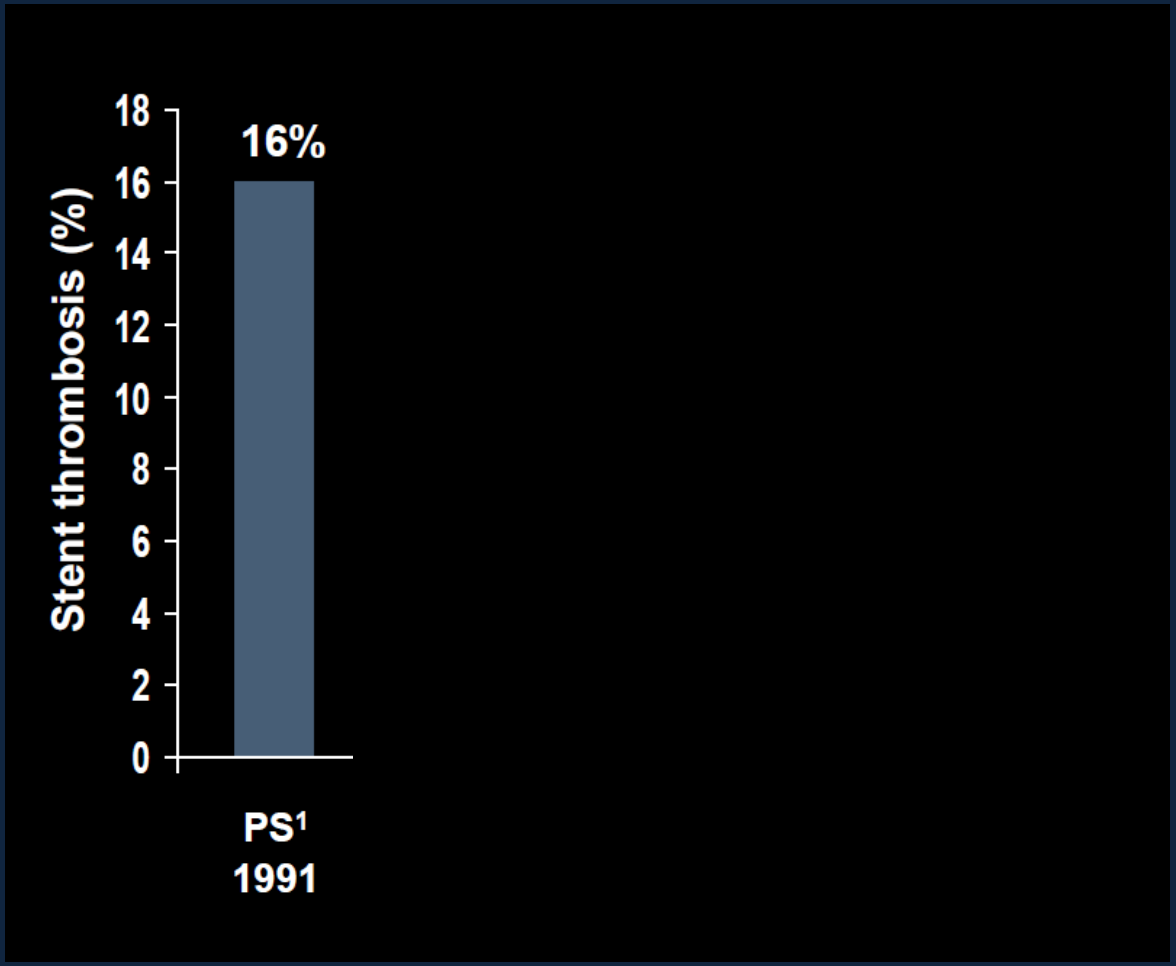
Θρόμβωση ενδοστεφανιαίων προθέσεων

Σταύρος Χατζημιλτιάδης

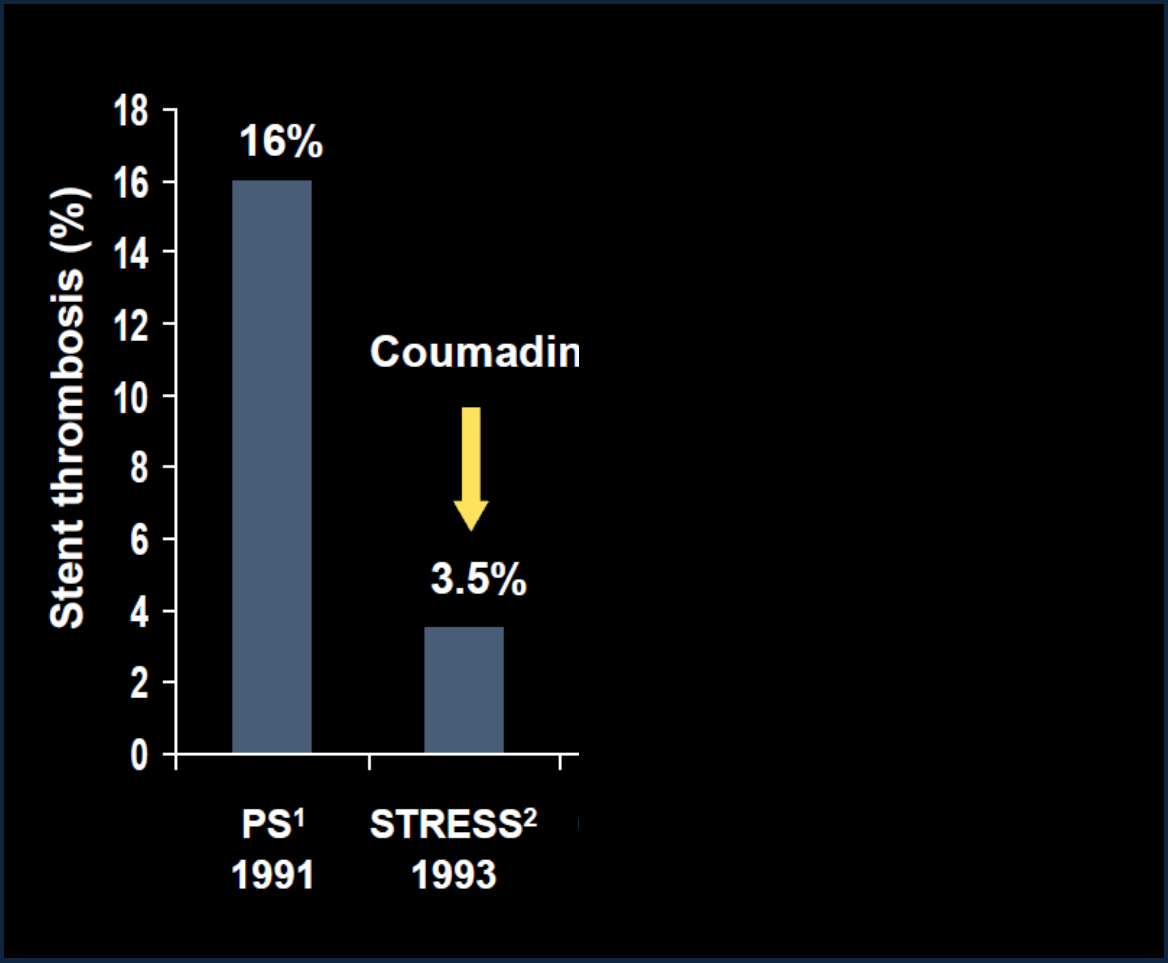
Αναπληρωτής Καθηγητής Καρδιολογίας ΑΠΘ

When BMS were first introduced, stent thrombosis occurred in up to 16% of patients



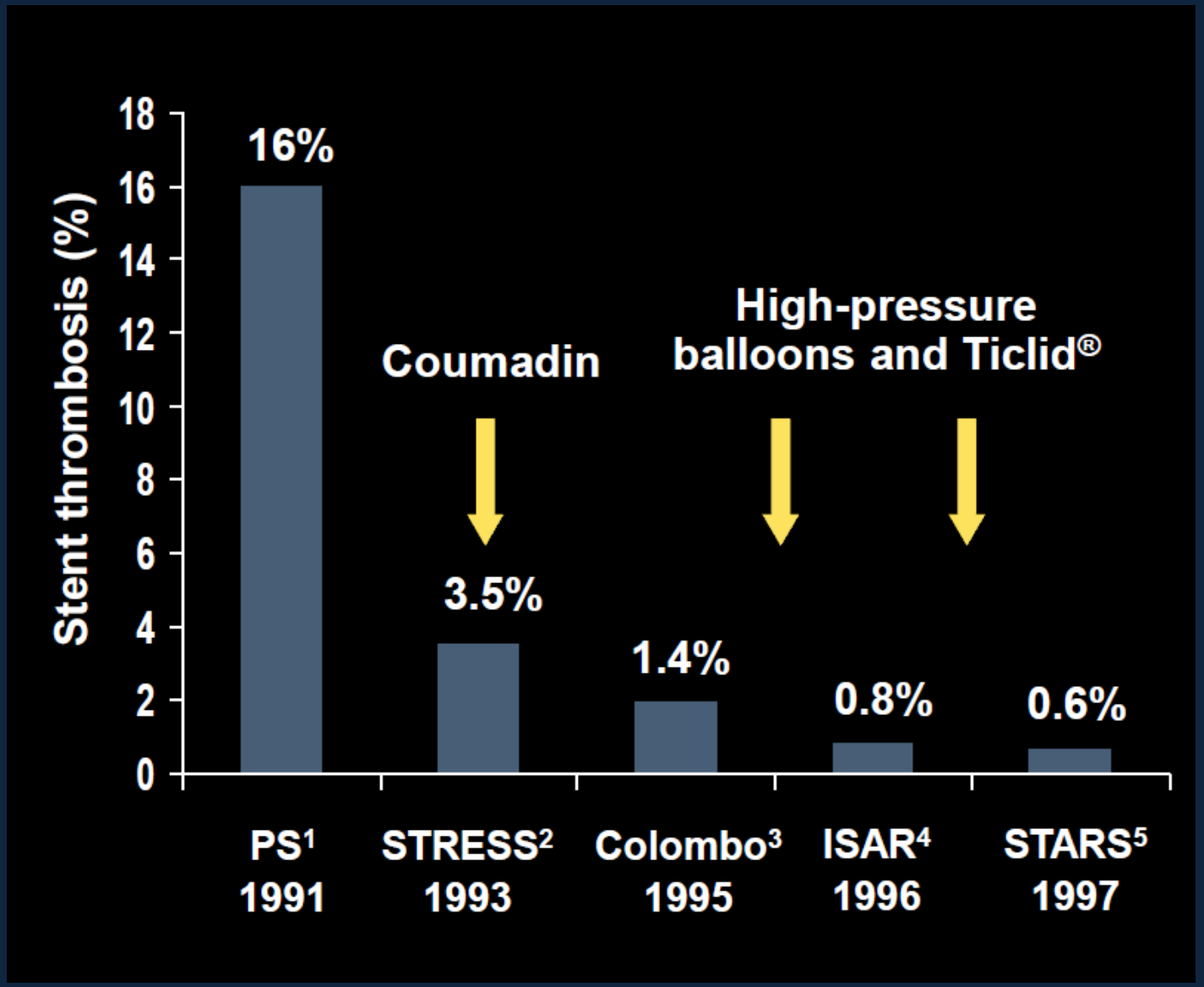
1. Schatz RA, Baim DS, Leon M, et al. Clinical experience with the Palmaz-Schatz coronary stent. Initial results of a multicenter study. Circulation 1991;83:148-61

The STRESS and BENESTENT era - a major step forward



The heparin coated stent

Stent Thrombosis rate 0.4%

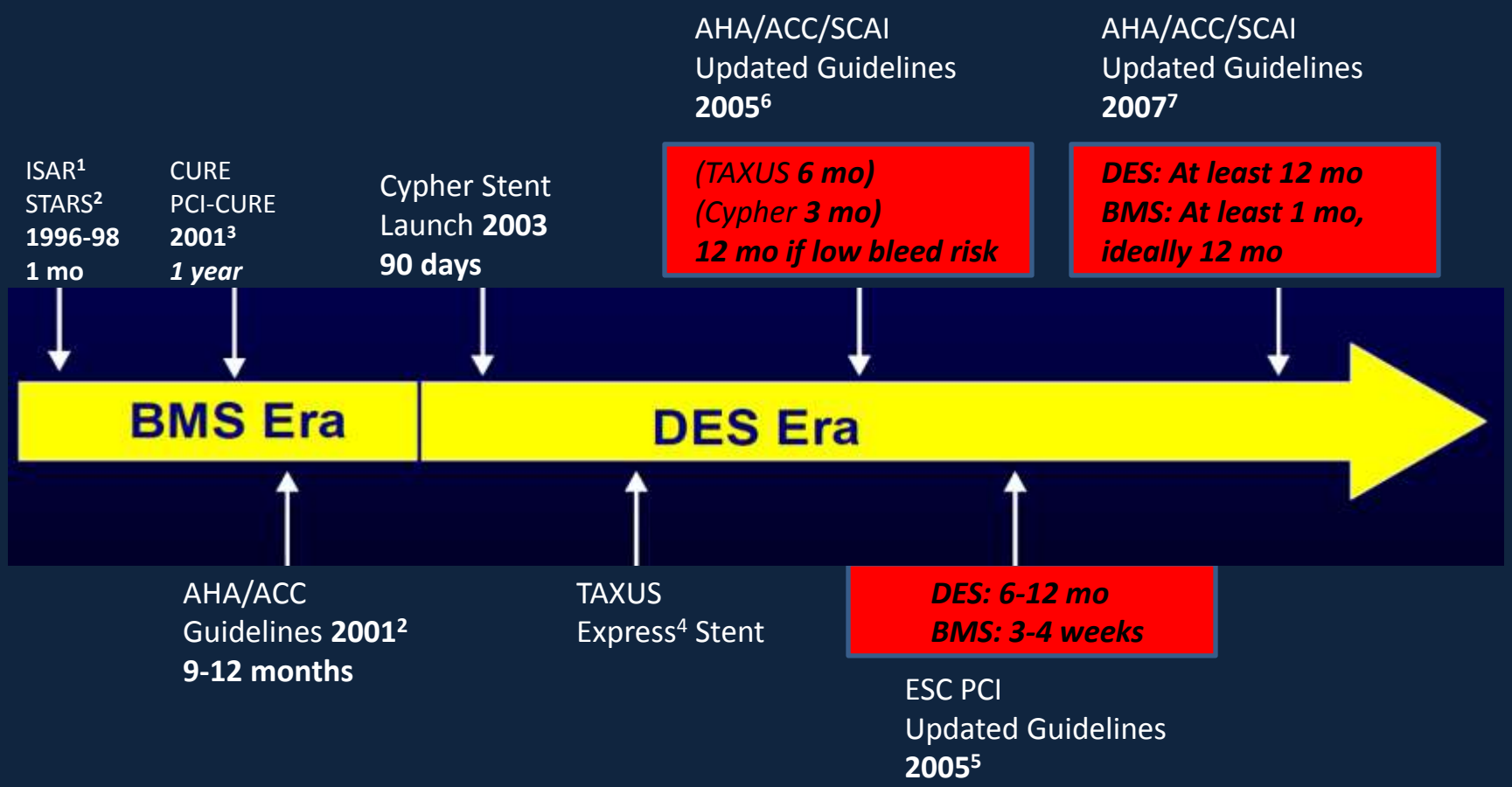


3. Colombo A. et al, Circulation. 1995;91:1676.

4. Schöming A. et al, Circulation. 1994;90:2716.

5. Leon MB. et al, N Engl J Med 1998;339:1665.

Uncertainty regarding optimal duration of thienopyridine therapy after DES



5. Silber et al. Eur Heart J. 2005;26:804;
6. Smith et al. *Circulation. 2006;113:e166;*
7. King et al. Circulation 2008; 117: 261 – 295

ARC Proposed Standard Definition

1) Stent Thromboses will fall into one of three types of evidence:

Definite / Confirmed

Acute Coronary Syndrome (ACS) AND Angiographic/Pathologic Confirmation

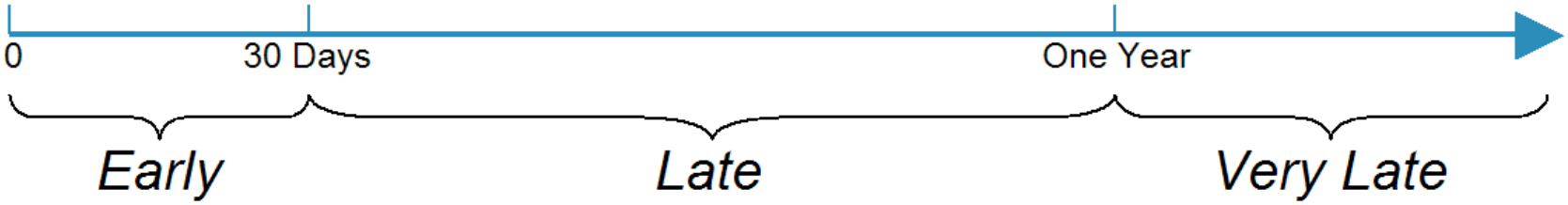
Probable

Unexplained Death (≤ 30 days) OR Target Vessel MI without angiographic confirmation of stent thrombosis or other identified culprit lesion

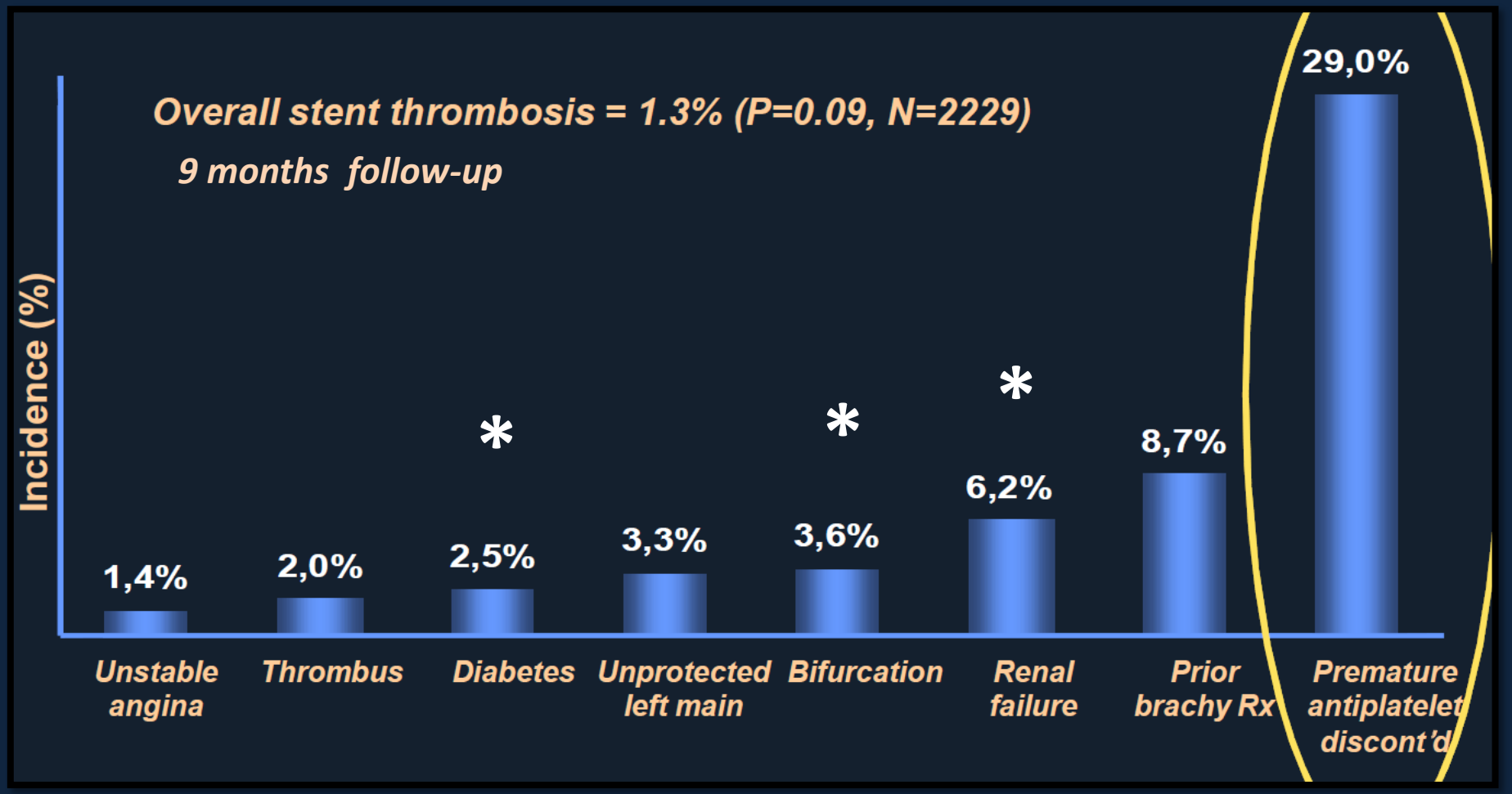
Possible

Unexplained Death (>30 days)

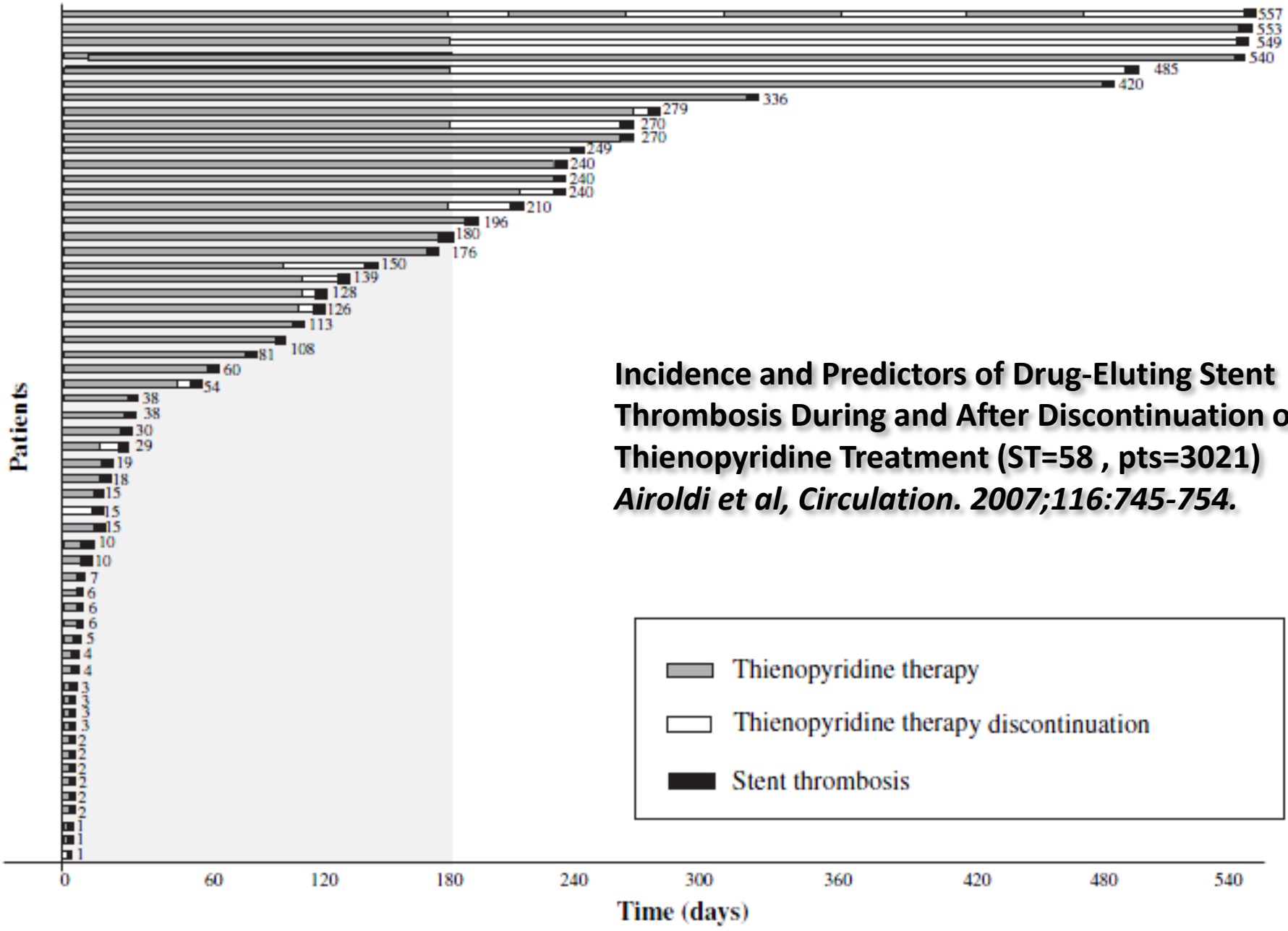
2) Stent Thromboses will also fall into one of three time periods:



Incidence, Predictors, and Outcome of Thrombosis After Successful Implantation of Drug-Eluting Stents



Iakovou I et al, JAMA. 2005;293:2126-2130



Incidence and Predictors of Drug-Eluting Stent Thrombosis During and After Discontinuation of Thienopyridine Treatment (ST=58 , pts=3021)

Airoldi et al, Circulation. 2007;116:745-754.

Clinical, Angiographic, and Genetic Factors Associated With Early Coronary Stent Thrombosis

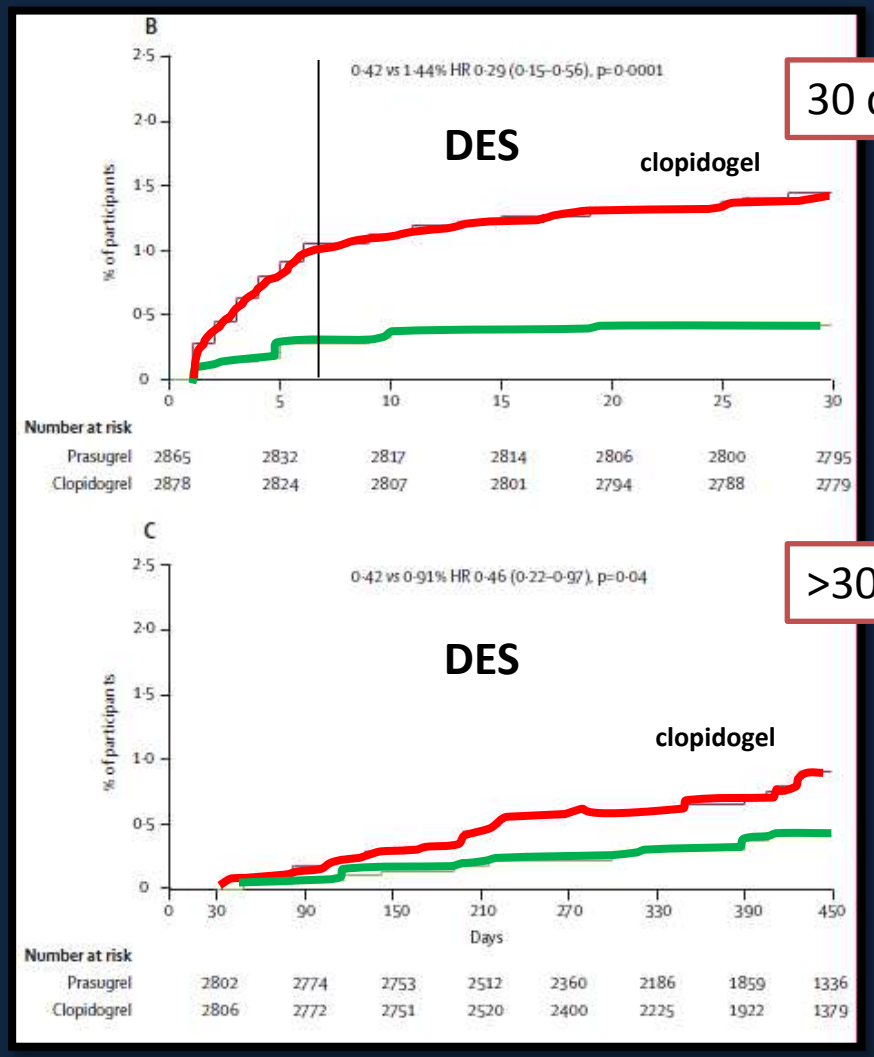
Gayla G, et al. JAMA. 2011; 306(16):1765-1774

Table 5. Stepwise Multivariable Analysis for the Combined Model

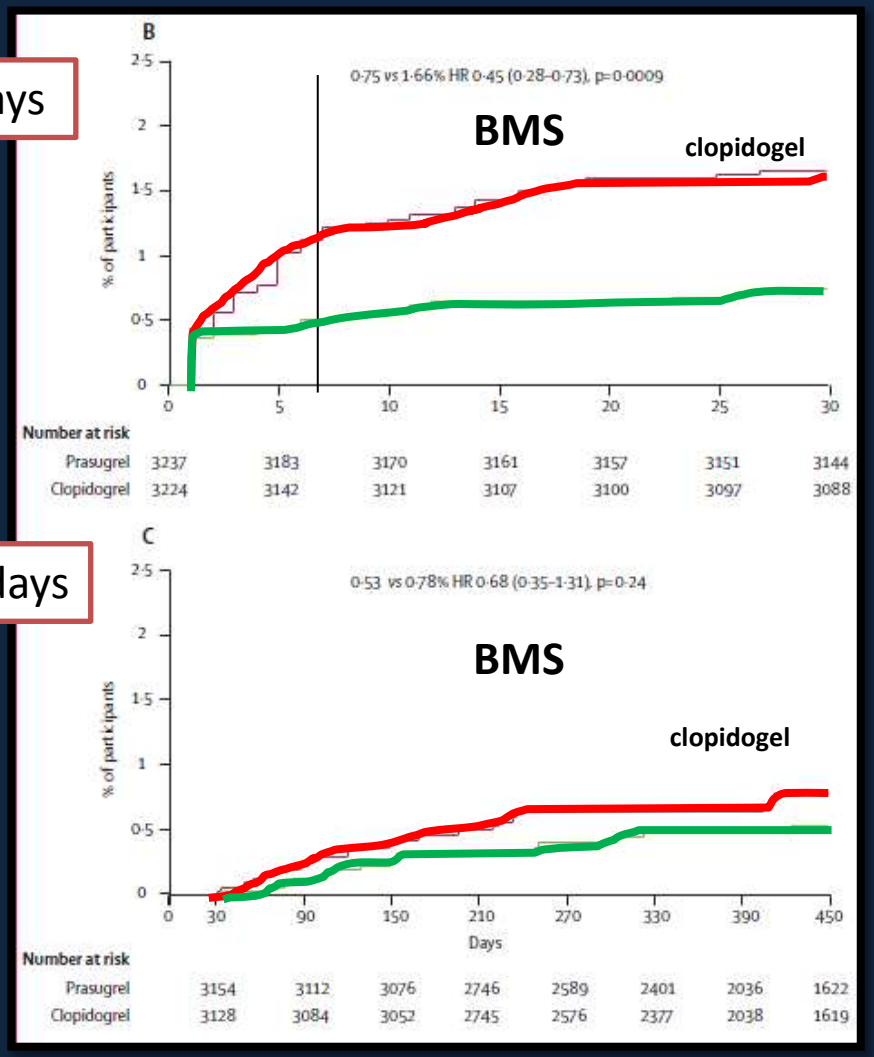
	Variables	Univariable Analysis		Multivariable Analysis	
		Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
*	Diabetes	1.76 (1.08-2.85)	.02	1.82 (1.02-3.24)	.04
	Prior myocardial infarction	1.48 (0.96-2.28)	.08		
*	Left ventricular ejection fraction <40%	2.59 (1.40-4.83)	.003	2.25 (1.09-4.70)	.03
*	ACC/AHA type C lesion	2.30 (1.48-3.60)	<.001	2.33 (1.40-3.89)	.001
	Number of vessels	1.44 (0.89-2.32)	.13		
*	Percutaneous coronary intervention in acute setting	3.06 (1.64-5.70)	<.001	3.05 (1.54-6.07)	.001
	Dissection	2.31 (1.10-4.86)	.03		
	Minimum stent diameter	0.69 (0.40-1.17)	.17		
*	High clopidogrel loading dose	0.80 (0.65-0.98)	.03	0.73 (0.57-0.93)	.01
*	Use of proton pump inhibitors	1.96 (1.24-3.10)	.004	2.19 (1.29-3.75)	.004
	Use of calcium channel blockers	0.62 (0.35-1.12)	.11		
*	CYP2C19 metabolic status	2.01 (1.52-2.65)	<.001	1.99 (1.47-2.69)	<.001
	PON1 QQ192 vs *QR* or *RR192*	1.36 (0.88-2.10)	.17		
*	*ABCB1* TT vs CC or CT	2.01 (1.22-3.30)	.006	2.16 (1.21-3.88)	.009
*	*ITGB3* (*PLA2* carriers vs noncarriers)	0.50 (0.29-0.87)	.01	0.52 (0.28-0.95)	.03
	P2Y12 H2/H2 vs *H1/H1* or *H1/H2*	4.14 (1.02-16.83)	.05		

The Online Assistance for Stent Thrombosis (ONASSIST) project

Kaplan–Meier curves of Academic Research Consortium definite or probable stent thrombosis for all patients (TRITON-38 prasugrel vs clopidogrel)



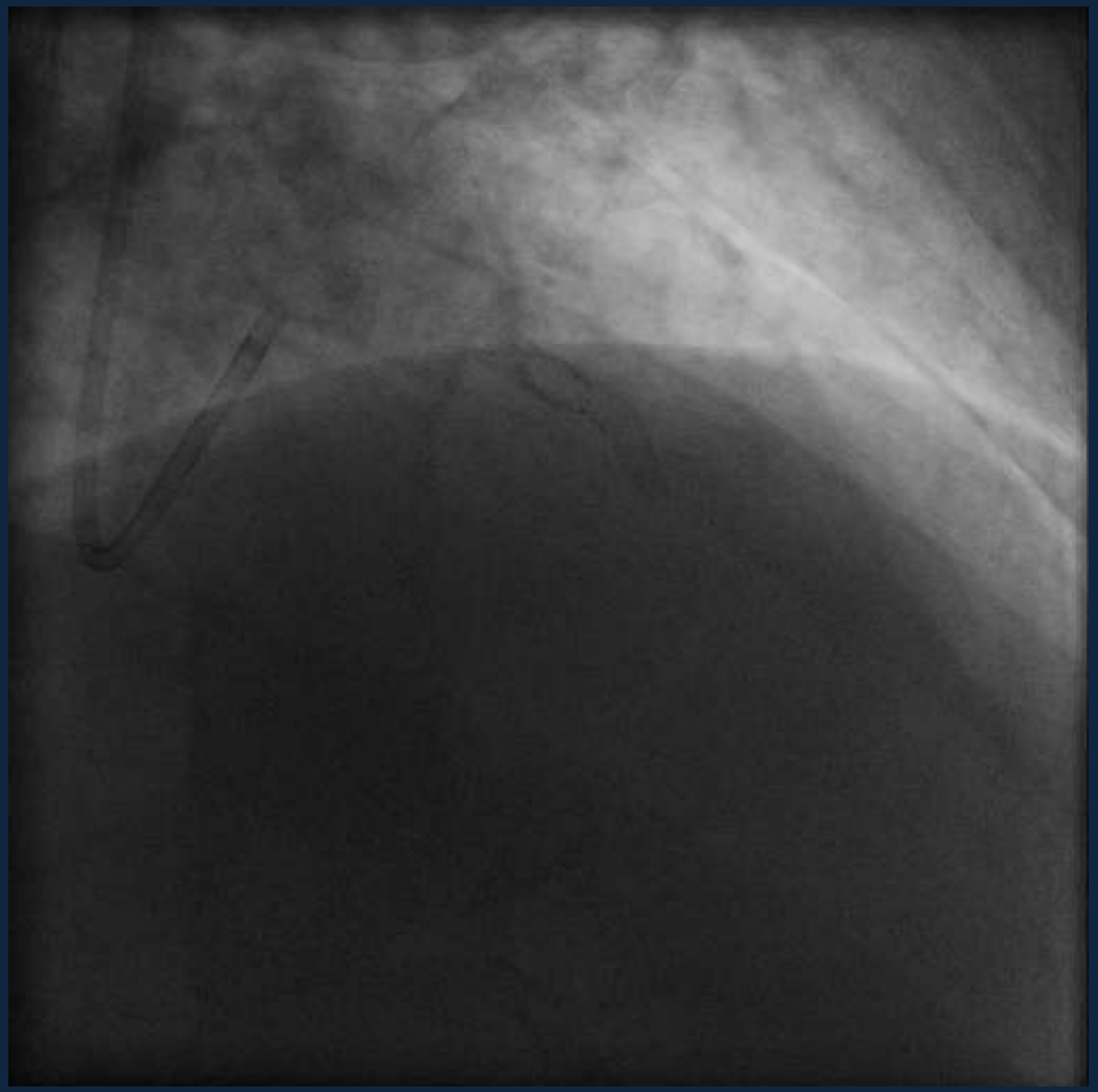
30 days



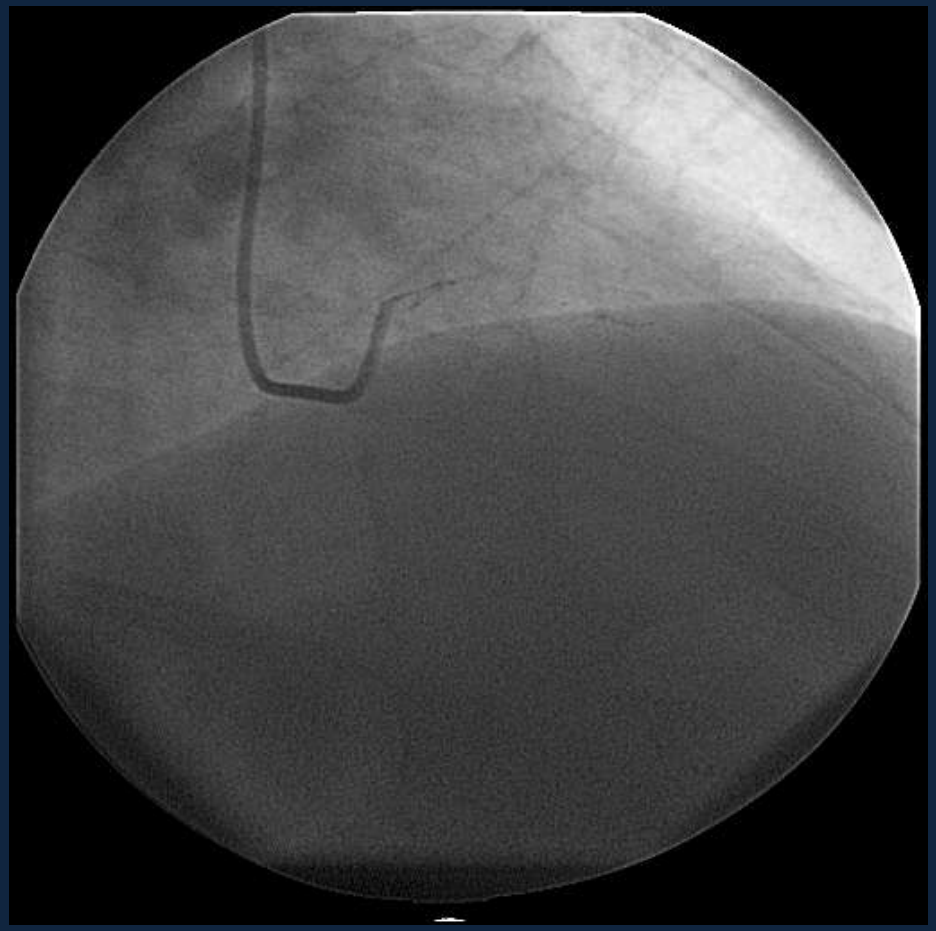
>30 days

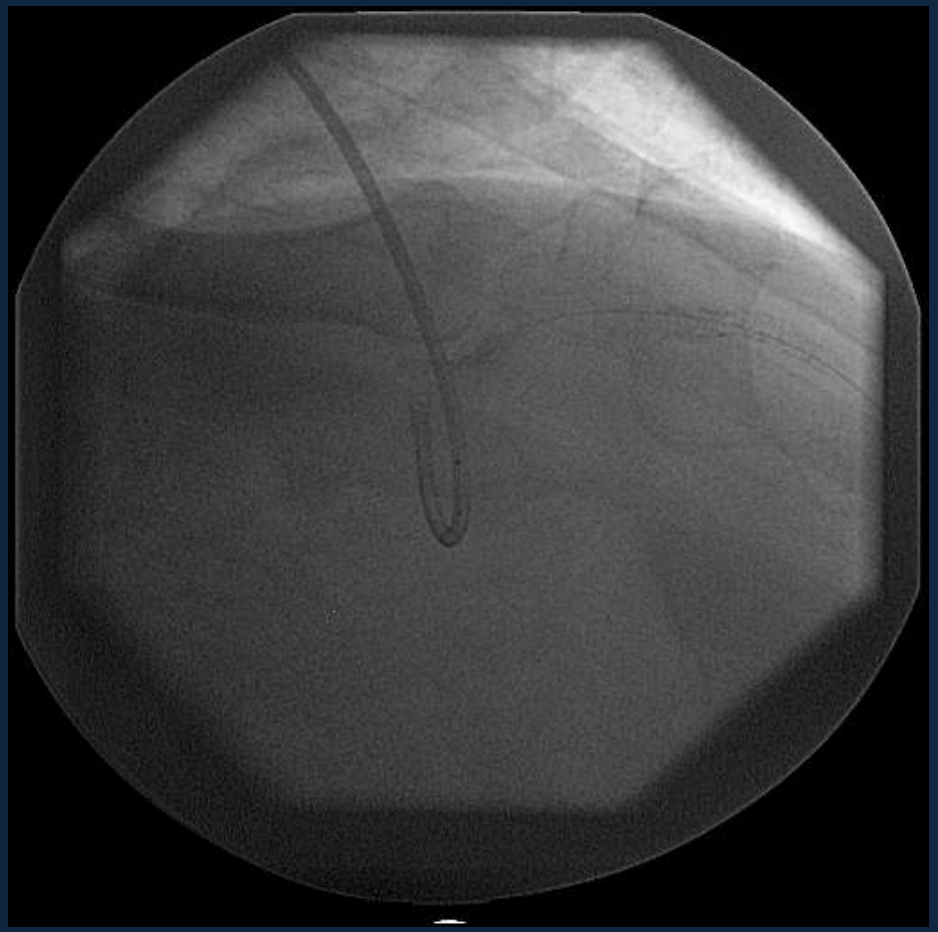
Wiviott SD et al, Lancet 2008; 371: 1353–63

Early stent thrombosis

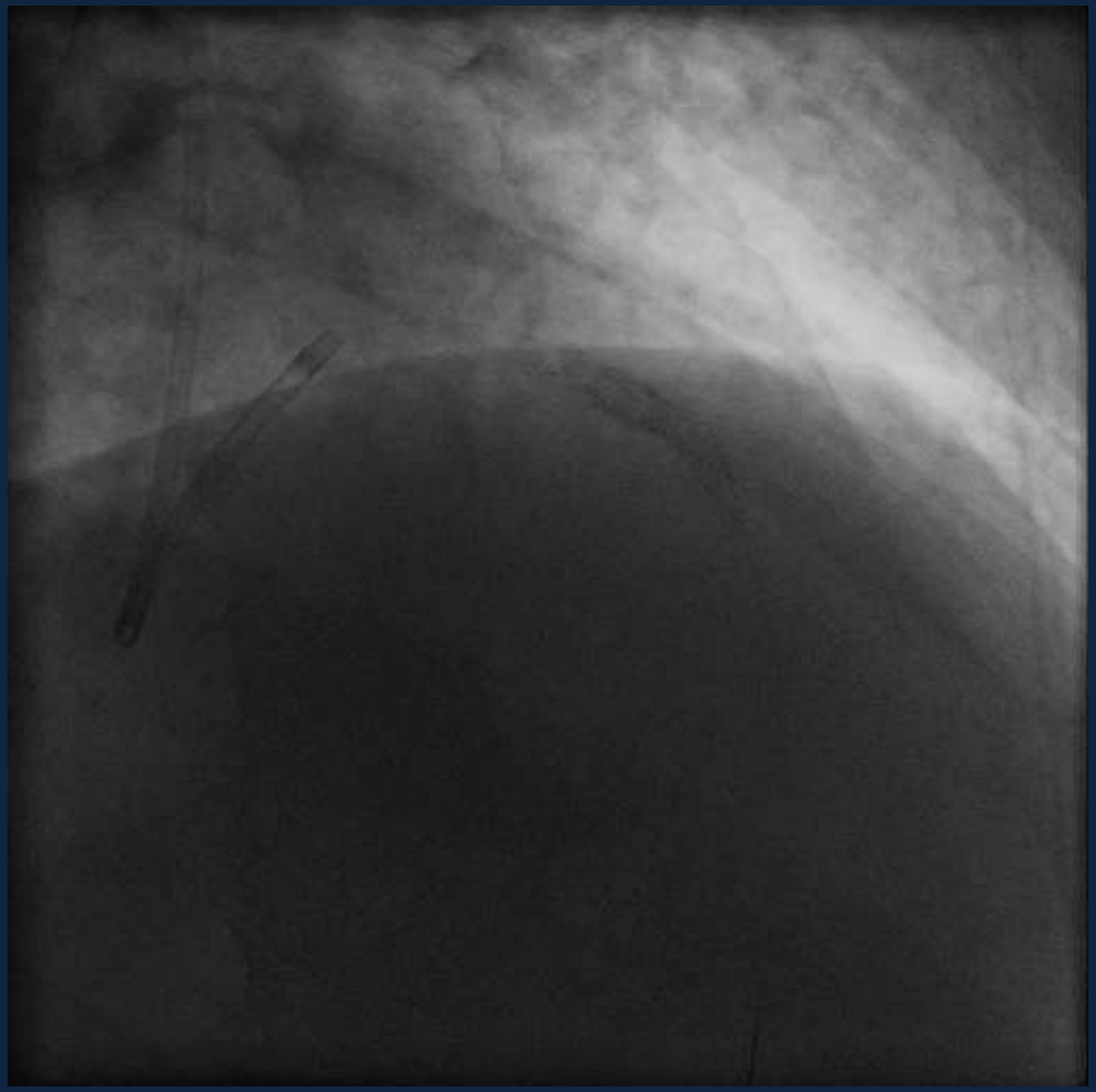


7 days earlier





Thrombus at the site of the incomplete stent expansion



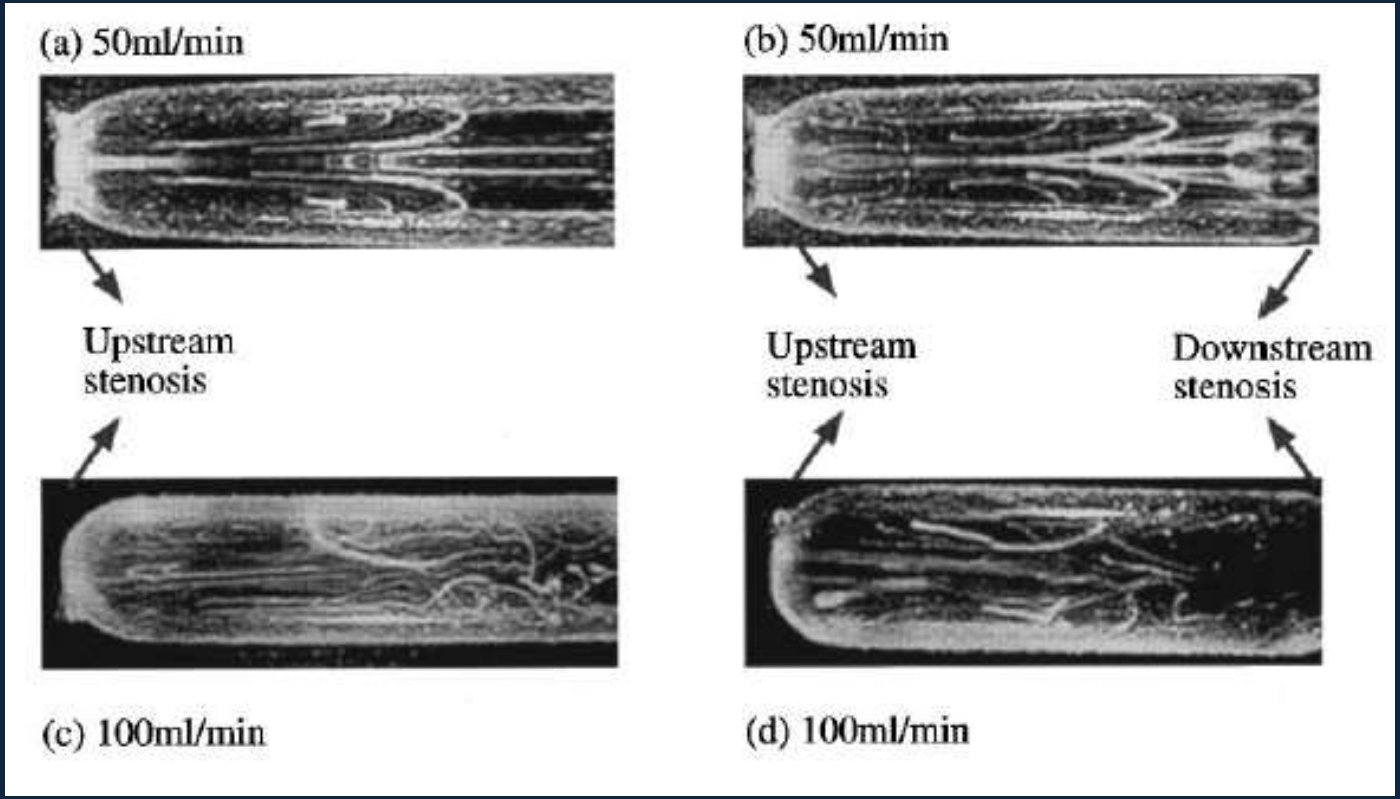
Early Stent Trombosis after Sirolimus-Eluting Stent Implantation: An Intravascular Ultrasound Study

Procedural Characteristics and Angiographic and IVUS Findings

	Stent Thrombosis (n = 15)		Matched Control Group (n = 45)	p Value
Reference (minimum lumen segment)				
Lumen CSA (mm^2)	3.9 ± 1.6		5.3 ± 1.7	0.007
EEM CSA (mm^2)	10.8 ± 4.2		9.9 ± 3.2	0.4
Plaque burden (%)	62 ± 13		46 ± 9	<0.001
Significant residual stenosis	10 (67%)	*	4 (9%)	<0.001
Stent segment				
Minimum stent CSA (mm^2)	4.3 ± 1.6	*	6.2 ± 1.9	<0.001
Stent expansion	0.65 ± 0.18		0.85 ± 0.14	<0.001

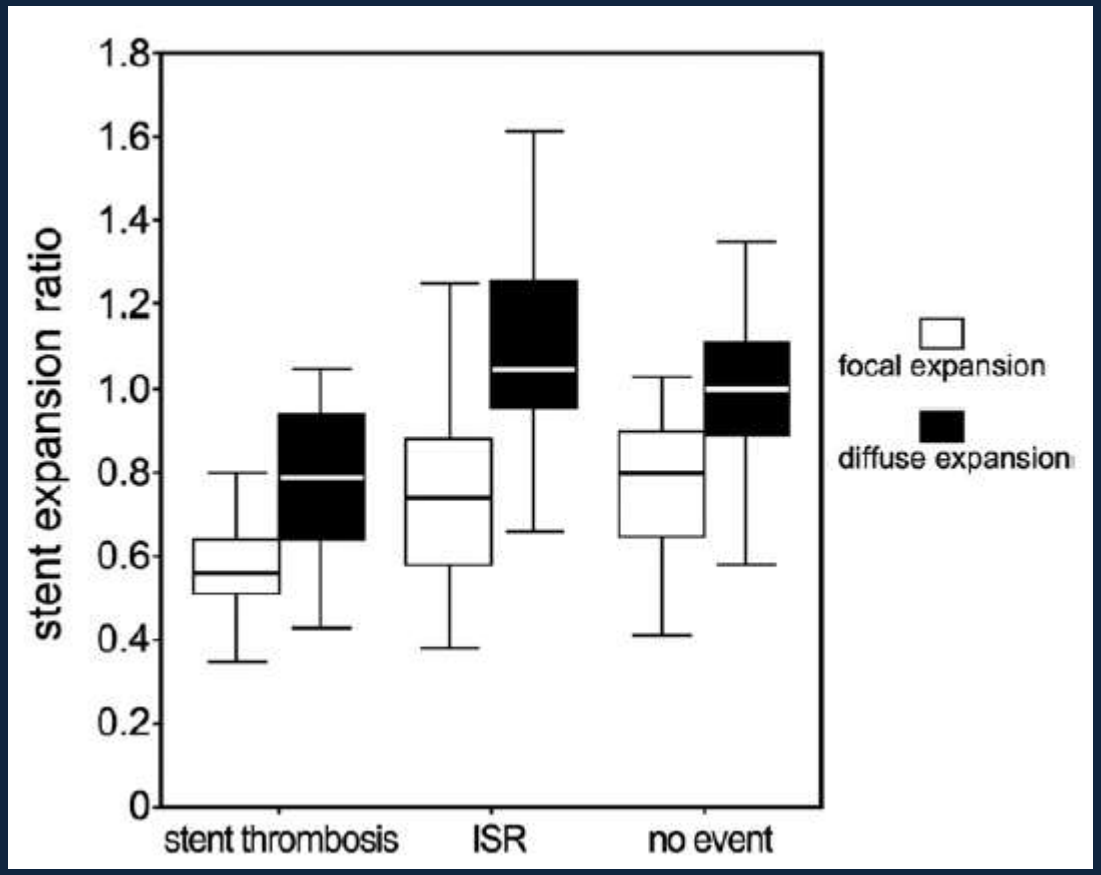
Fujii K et al, J Am Coll Cardiol 2005;45:995– 8

Enhancement of Stent-Induced Thromboembolism by Residual Stenoses: Contribution of Hemodynamics



Sukavaneshvar S et al. *Annals of Biomedical Engineering 2000 ; 28:182–193.*

Underexpansion in DES that thrombose is more severe, more diffuse, and more often proximal in location.

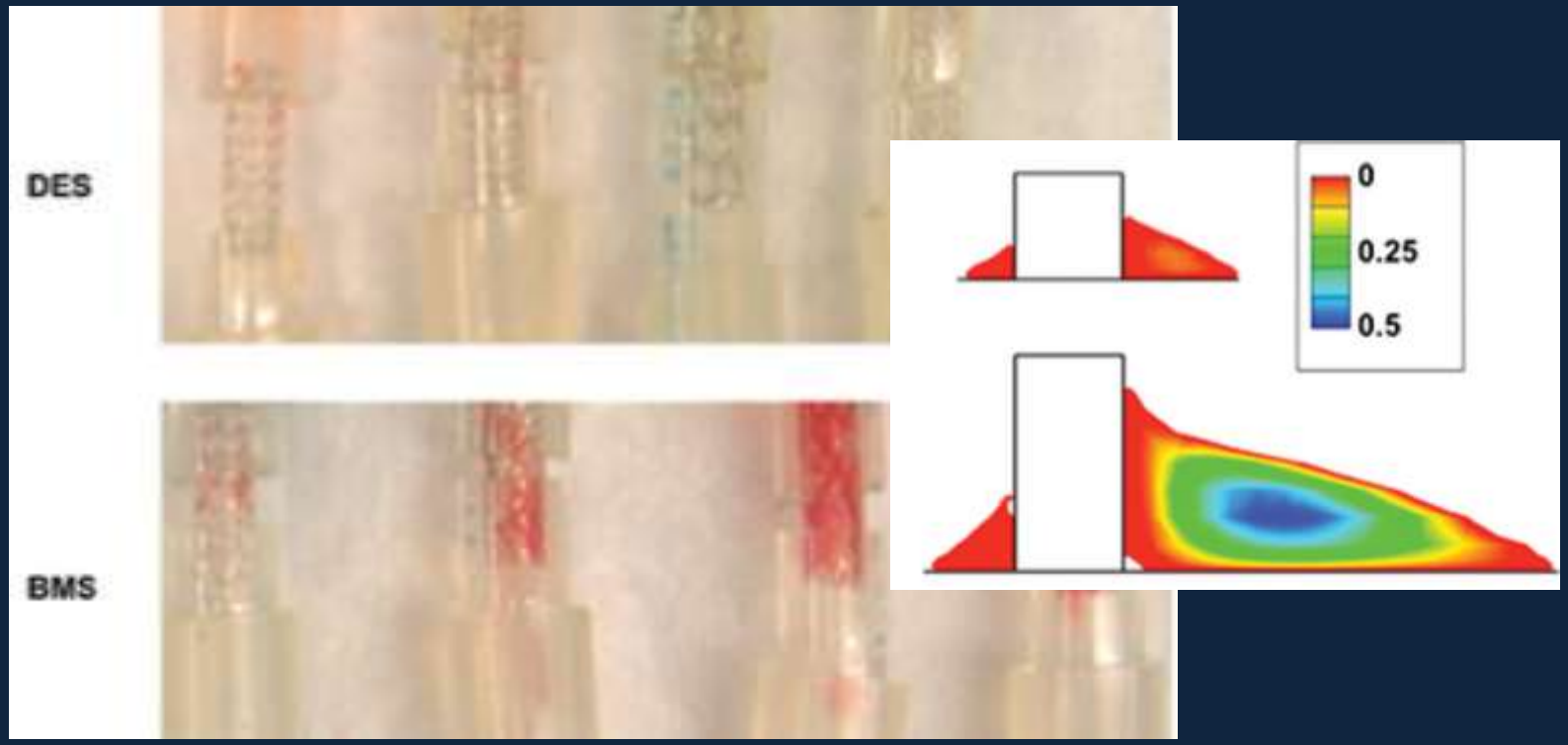


minimum stent area (MSA)/mean reference lumen CSA

mean stent CSA /mean reference lumen CSA

Liu et al. A Volumetric Intravascular Ultrasound Comparison of Early Drug-Eluting Stent Thrombosis Versus Restenosis. J Am Coll Cardiol Intv 2009;2:428 –34.

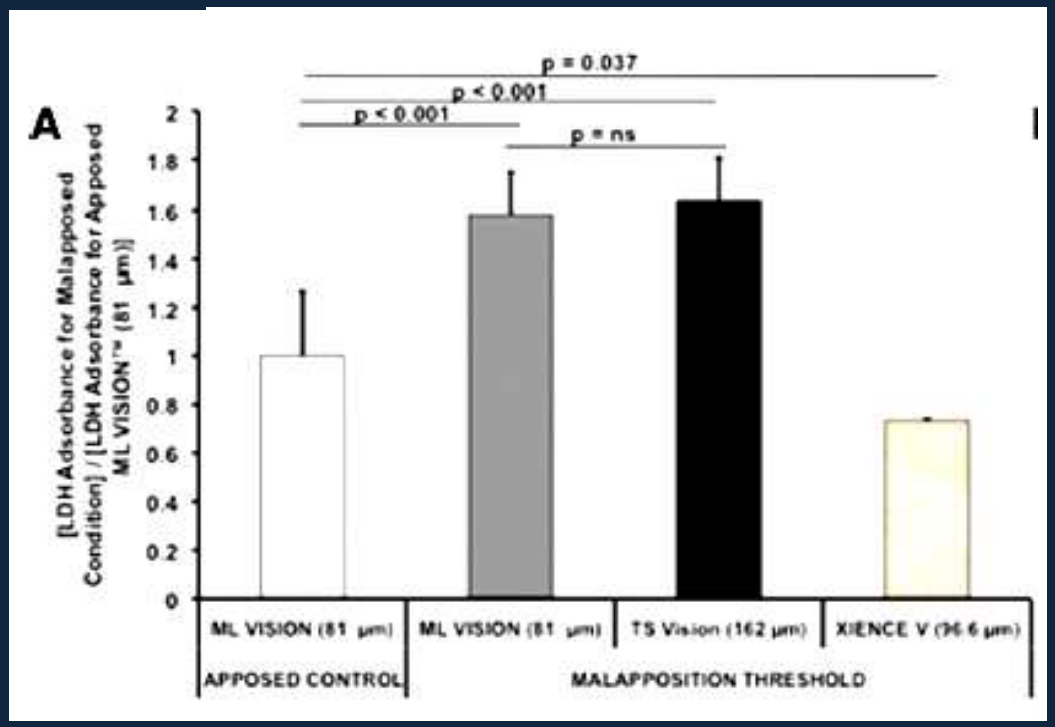
Stent Thrombogenicity is Driven by Stent Design and Deployment

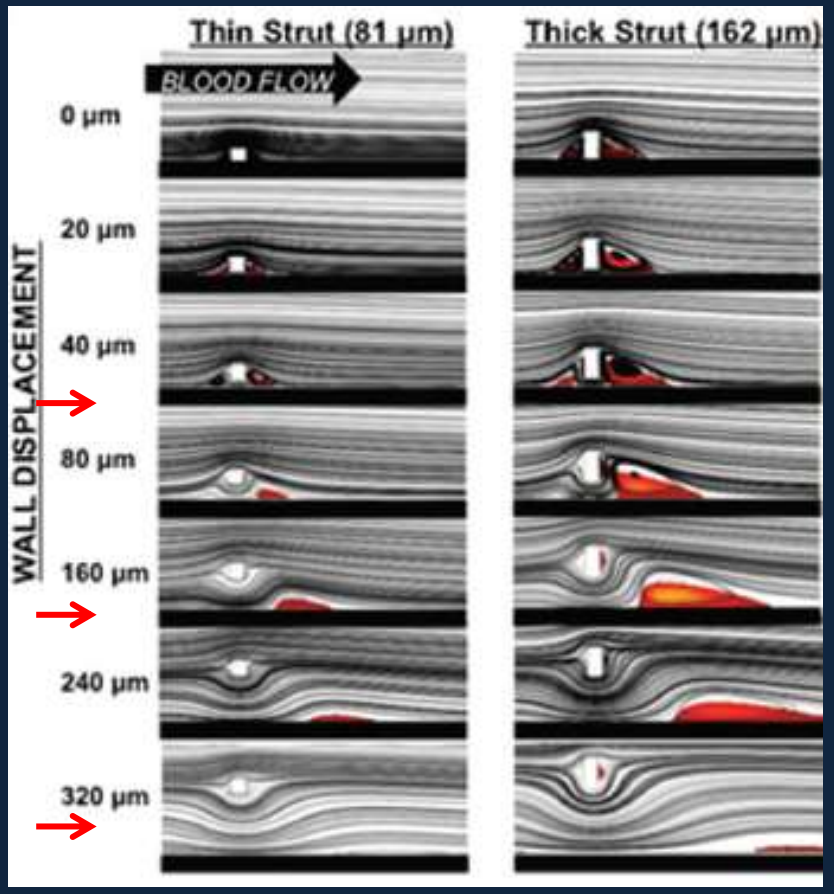


Kolandaivelu K, et al. Circulation. **2011;123:1400-1409**

Stent Thrombogenicity is Driven by Stent Design and Deployment and Protected by Polymer-Drug Coatings

Malapposition

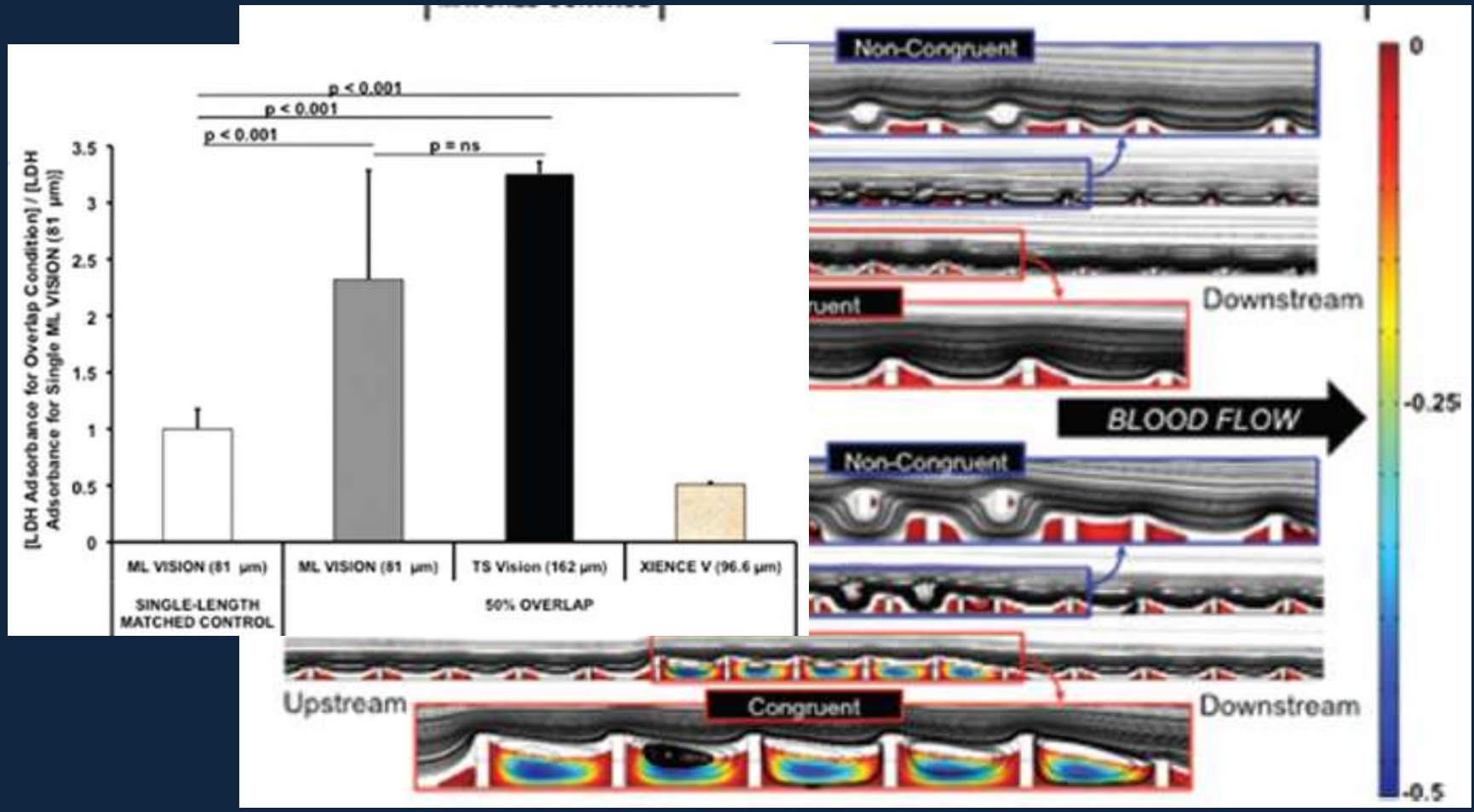




Kolandaivelu K, et al. Circulation. 2011;123:1400-1409

Stent Thrombogenicity is Driven by Stent Design and Deployment and Protected by Polymer-Drug Coatings

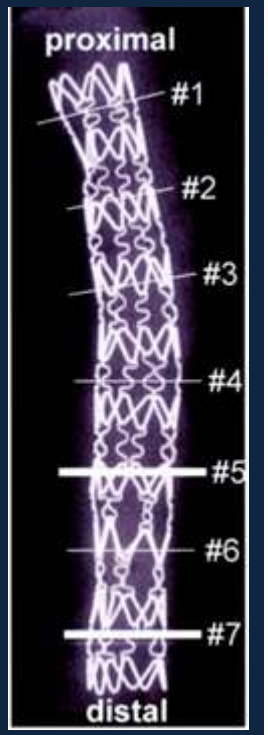
Overlapping stents

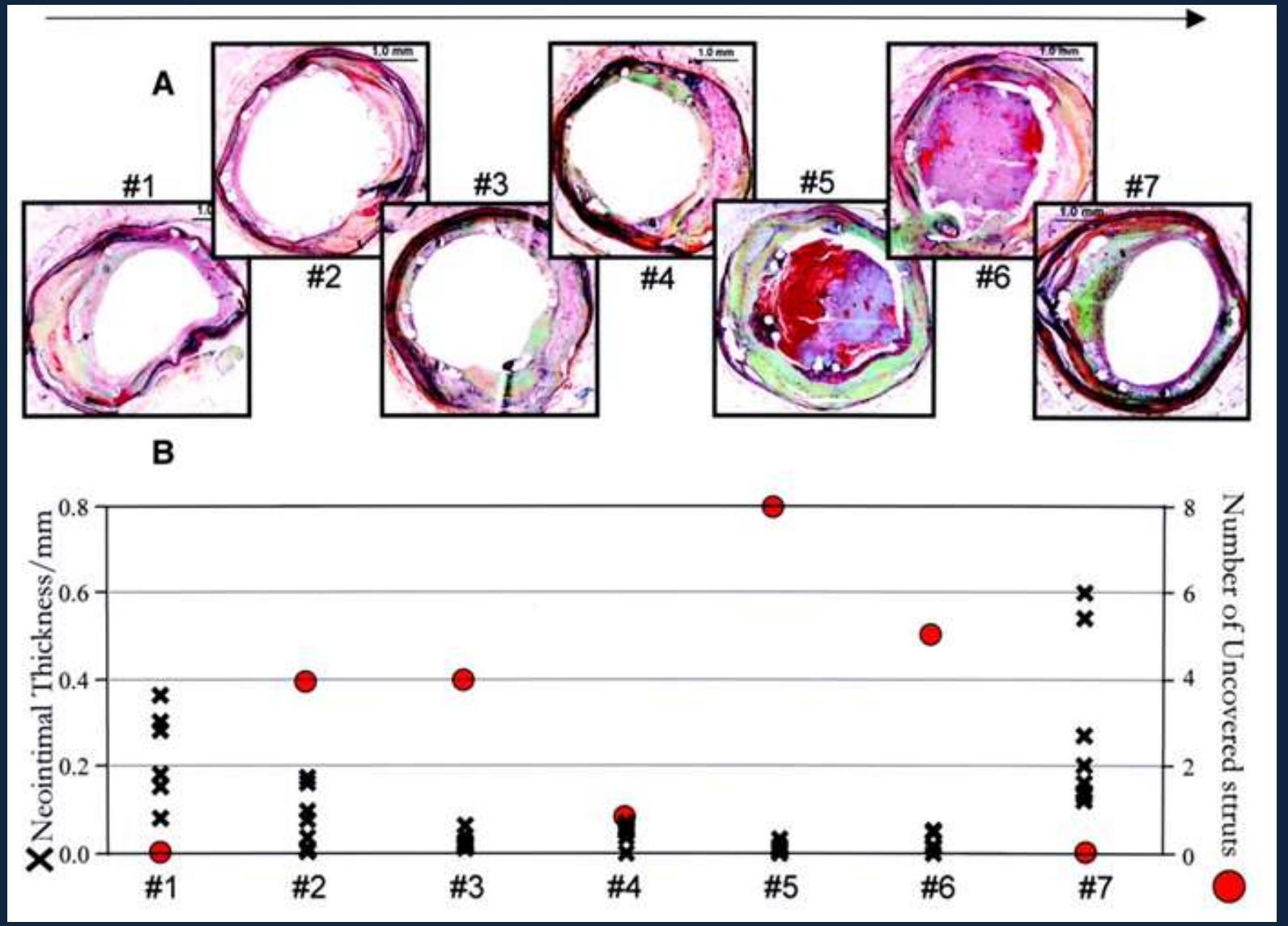


Kolandaivelu K, et al. Circulation. 2011;123:1400-1409

Pathological Correlates of Late Drug-Eluting Stent Thrombosis

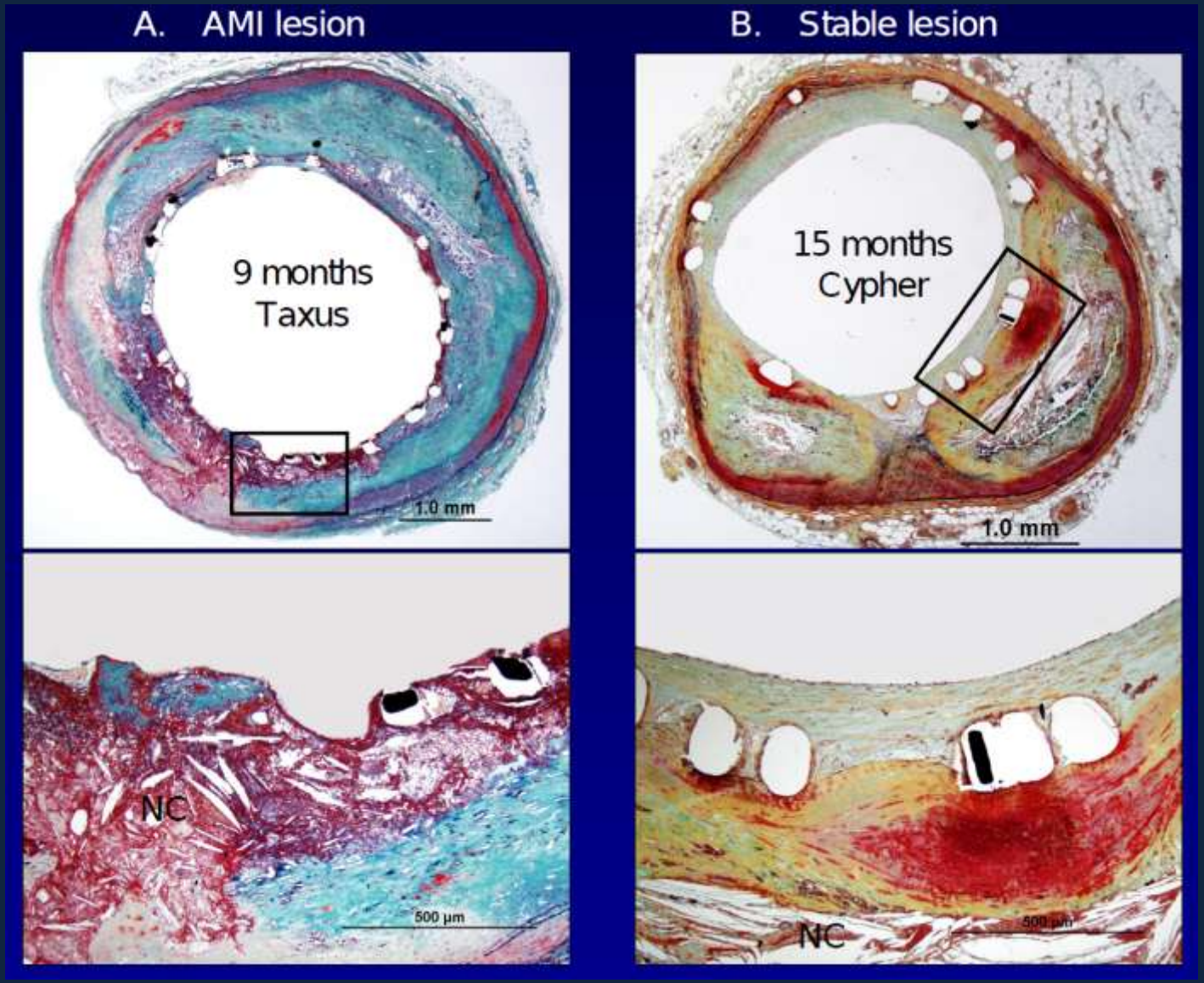
Strut Coverage as a Marker of Endothelialization (34 y/o woman 2 years post primary PCI)





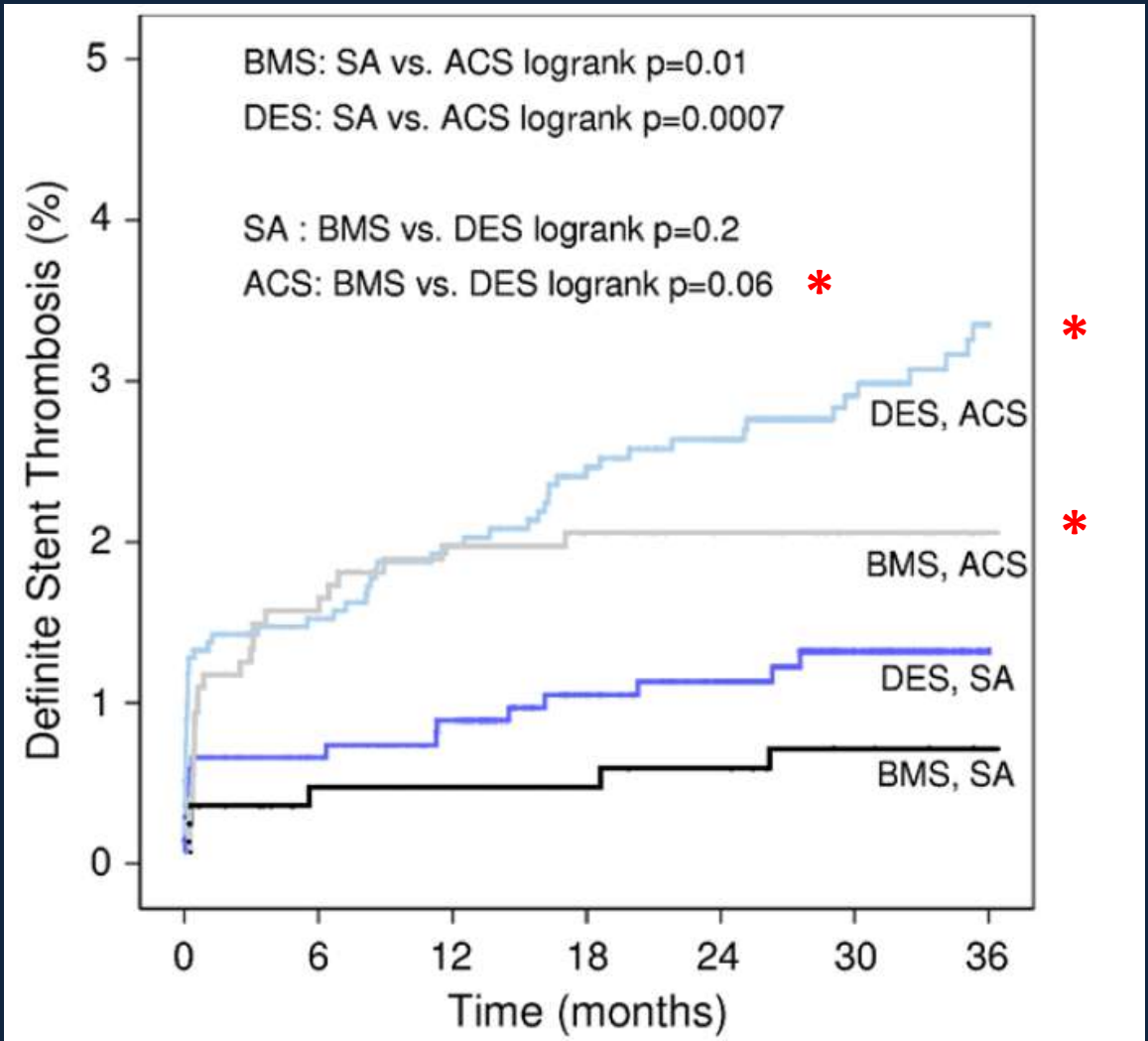
A Finn et al, (*Circulation. 2007;115:2435-2441*

Vessel healing at the culprit site in AMI patients treated with DES is substantially delayed compared with the culprit site in patients receiving DES for stable angina



NakazawaG, Circulation. 2008;118:1138-1145

The Risk of Stent Thrombosis in Patients With Acute Coronary Syndromes Treated With Bare-Metal and Drug-Eluting Stents



(Kukreja N et al, J Am Coll Cardiol Intv 2009;2:534–41)

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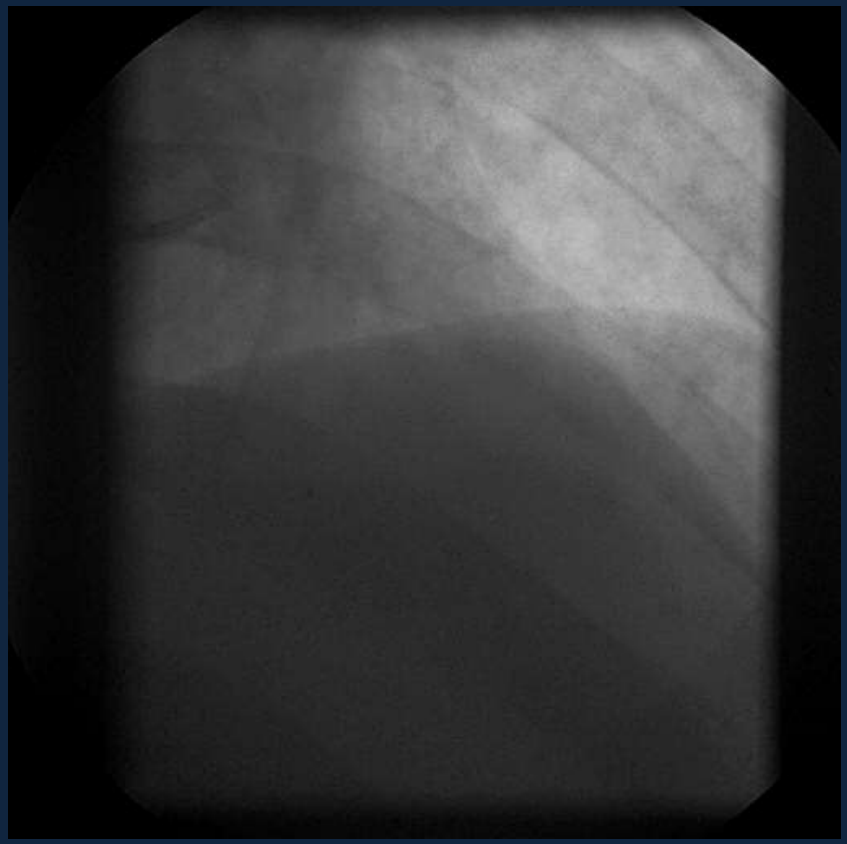
DOI: 10.1016/j.jcin.2009.07.006

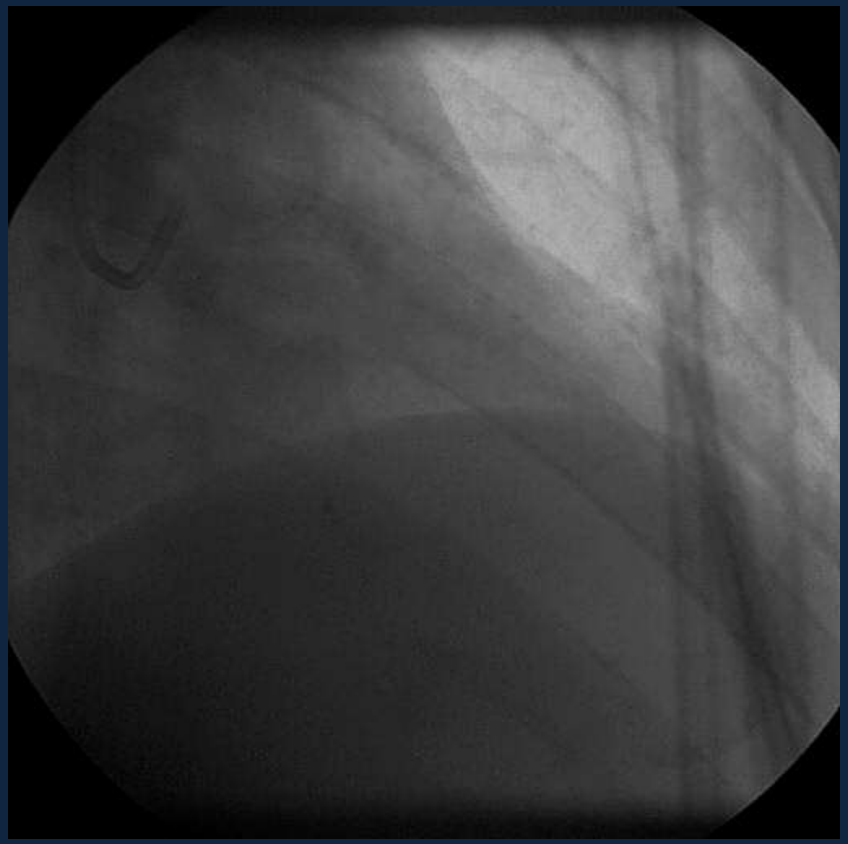
Optimal Stent-Sizing With Intravascular Ultrasound Contributes to Complete Neointimal Coverage After Sirolimus-Eluting Stent Implantation Assessed by Angioscopy

Fusako Sera, MD,* Masaki Awata, MD,* Masaaki Uematsu, MD, PhD,*
Jun-ichi Kotani, MD, PhD,† Shinsuke Nanto, MD, PhD,*† Seiki Nagata, MD, PhD*

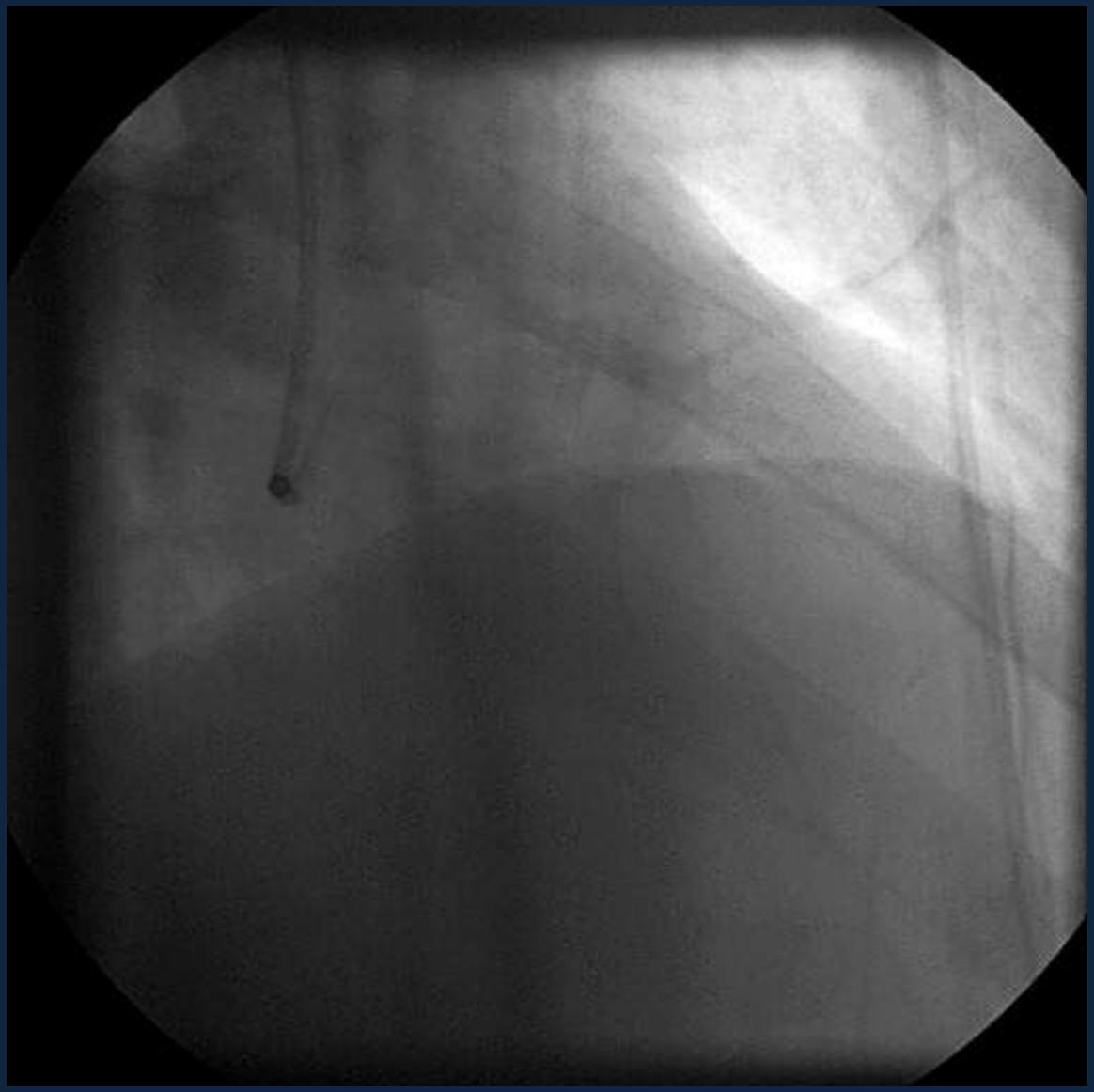
Amagasaki and Suita, Japan

PCI with a Cypher stent with good angiographic expansion

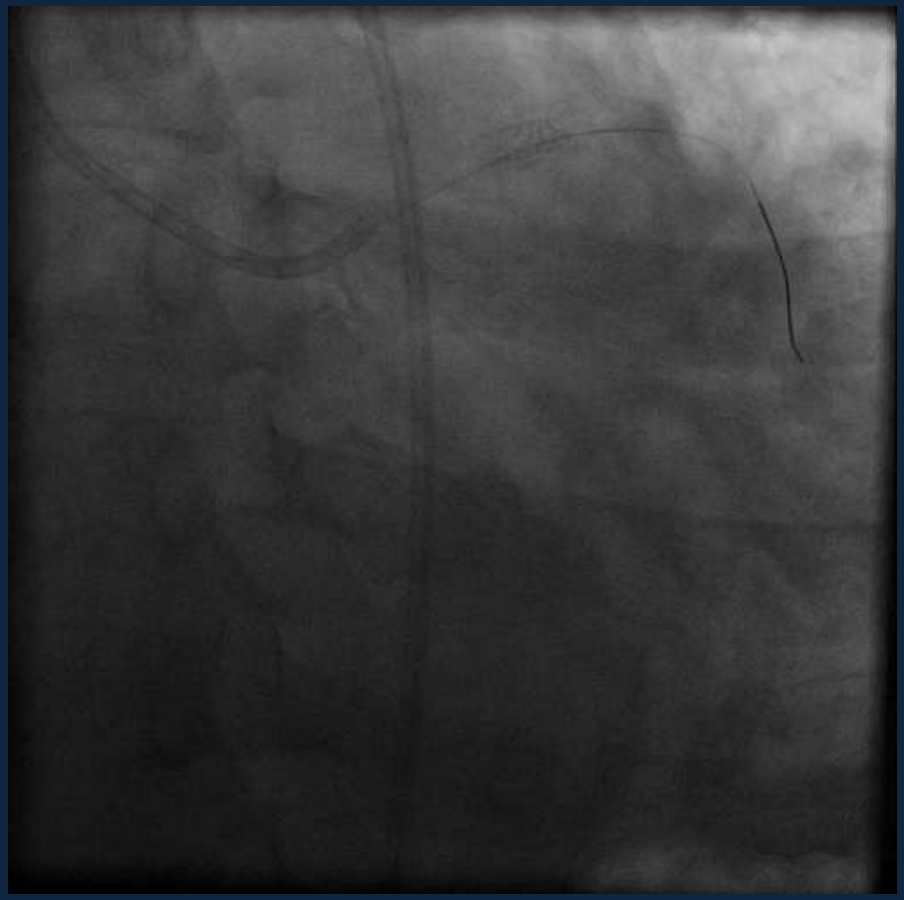




Scheduled angiographic evaluation 16 months post-PCI

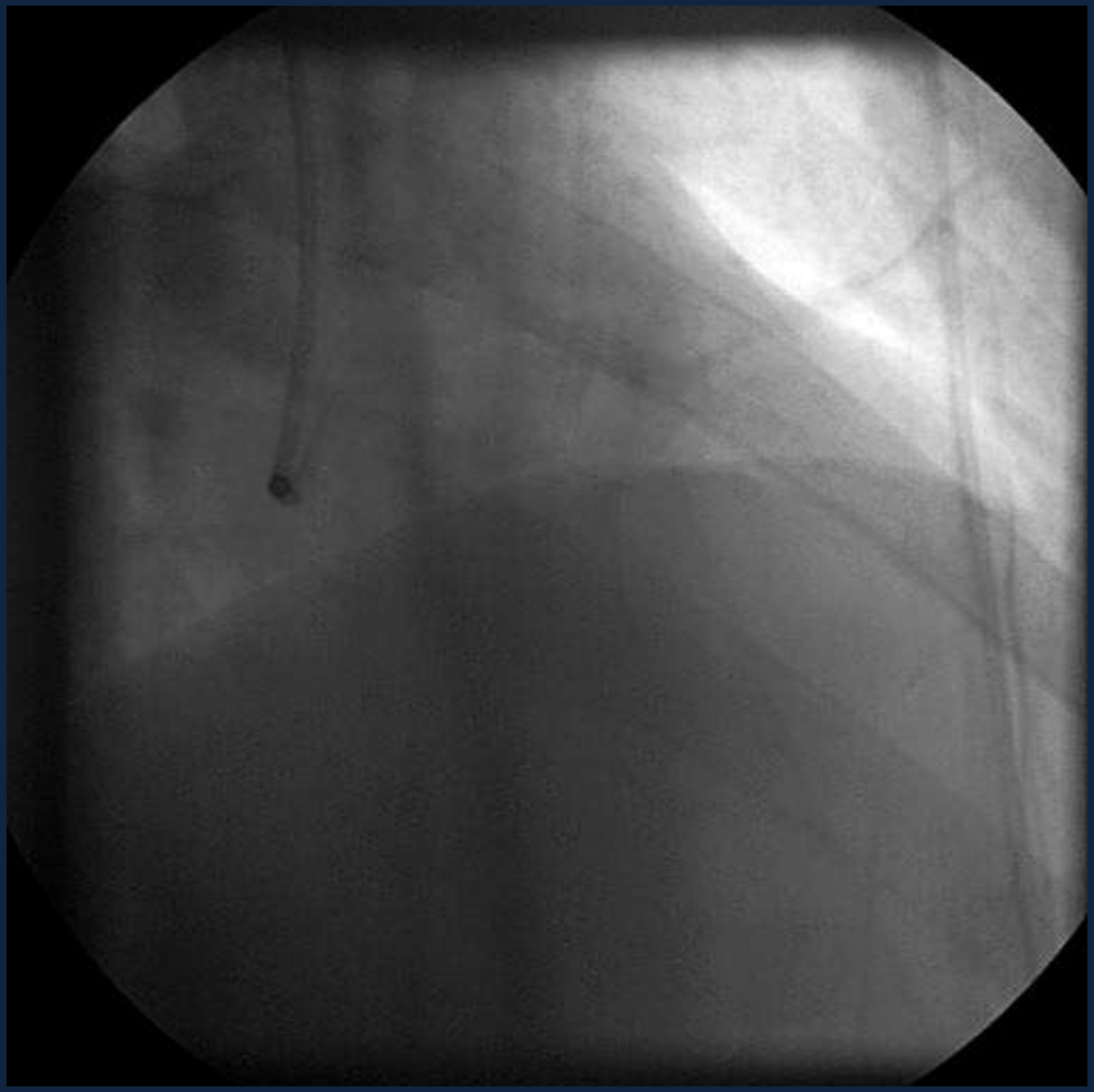


Stent thrombosis 3 years post PCI
(post-thrombectomy the pathology is limited to the stent)



Scheduled angiographic evaluation 16 months post-PCI

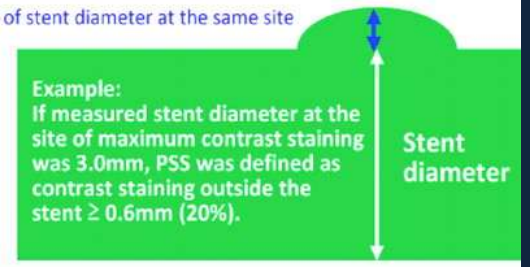
Dye outside the borders of the stent

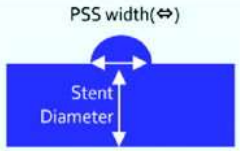
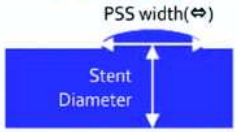


Definition and morphological classification of peri-stent contrast staining (PSS)- angiographic late malapposition.

Definition*:

PSS was defined as contrast staining outside the stent contour extending to ≥20% of stent diameter measured by quantitative coronary angiography.



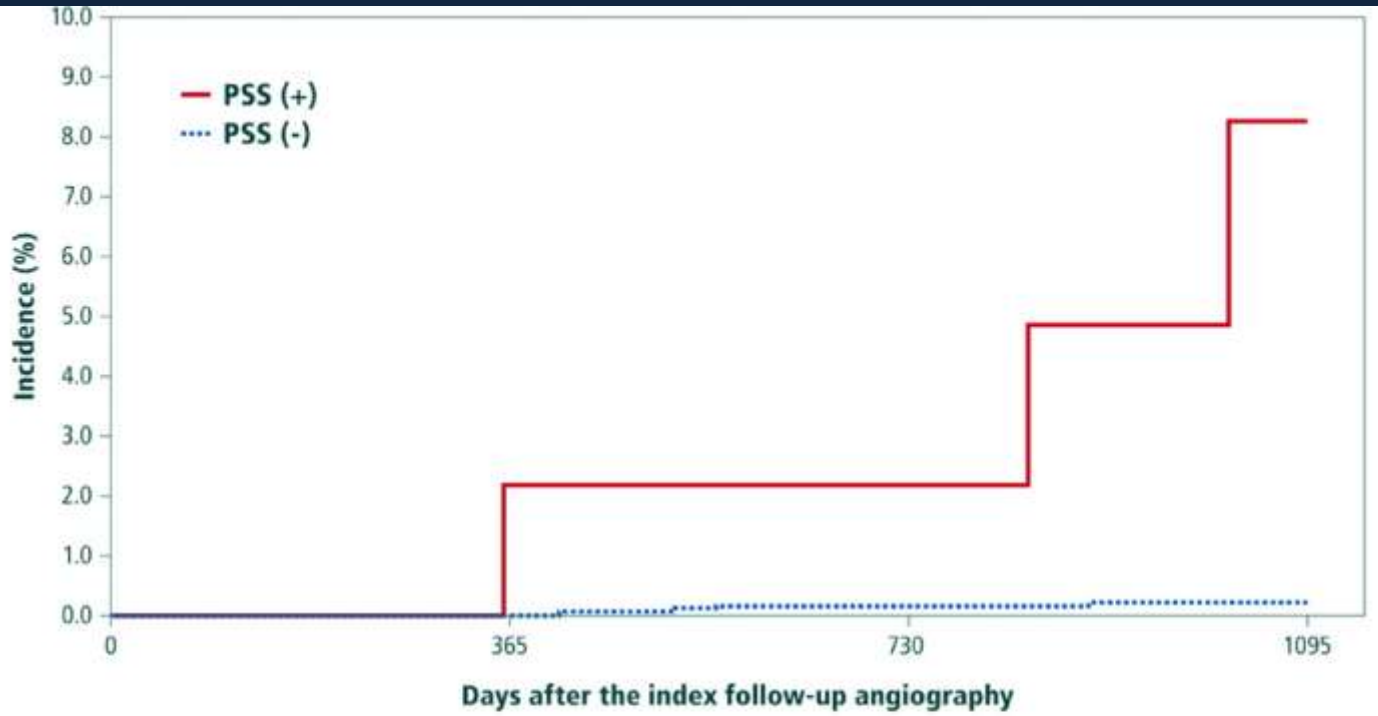
Classification of PSS Morphology		Definition
Focal		PSS width ≤ Stent diameter
Mono-focal		Single focal PSS at the stented segment
Multi-focal		Multiple focal PSS at the stented segment
Segmental**		PSS width > Stent diameter
Irregular-contour***		Segmental PSS with irregular contour
Smooth-contour		Segmental PSS with smooth contour

*: Maximum contrast staining outside stent ≥50% of stent diameter was classified as severe PSS.

:Including coexisting focal type PSS *:including coexisting smooth contour type

Imai M et al. Circulation 2011;123:2382-2391

Cumulative incidence of ST after the index follow-up angiography: PSS group versus non-PSS group.

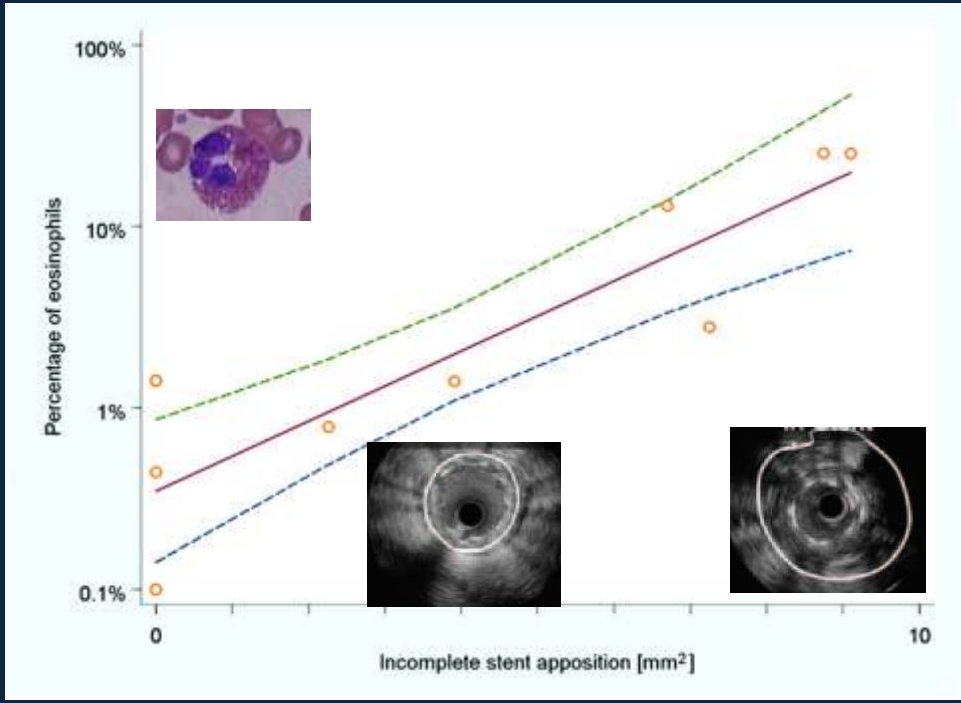


Days	0	365	730	1095
PSS (+) N of lesions at risk	51	46	40	26
N of lesions with events	0	1	1	3
Cumulative incidence	0%	2.1%	2.1%	8.2%
PSS (-) N of lesions at risk	2761	2532	1847	580
N of lesions with events	0	0	3	4
Cumulative incidence	0%	0%	0.13%	0.2%

Imai M et al. Circulation 2011;123:2382-2391

Correlation of Intravascular Ultrasound Findings With Histopathological Analysis of Thrombus Aspirates in Patients With Very Late Drug-Eluting Stent Thrombosis

	#	WBCs	p-ANOVA	Eosinophils	P-ANOVA
Controls	26				
Spontaneous MI	7	291±94	0.0001	7±10	0.038
Early ST-BMS	4	146±117		1±1	
Early ST-DES	10	73±117		1±2	
Very late ST-BMS	5	84±50		2±3	
Very late ST-DES	28	283±149		20±24	

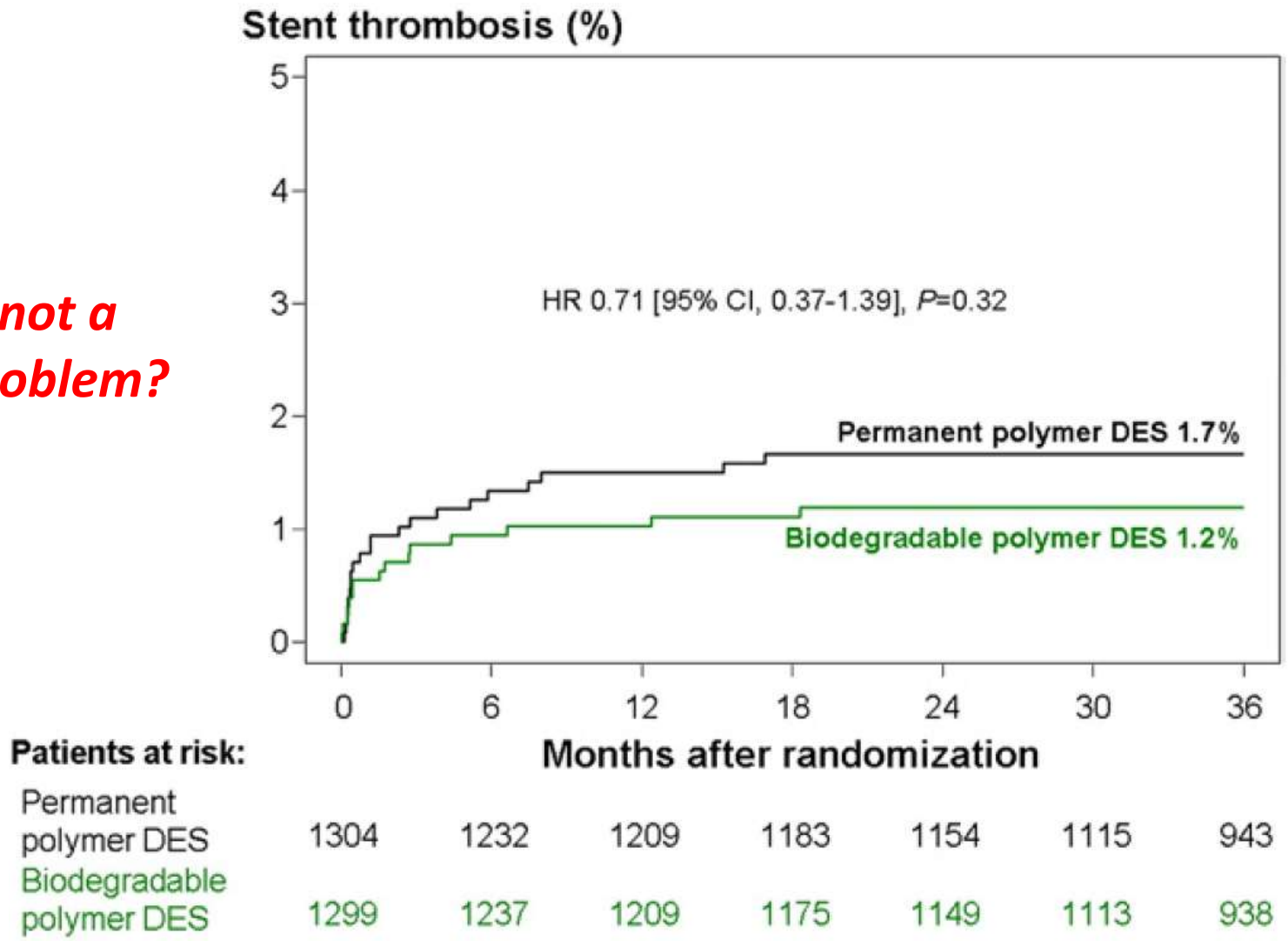


Cook S et al, Circulation. 2009;120:391-399

Stent Thrombosis

ISAR-TEST 4 comparing two permanent polymer DES and a biodegradable polymer DES (3 year results)

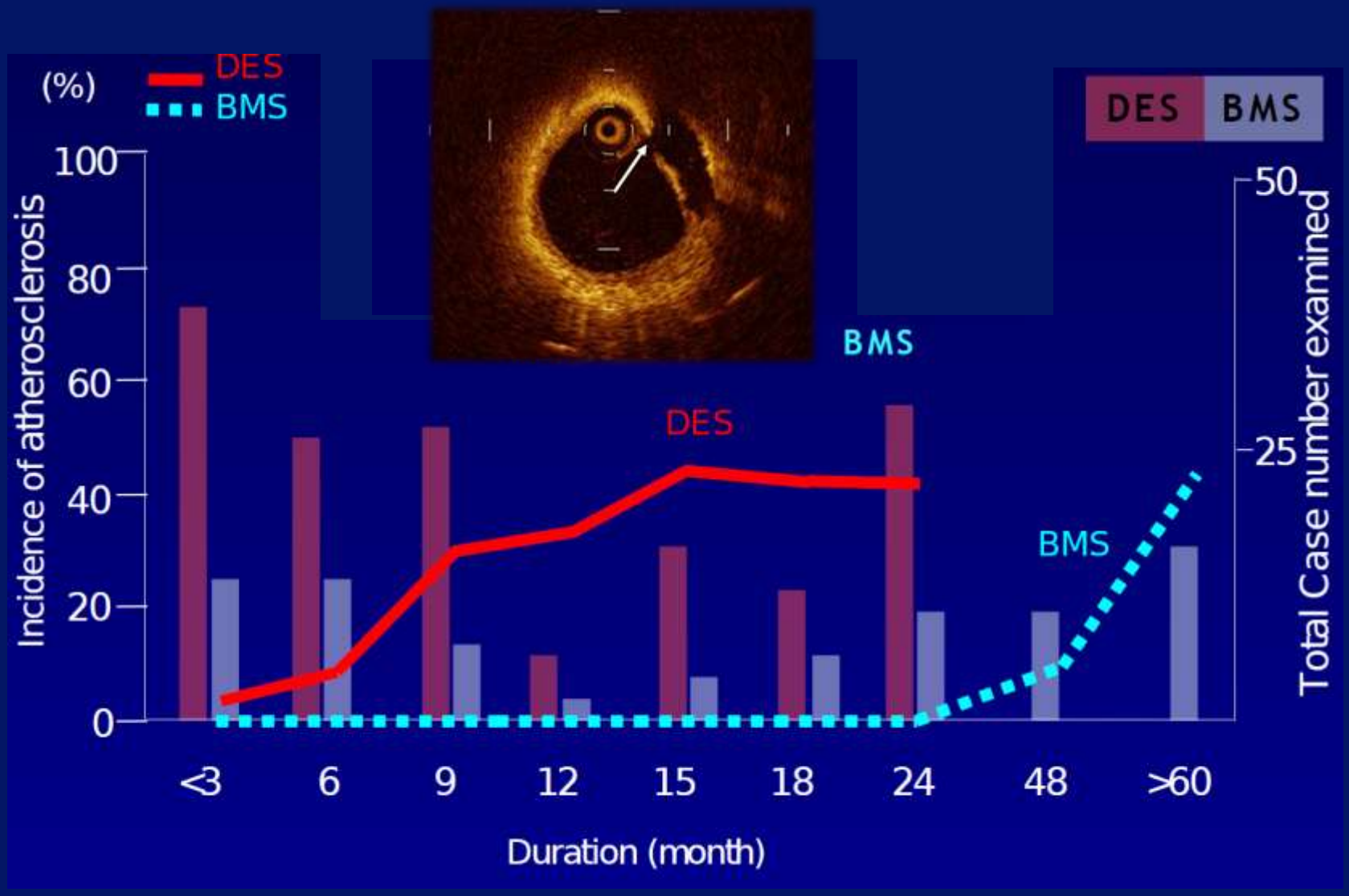
At the end not a polymer problem?



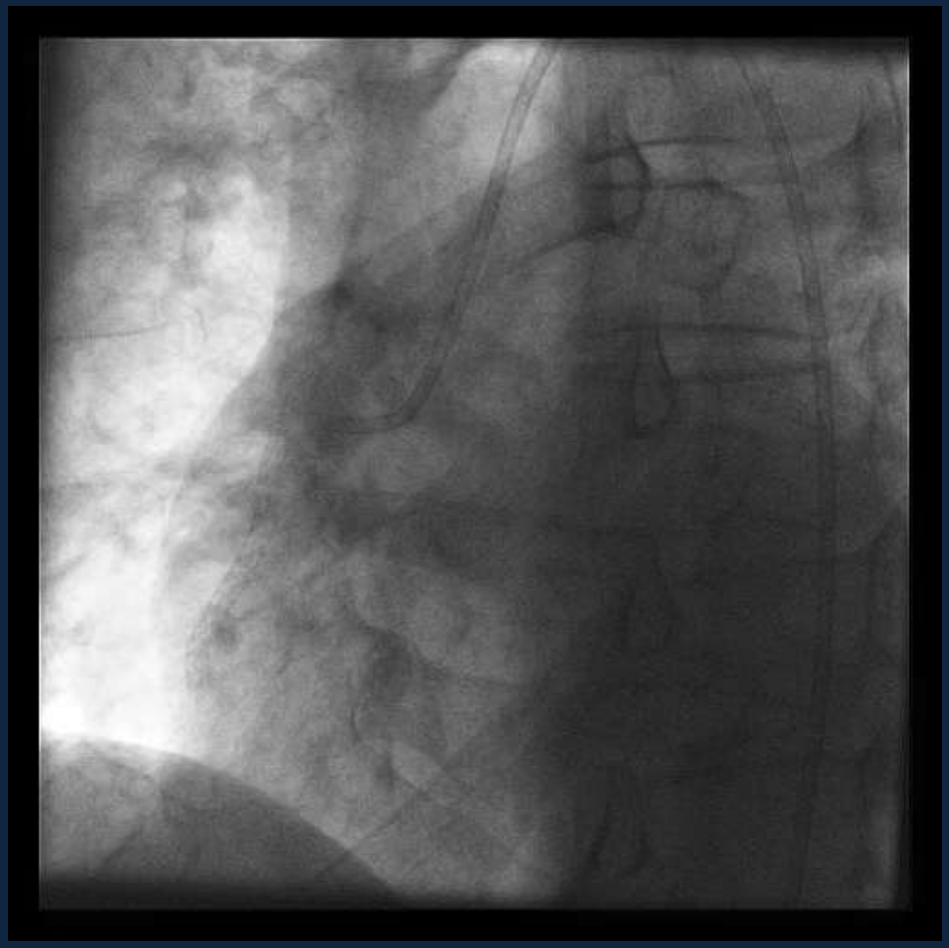
Byrne et al, J Am Coll Cardiol 2011;58:1325–31

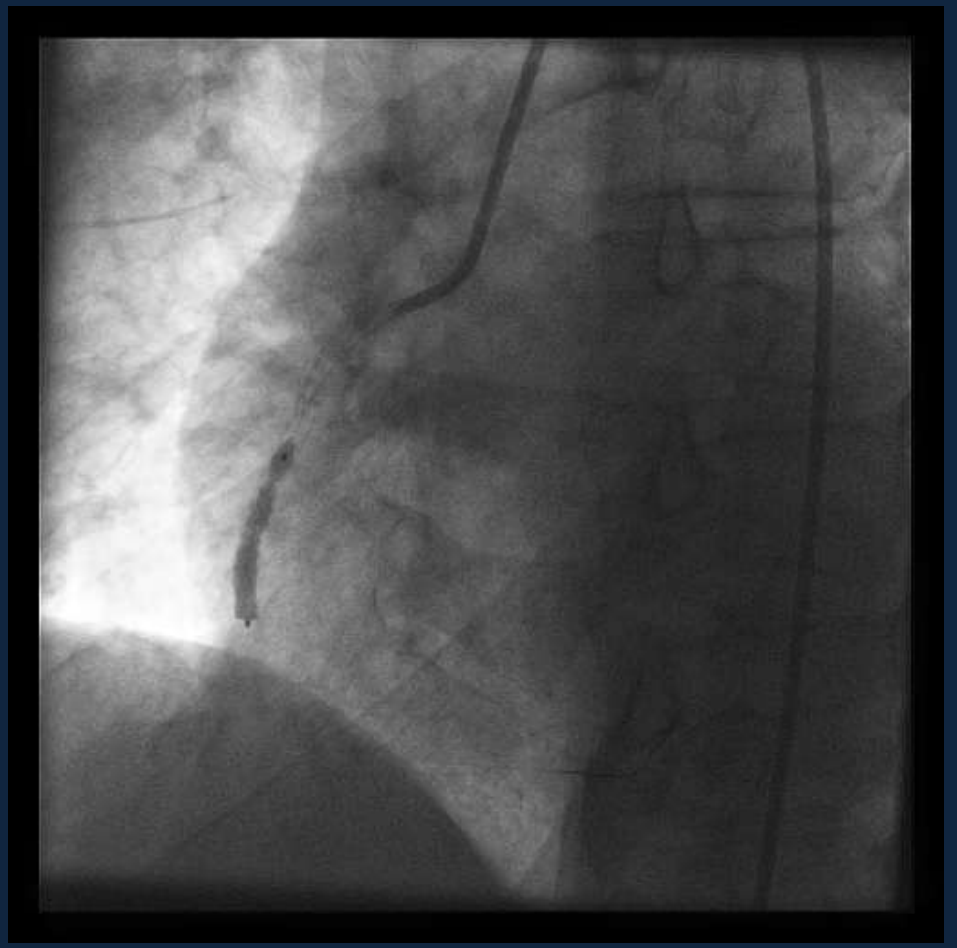
Incidence and Timing of Atherosclerotic Change

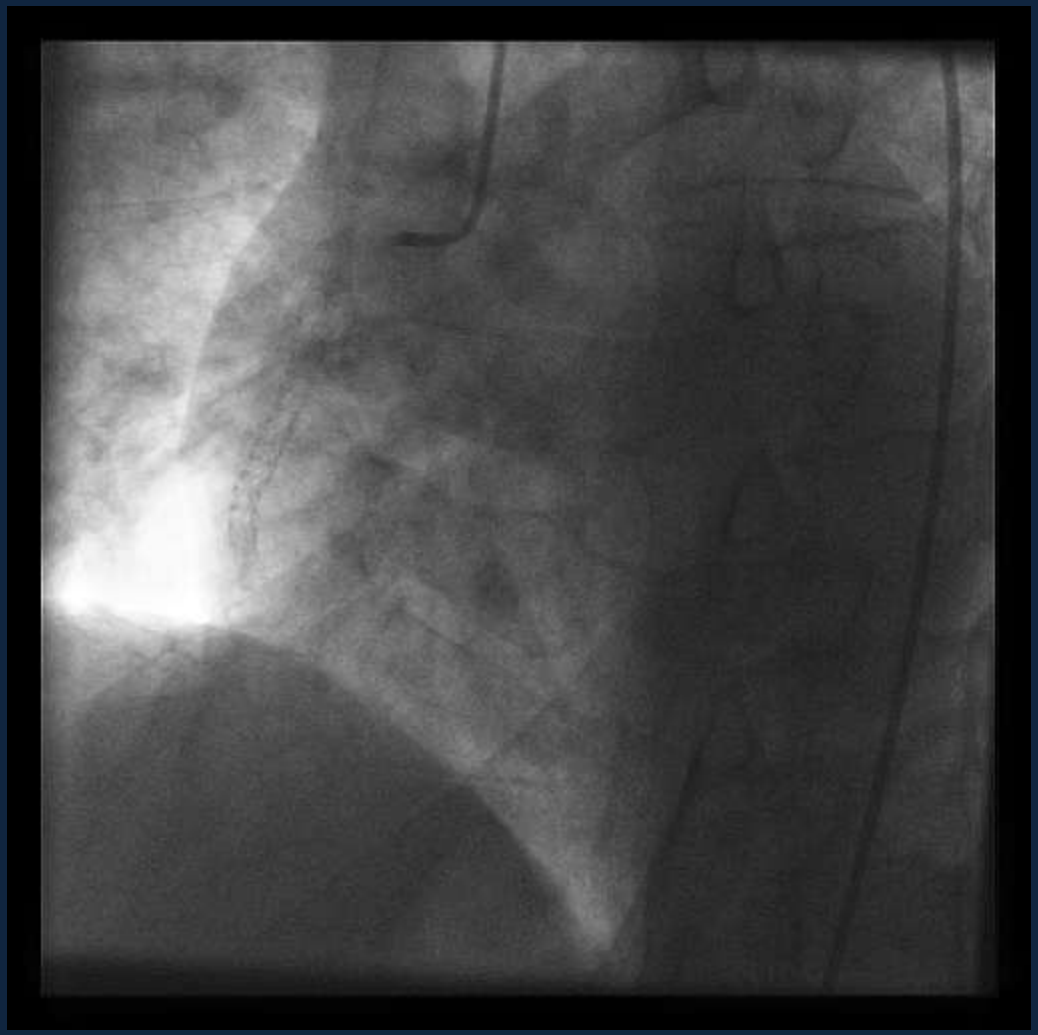
Autopsy study based on angioscopic findings by Higo et al ,JACC Cardiol Img 2009;2:616



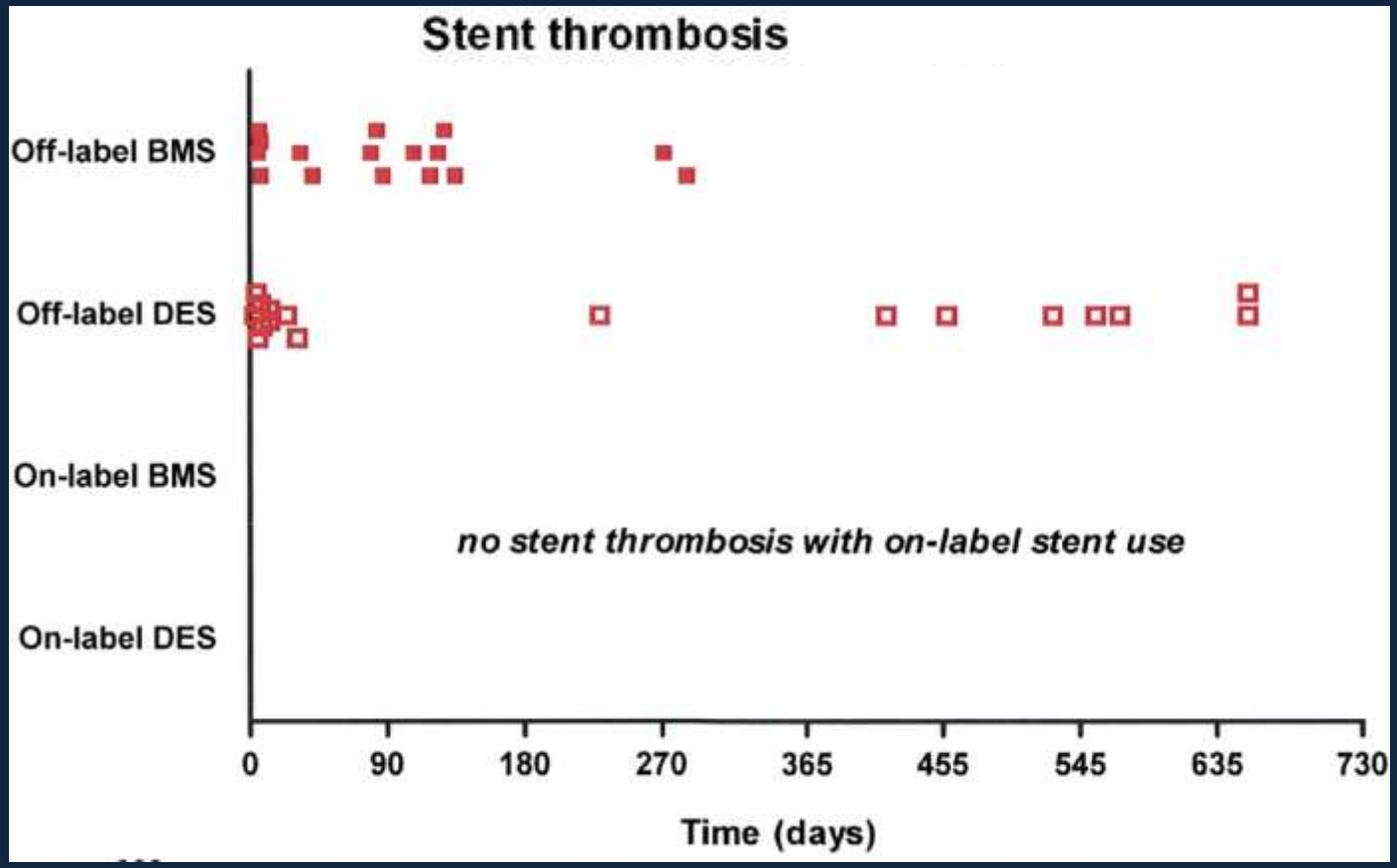
Acute Inferior wall myocardial infarction,
4 years post PCI of the RCA (cypher stents for an inferior wall MI)
On aspirine (one year on clopidogrel)







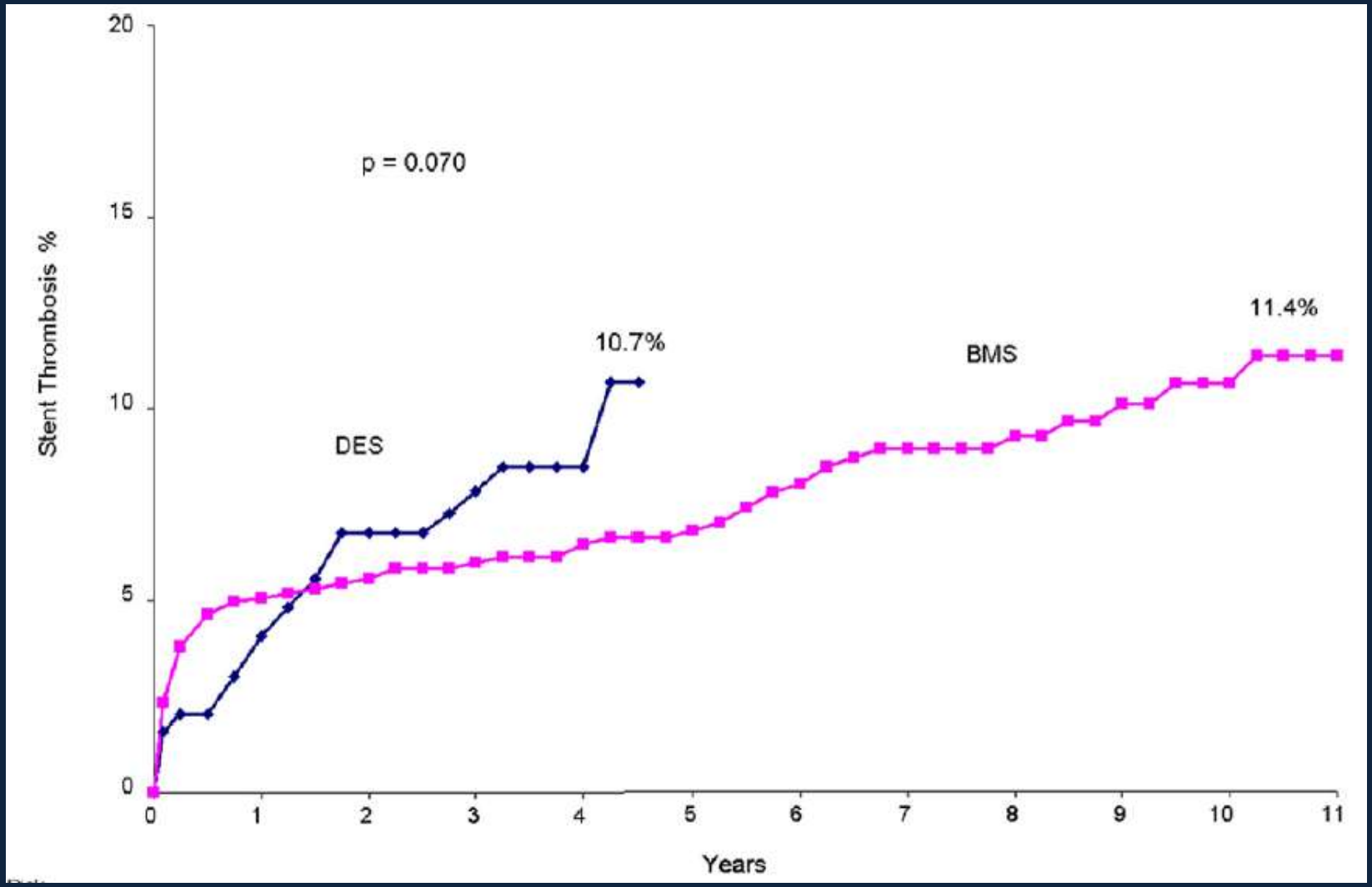
Timing of Stent Thrombosis up to 2 Years in on-label and off-label BMS and DES indications



* >18 years old,
* single de novo native lesions <30 mm L
* without thrombus
* LVEF >25%,
*no MI < 7 days
*creatinine <2.0 mg/dl)

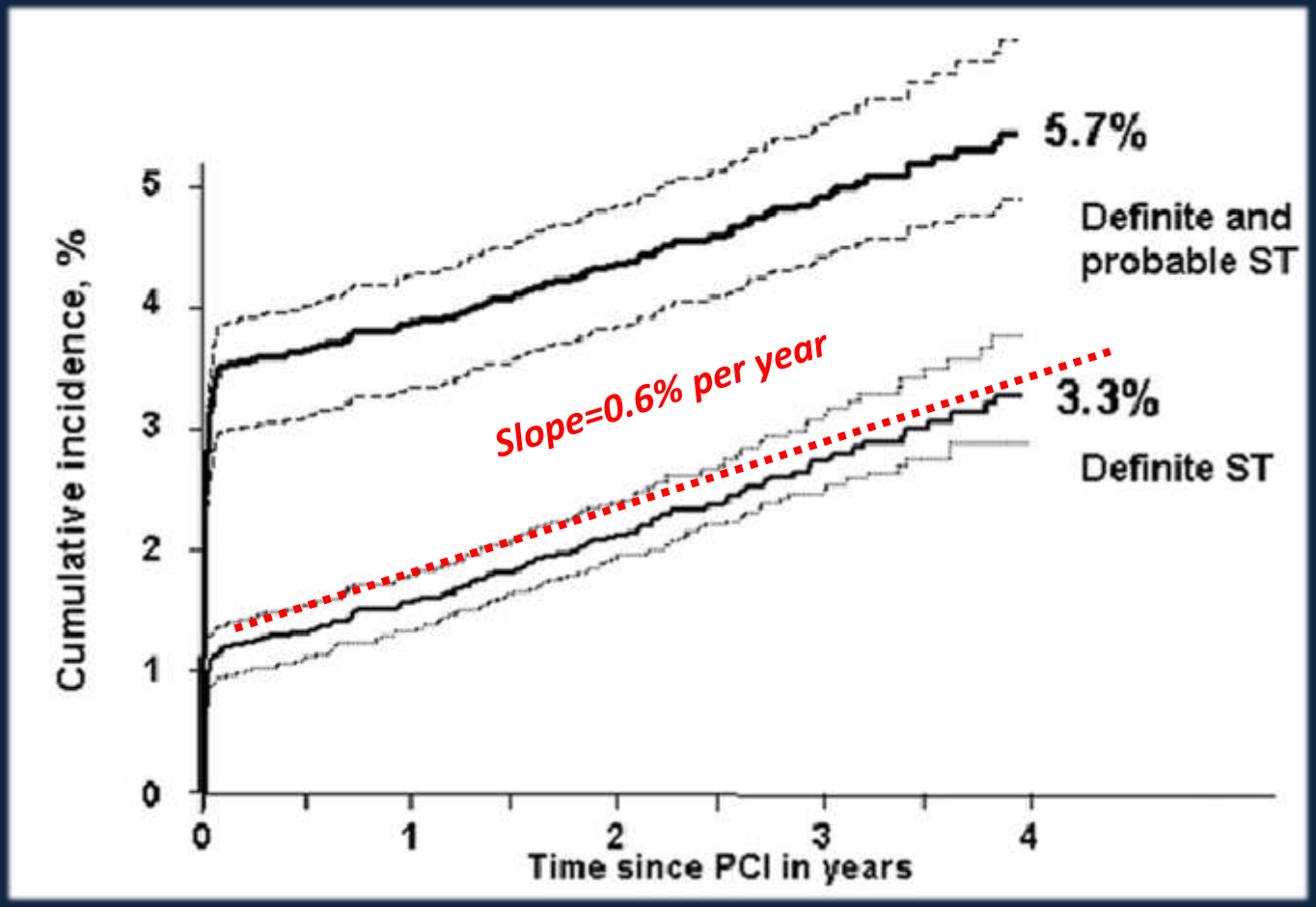
Applegate, R. J. et al. J Am Coll Cardiol 2008;51:607-614

Kaplan-Meier Estimates of ST Rates After Primary PCI With BMS and DES for STEMI



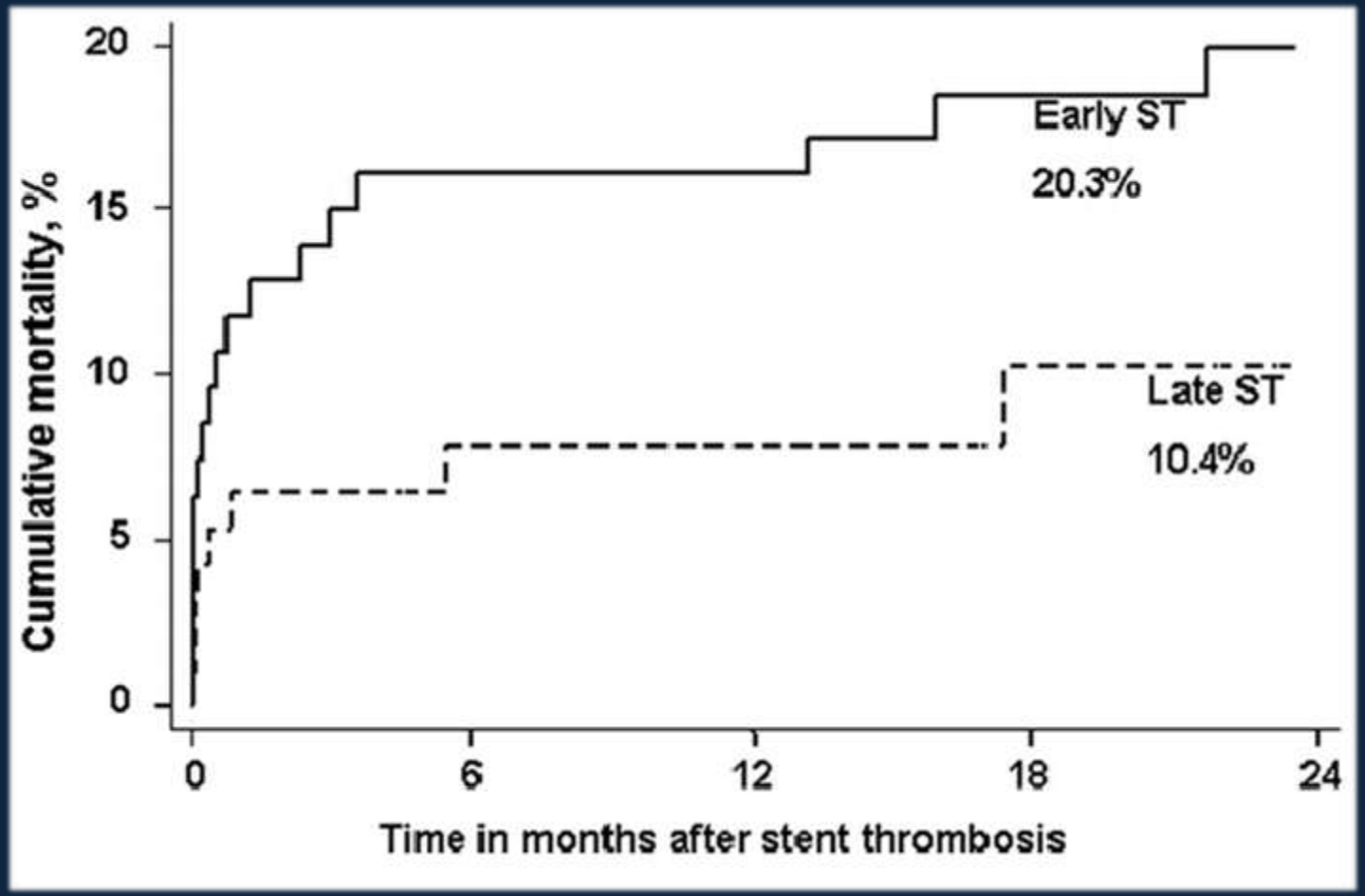
Brodie et al,J Am Coll Cardiol Intv 2011;4:30–8

Stent Thrombosis (SES PES)
Bern Rotterdam cohort study



Wenaweser P et al, J Am Coll Cardiol 2008;52:1134–40

Cumulative Incidence of Death in Patients With Definite ST Stratified According to Early and Late ST
Bern Rotterdam cohort study



Wenaweser P et al, J Am Coll Cardiol 2008;52:1134–40

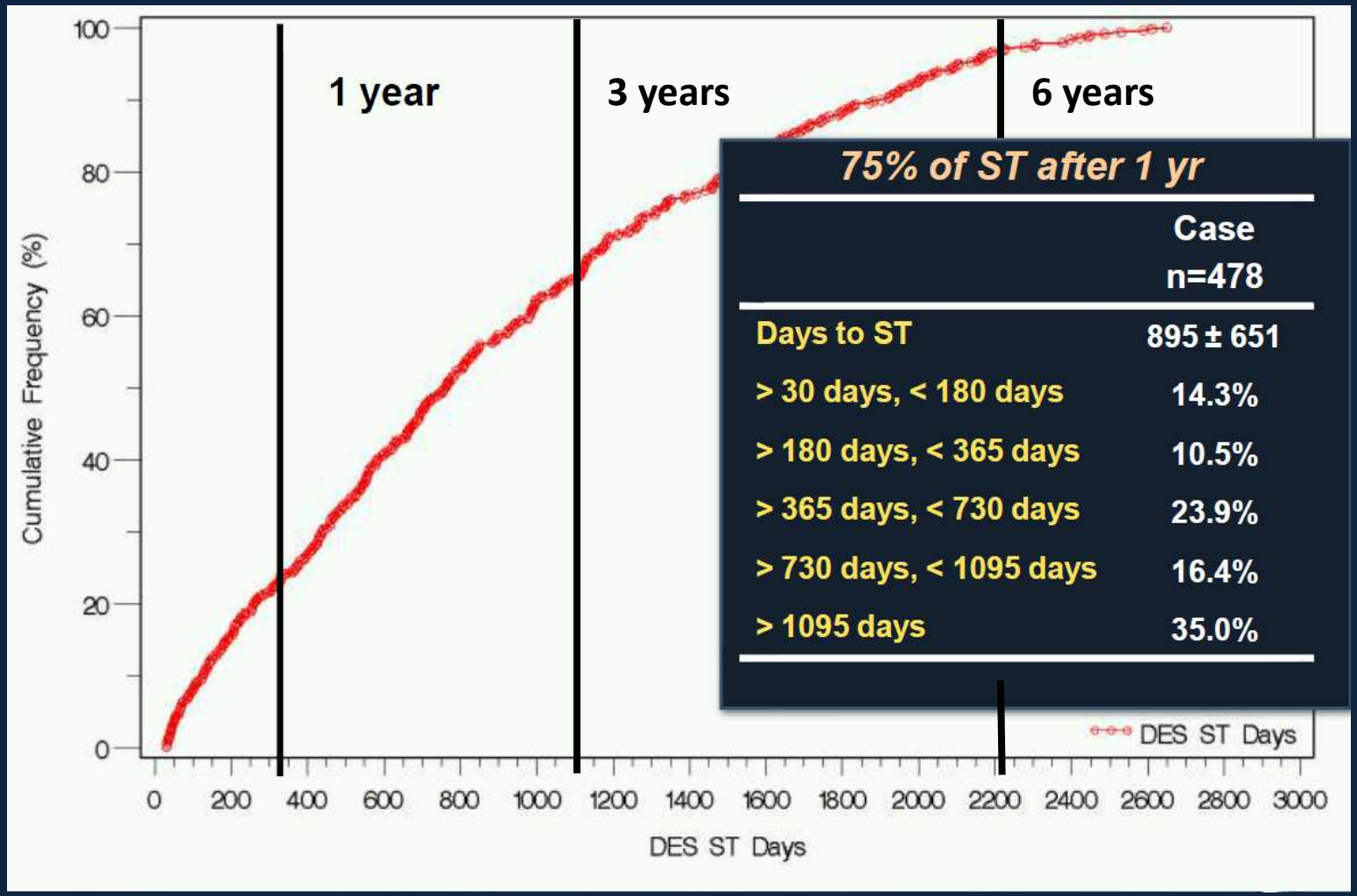
DESERT: Study Objectives*

- To describe the correlates (clinical, procedural, and angiographic) of late (FDA approved) DES thrombosis (>30 days from stent implantation) using an adequately sized and powered case-control study design
  - 500 total late Stent thrombosis events
- To describe the outcomes of patients with stent thrombosis in the DES era

Drug-**E**luting **S**tent **E**vent **R**egistry of **T**hrombosis

TCT 2011

Time of implantation to ST event presentation-DESERT registry



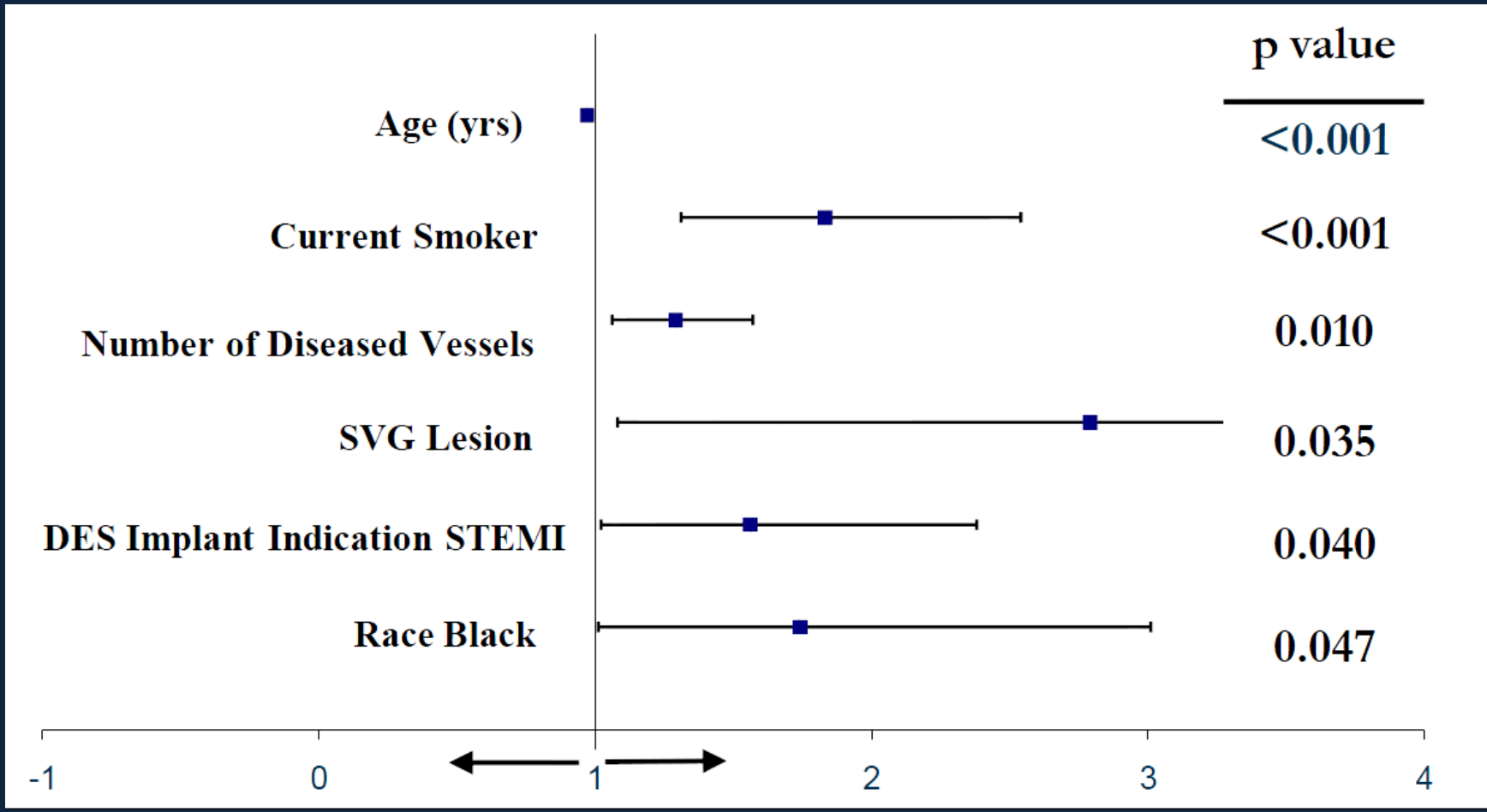
1 year

2 years

3 years

>3 years

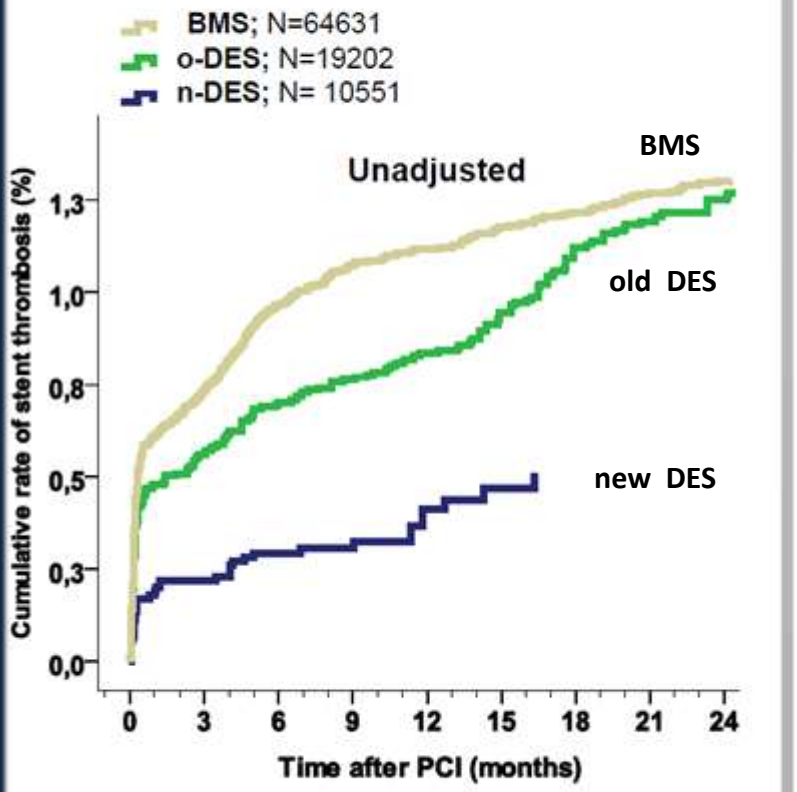
Independent correlates of Late Stent Thrombosis- DESERT registry

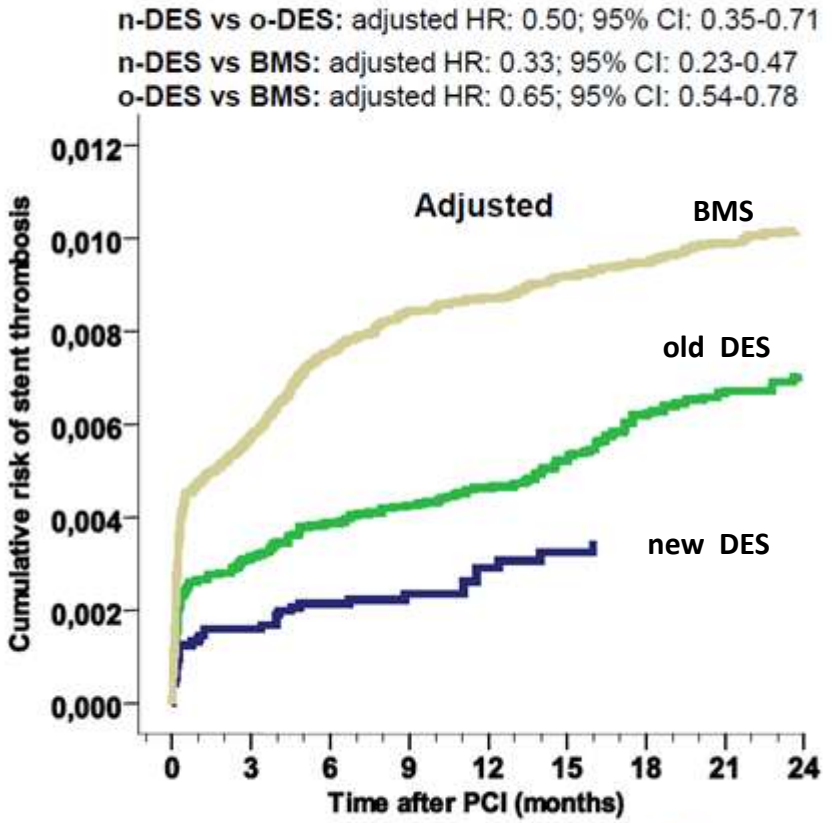


- DESERT is the largest case-control registry of late and very late DES Stent Thrombosis
- In DESERT, the majority of the Late ST occurred after one year (~75%) and continued to occur up to 7.3 years
- The clinical presentation of late ST was mainly MI (66.9% STEMI and 22% NSTEMI)
- Nearly 30% of the patients with Late ST were on DAPT at the time of the event
- In hospital mortality of patients who presented with late ST was 3.8% and 1.67% at one year

a report from the nation wide Swedish Coronary Angiography and Angioplasty Registry (SCAAR)

Stent Thrombosis up to 2 years



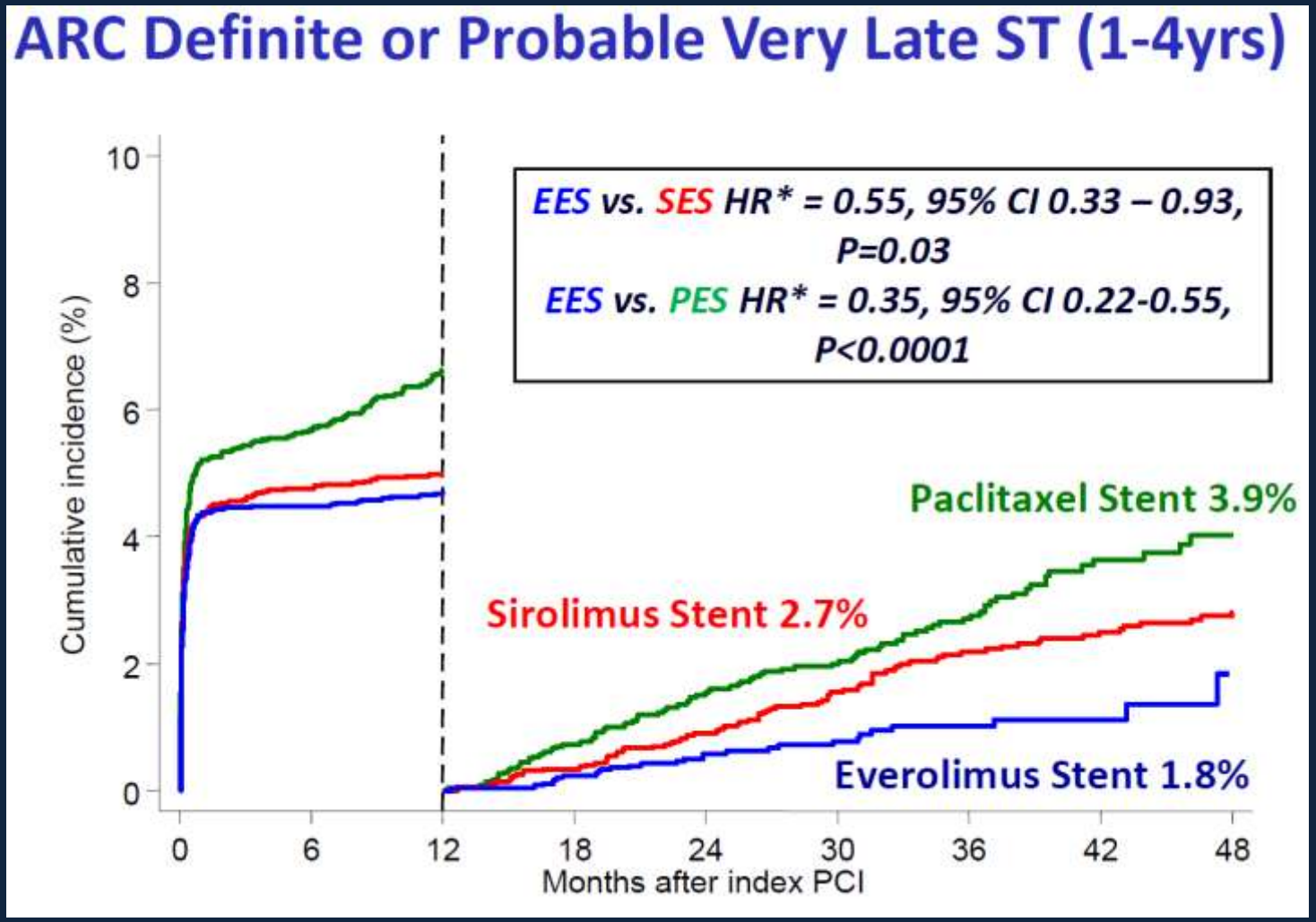


UCR UPPSALA CLINICAL RESEARCH CENTER

AKADEMISKA SJUKHUSET

Sarno G, ESC Congress 2011

Newer generation everolimus-eluting stents eliminate the risk of very late stent thrombosis? (Bern-Rotterdam cohort –clopidogrel<12 ms)



Raber L et al, ESC Congress 2011

Association of Cardiac Death or MI With ARC Definite ST

Cardiac Death or MI associated with ST

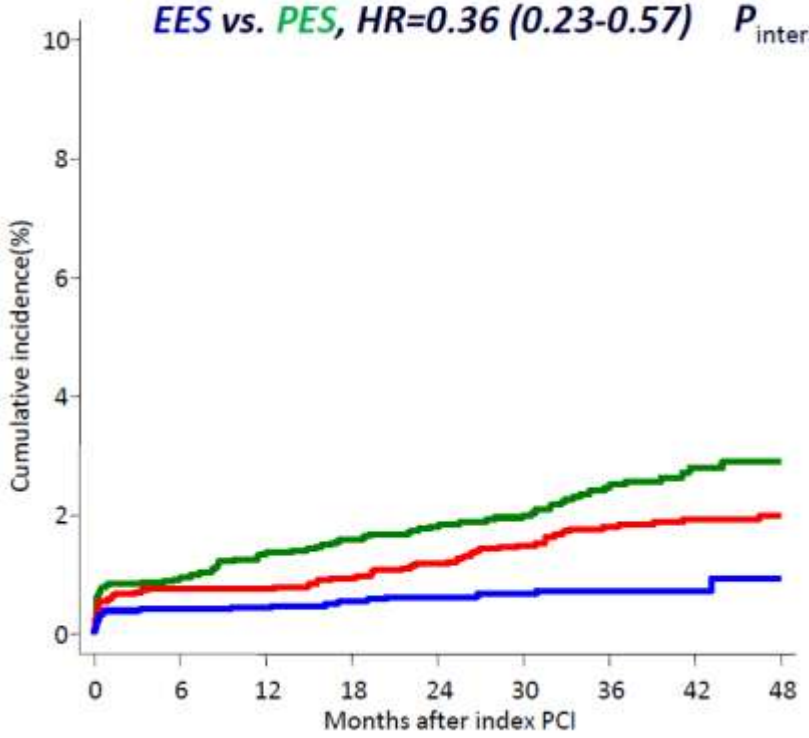
EES vs. SES HR = 0.46 (0.26-0.81) $P_{interaction}$=0.01

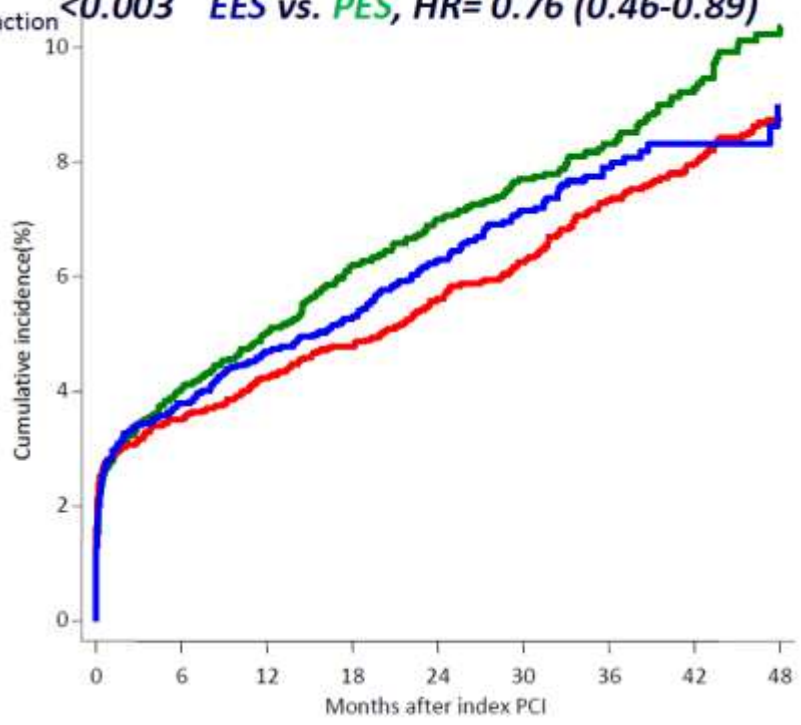
EES vs. PES, HR=0.36 (0.23-0.57) $P_{interaction}$<0.003

Cardiac Death or MI not associated with ST

EES vs. SES, HR = 1.00 (0.84-1.20)

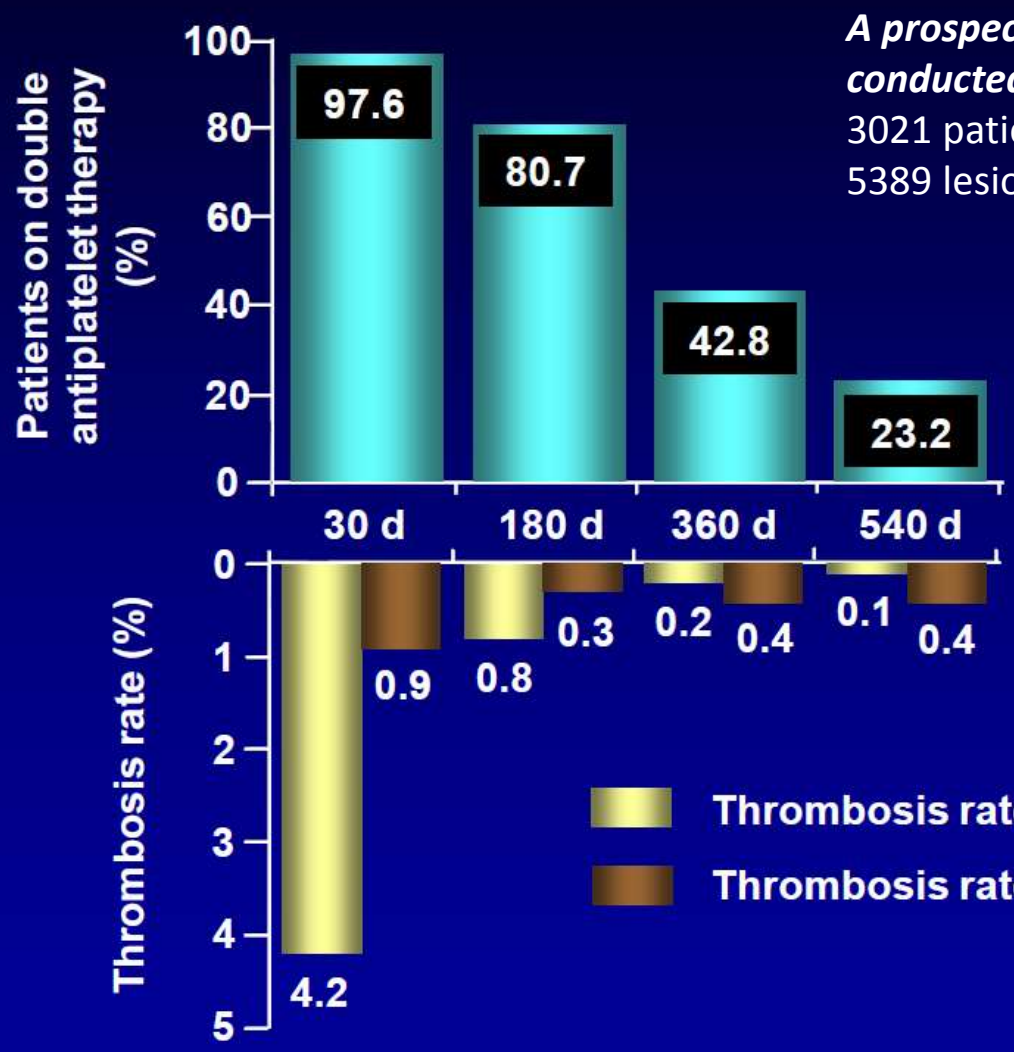
EES vs. PES, HR= 0.76 (0.46-0.89)





Raber L et al, ESC Congress 2011

Do we need dual antiplatelet therapy beyond 6 months?

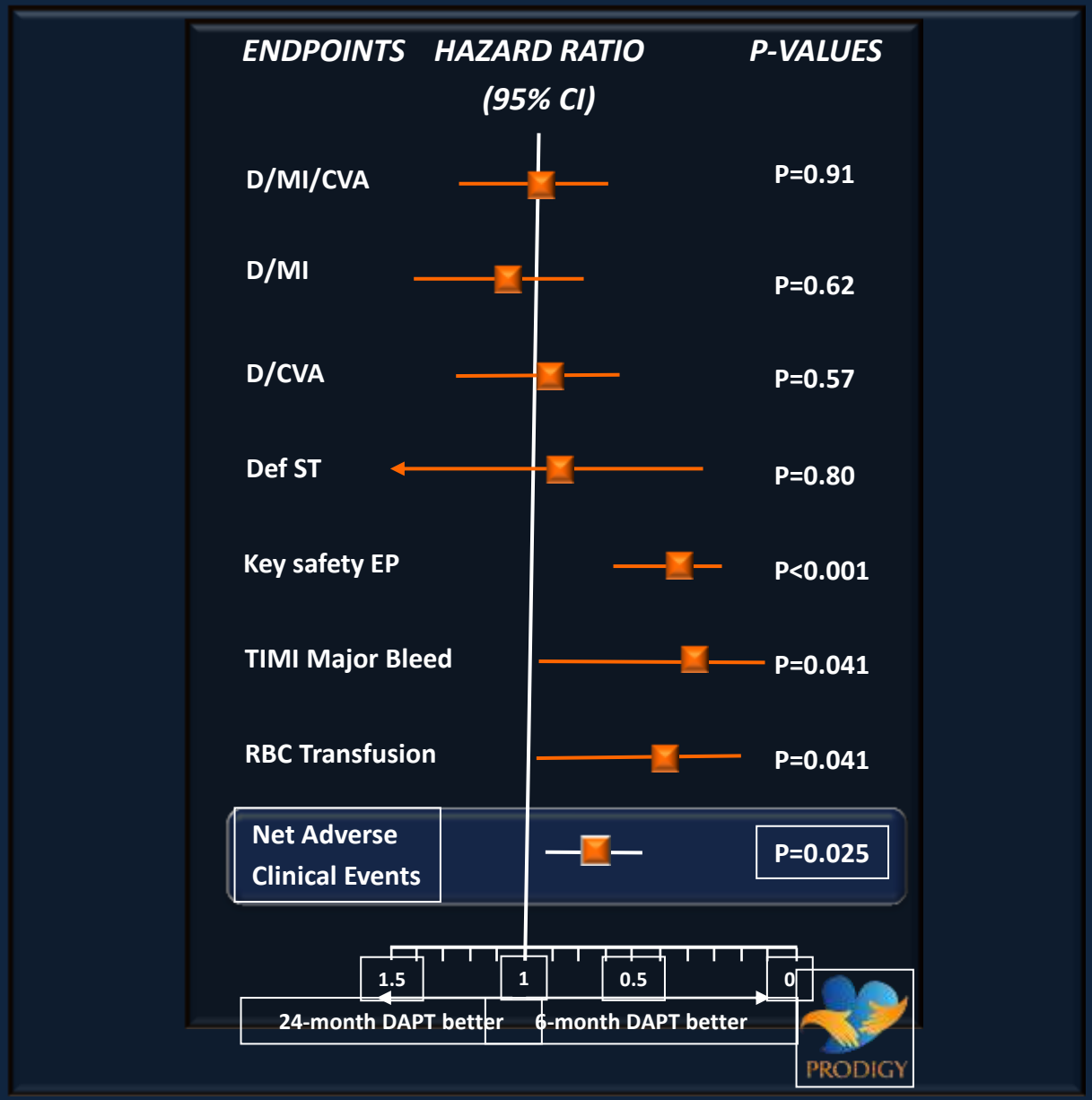


A prospective observational cohort study was conducted between June 2002 and January 2004 on 3021 patients consecutively and successfully treated in 5389 lesions with drug-eluting stents

Airoldi F, *et al. Circulation.* 2007;116:745-754.

Hypothesis

24 months duration of aspirin and clopidogrel is *superior* to a short course of up to 6 month aspirin and clopidogrel therapy



Conclusions

- ST with either DES or BMS remains catastrophic and, although infrequent, occupies a central place in the risk-benefit equation of PCI.

- The timing of ST between DES and BMS differs.

- Factors associated with ST may be categorized into several groups:

  1)the stent, including its geometry, polymer, and drug

  2) The patient, including clinical presentation and comorbid conditions

  3) the procedure, including residual dissection or incomplete expansion

  4) the extent and duration of antiplatelet therapy and the patient-specific response to this therapy.

Improved understanding of these factors will facilitate identification of optimal preventive strategies.