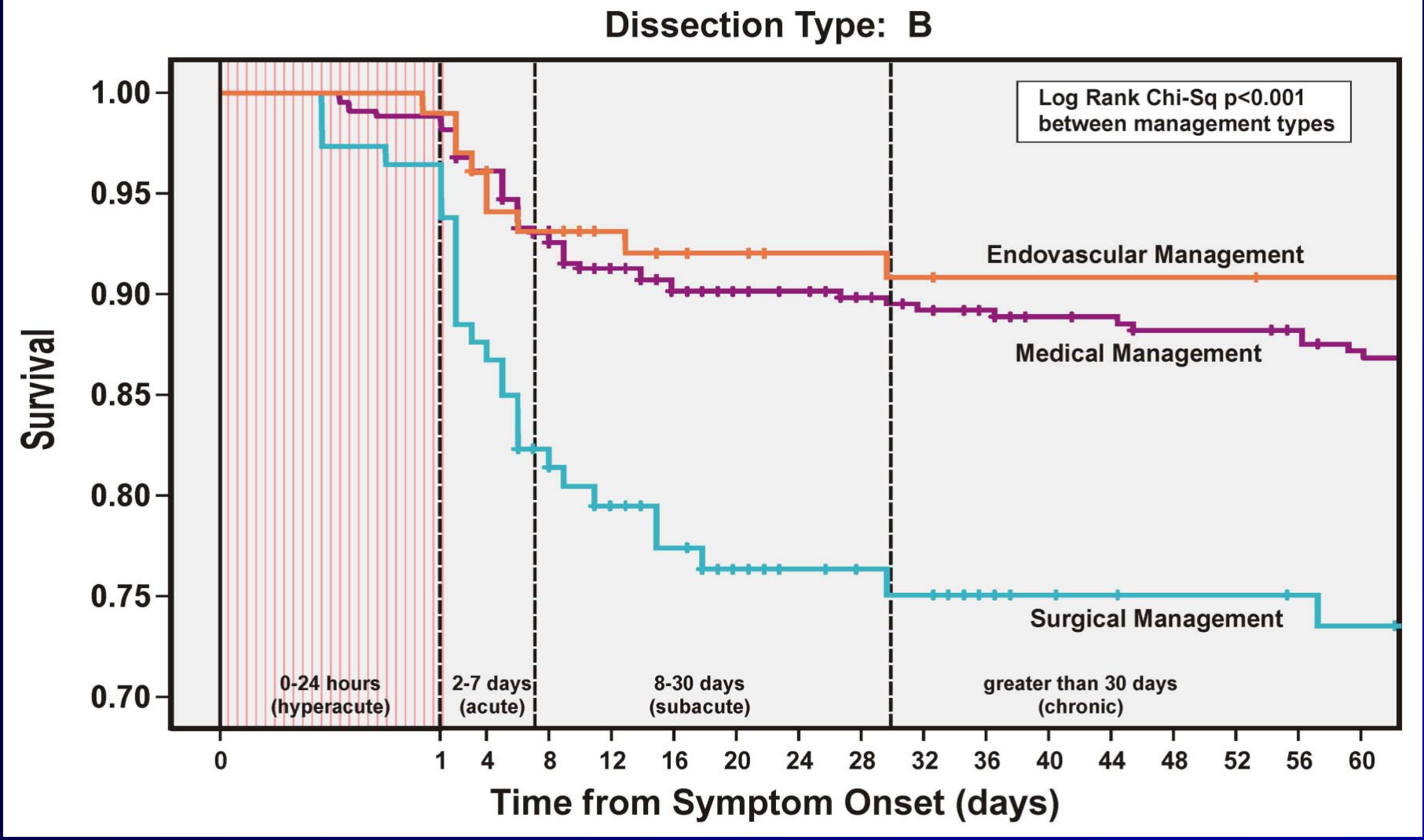
Hirst, Johns, and Kime; *Medicine* 1958; 37:217-279.

Survival Curve – Type A Dissection



Am J Med (in press).

Survival Curve – Type B Dissection



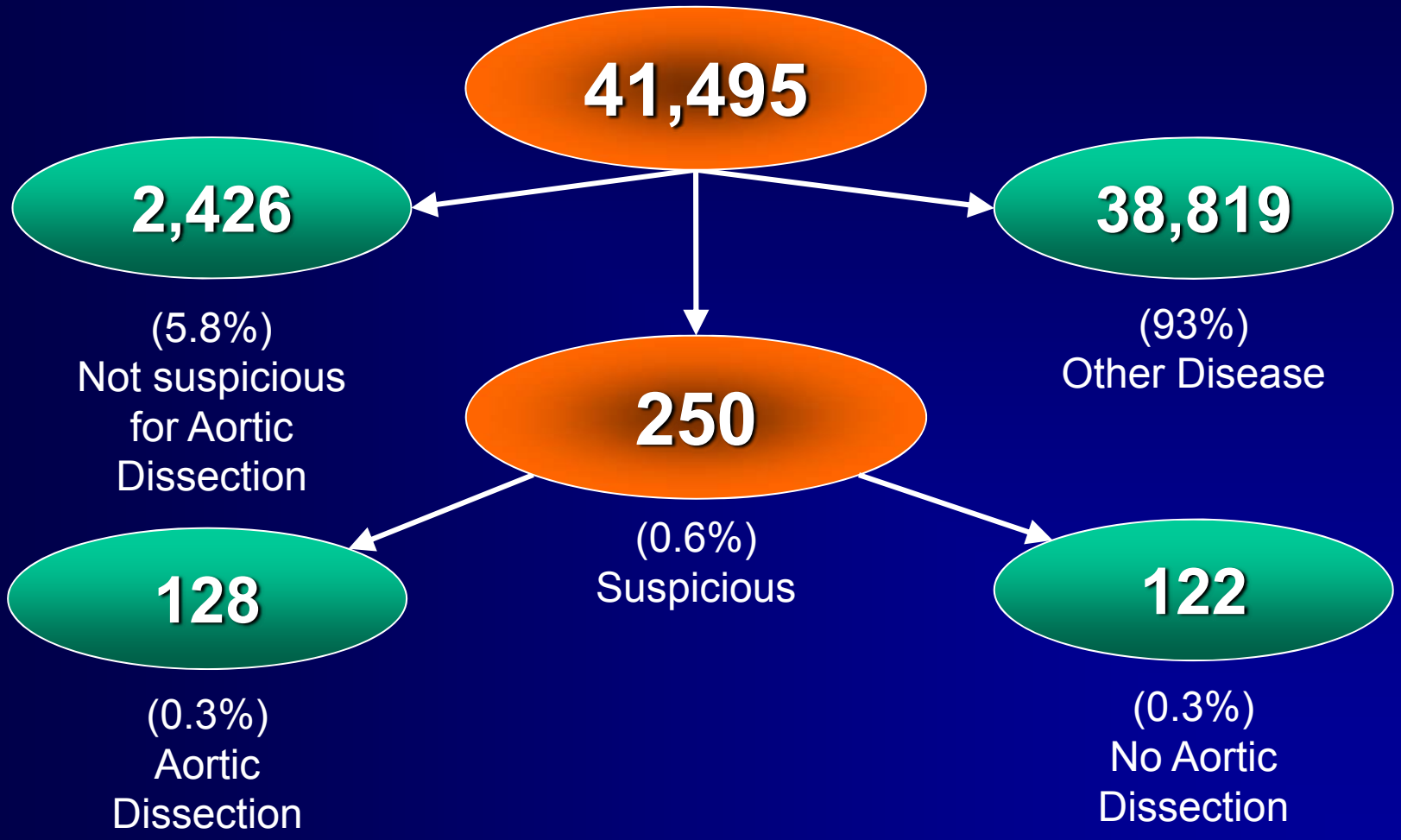
Am J Med (in press).

Demographics and Past History

Variable	All	Type A	Type B	p-value
	(n=3037)	*(n=1924)*	*(n=1113)*	
Age (yrs)	61.9	61.3	63.0	0.003
Male	67.1%	67.2%	67.1%	NS
HTN	75.2%	72.0%	80.7%	<0.001
Marfan	4.3%	4.5%	3.8%	NS
Prior Heart Surgery	**16.9%**	**15.3%**	**19.8%**	**0.002**
Iatrogenic	3.3%	3.8%	2.6%	0.09

IRAD Investigators

How Common is Aortic Dissection in ED Patients with Thoracic Pain?



Von Kodolitsch et al., *Arch Intern Med.* 2000;160:2977-2982.

Pain attending the splitting of the aortic wall is usually excruciating and extensive, radiating from midthorax front or back through the chest, down the back, and even into the thighs or up into the neck. The pain in the thorax or back comes suddenly at its maximum and is often prostrating, inducing a state of shock or even death.

- Paul Dudley White, 1944

IRAD
Presenting Symptoms

Variable	All	Type A	Type B	p-value
• ***Pain***	94.0%	92.6%	96.5%	<0.001
Abrupt	**84.0%**	**82.9%**	**85.7%**	**0.06**
Anterior	71.9%	78.0%	61.1%	<0.001
Back	53.1%	42.8%	70.5%	<0.001
Abdominal	31.2%	25.5%	40.8%	<0.001
Sharp	62.8%	58.4%	69.4%	<0.001
Tearing	47.1%	44.0%	52.0%	0.004
• ***Syncope***	12.6%	18.3%	2.9%	<0.001

(n=2807)

IRAD Investigators

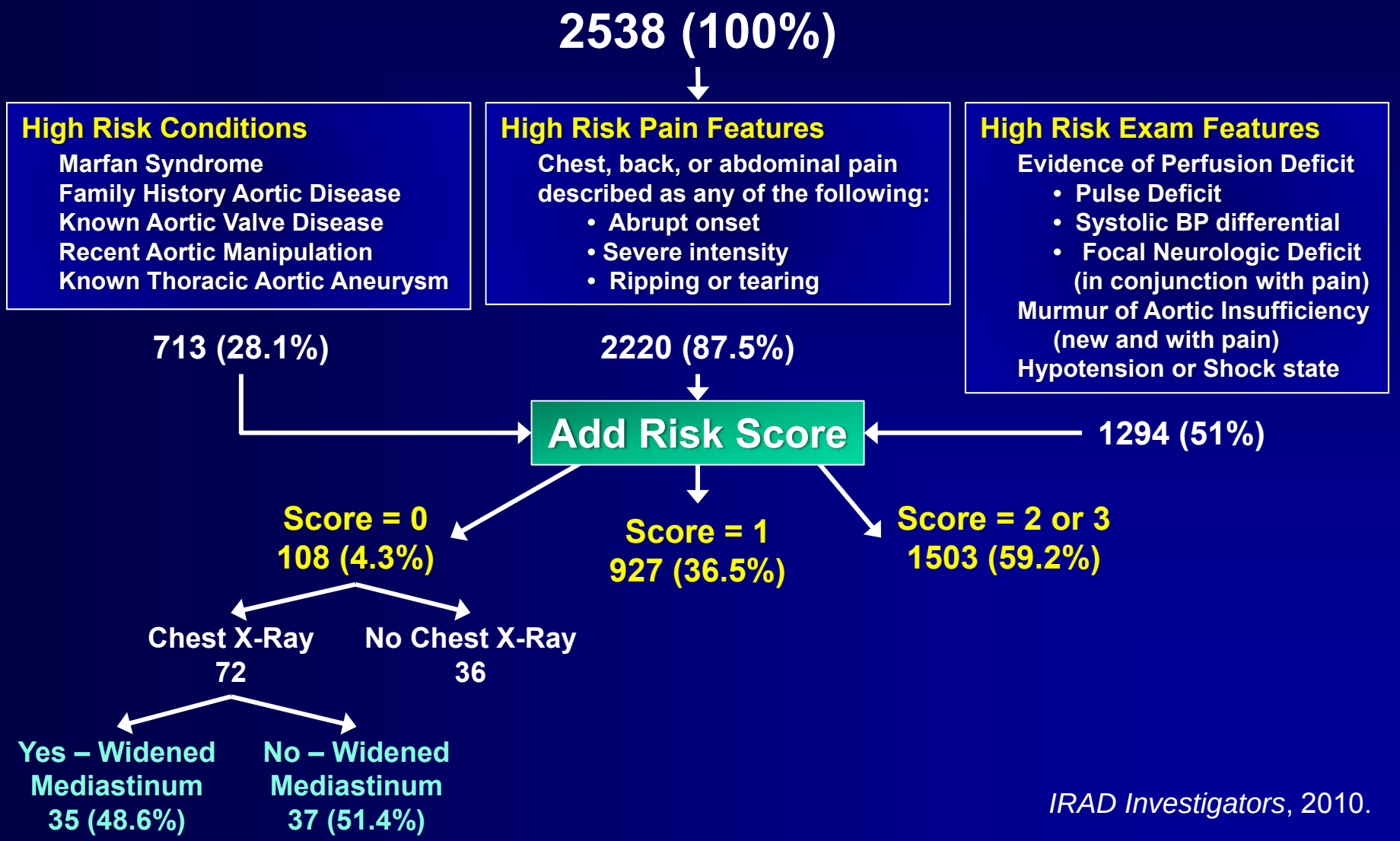
IRAD
Physical Exam

Variable	All	Type A	Type B	p-value
High BP	43.3%	30.3%	65.3%	<0.001
Low BP	11.4%	16.0%	3.5%	<0.001
Shock/Tamponade	8.0%	12.0%	1.3%	<0.001
Murmur AI	**27.6%**	**38.3%**	**10.7%**	**<0.001**
Pulse Deficit	**25.7%**	**30.5%**	**18.1%**	**<0.001**
Stroke	6.5%	9.1%	2.2%	<0.001

(n=2820)

IRAD Investigators

Sensitivity of ACC/AHA Guidelines for Acute Aortic Dissection



IRAD Investigators, 2010.

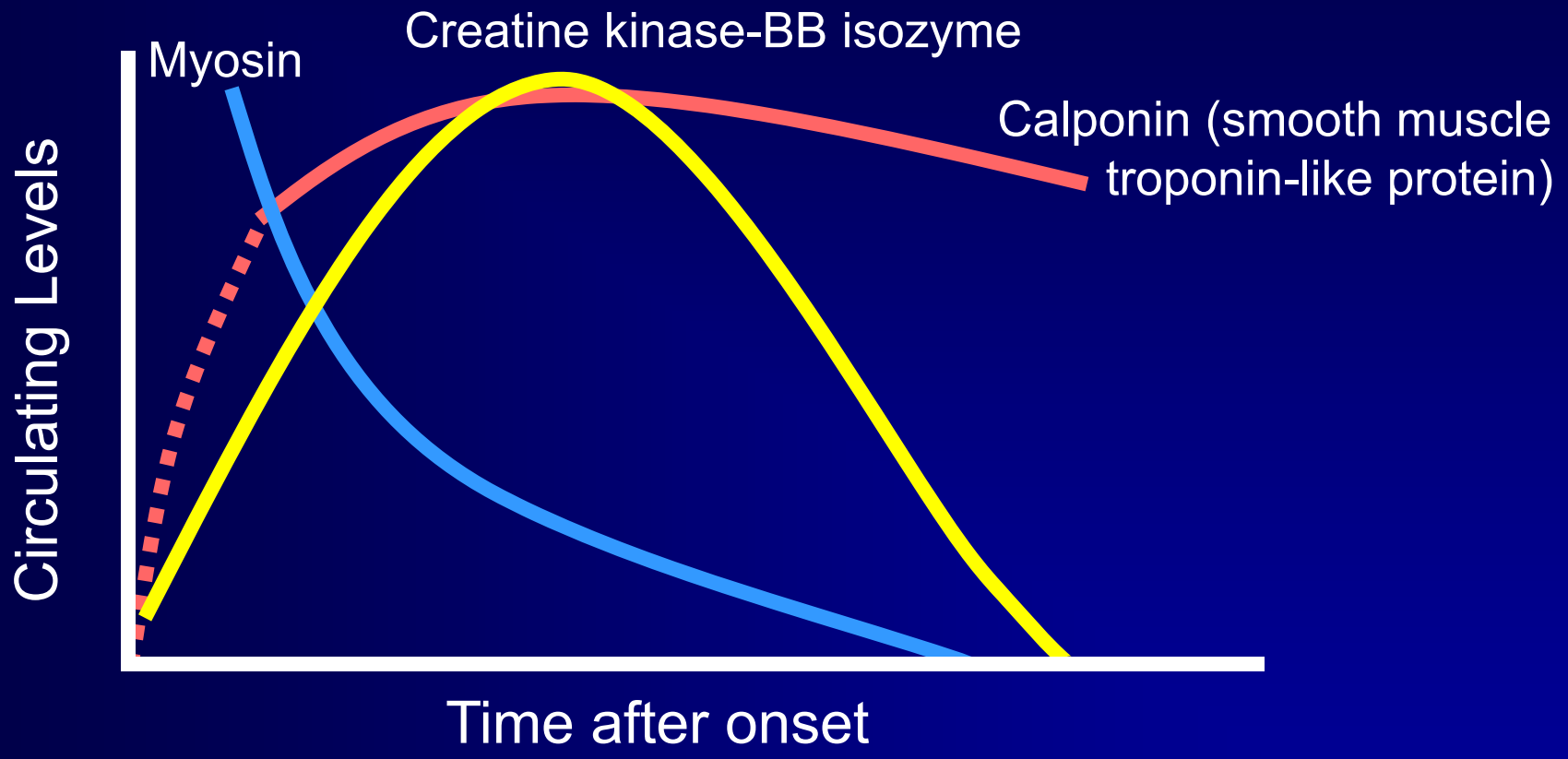
IRAD
EKG & CXR

Variable	All	Type A	Type B	p-value
• *CXR*				
Normal	22.4%	20.2%	25.9%	0.001
Wide Mediast. or Aorta	67.6%	69.5%	64.5%	0.012
PL. Effusion	14.4%	12.5%	17.3%	0.002
• *EKG*				
Normal	32.2%	29.9%	36.2%	0.001
NSST-T △'s	40.7%	41.2%	39.8%	NS
Ischemia	14.3%	17.1%	9.6%	<0.001
New MI	5.5%	7.4%	2.1%	<0.001

(n=2353)

IRAD Investigators

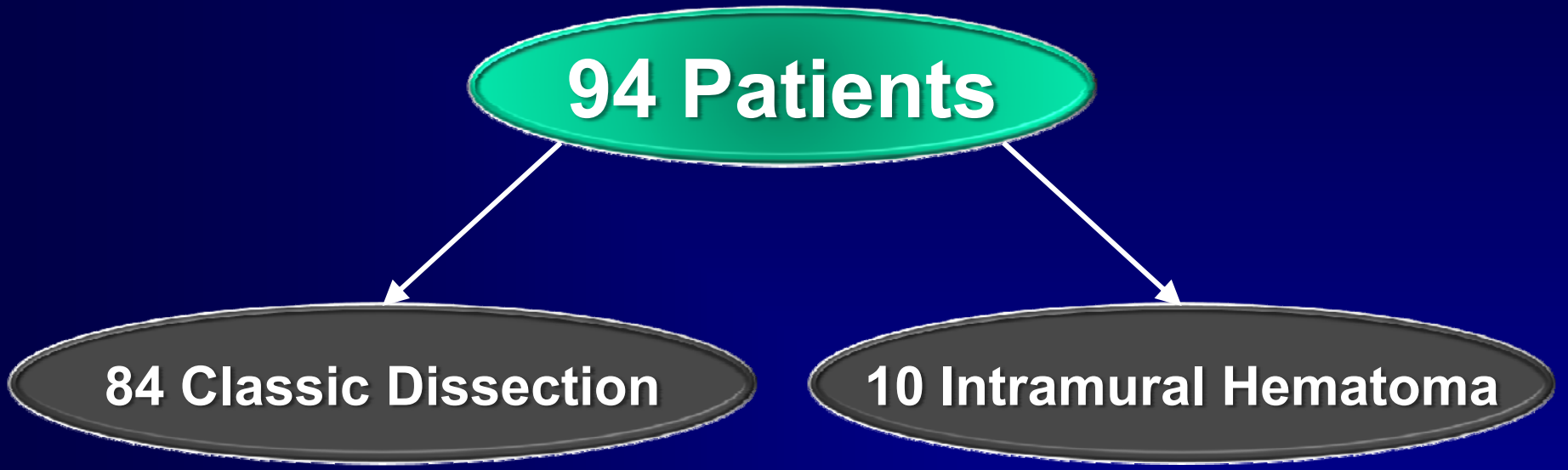
Smooth Muscle Proteins as Biomarkers of Dissection



- ***Promising results but not yet clinically available***

Refs. Myosin Suzuki T et al. *Circulation* 93:1244-9, 1996, *Ann Intern Med* 133:537-541, 2000.
CK-BB Suzuki T et al. *Lancet* 350:784-5, 1997.
Calponin Suzuki T et al. *Eur. Heart J.* 29:1439-45, 2008.

D-Dimer in Acute Aortic Syndromes

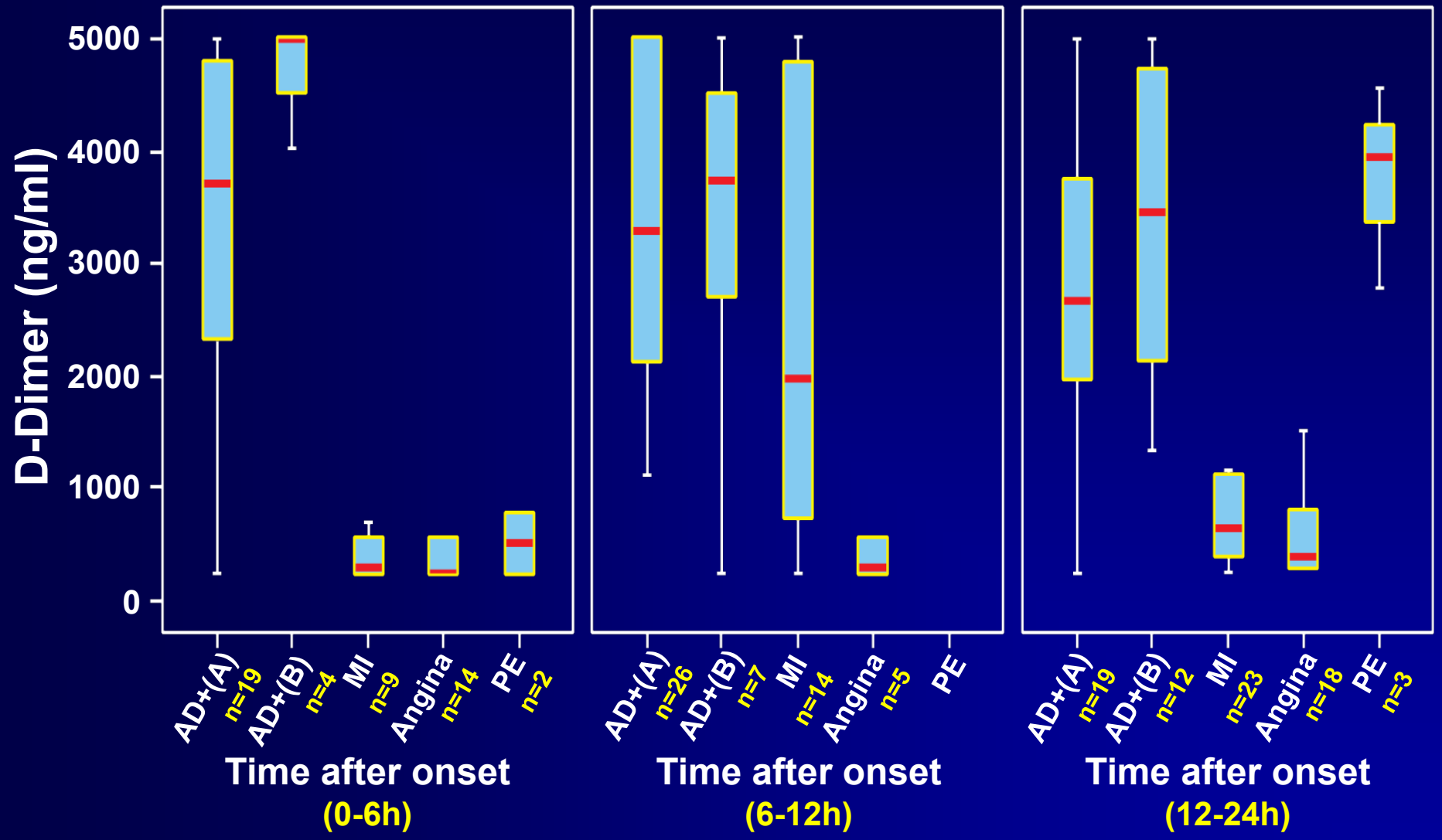


- Median D-Dimer
  9,290 ng/ml
- 100% ≥ 400 ng/mL
- Mortality - 26%

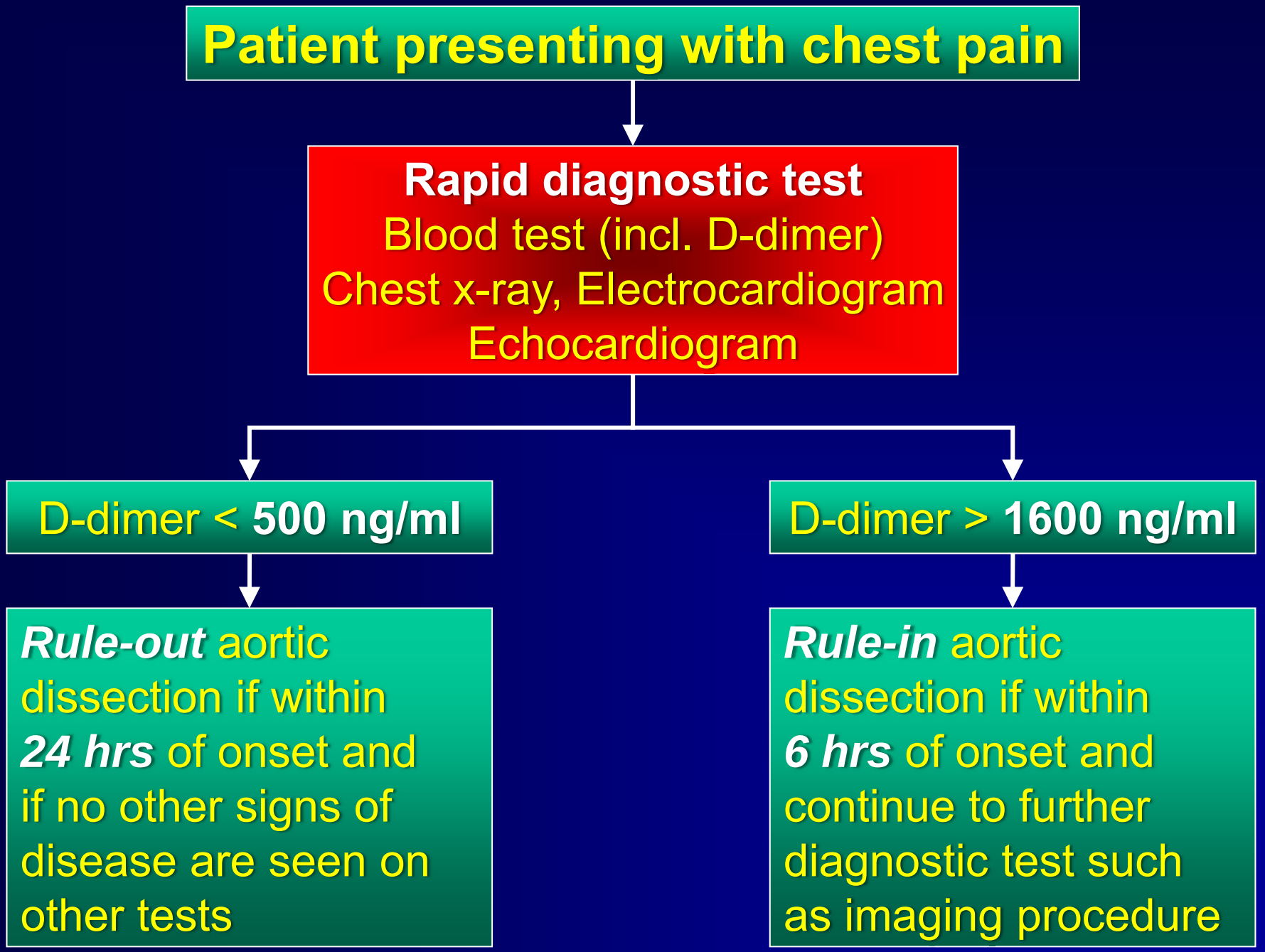
- Median D-Dimer
  1,230 ng/ml
- 90% (9/10) ≥ 400 ng/mL
- Mortality - 0%

Ohlmann PA, et al. *Crit Care Med.* 2009;37:899-901.

D-Dimer Levels in Aortic Dissection

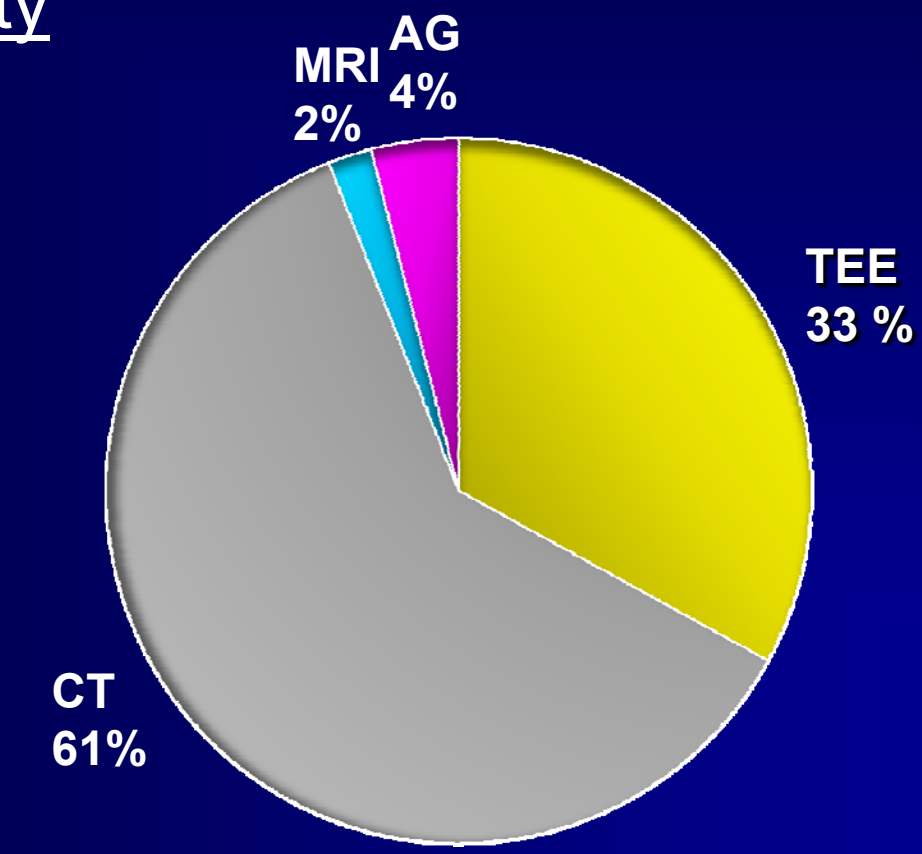


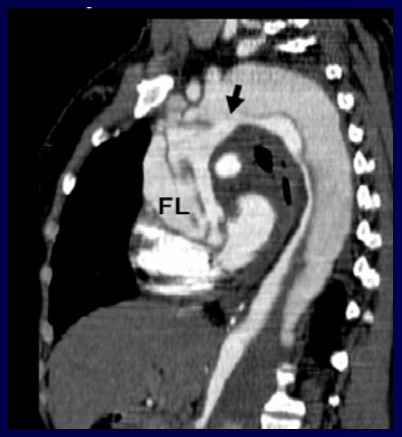
Suzuki T, et al. *Circulation* 2009;119:2702-07.


Patient presenting with chest pain
Rapid diagnostic test
Blood test (incl. D-dimer)
Chest x-ray, Electrocardiogram
Echocardiogram
D-dimer < 500 ng/ml
D-dimer > 1600 ng/ml
Rule-out aortic dissection if within 24 hrs of onset and if no other signs of disease are seen on other tests
Rule-in aortic dissection if within 6 hrs of onset and continue to further diagnostic test such as imaging procedure

IRAD Diagnostic Tests
Imaging test 1.8/case (60% > 1)

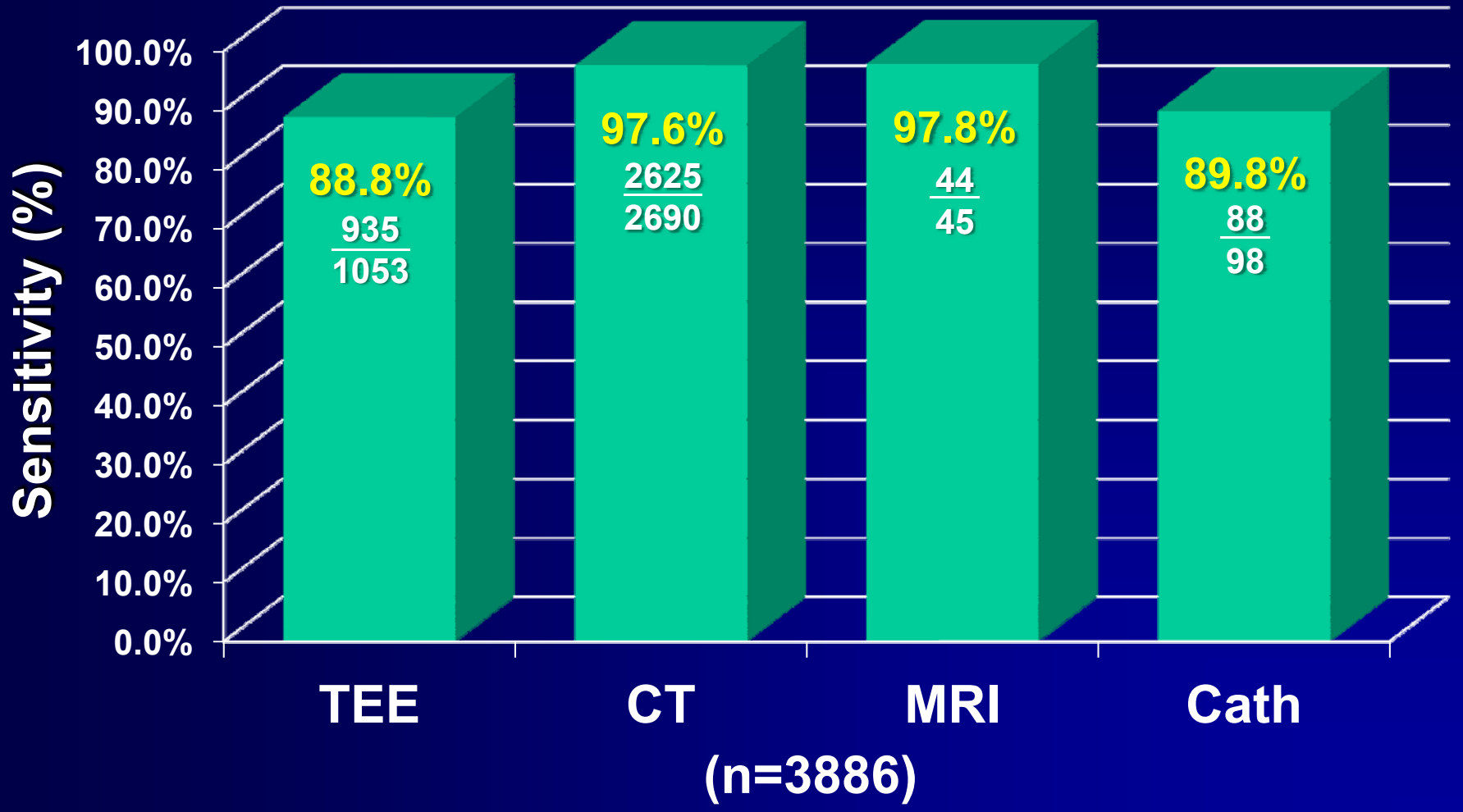
First Modality





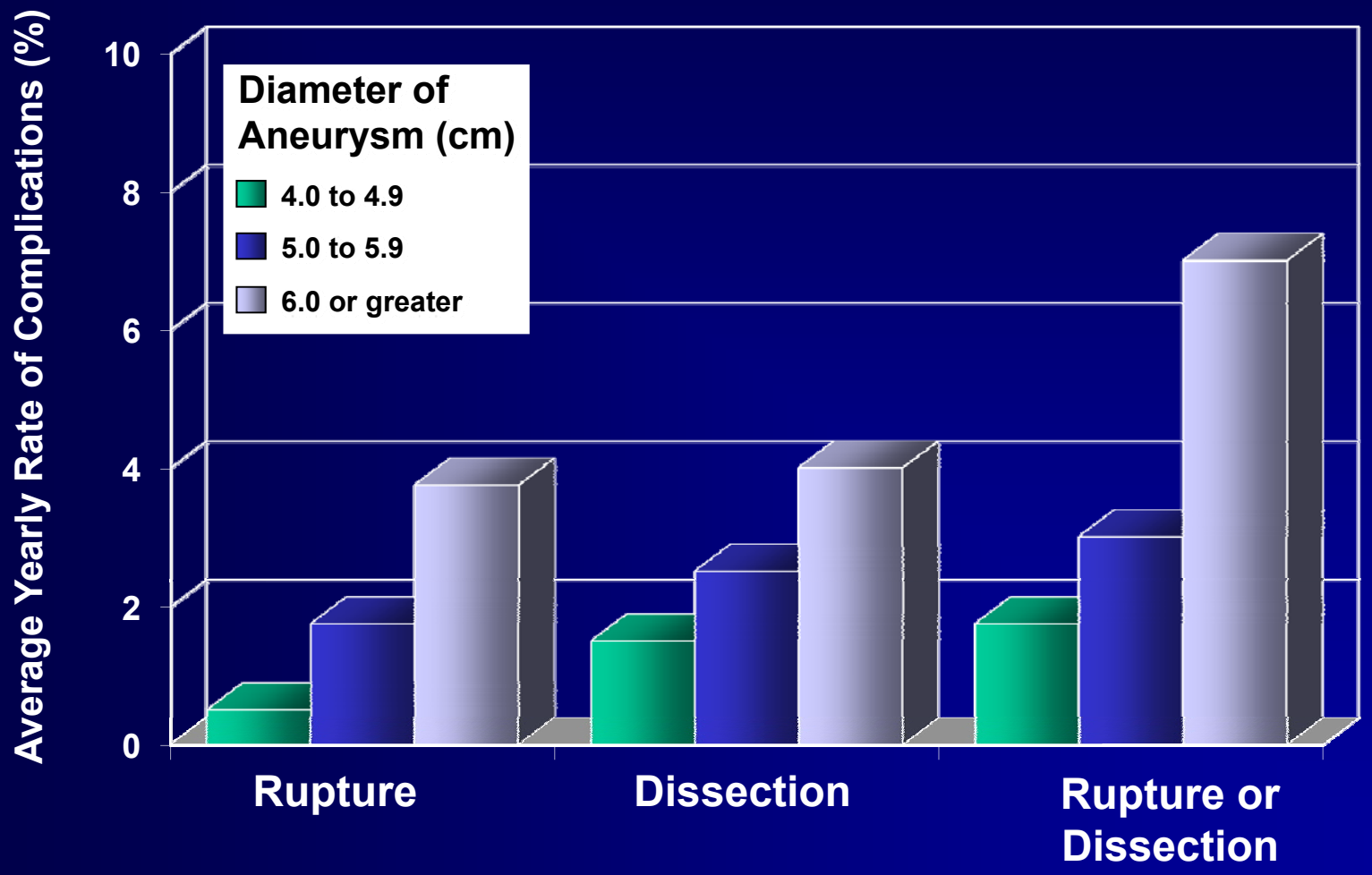
Moore AG, et al. *Am J Cardiol* 2002;89:1235-1238.

Sensitivity of the First Imaging Study to Detect AoD and Intramural Hematoma



IRAD Investigators

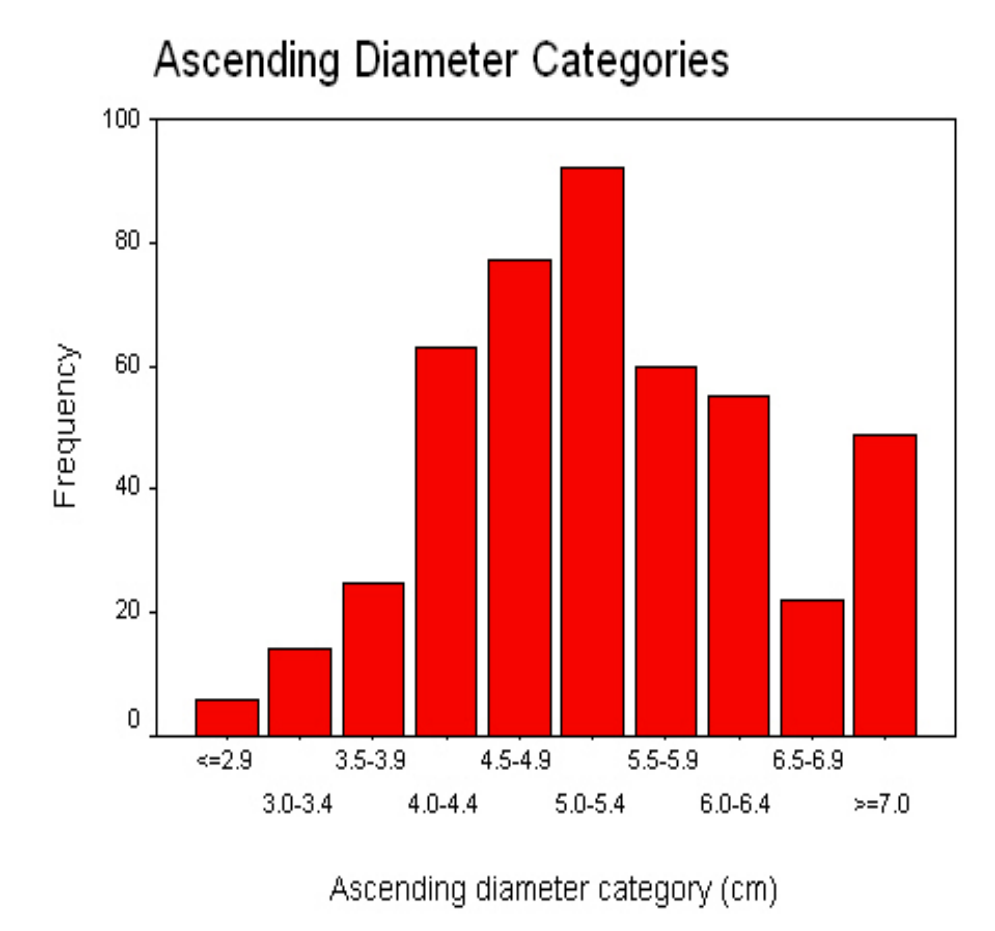
Aortic Aneurysms: Yearly Risk of Complications



Scientific American, August: 2005.

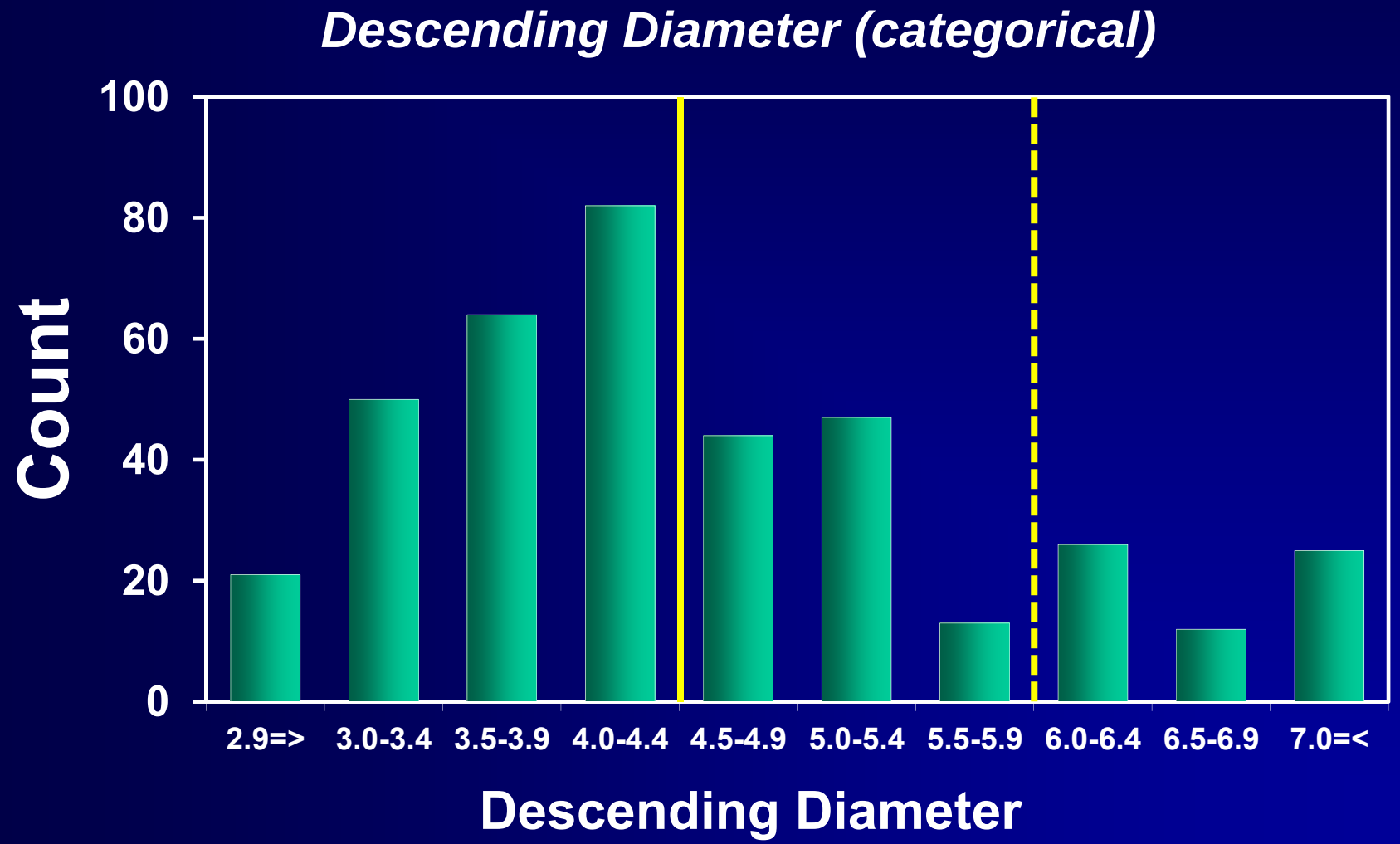
Maximum Aorta Diameter: Type A Dissection

(59% < 5.5 cm)



Pape et al. *AHA* 2005.

Descending Aortic Diameter ≥ 6.0cm: A Poor Predictor of Type B Aortic Dissection



Trimarchi S, et al. *J Am Coll Cardiol* 2009;53: A452.

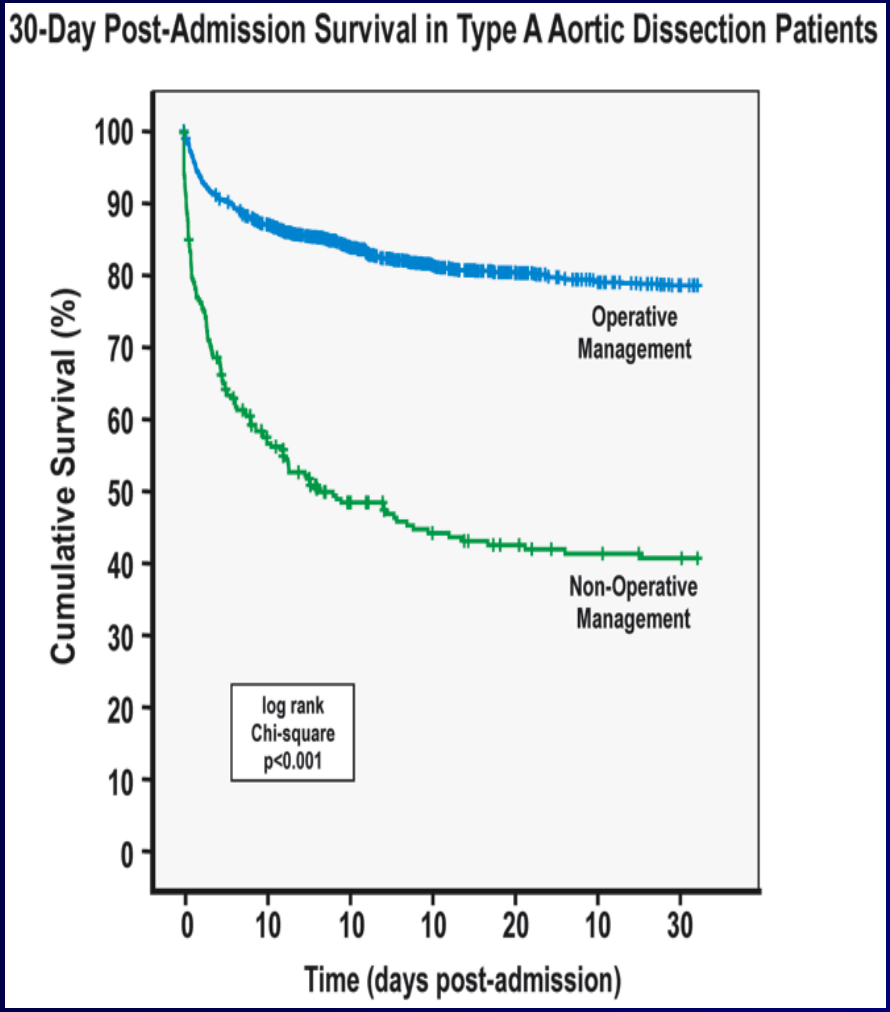
2013

How Should I Treat Acute Aortic Syndromes?

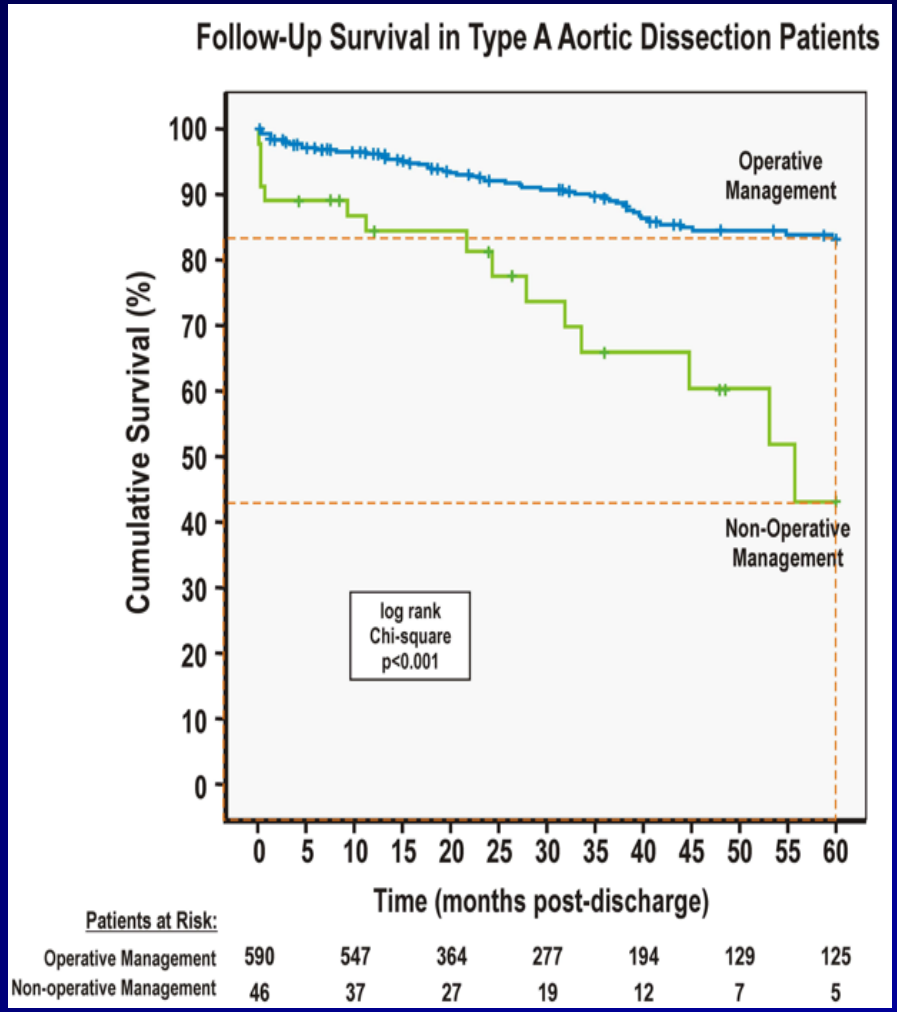
Type A Dissection

- Medical Therapy for all, for life
- Surgery if possible
- Consider fenestration if surgery not possible, especially if malperfusion occurs

In-hospital Survival in TA-AAD

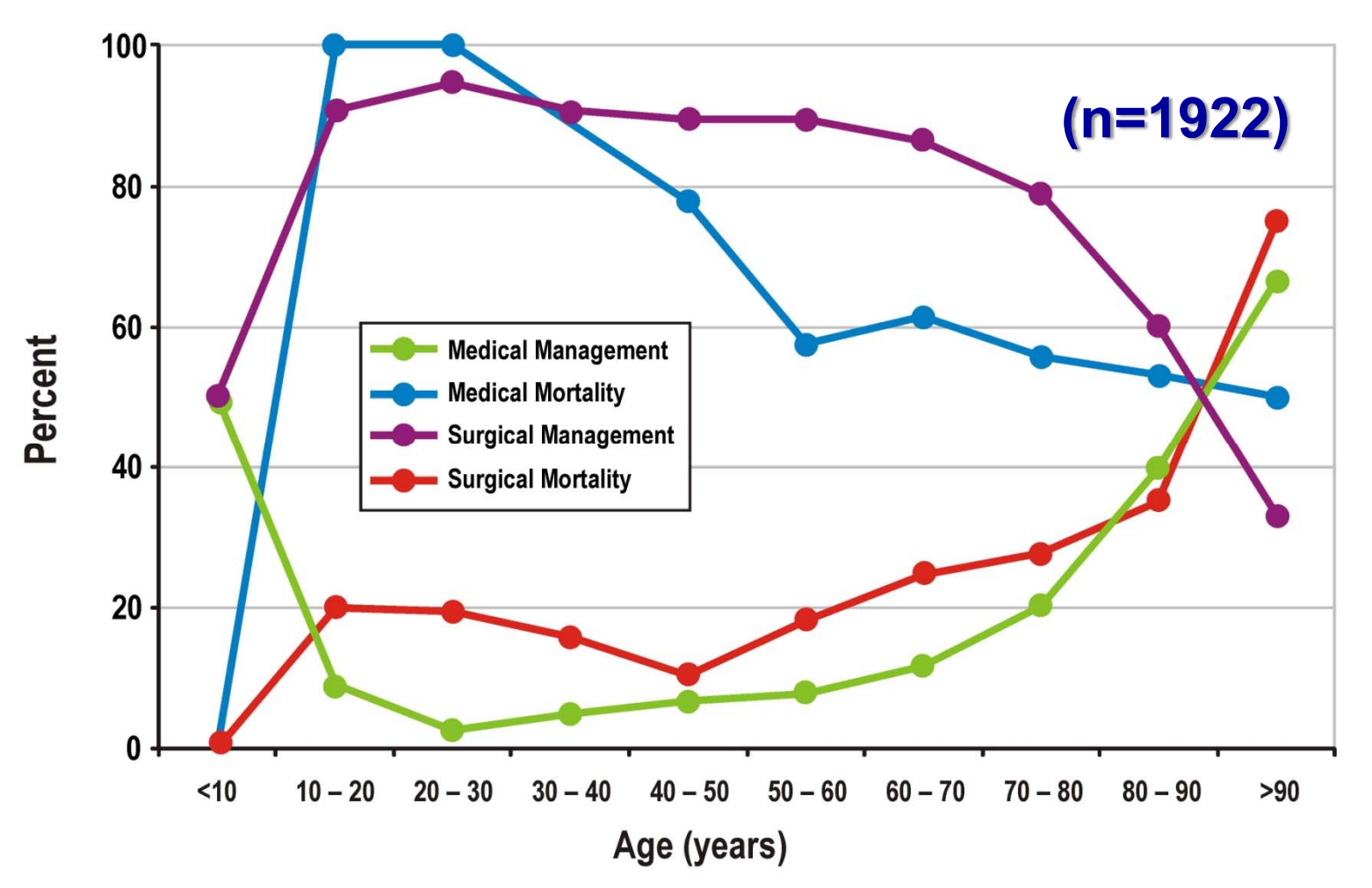


Follow-up Survival in TA-AAD

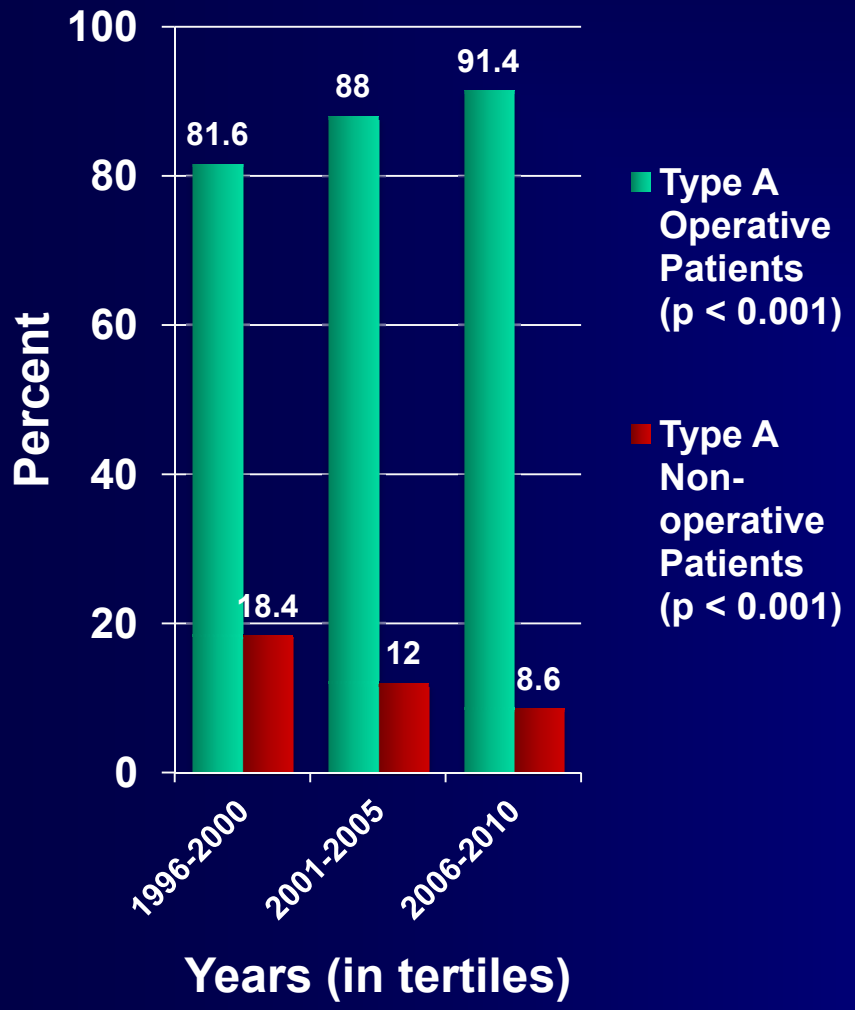


Sinha S, presented ACC 2011.

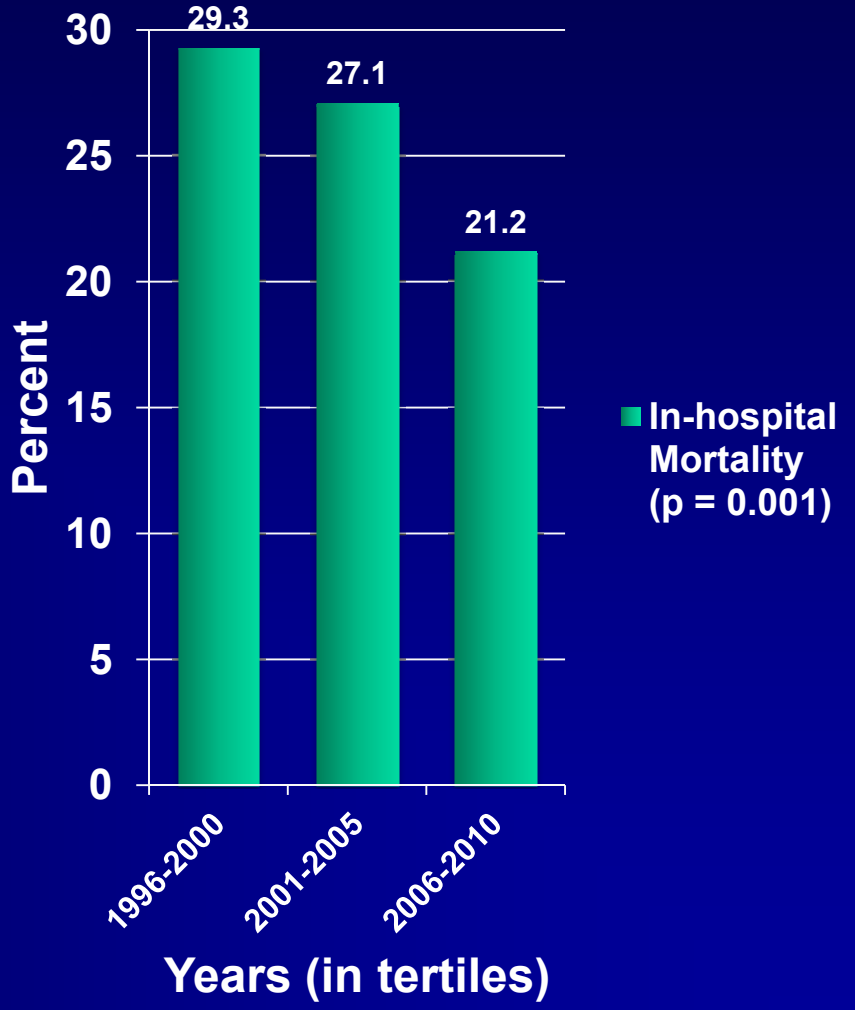
Mortality in Type A Aortic Dissection: Relation to Age and Type of Therapy



Percentage of Non-operative TA-AAD Patients Over Time



Percentage of In-hospital Mortality of All TA-AAD Patients Over Time



Sinha S, presented ACC 2011.

Type B Dissection

- Uncomplicated - No false lumen: Medical
- Uncomplicated - False channel +/- aneurysm - consider stent
- Complicated - stent +/- surgery

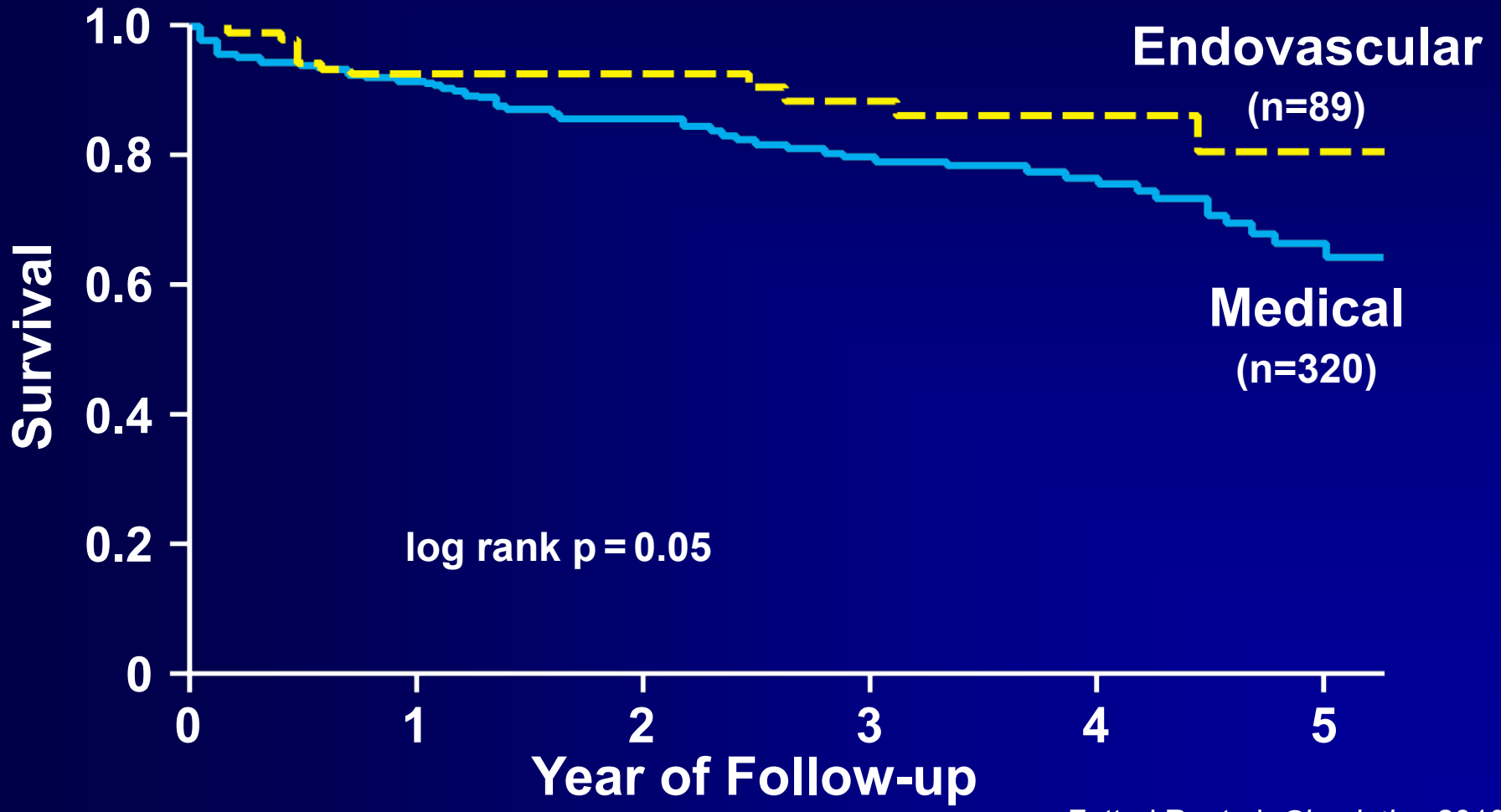
Nienaber CA, et al. *Circulation* 2003;108:628-635.
Nienaber CA, et al. *Circulation* 2003;108:772-778.

Stable Type B Dissection "Instead" 1 – Yr. Mortality

	#	Mortality
Medical Treatment	66	3%
Stent Graft	70	10%

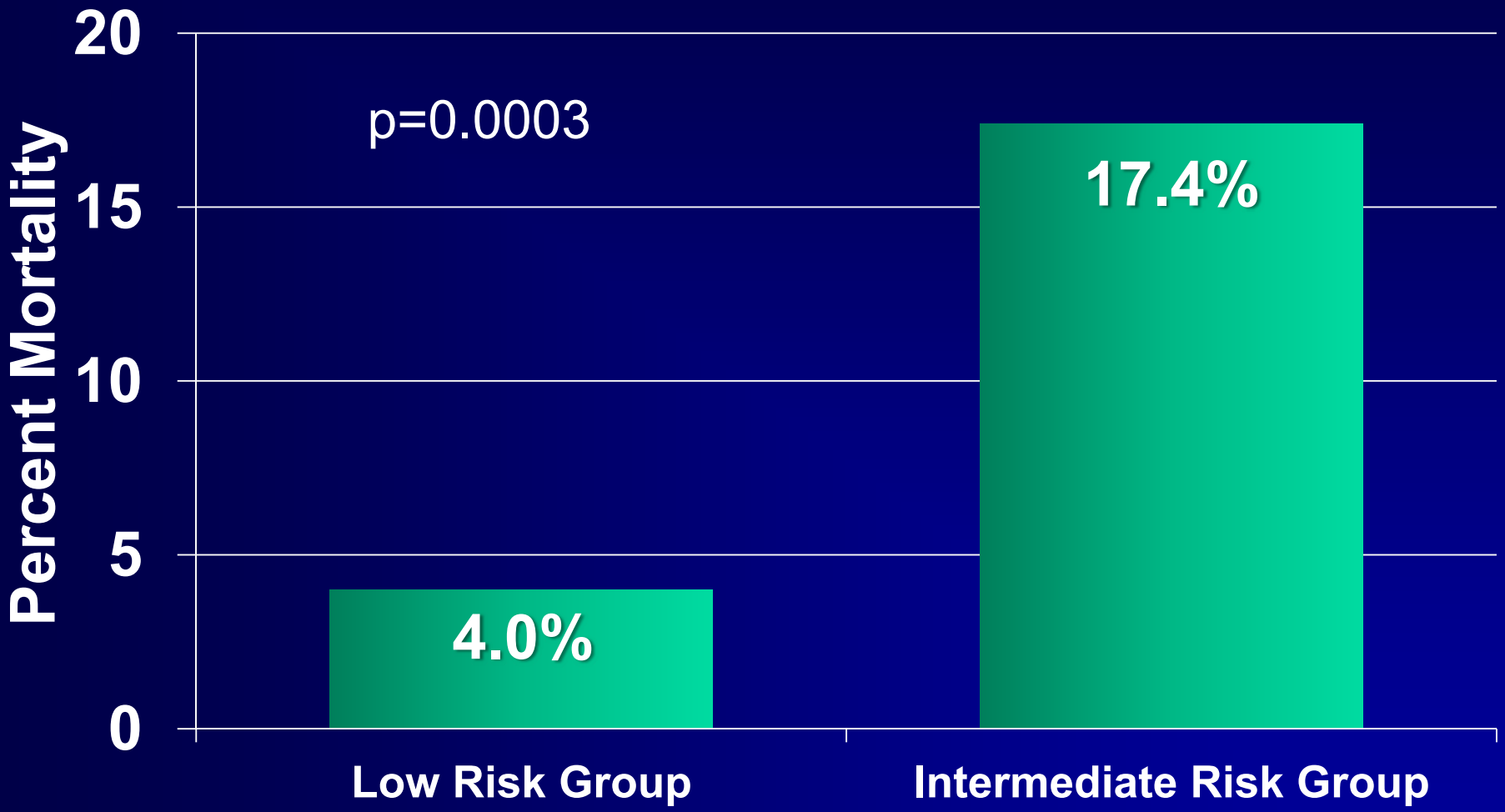
Nienaber C, et al. *Circulation 2009;120:2519-28.*

Comparison of Medical Therapy to Endovascular Treatment in Type B Dissection: *Long Term Follow-Up*



Fattori R, et al. *Circulation* 2010.

Refractory Pain or Hypertension: Type B



Overall in-hospital mortality rates in the low-risk and intermediate-risk groups. The intermediate-risk group consists of ABAD patients with recurrent/refractory pain or refractory hypertension but no other clinical complications.

Trimarchi S, Eagle KA, Nienaber CA, et al. *Circulation* 2010;122:1283-1289.

Endovascular Treatment

Indication for treatment
- Dilatation > 5.5cm
- Symptomatic dilatation
- Rapid expansion 1cm per year

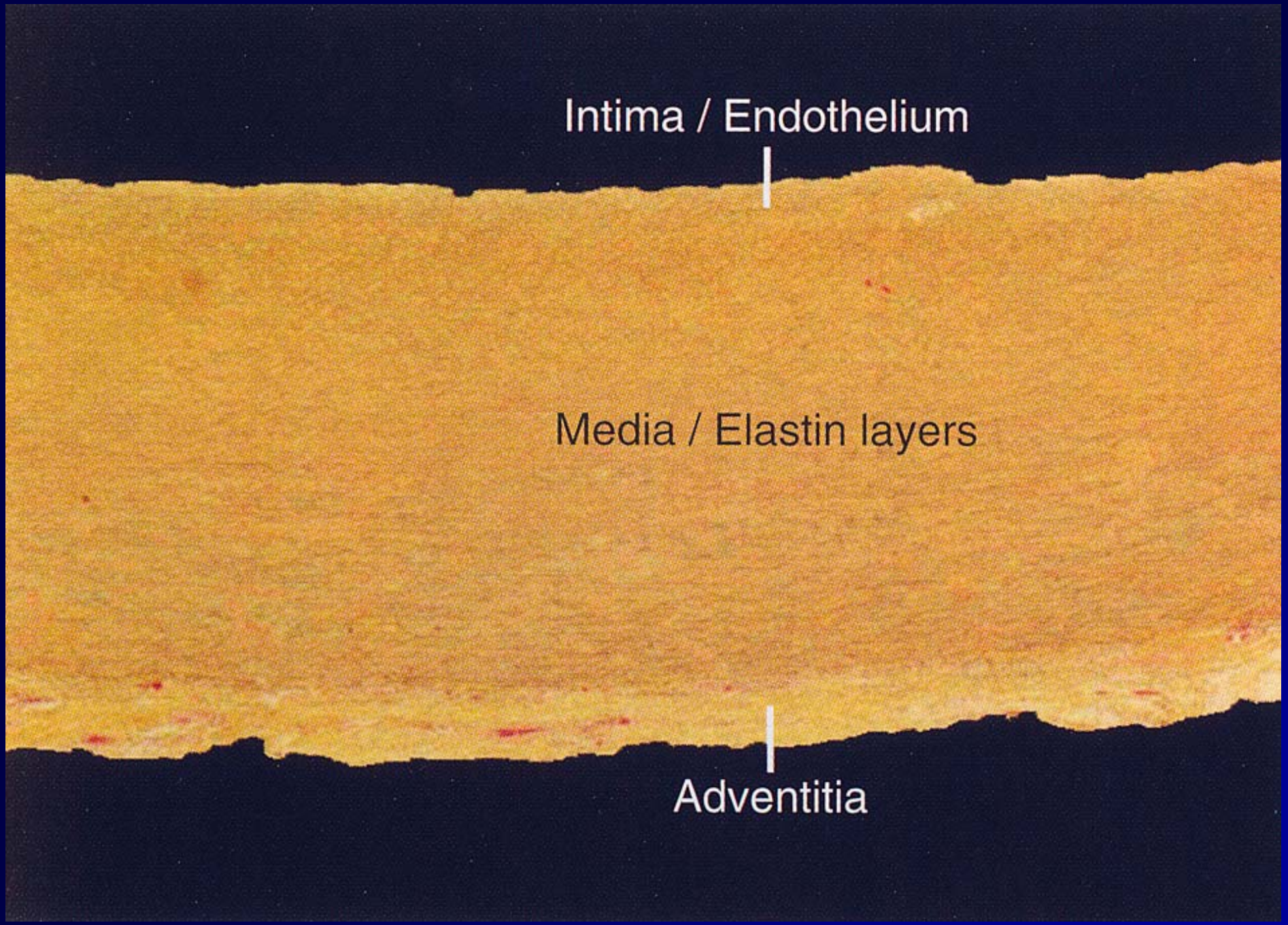
Aim
- De-pressurise false lumen
- Prevent rupture

Issues
- Multiple re-entries
- Aortic remodelling

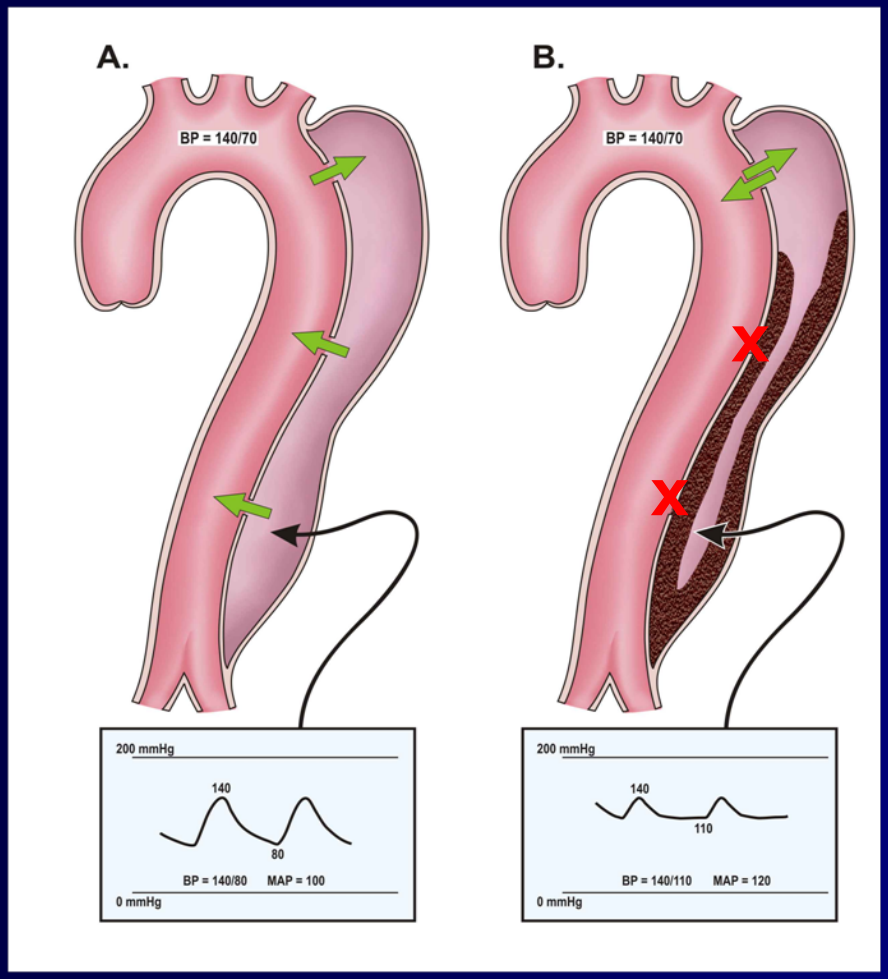
Nienaber CA, et al. *Circulation* 2003;108:628-635.
Nienaber CA, et al. *Circulation* 2003;108:772-778.

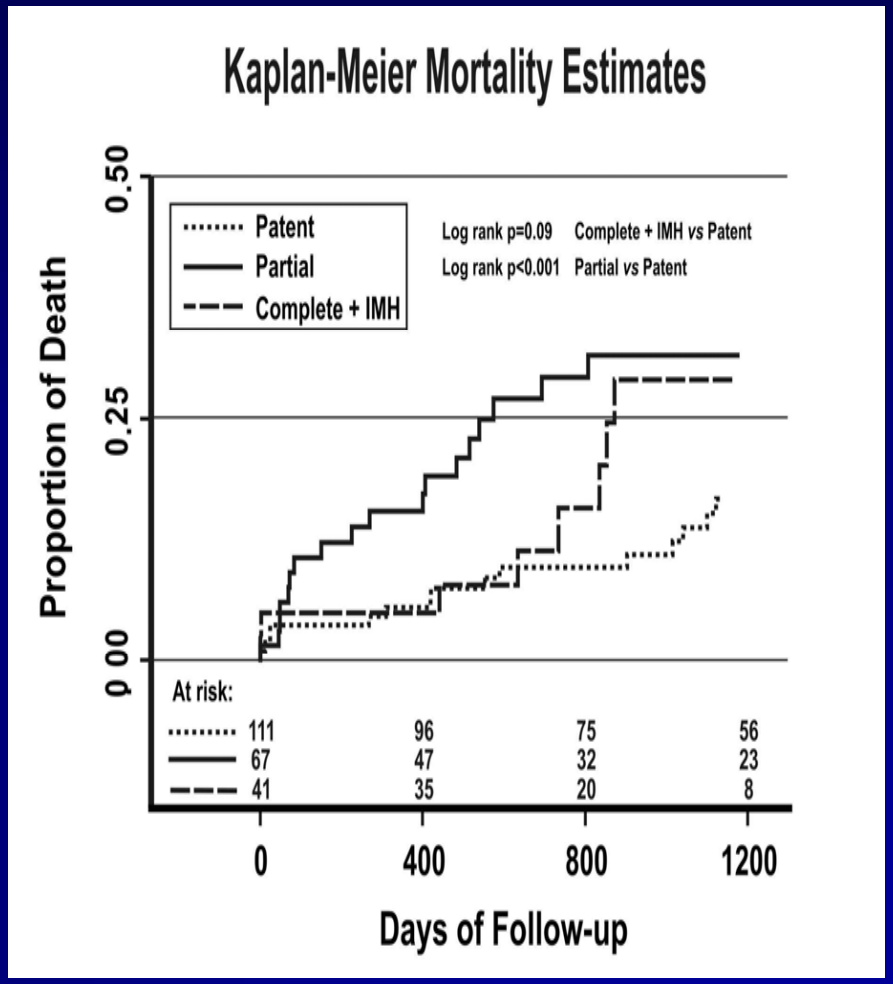
How to Follow?

1. Treatment
2. Surveillance
3. Patient Education

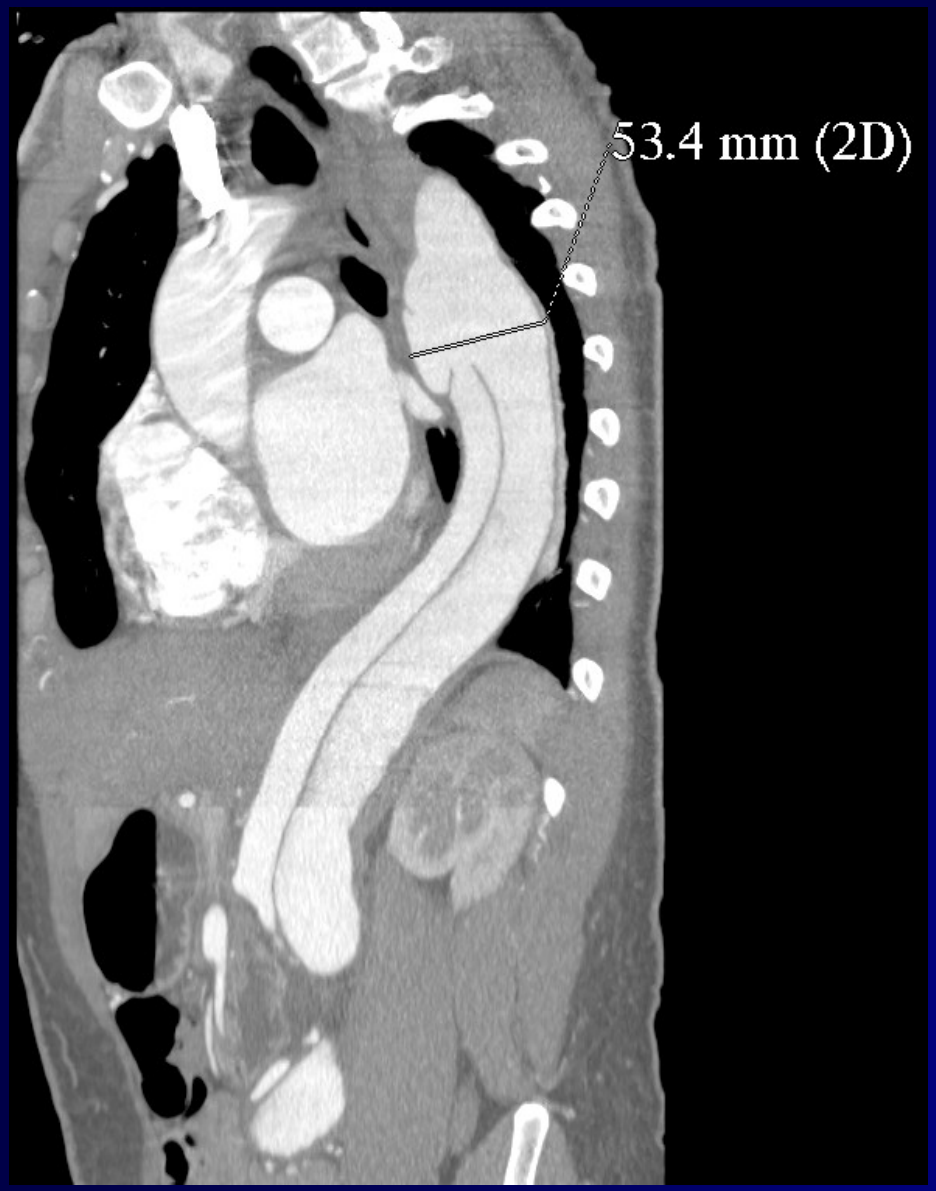

Intima / Endothelium
Media / Elastin layers
Adventitia

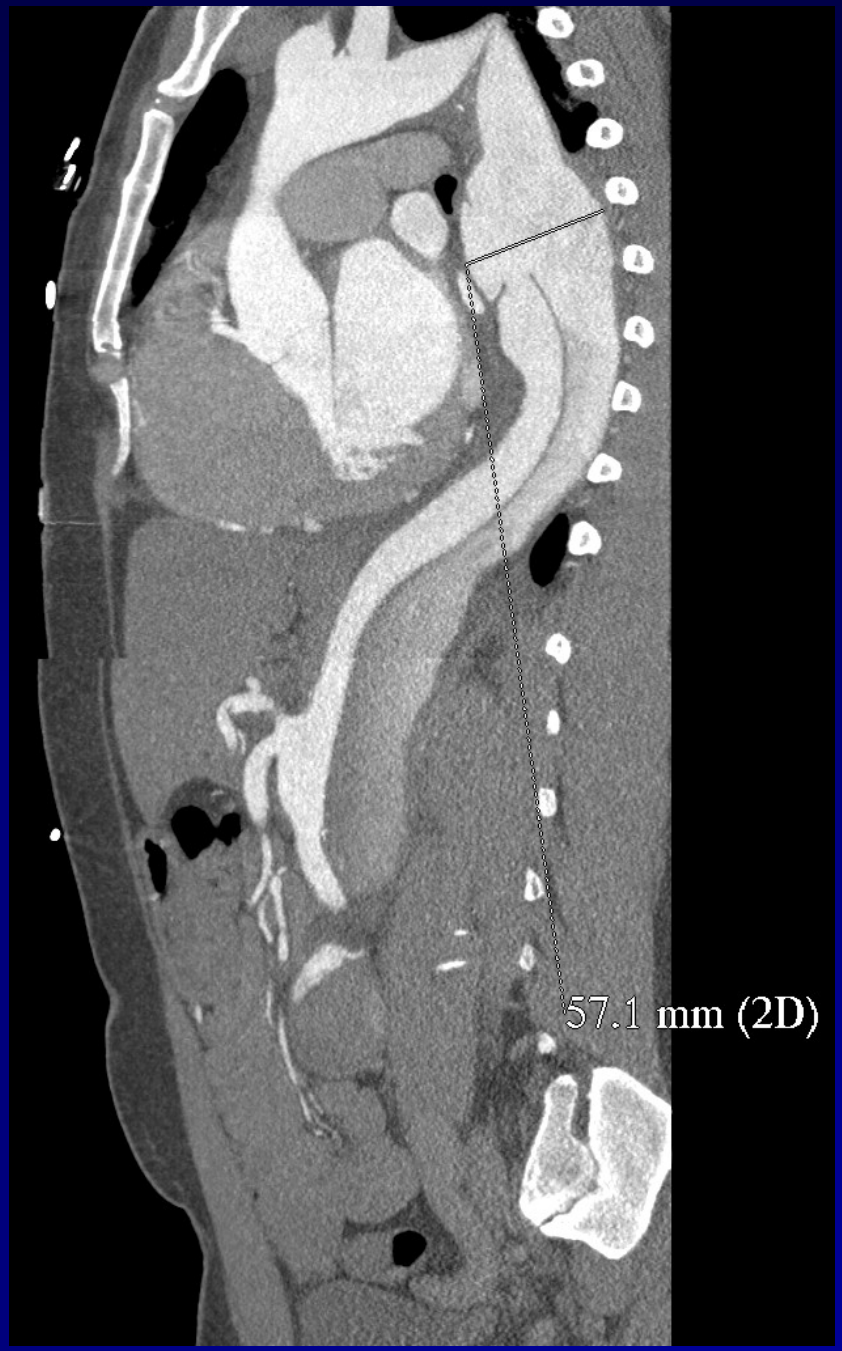
Partial Thrombosis of False Lumen in Acute Type B Dissection





Tsai TT, Evangelista A; *N Engl J Med* 2007;357:349-359.


53.4 mm (2D)

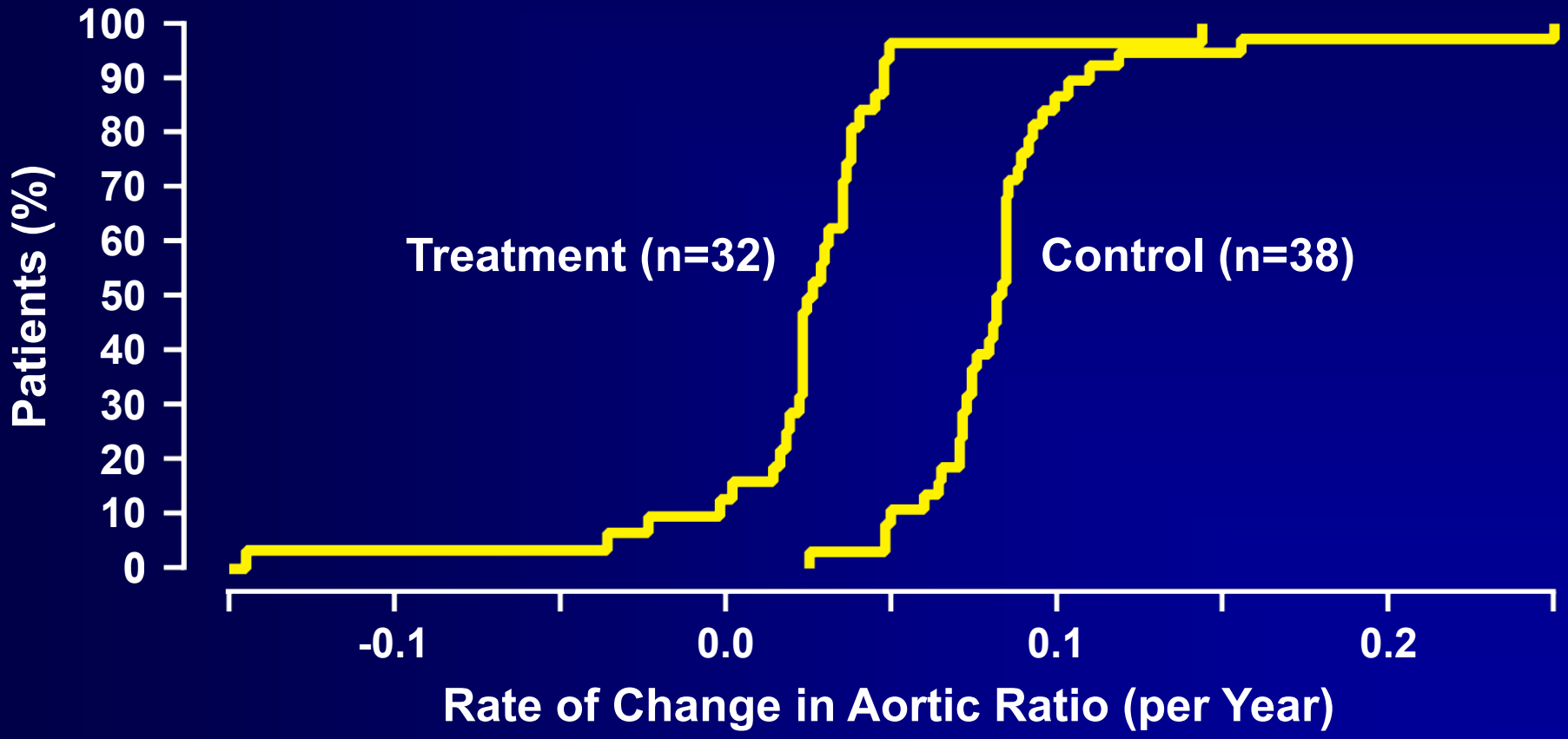

57.1 mm (2D)

Follow-up Treatment?

1. Beta-blockers
2. ACE/ARB
3. Statins
4. Anticoagulants?

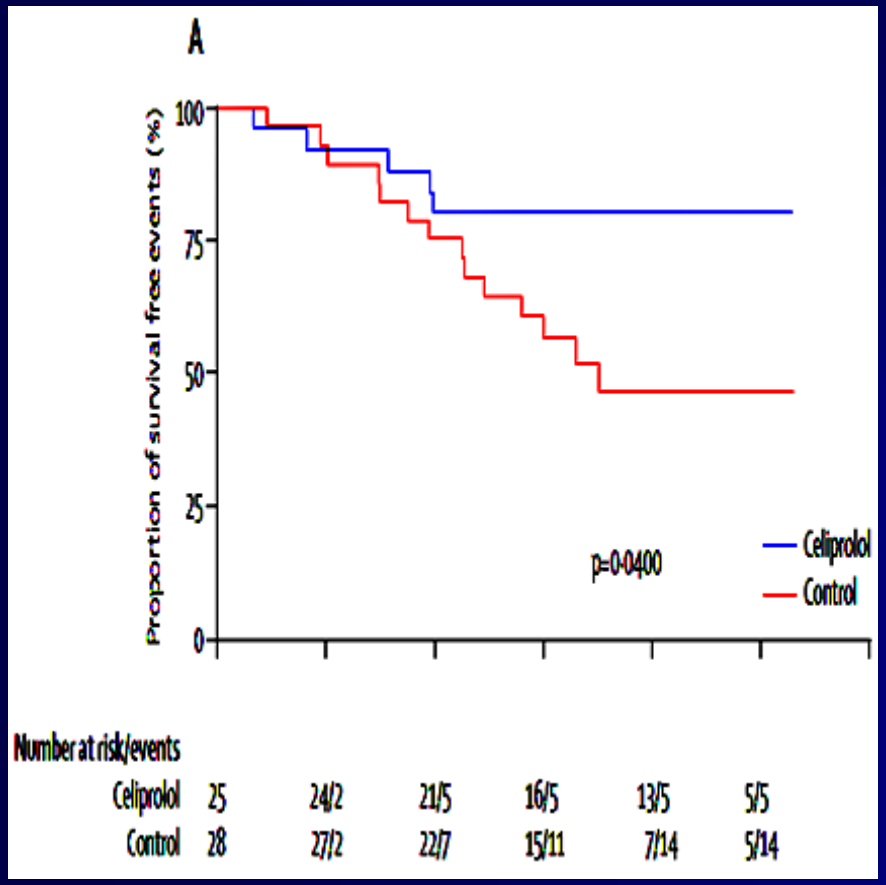
Beta Adrenergic Blockade Slows Aorta Growth in Marfan's

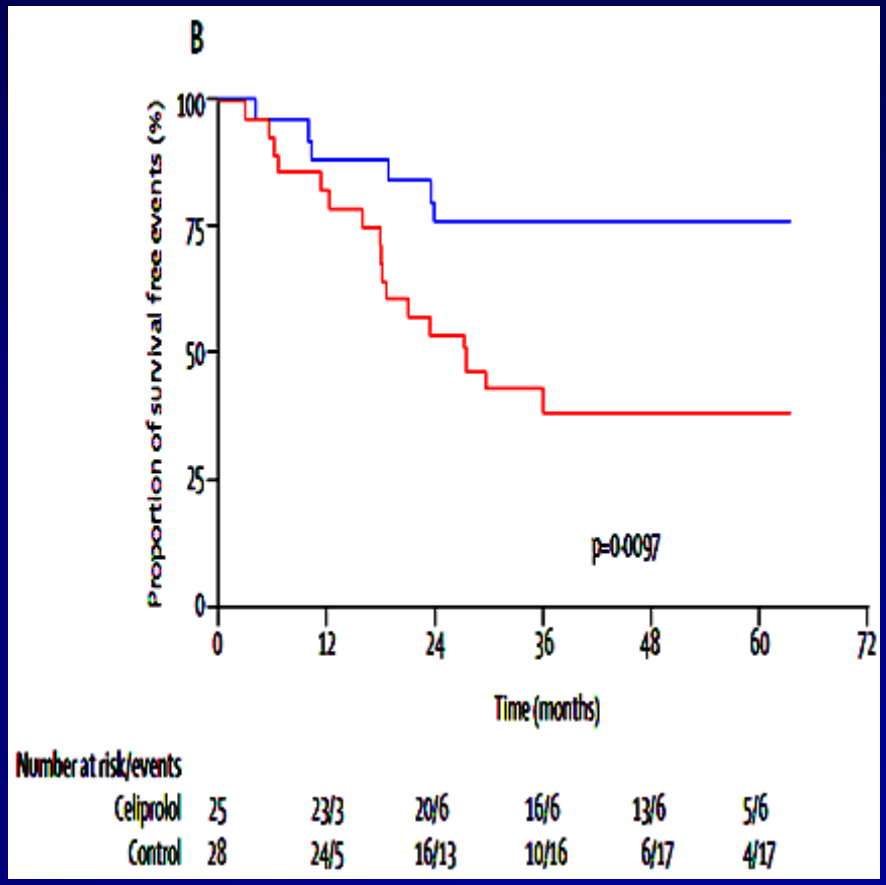
Randomized trial of propranolol in 70 adolescent and adult patients with classic Marfan's syndrome



Shores J. *NEJM* 1994;330:1335-1341.

Beta-Blockers Lower Risk in Ehler-Danos

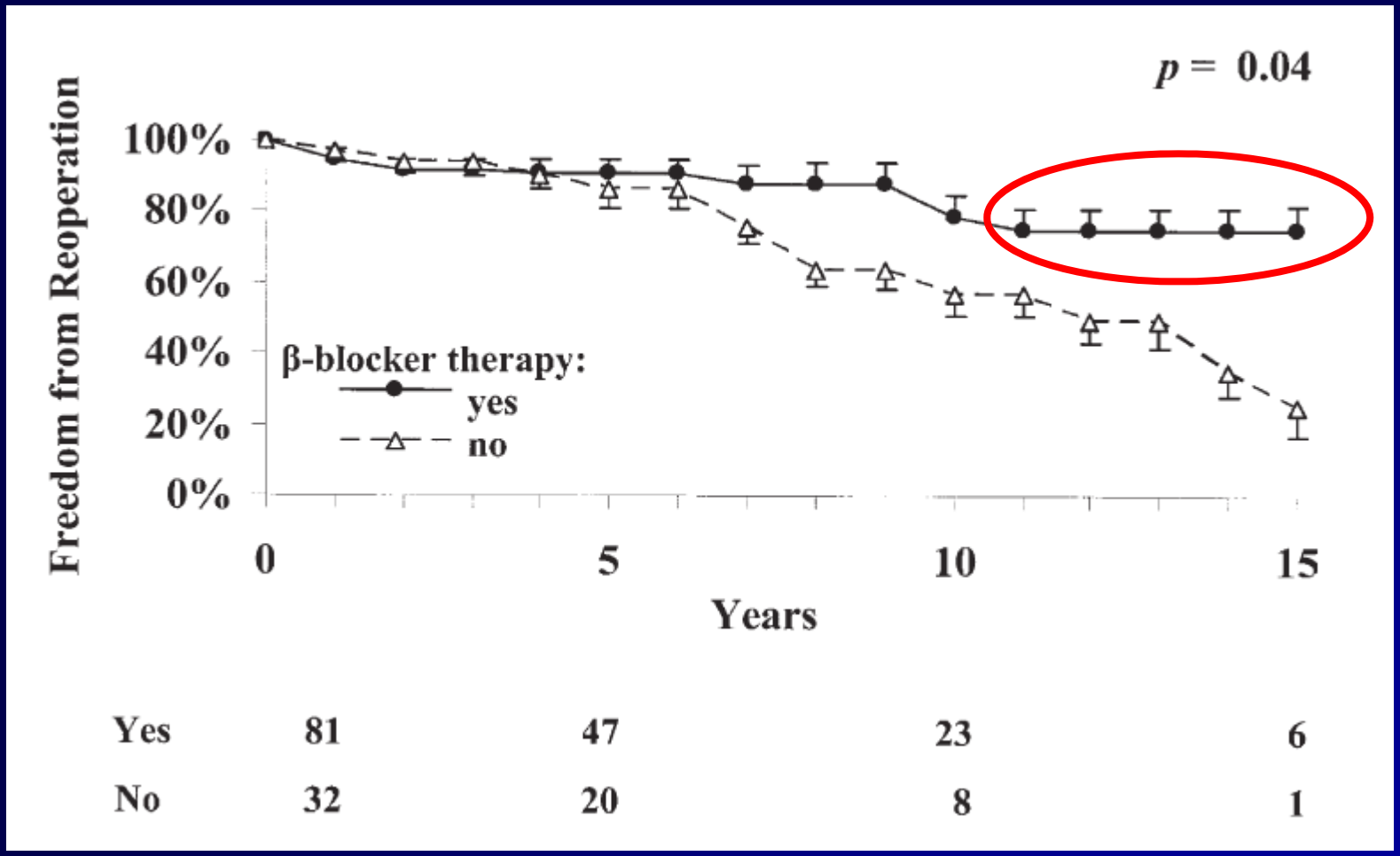




Kaplan-Meier curves of event-free survival in 53 patients with vascular Ehlers-Danlos Primary endpoint (A). Primary and secondary endpoints (B).

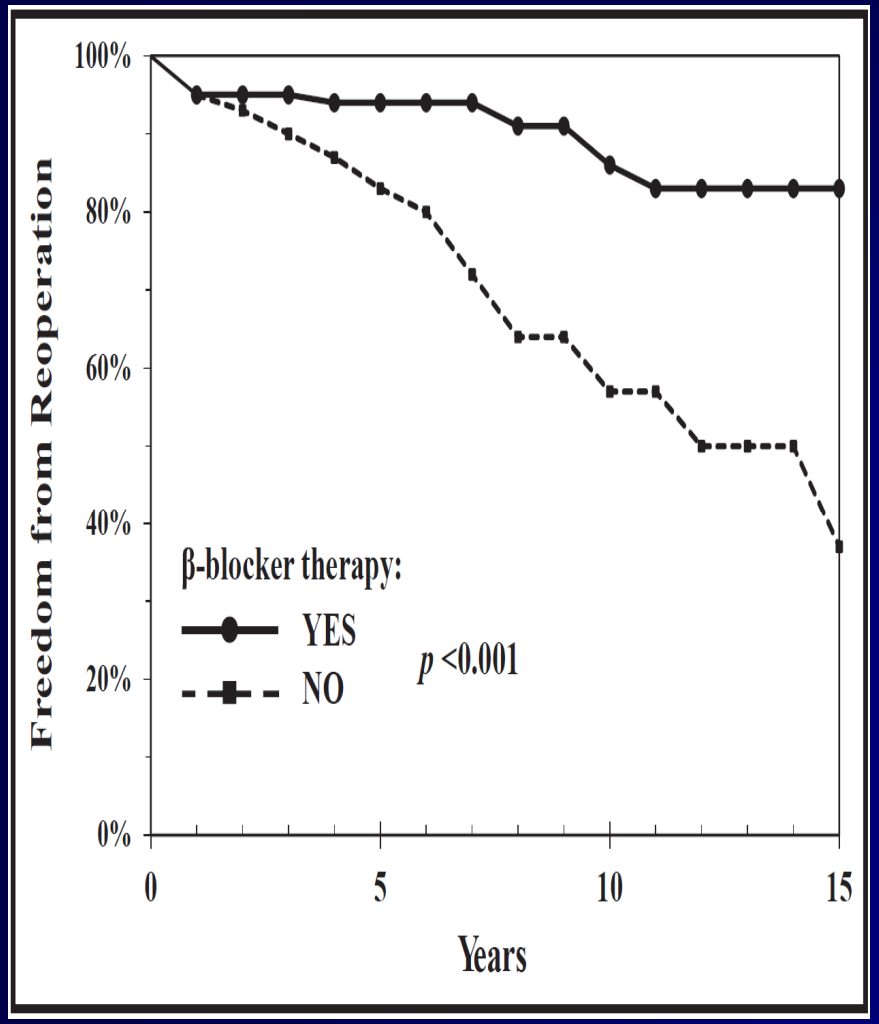
Kim-Thanh Ong et al. *www.thelancet.com* 2010:376;1476-84.

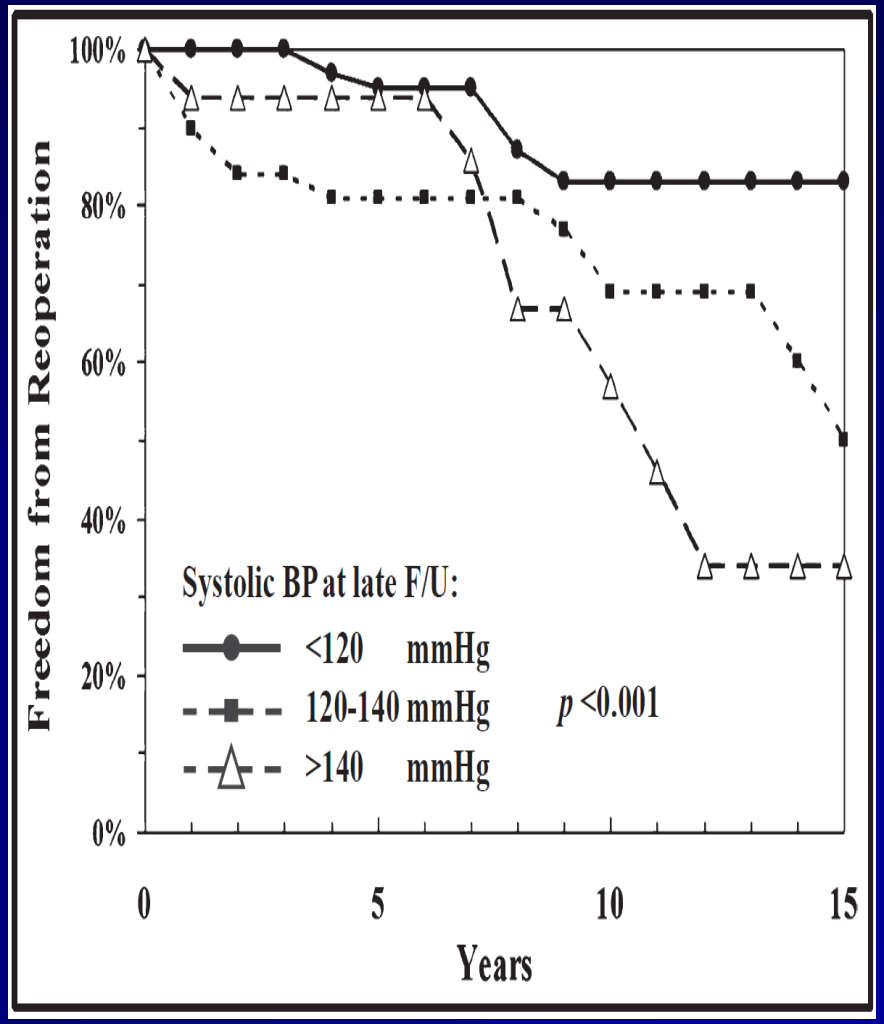
Freedom from Reoperation After Repair of Type A AoD vs. Postoperative β-blocker Therapy



Zierer A, et al. *Ann Thorac Surg* 2007;84:479-87.

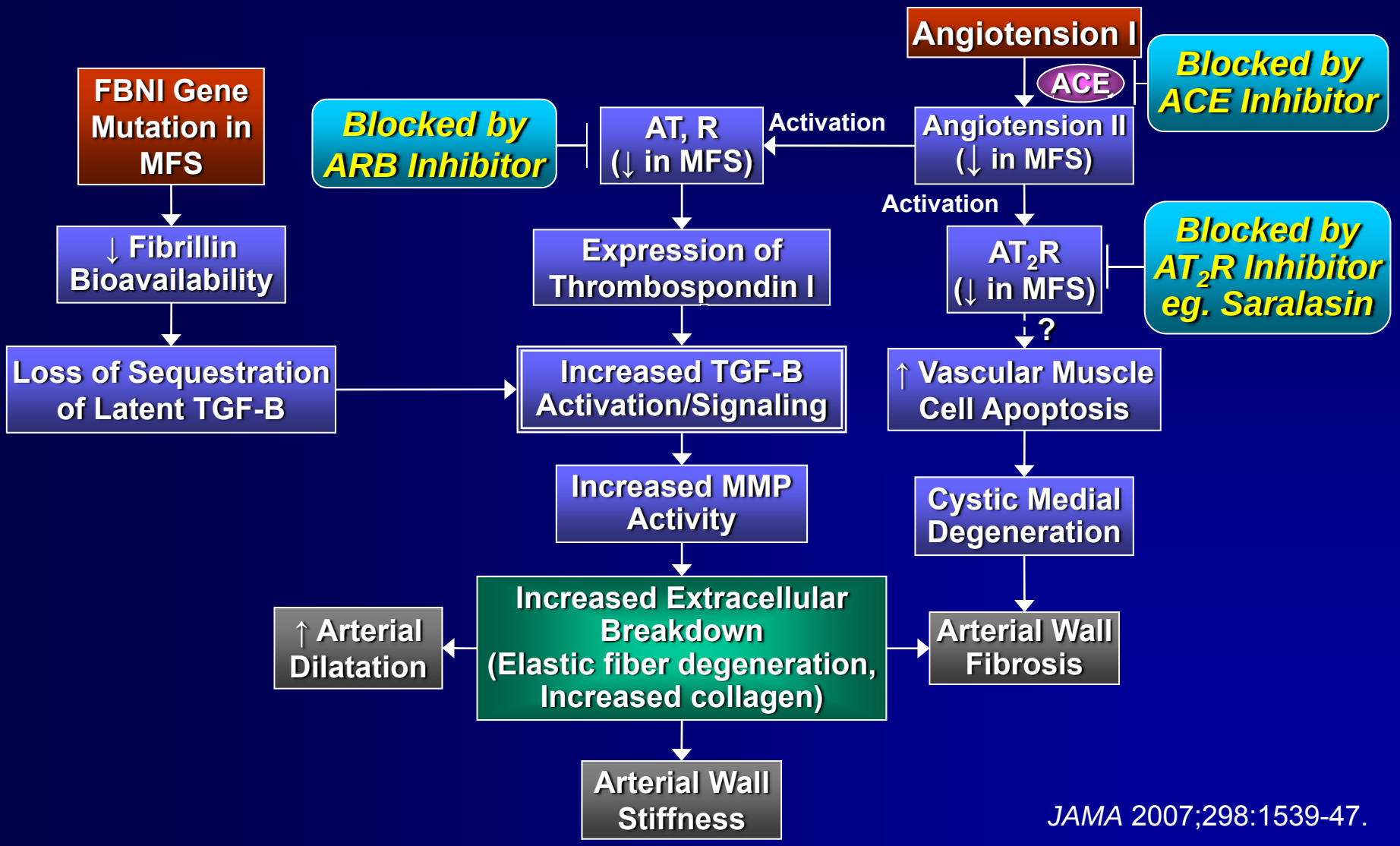
Beta-Blocker after Dissection





Melby SJ, et al. *J Clin Hypertens* 2013:16:63-68.

How Would ACE/ARB's Have Aortic Benefit?



JAMA 2007;298:1539-47.

Jikei Heart Study

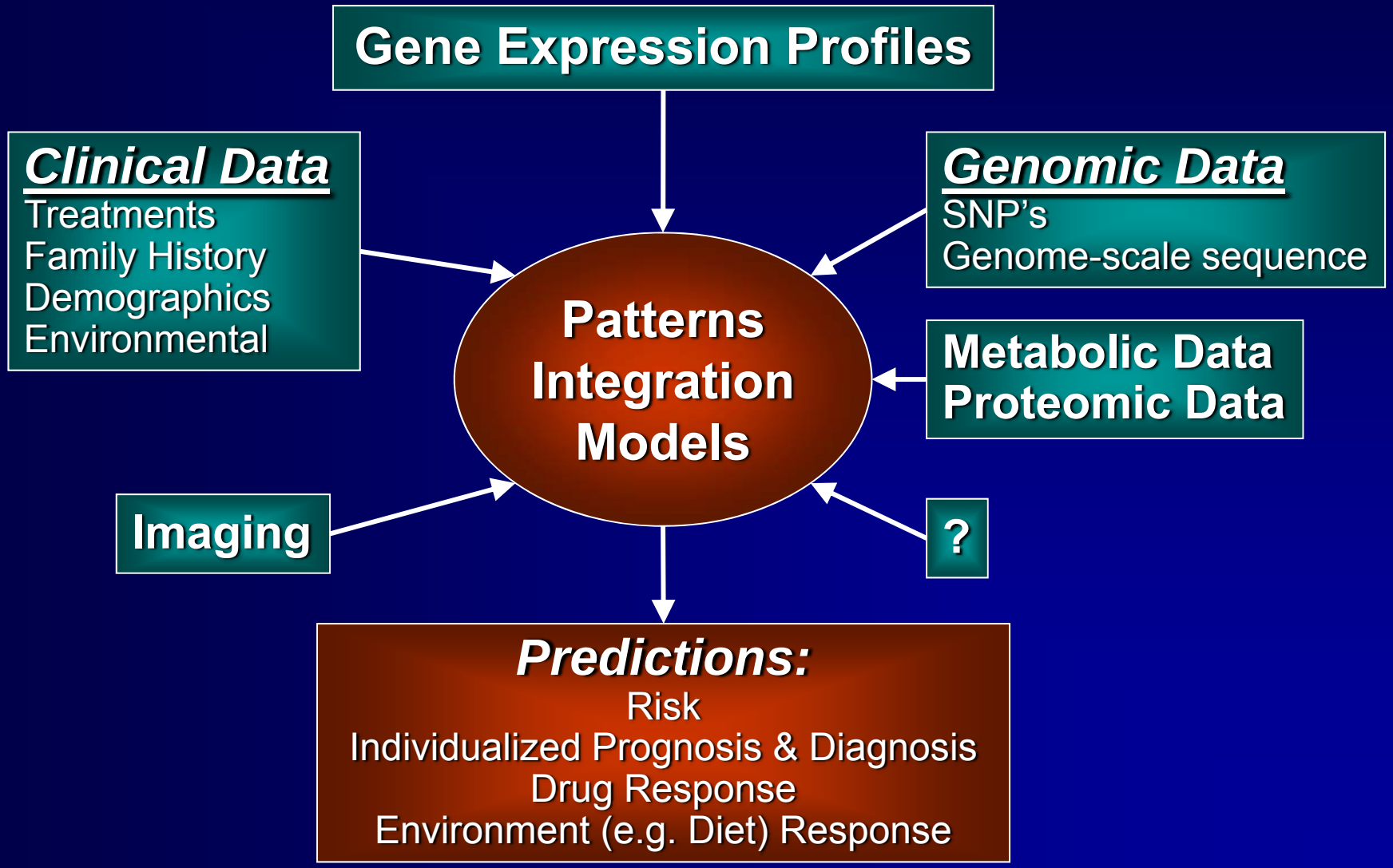
	All Patients	Valsartan Group	Non-ARB Treatment Group
Calcium-channel blocker	2052 (67%)	1041 (68%)	1011 (66%)
ACE inhibitor	1073 (35%)	548 (36%)	525 (34%)
α Blocker	988 (32%)	486 (32%)	502 (33%)
β Blocker	167 (5%)	74 (5%)	93 (6%)
Thiazide	68 (2%)	29 (2%)	39 (3%)
Antialdosterone agent	116 (4%)	52 (3%)	64 (4%)
Other diuretics	243 (8%)	117 (8%)	126 (8%)
Statin	951 (31%)	461 (30%)	490 (32%)
Fibrate	79 (3%)	42 (3%)	37 (2%)
Dissection	**12 (0.7%)**	**2 (0.1%)**	**10 (0.6%)**

Mochizuki S, et al. *Lancet* 2007;369:1431-39.

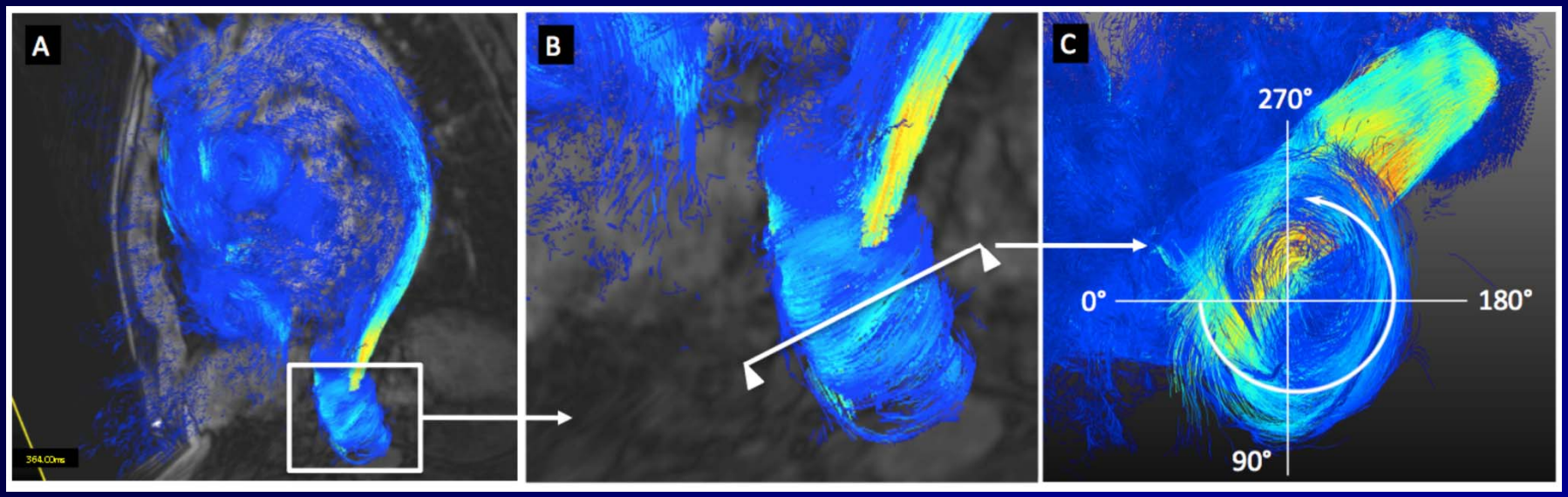
Long-Term

- B-Blockers: HR <60BPM
- Control Blood Pressure: <120/80 - Prefer ARB's or ACE's
- Statins for atherosclerosis
- Anticoagulants?
- "Watch" for aneurysm formation: 1, 3, 6, 12 months to start
- Educate the patient: a lifelong disease; sx, activity, meds, f/up

Where is the Future?

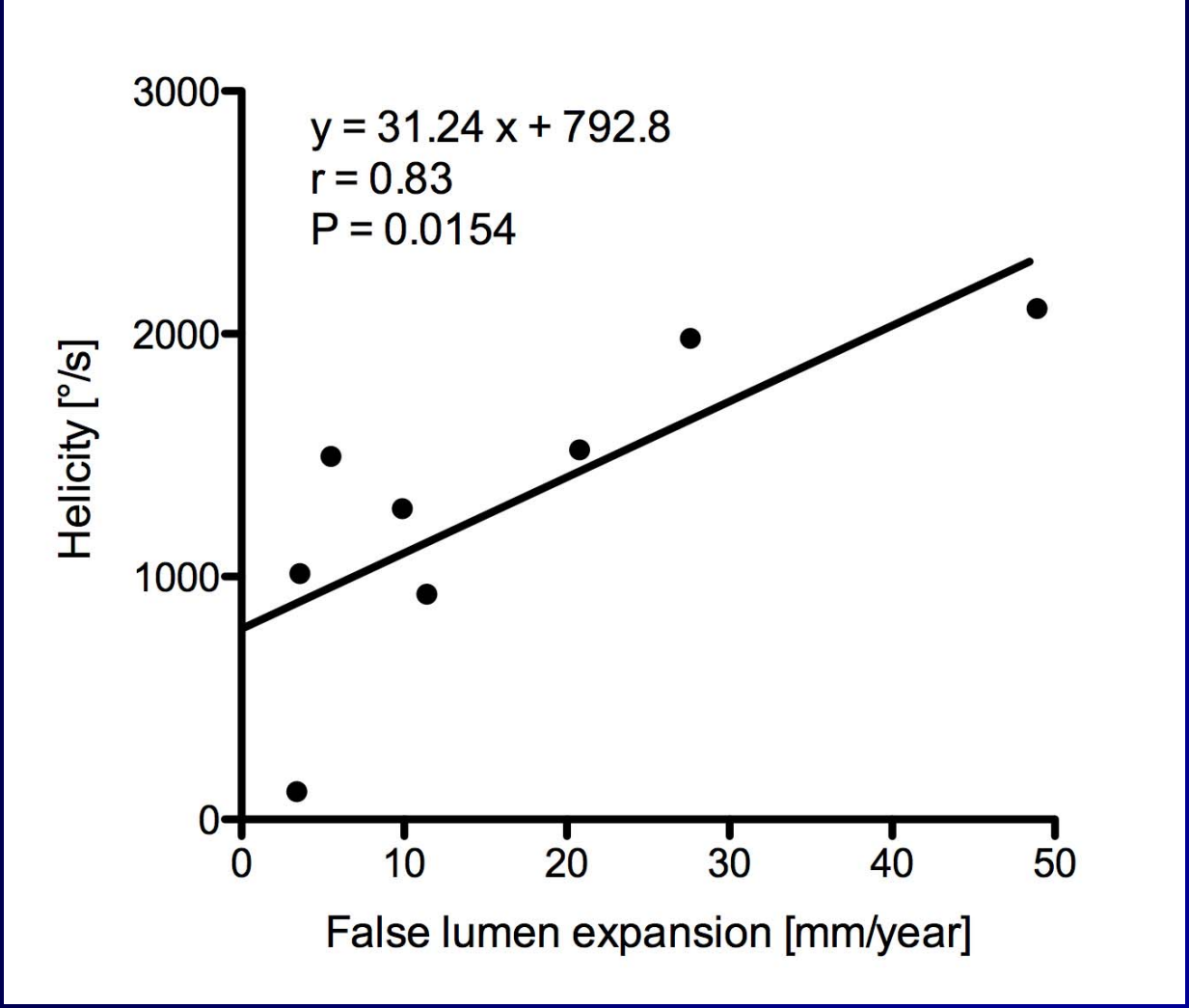


Helicity Quantification



RE Clough et al. *J Vasc Surg*. 2012; 55:914-23

Helicity

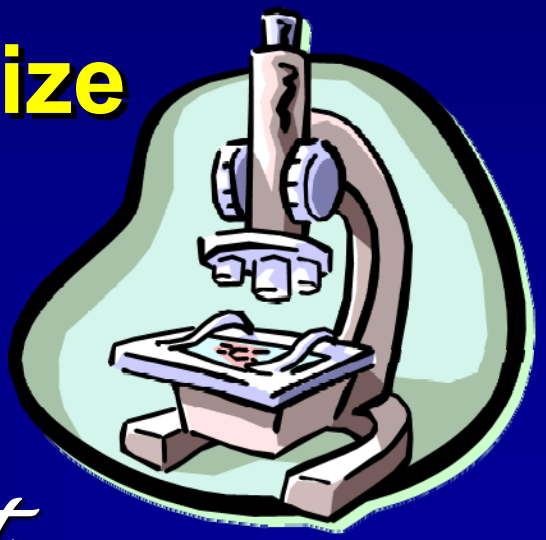


RE Clough et al. *J Vasc Surg*. 2012; 55:914-23

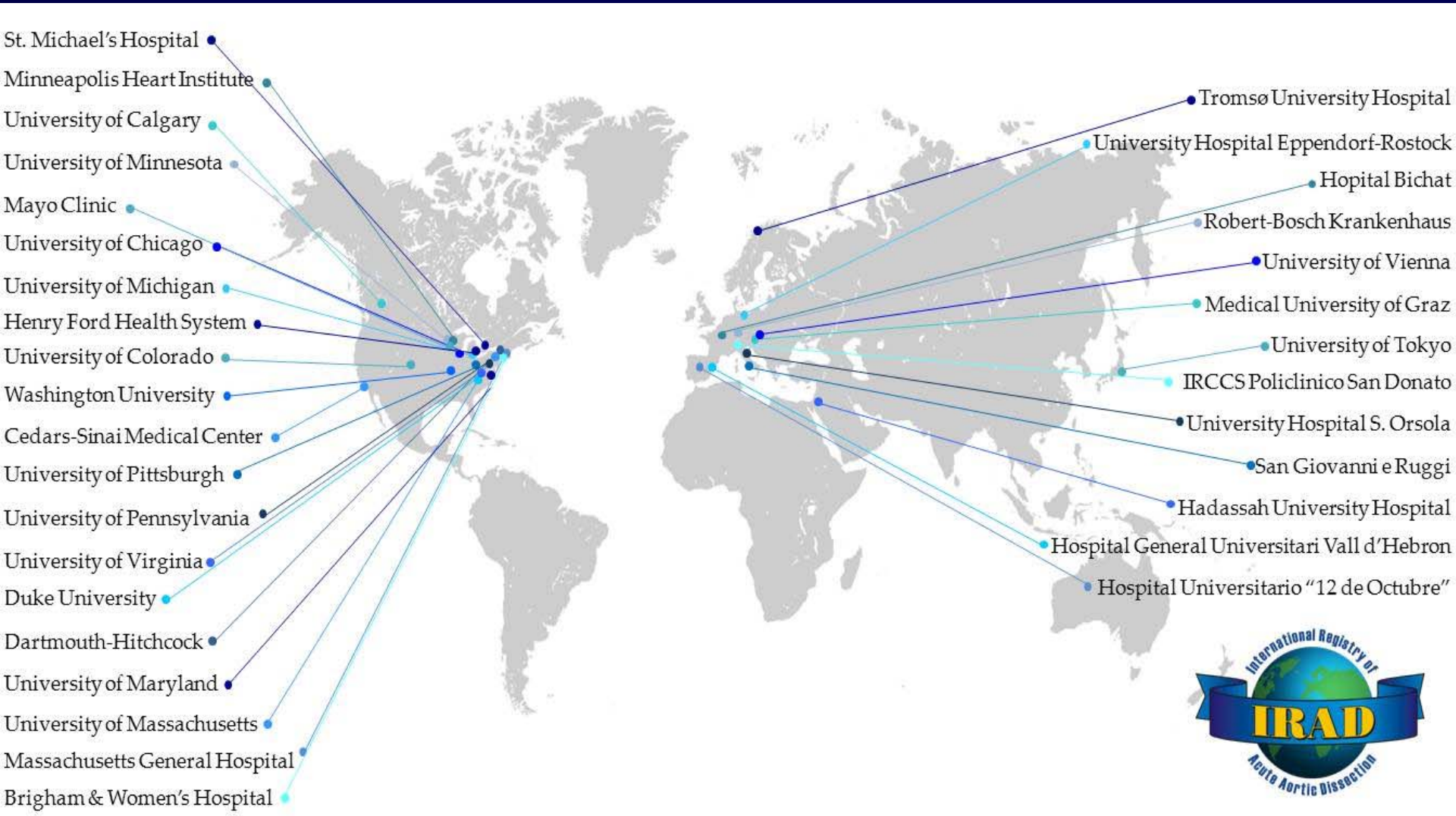
Disease is very old, and nothing about it has changed.

It is we who change as we learn to recognize what was formerly imperceptible.

- Charcot



IRAD Hospitals



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“There is no disease more conducive to clinical humility than aneurysm of the aorta”

- Sir William Osler