Management of Multivessel CAD: Stenting or CABG ?

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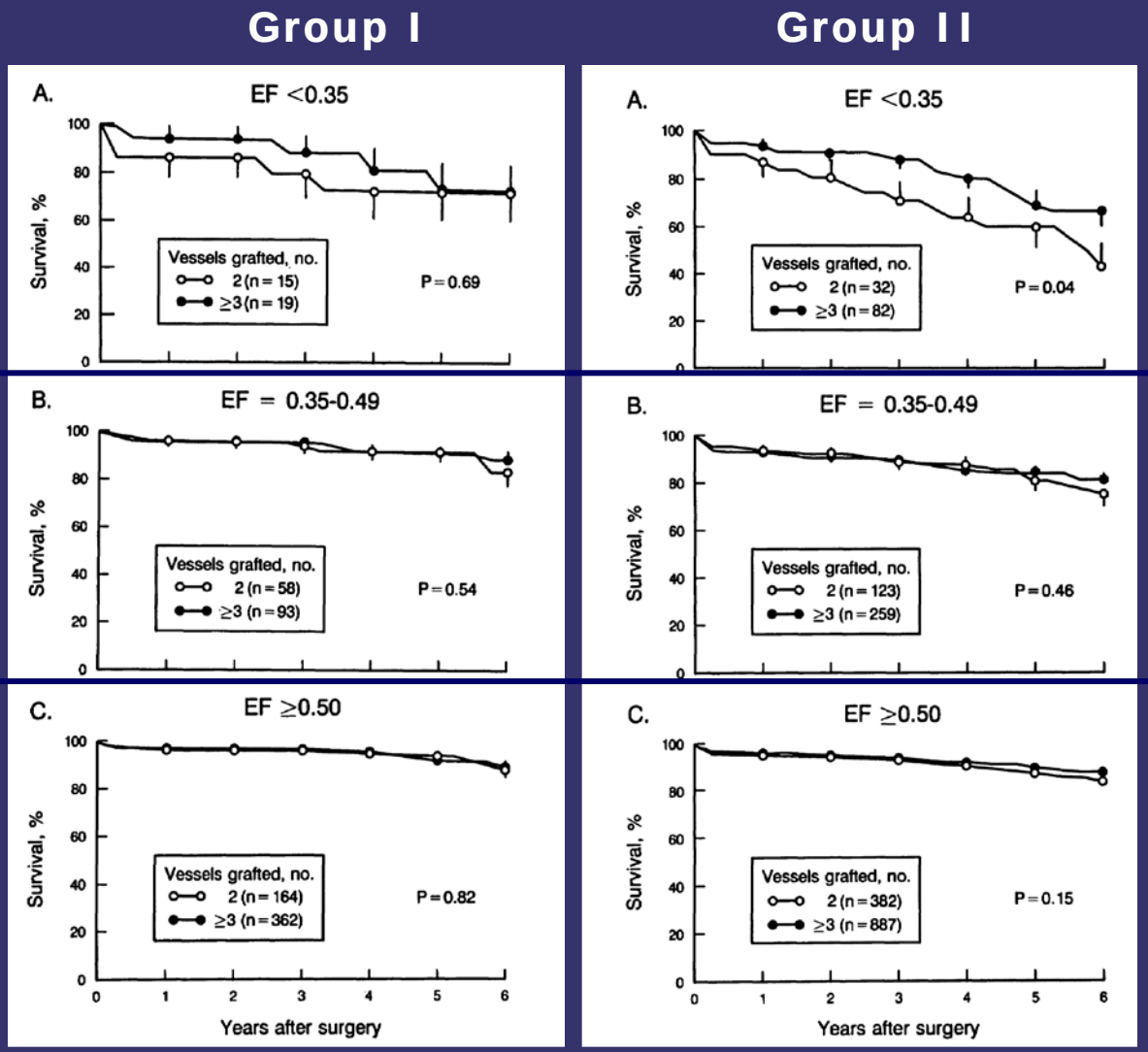
Long-term Outcome of Patients With 3VD Undergoing CABG A Report from CASS Registry

The study was performed as a retrospective analysis of 3,372 nonrandomized surgical patients from the Coronary Artery Surgery Study (CASS) Registry who had three-vessel coronary disease. Group 1 (894 patients) had class I or H angina (Canadian Cardiovascular Society criteria) and group 2 (2,478 patients) had class III or IV angina.

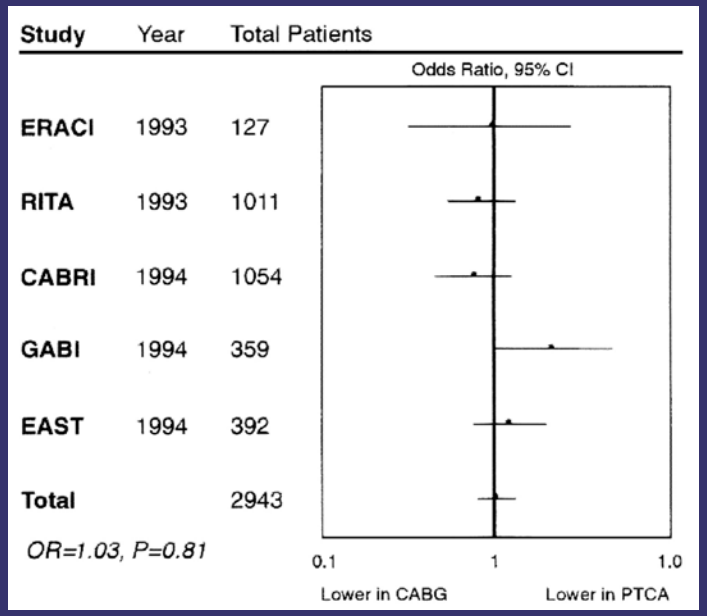


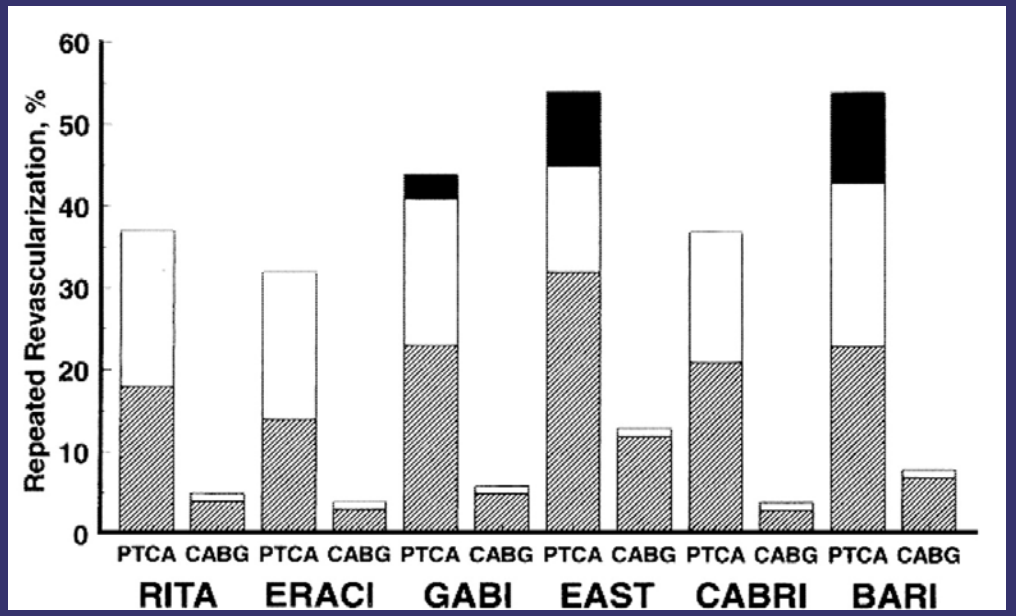
Bell, et al. Circulation 1992;86;446-57

Management of Chronic Stable Angina: Lessons from the Randomized Trials

Characteristic	RITA (21)	ERACI (22)	GABI (23)	EAST (24)	CABRI (25)	BARI (26)
Patients enrolled, *n*	1011	127	359	392	1054	1829
Patients screened, *n*	27 975	1409	8981	5118	23 047	25 200
Median age, *y*	57	58	59	62	61	62
Men, %	81	85	89	74	78	73
Diseased vessels, *n*	≥1	≥2	≥2	≥2	≥2	≥2
Mean ejection fraction	–	0.61	–	0.61	0.63	0.57
Class III–IV angina, %	59	–	65	80	62	–

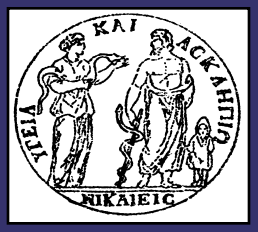
* BARI = Bypass Angioplasty Revascularization Investigation; CABRI = Coronary Angioplasty Bypass Revascularization Investigation; EAST = Emory Angioplasty versus Surgery Trial; ERACI = Argentine Trial of PTCA versus CABG; GABI = German Angioplasty Bypass Surgery Investigation; RITA = Randomised Intervention Treatment of Angina Trial.





Solomon and Gersh. Ann Intern Med 1998;128:216-223

Management of Chronic Stable Angina: Lessons from the Randomized Trials



……..When revascularization is considered for the treatment of multivessel CAD, the selection of PTCA or CABG depends on the coronary anatomy, LV function, need for complete revascularization, and patient preference. In high-risk patients who have left main coronary artery disease or three-vessel coronary artery disease with impaired LV function, current data support surgical revascularization as the treatment of choice to achieve complete revascularization……..

Solomon and Gersh. Ann Intern Med 1998;128:216-223

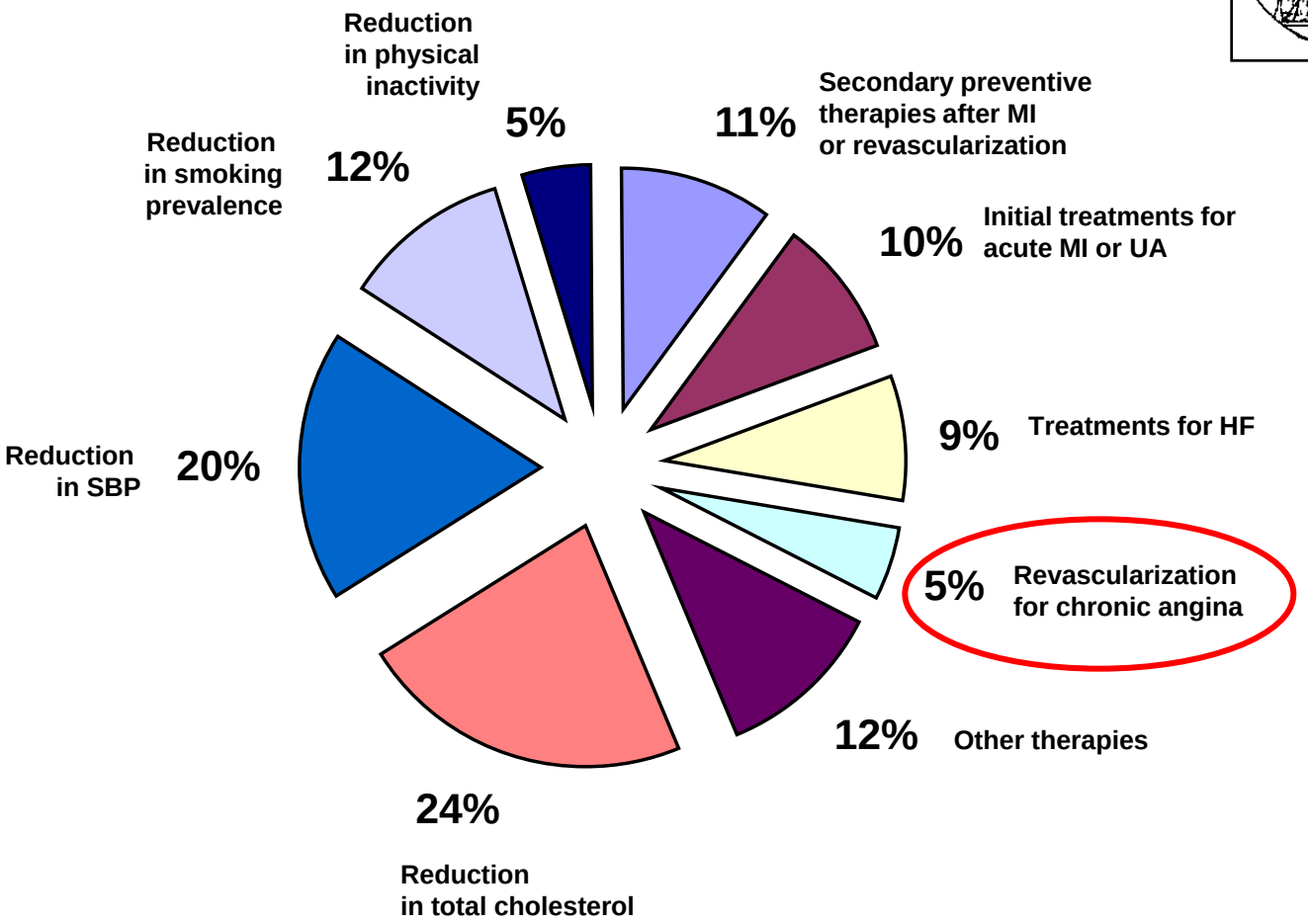
- About 40-50% of all cardiovascular deaths are sudden cardiac deaths.

Mehra R. J Electrocardiol 2007;40(6 Suppl):S118-22.

- Nearly 50% of all SCDs occurr in subjects without a prior history of heart disease.

Fox, et al. Circulation. 2004;110:522-527

Explaining the Decrease in U.S. Deaths from Coronary Disease, 1980–2000



Ford, et al. N Engl J Med 2007;356:2388-98

Reperfusion Management of CAD

- Pathogenesis of atherosclerosis and its complications
- Coronary imaging
- Target and mechanism of intervention
- Reperfusion techniques
- Prospective randomized trials and registries

Pathogenesis of Atherosclerosis

Pathogenesis of Atherosclerosis

❖ Atherosclerosis is a ***multifocal***, smoldering, immuno-inflammatory disease of medium-sized and large arteries fuelled by lipids.

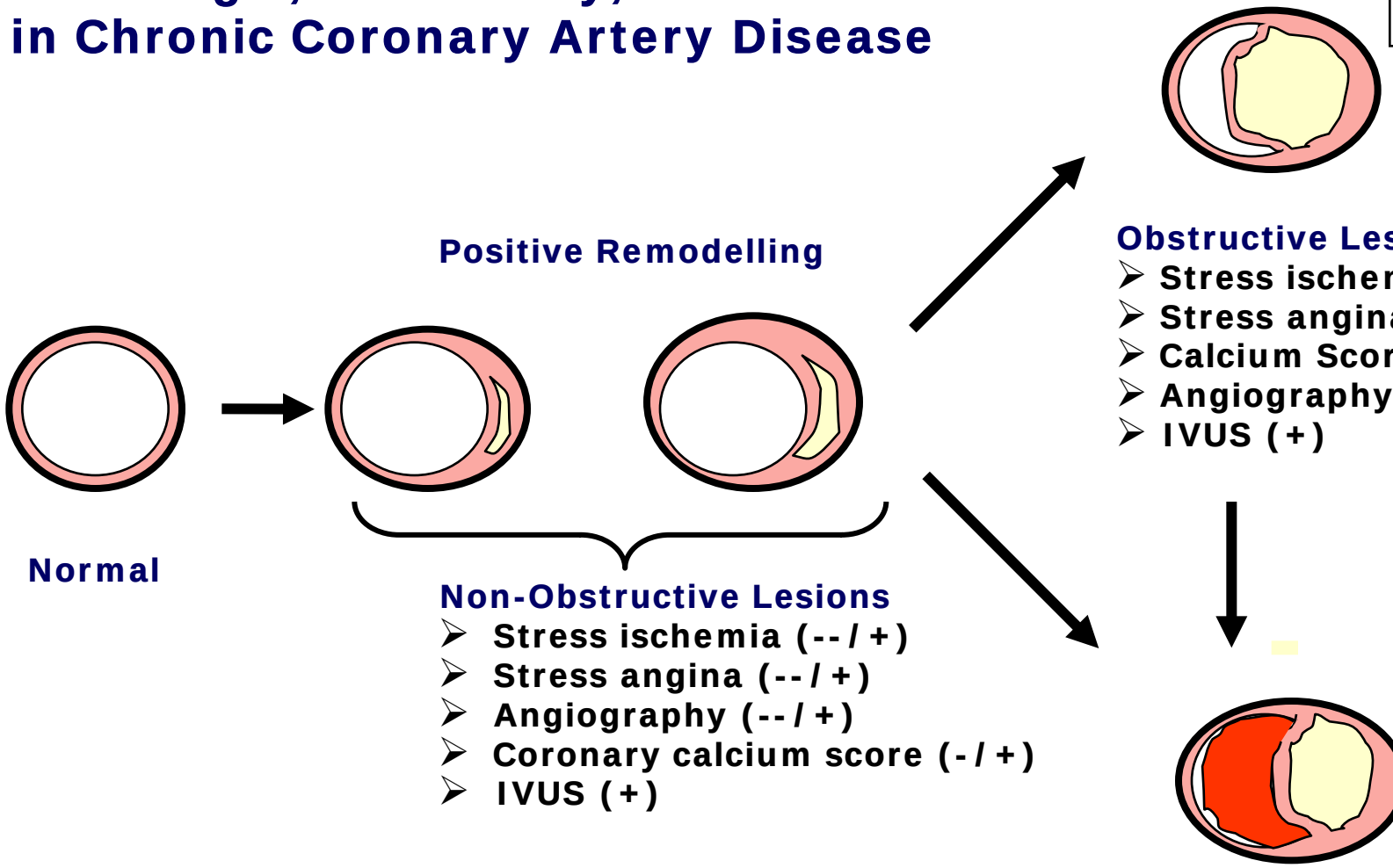
❖ The most devastating consequences of atherosclerosis, such as heart attack and stroke, are caused by superimposed ***thrombosis***.

❖ Approximately 76% of all fatal coronary thrombi are precipitated by ***plaque rupture***. Plaque rupture is a more frequent cause of coronary thrombosis in men (80%) than in women (60%).

❖ Ruptured plaques are characterized by a ***large lipid-rich core, a thin fibrous cap*** that contains few smooth muscle cells and many macrophages, angiogenesis, adventitial inflammation, and outward remodeling.

Falk E. J Am Coll Cardiol 2006;47:C7–12

Pathologic, Laboratory, and Clinical Correlates in Chronic Coronary Artery Disease



Triposkiadis, Starling, Stefanadis
Curr Cardiol Rev 2007;3:221-31

Controversies in stable coronary artery disease

Lionel H Opie, Patrick J Commerford, Bernard J Gersh

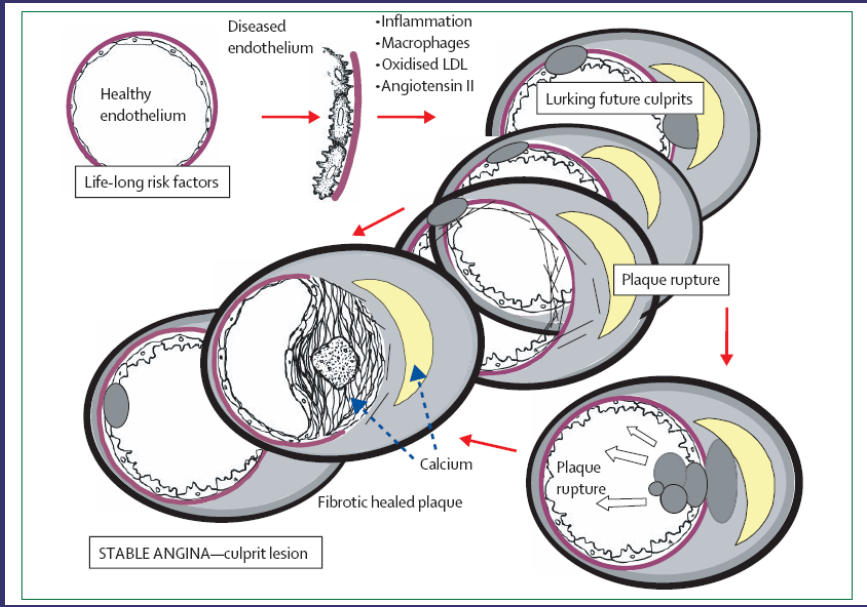


Figure 2: **Role of culprit lesion in stable effort angina**

The multiplicity of potential future culprit lesions is striking; multiple plaques and mature and dynamic evolving lesions can greatly change the clinical outlook. The major aspect of this model (compared with previous theories) is the potentially high number of vulnerable early plaques that could become unstable, some at the stage when the coronary arteries have been eccentrically deformed (lurking future plaques) so that the lumen diameter is virtually unchanged. Thus, there may be no angiographic traces. Once the lumen diameter is much narrowed (culprit lesion), the plaque is relatively stable. Therefore, severe coronary disease seen on a coronary angiogram might paradoxically be safer than an apparently healthy lumen.

Lancet 2006; 367: 69–78

Coronary Imaging

Coronary Angiography

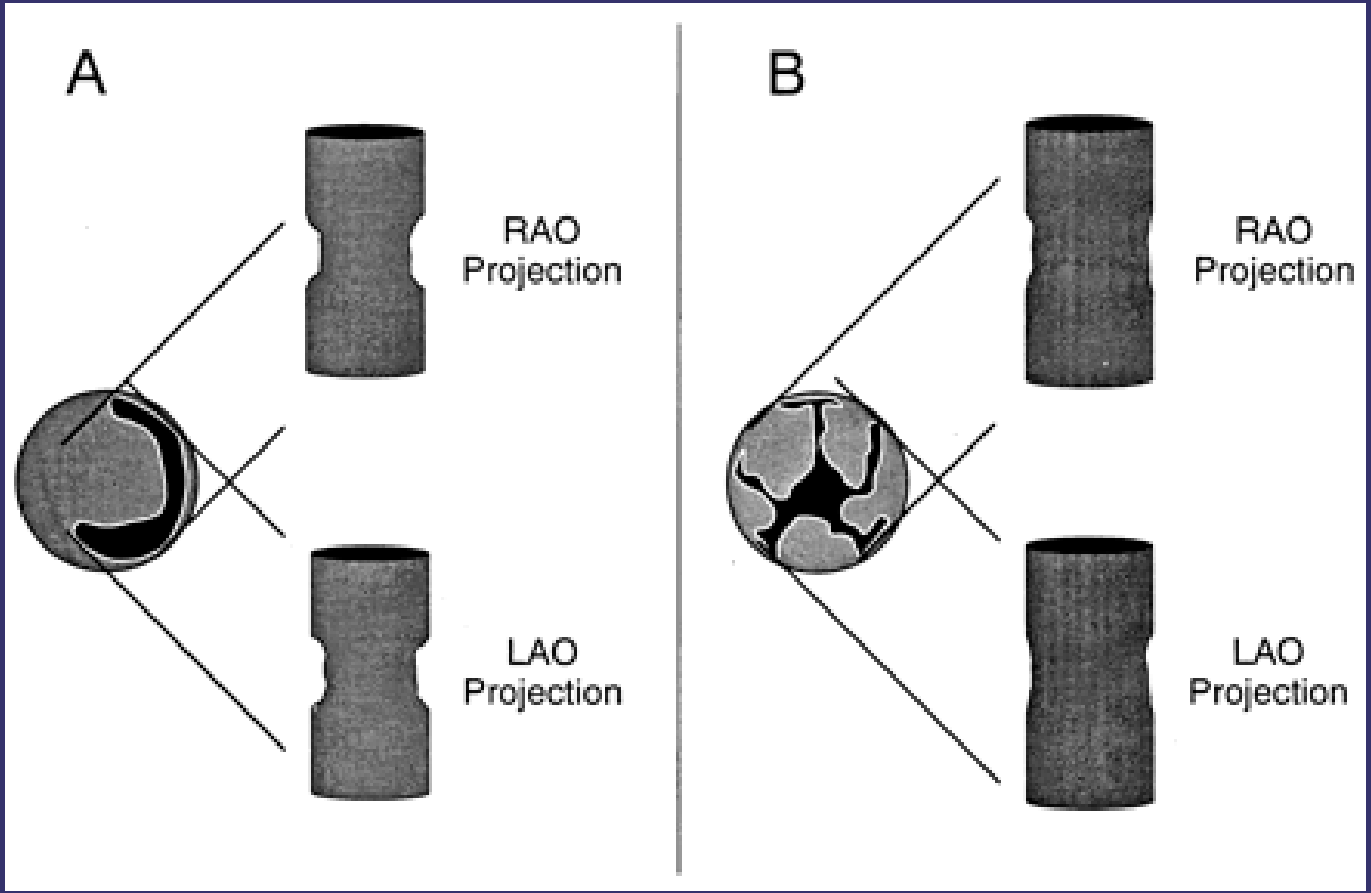
- Stenosis severity

- Qualitative descriptors of lesion complexity
  - -Eccentricity
  - -Irregularities
  - -Ulcerations
  - -Intraluminal filling defects and occlusions

  (Sensitivity: 36%; Specificity: 86%)

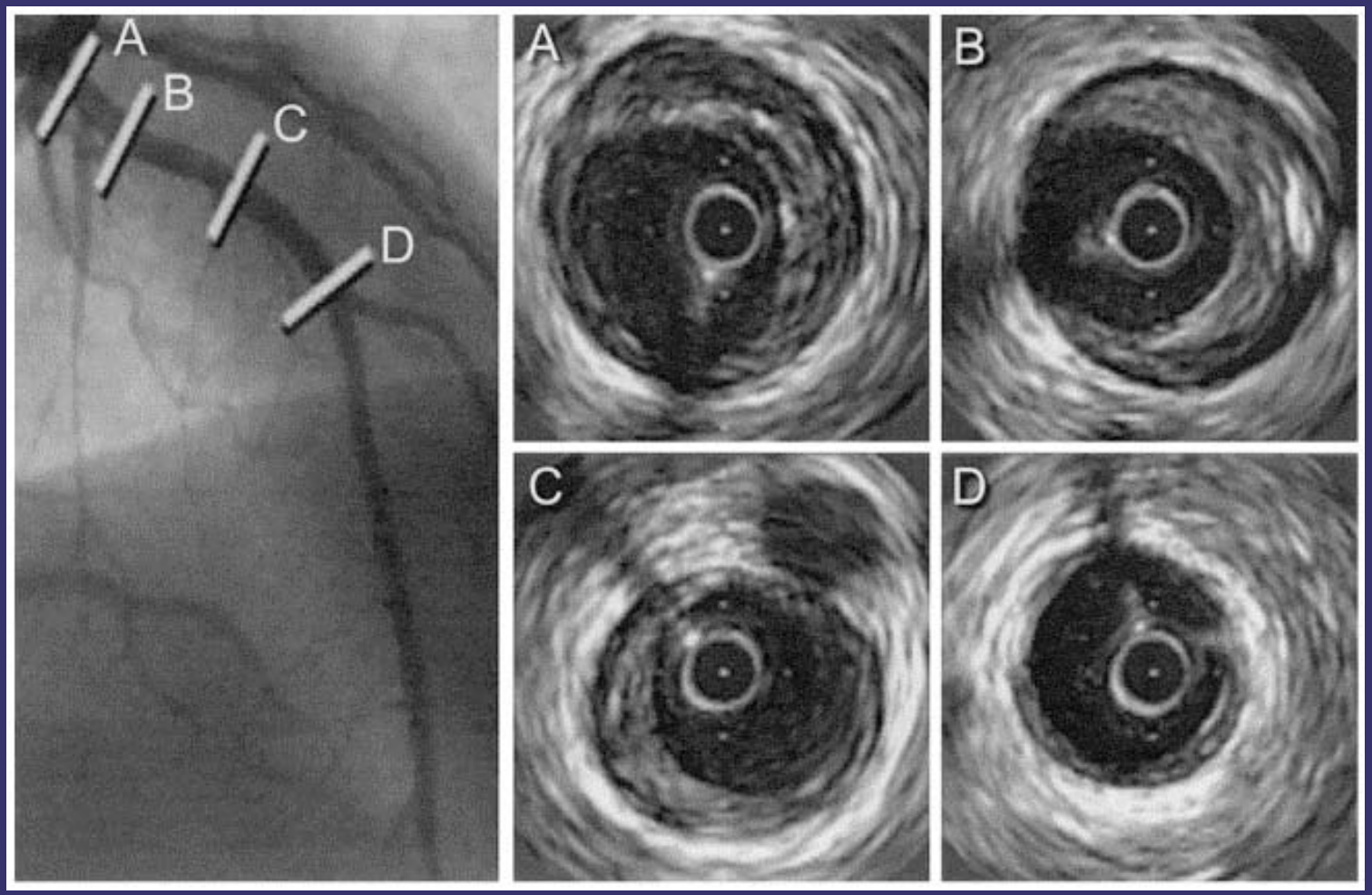
Am J Cardiol 1998;82:1273-75

Limitations of Projection Imaging



Circulation 1995;92:2333-2342

Coronary Remodeling Conceals Extensive Disease



J Am Coll Cardiol 2003;41:103S–112S

Drawbacks of Coronary Angiography

- Depicts rather poor representation of cross-sectional coronary anatomy from simple planar silhouette or luminogram of the contrast-filled lumen.

- Confounded by observer variability, with differences in the estimation of stenosis approaching 50%.

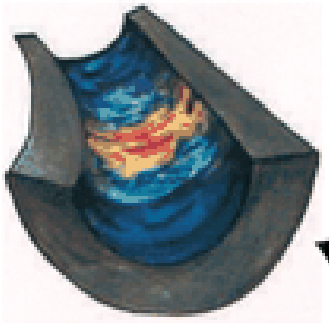
- Functional testing often reveals discordance between the severity of angiographic lesions and physiologic effects.

- Necropsy studies and IVUS demonstrate that coronary lesions, particularly after plaque rupture, are complex, with distorted luminal shapes that are difficult to assess using a planar angiographic silhouette.

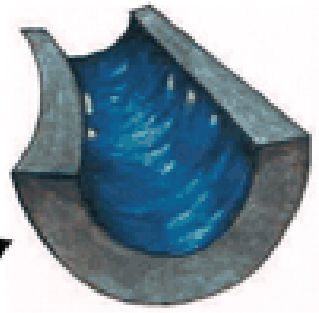
JACC 2003; 41: 103S-112S

Morphology vs. Activity Imaging

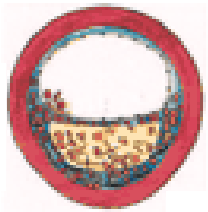
Thermography, Spectroscopy,
Molecular Imaging,
(radionuclear, MRI, CT……)
targeted to markers of activity
(MMP, Ox-LDL, LOX)



Different Activity



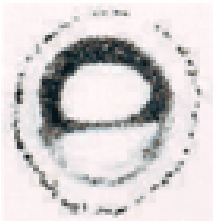
Active and inflamed plaque



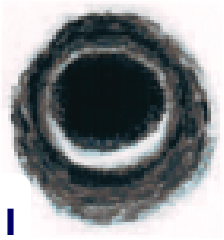
Inactive and non-inflamed plaque

Similar Morphology

IVUS



OCT

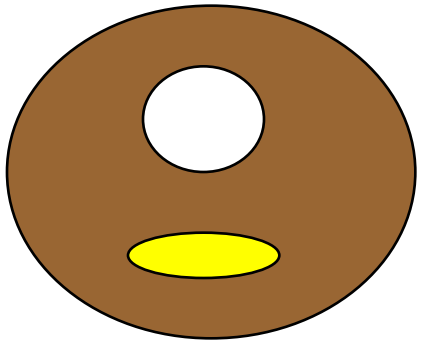


MRI

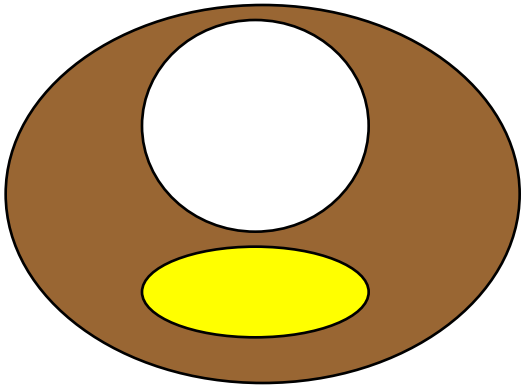
Circulation 2003; 108:1064-72

Target and Mechanism of Intervention

Coronary Revascularization in CAD: Are We Treating The Wrong Plaques?



- ✓ PCI
- ✓ CABG



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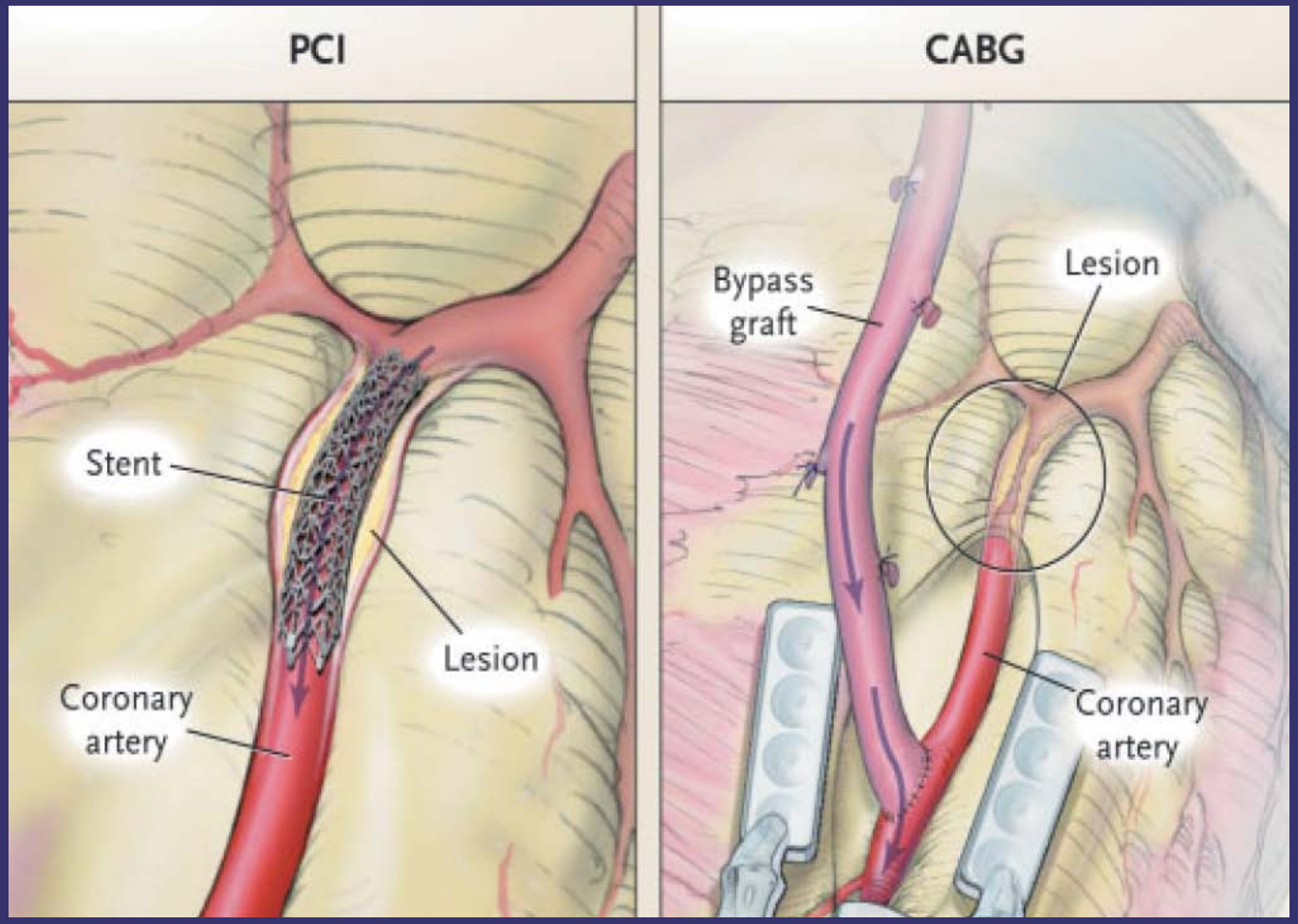
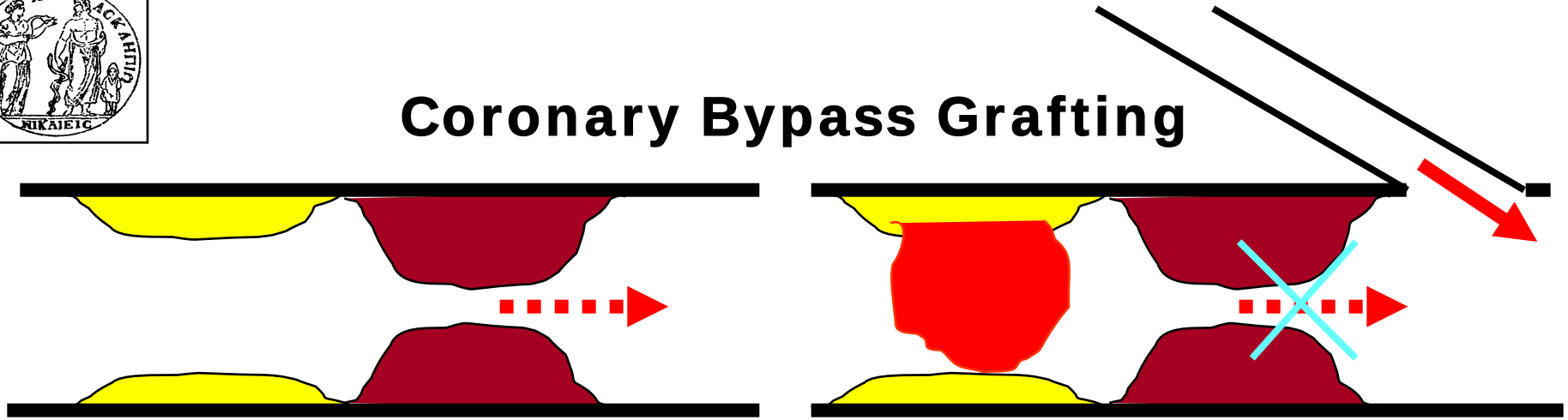
Methods of Coronary Revascularization: Things May Not Be as They Seem !!

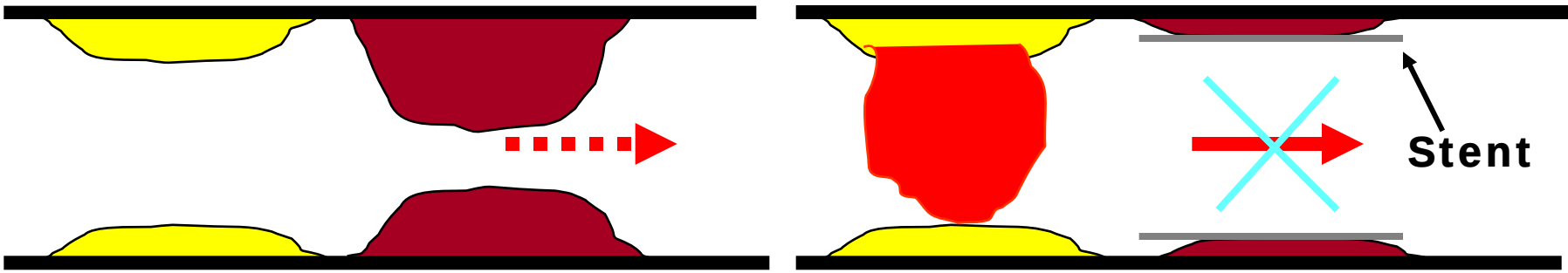


N Engl J Med 2005; 3522235-7

Coronary Bypass Grafting



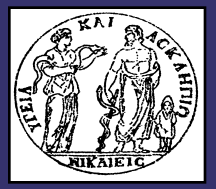
Percutaneous Coronary Intervention



Triposkiadis, Starling, Stefanadis. Curr Cardiol Rev 2007;3:221-31

Reperfusion Techniques

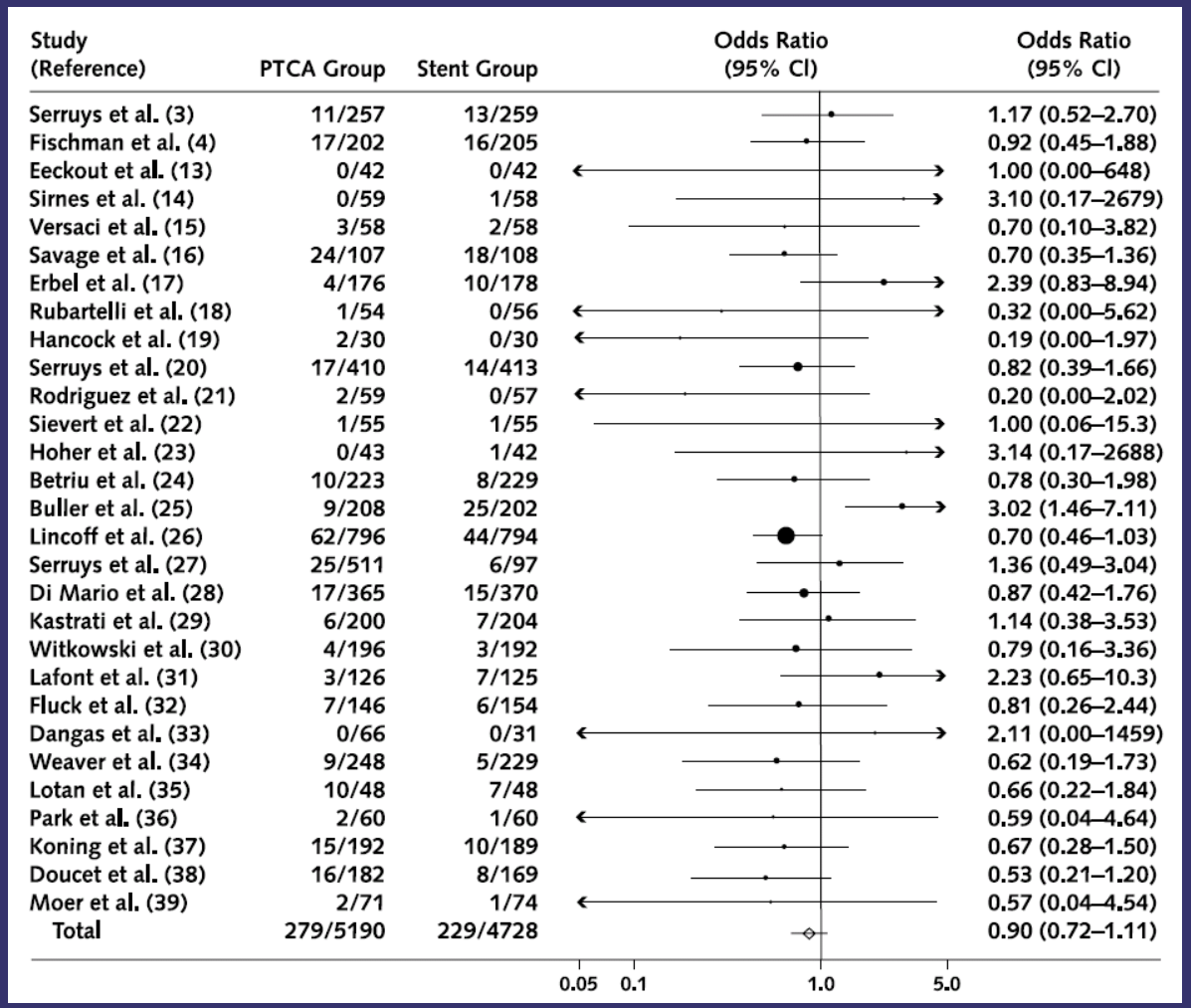
POBA vs. Stent: Rate of Restenosis



Study (Reference)	PTCA Group	Stent Group	Odds Ratio (95% CI)
Serruys et al. (3)	82/240	57/237	0.61 (0.41–0.91)
Fischman et al. (4)	67/159	56/177	0.64 (0.41–0.99)
Eeckout et al. (13)	14/40	19/40	1.66 (0.69–4.17)
Sirnes et al. (14)	42/47	18/57	0.06 (0.02–0.15)
Versaci et al. (15)	18/46	9/49	0.36 (0.13–0.88)
Savage et al. (16)	41/90	35/95	0.70 (0.39–1.25)
Erbel et al. (17)	51/158	28/156	0.46 (0.27–0.78)
Rubartelli et al. (18)	32/47	16/50	0.23 (0.09–0.51)
Hancock et al. (19)	16/28	8/29	0.30 (0.09–0.84)
Serruys et al. (20)	65/209	33/207	0.42 (0.26–0.67)
Rodriguez et al. (21)	9/56	11/56	1.26 (0.49–3.39)
Sievert et al. (22)	39/52	14/51	0.13 (0.05–0.30)
Hoher et al. (23)	29/43	12/42	0.20 (0.07–0.48)
Betriu et al. (24)	74/199	44/198	0.49 (0.31–0.75)
Buller et al. (25)	141/201	105/191	0.52 (0.34–0.79)
Lincoff et al. (26)	NA	NA	–
Serruys et al. (27)	NA	NA	–
Di Mario et al. (28)	NA	NA	–
Kastrati et al. (29)	61/163	61/171	0.93 (0.59–1.45)
Witkowski et al. (30)	48/193	34/187	0.67 (0.41–1.09)
Lafont et al. (31)	32/118	25/117	0.73 (0.40–1.33)
Fluck et al. (32)	17/101	24/112	1.34 (0.68–2.71)
Dangas et al. (33)	16/42	8/17	1.44 (0.46–4.51)
Weaver et al. (34)	NA	NA	–
Lotan et al. (35)	22/31	16/38	0.31 (0.11–0.80)
Park et al. (36)	17/55	20/56	1.24 (0.56–2.76)
Koning et al. (37)	93/192	41/189	0.30 (0.19–0.46)
Doucet et al. (38)	50/152	41/146	0.80 (0.48–1.30)
Moer et al. (39)	13/69	7/72	0.48 (0.17–1.21)
Total	1089/2731	742/2740	0.52 (0.37–0.69)

Ann Intern Med 2003;138:777-786

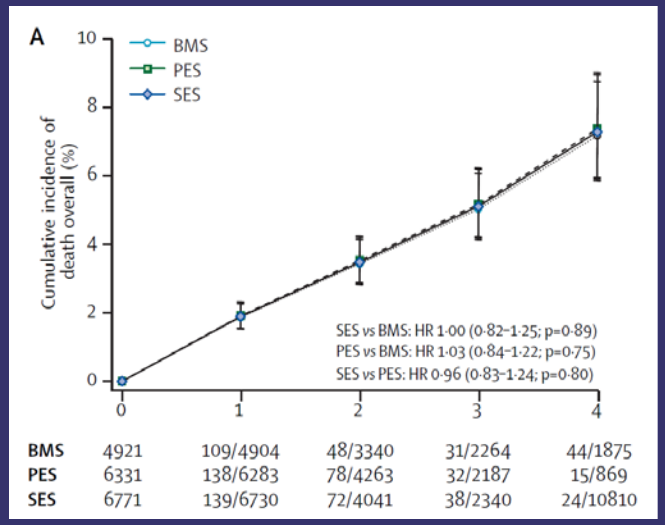
POBA vs. Stent: Rate of Death or MI

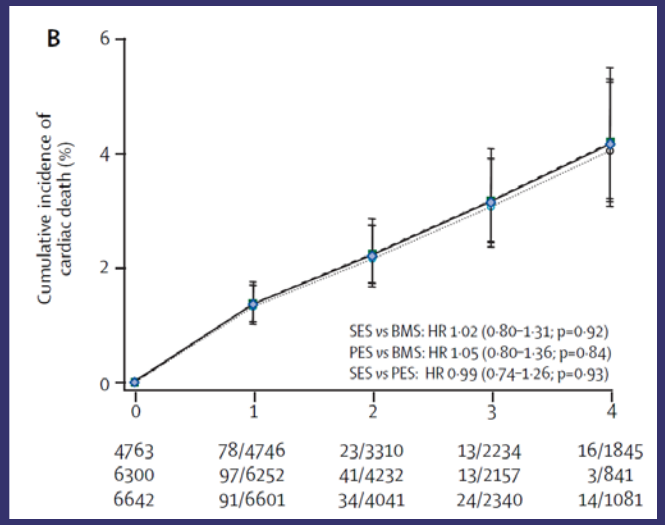


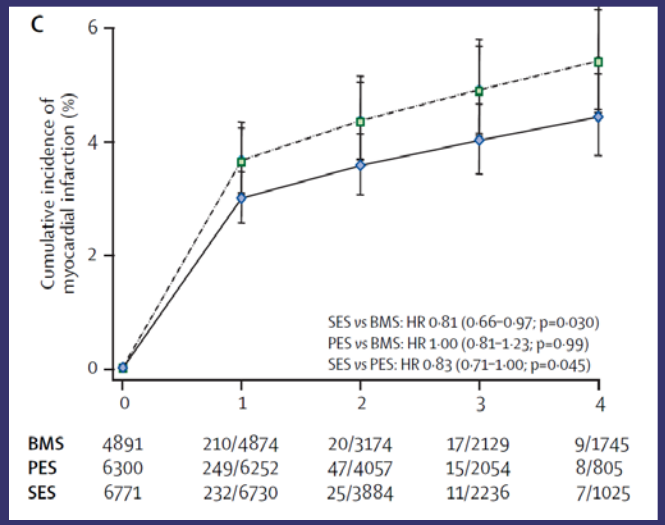
Ann Intern Med 2003;138:777-786

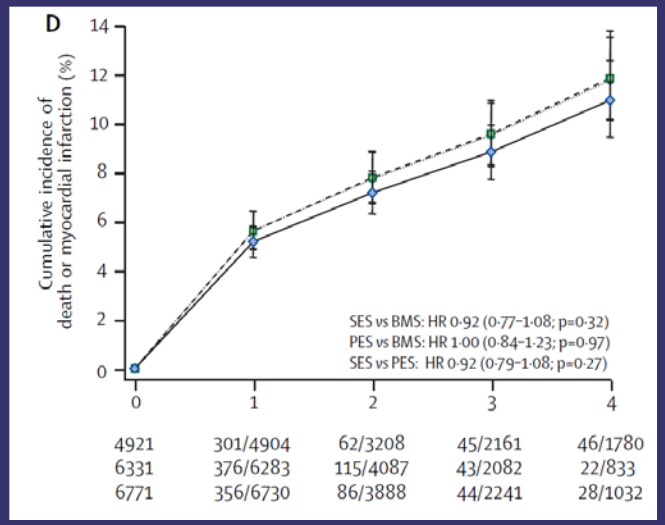
Outcomes Associated with DES and BMS: A Collaborative Network Meta-Analysis

- 38 trials (18,023 patients) with a follow-up of up to 4 years were included.
- Safety outcomes included mortality, MI, and definite stent thrombosis; the effectiveness outcome was TLR.
- Trialists and manufacturers provided additional data on clinical outcomes for 29 trials.
- We did a network meta-analysis with a mixed-treatment comparison method to combine direct within-trial comparisons between stents with indirect evidence from other trials while maintaining randomisation.





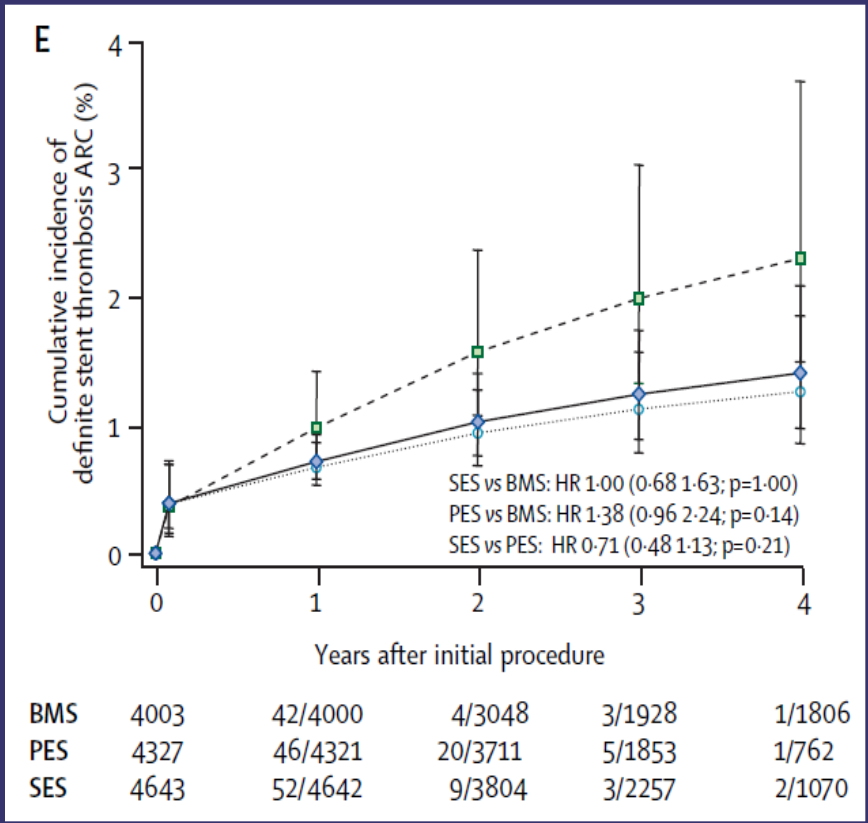


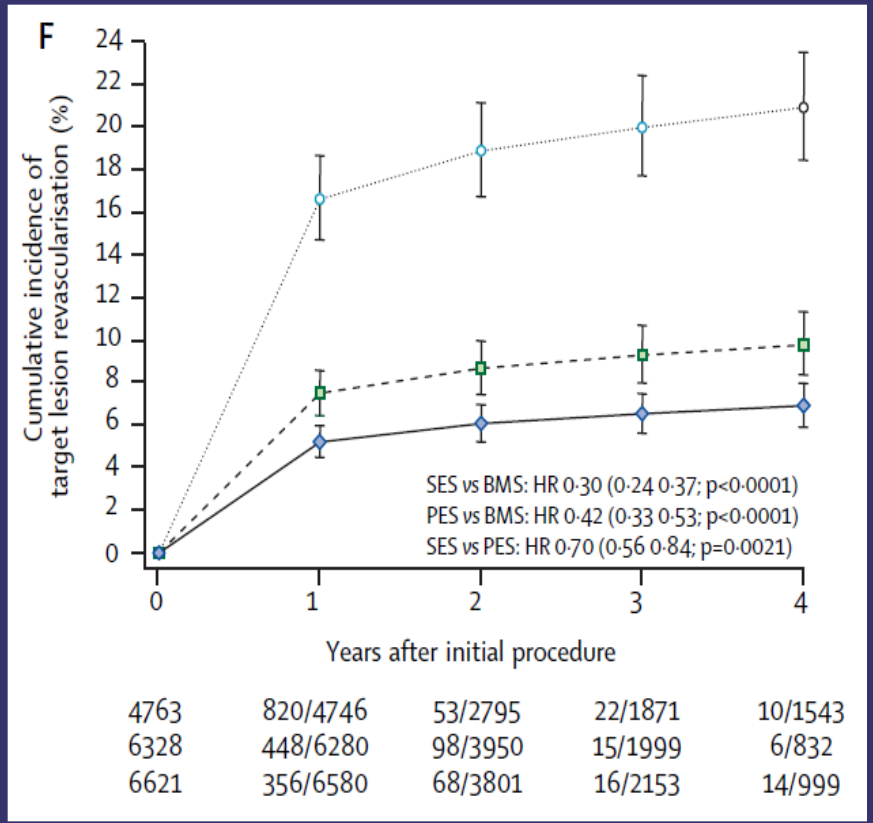


Stettler, et al. Lancet 2007; 370: 937–48

Stent Thrombosis

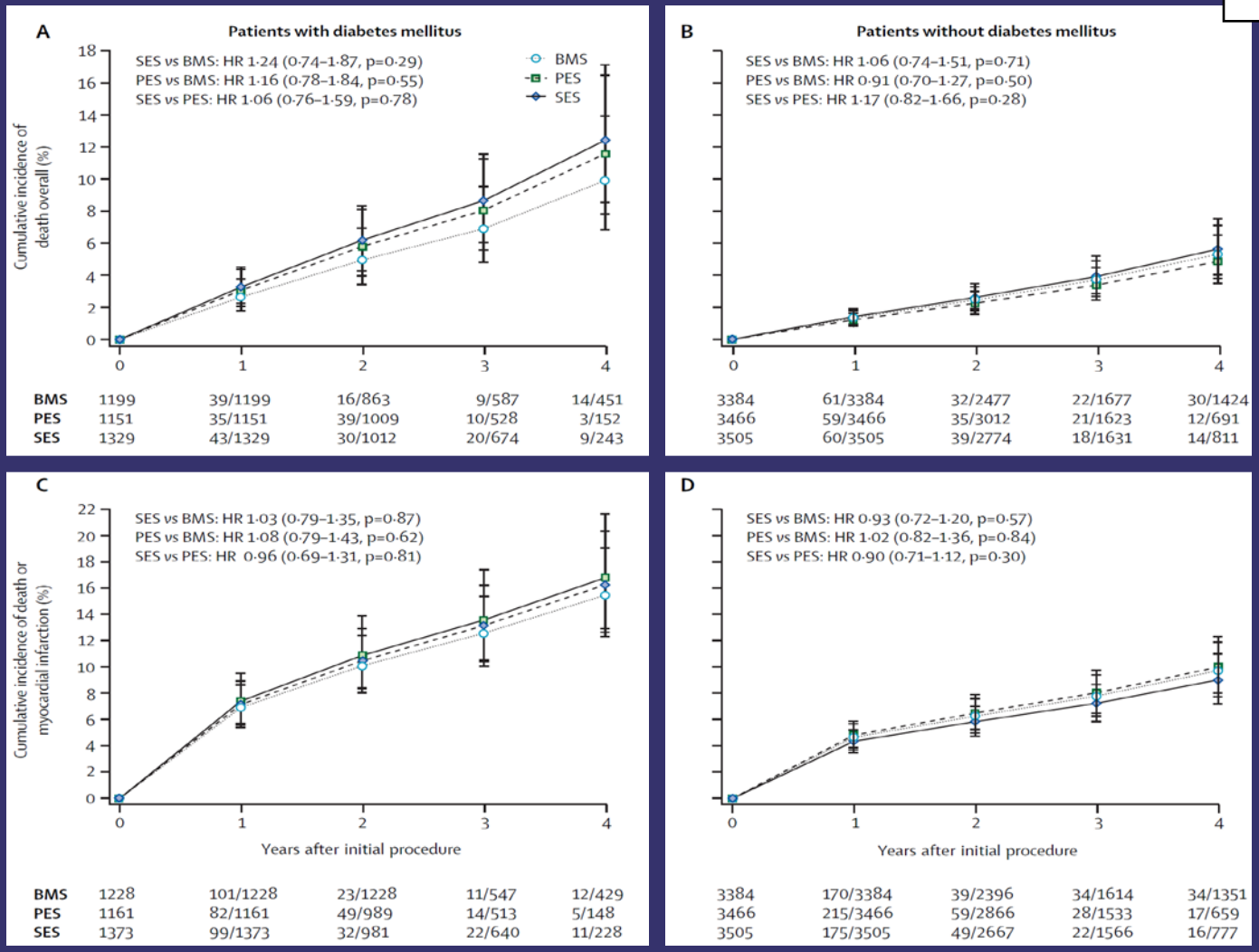
TLR





Stettler, et al. Lancet 2007; 370: 937–48

Stratified Analysis According to Presence or Absence of Diabetes Mellitus



Stettler, et al. Lancet 2007; 370: 937–48

Randomized Controlled Trials and Registries: CABG vs. PCI

Long-Term Safety and Efficacy of PCI With Stenting and CABG for Multivessel CAD

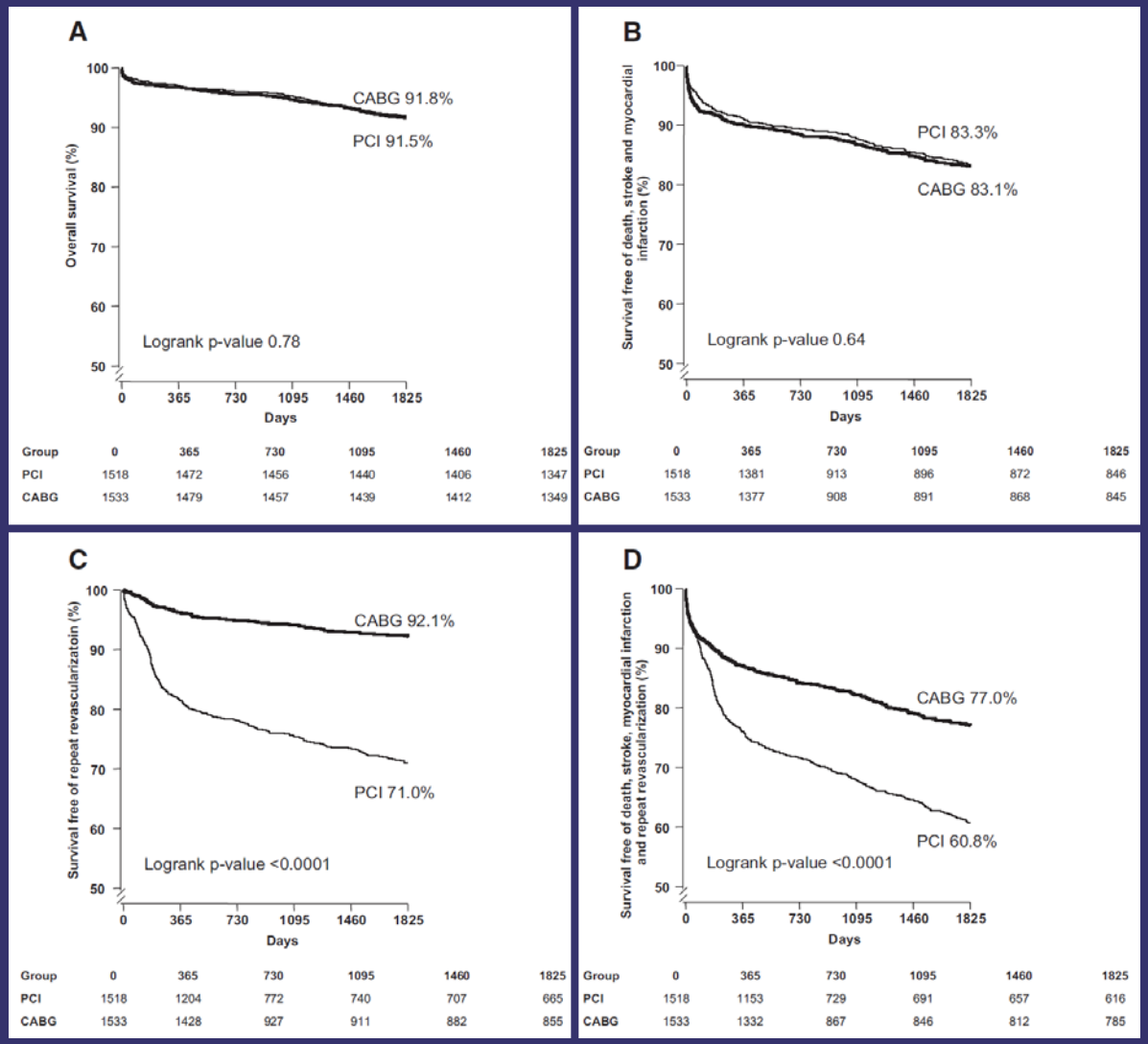
A Meta-Analysis With 5-Year From ARTS, ERACI-II, MASS-II, and SoS

We performed a pooled analysis of 3051 patients in 4 randomized trials evaluating the relative safety and efficacy of PCI with stenting and CABG at 5 years for the treatment of multivessel coronary artery disease.
The primary end point was the composite end point of death, stroke, or myocardial infarction.
The secondary end point was the occurrence of major adverse cardiac and cerebrovascular accidents, death, stroke, myocardial infarction, and repeat revascularization.

	PCI With Stenting (n=1518 Patients)	CABG (n=1533 Patients)	*P*
Age, y			
Median	61.6	61.6	0.37
IQR	53.5–68.0	54.6–68.3	
Range	30.2–85.4	31.9–86.0	
Men, %	76.5 (1162/1518)	77.1 (1182/1533)	0.73
Diabetes mellitus, %	18.1 (275/1518)	17.5 (268/1533)	0.67
Statins, %	40.9 (621/1517)	39.5% (606/1533)	0.44
Enrollment diagnosis, %*			
Stable angina	68.2 (1036/1518)	68.9 (1057/1533)	0.70
Unstable angina	28.5 (432/1518)	27.3 (418/1533)	0.47
Silent ischemia	3.5 (48/1358)	2.6 (34/1330)	0.15
Ejection fraction, %			0.91
Median	60	60	
Diseased vessels, n			0.017
1	4.6 (70/1518)	3.0 (46/1533)	
2	59.3 (900/1518)	57.0 (874/1533)	
3	36.1 (548/1518)	40.0 (613/1533)	

Daemen, et al. Circulation 2008;118:1146-54

Kaplan–Meier Event-Free Survival Analysis



Daemen, et al. Circulation 2008;118:1146-54

Characteristics of Patients in CABG vs. PCI Trials for Multivessel CAD

- The trials involved almost 9000 patients but probably only around 5% of the total eligible population
- There were no patients with left main stem stenosis
- Only about one third of patients had true 3VD
- Only about 40% of patients had proximal LAD disease
- Most patients had a LVEF > 0.50.

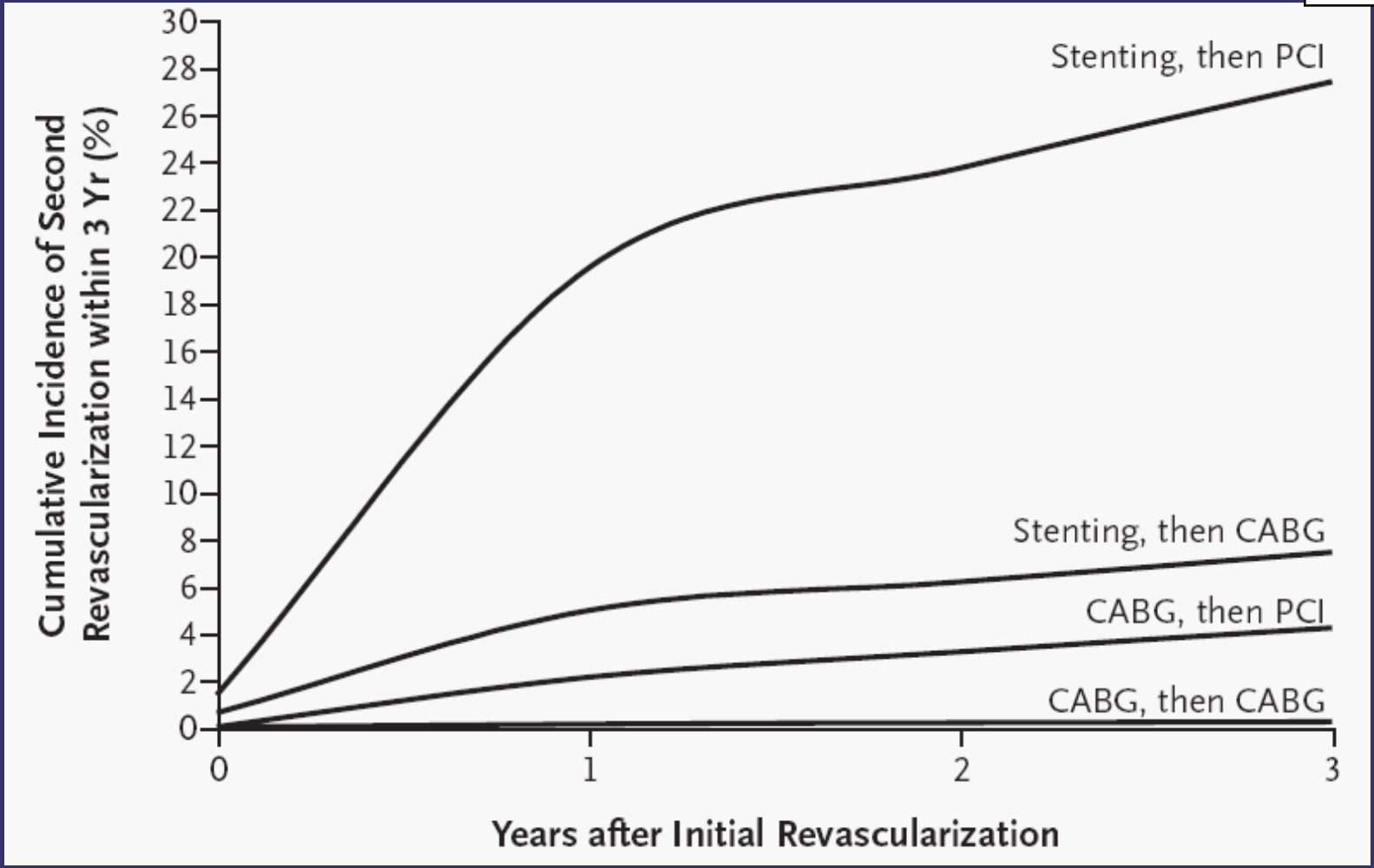
Long-Term Outcomes of CABG versus Stent Implantation (New York Registries)

New York's cardiac registries were used to identify 37,212 patients with MVD who underwent CABG and 22,102 patients with MVD who underwent PCI from January 1, 1997, to December 31, 2000. The rates of death and subsequent revascularization within three years after the procedure were determined in various groups of patients according to the number of diseased vessels and the presence or absence of involvement of the LAD.

Characteristic	Stenting (N=22,102)	CABG (N=37,212)	P Value
Median ejection fraction (%)	53	50	<0.001
Previous myocardial infarction	27.4	25.0	<0.001
1–7 days	22.8	16.3	<0.001
≥8 days	4.6	8.7	
Stroke	4.4	6.9	<0.001
Carotid or cerebrovascular disease	3.5	14.0	<0.001
Aortoiliac disease	2.9	4.6	<0.001
Femoral or popliteal disease	3.6	8.7	<0.001
Hemodynamic instability	0.5	0.7	0.001
Shock	0.1	0.2	0.16
Cardiopulmonary resuscitation	0.1	0	0.01
Electrocardiographic evidence of left ventricular hypertrophy	7.4	11.5	<0.001
Congestive heart failure	11.4	19.5	<0.001
Current admission	7.0	12.3	
Before this admission	4.4	7.2	
Malignant ventricular arrhythmia	1.3	1.8	<0.001
Chronic obstructive pulmonary disease	5.9	16.4	<0.001
Diabetes	25.3	33.2	<0.001
Renal failure	2.2	3.4	<0.001
Requiring dialysis	1.0	1.4	
Creatinine >2.5 mg/dl	1.2	2.0	
No. of diseased vessels (% of patients)†			<0.001
2	80.4	30.7	
3	19.6	69.3	

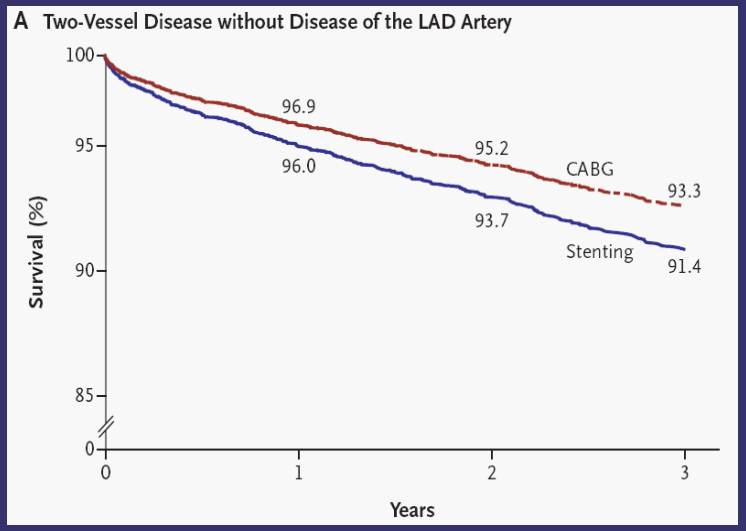
N Engl J Med 2005;352:2174-83

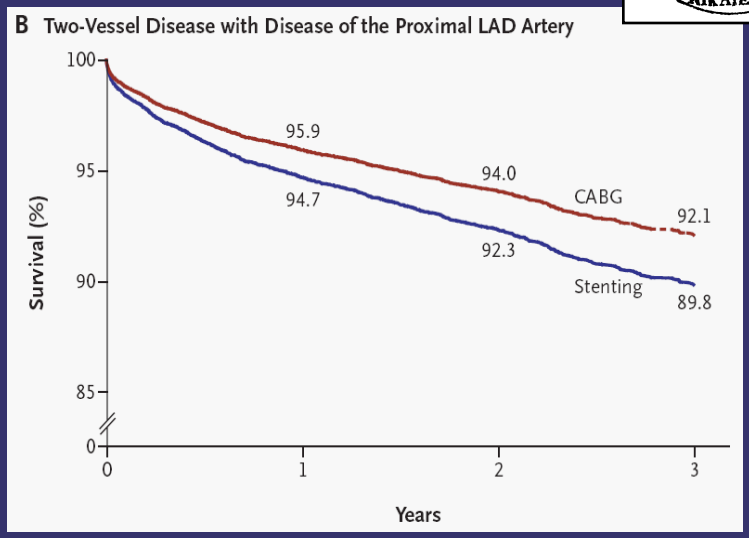
New York Registries

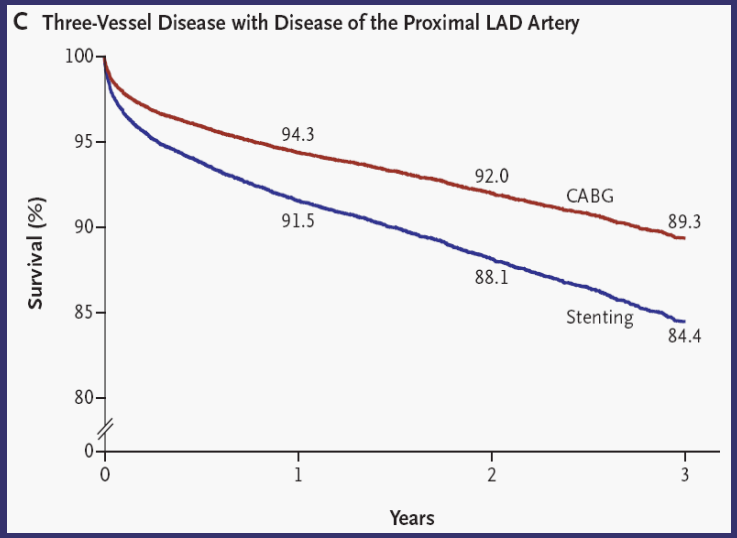


N Engl J Med 2005;352:2174-83

New York Registries







N Engl J Med 2005;352:2174-83

The Cleveland Clinic Experience

- More than 6,000 patients who underwent revascularization between 1995 and 2000 were followed for 5 years.

- CABG patients were more likely to have significant comorbidities such as diabetes and heart failure, while the PCI patients were slightly older and more likely to present with an ACS.

- Left main trunk stenosis and chronic total occlusions were significantly more common in the CABG cohort.

- The unadjusted mortality rate was 16% for PCI and 14% for CABG (*P* = .07). However, after adjusting for all baseline characteristics and the propensity to be selected for one revascularization method or the other, PCI was associated with a higher mortality rate at 5 years (hazard ratio 2.3 [1.9–2.9], *P* <0.001).

- **The excess mortality with PCI was present in nearly all subgroups of patients—just as in the New York registry study**.

Clev Clin J Med 2006; 73: 340-3

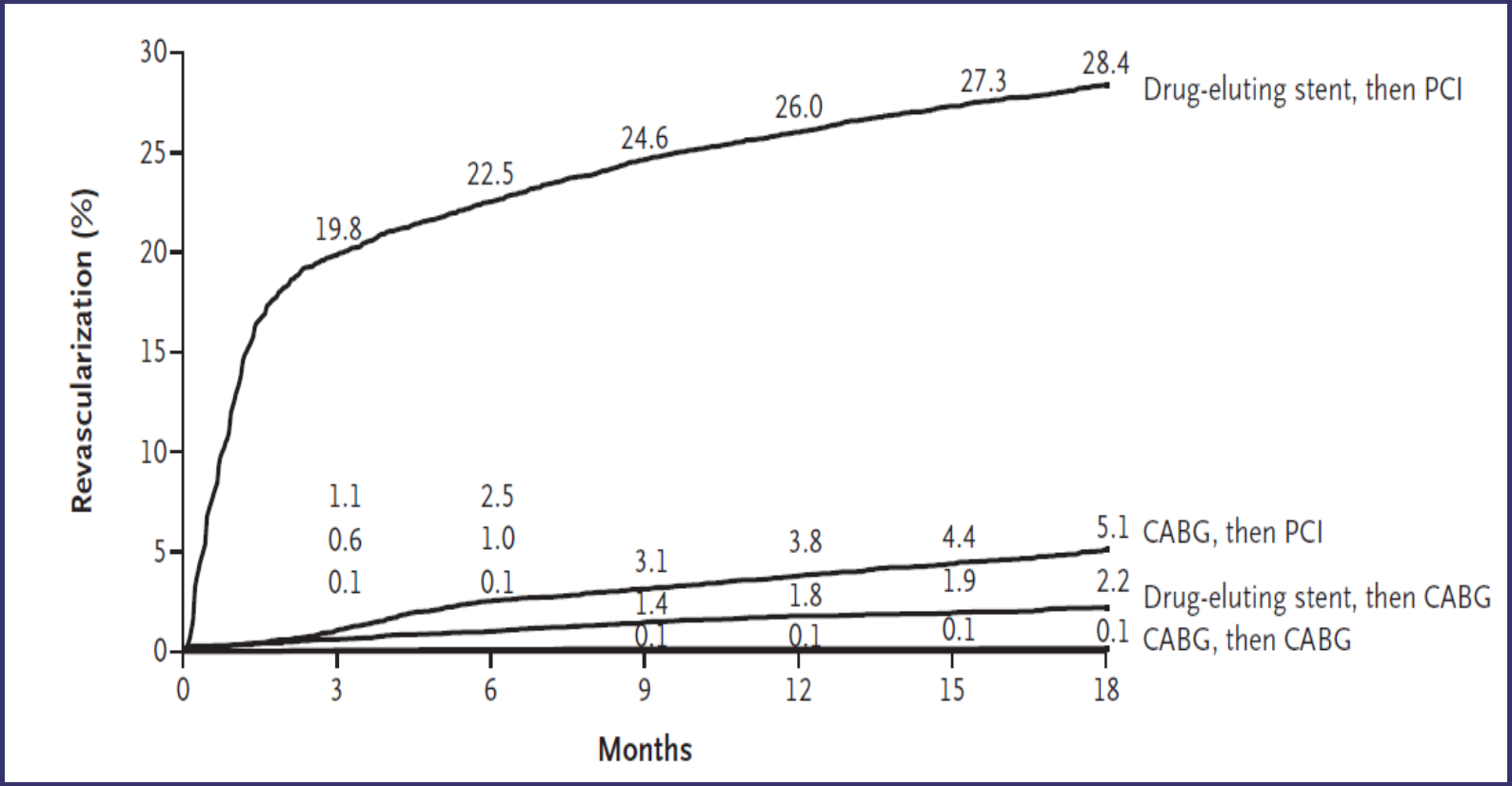
DES vs. CABG in Multivessel CAD

We identified patients with multivessel disease who received drug-eluting stents or underwent CABG in New York State between October 1, 2003, and December 31, 2004, and we compared adverse outcomes (death, death or myocardial infarction, or repeat revascularization) through December 31, 2005, after adjustment for differences in baseline risk factors among the patients.

Risk Factor	CABG (N=7437)	Stent (N=9963)	P Value
Mean age (yr)	66.0±10.9	65.4±11.9	<0.001
Sex (%)			<0.001
Male	72.5	67.2	
Female	27.5	32.8	
Ejection fraction (%)			<0.001
<20%	2.0	0.8	
20–29%	6.8	3.3	
30–39%	12.9	6.6	
≥40%	77.7	84.2	
Data missing	0.6	5.1	
Chronic obstructive pulmonary disease (%)	17.4	6.6	<0.001
Diabetes (%)	38.2	32.7	<0.001
No. of diseased vessels (%)‡			<0.001
3, with proximal LAD artery	51.5	11.8	
3, without proximal LAD artery	18.4	13.1	
2, with proximal LAD artery	20.0	26.1	
2, without proximal LAD artery	10.1	49.0	

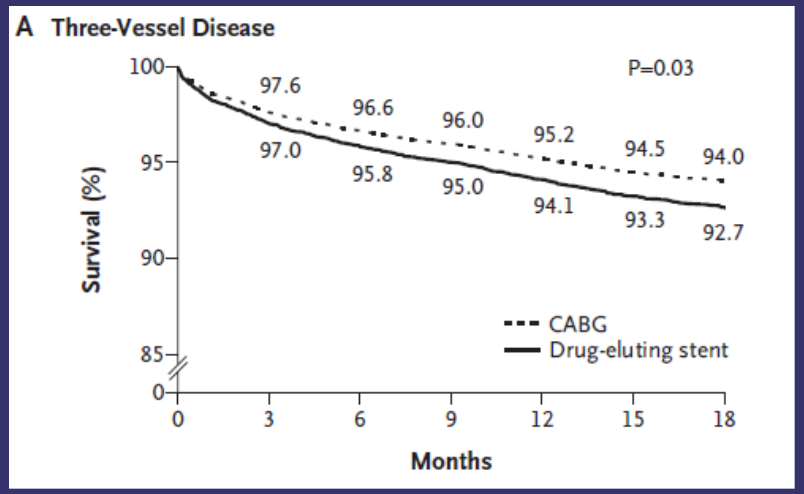
Hannan, et al. N Engl J Med 2008;358:331-41

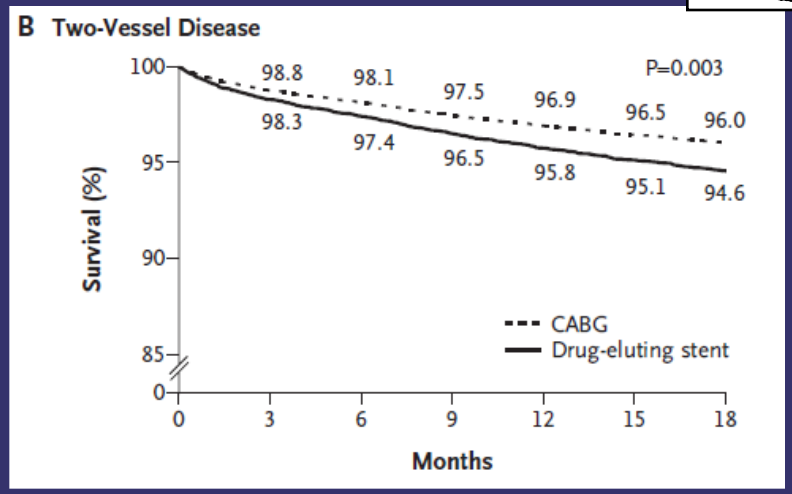
Revascularization within 18 Months after Initial Procedure

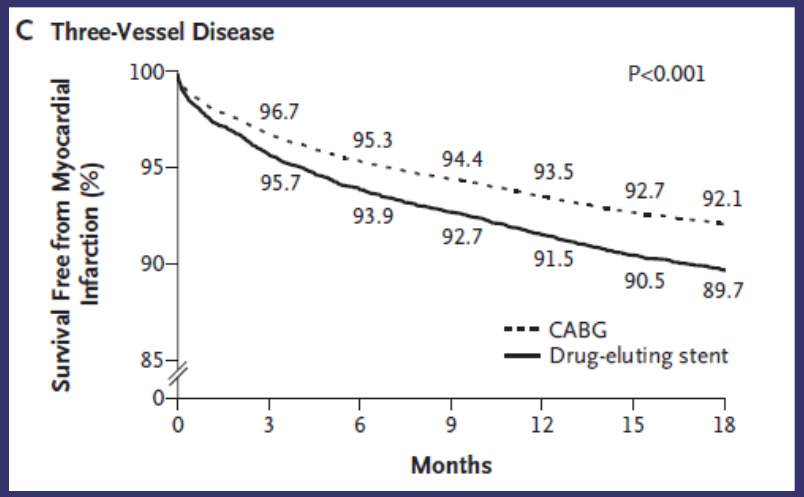


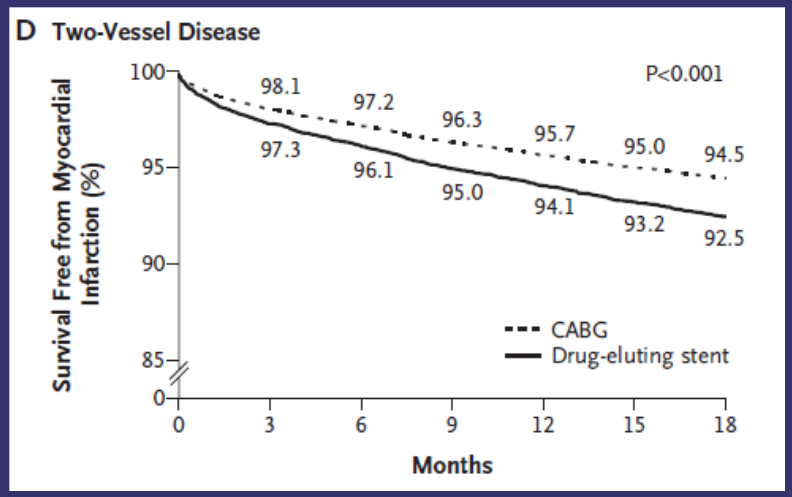
Hannan, et al. N Engl J Med 2008;358:331-41.

Adjusted Curves for Long-Term Survival and Survival Free from MI





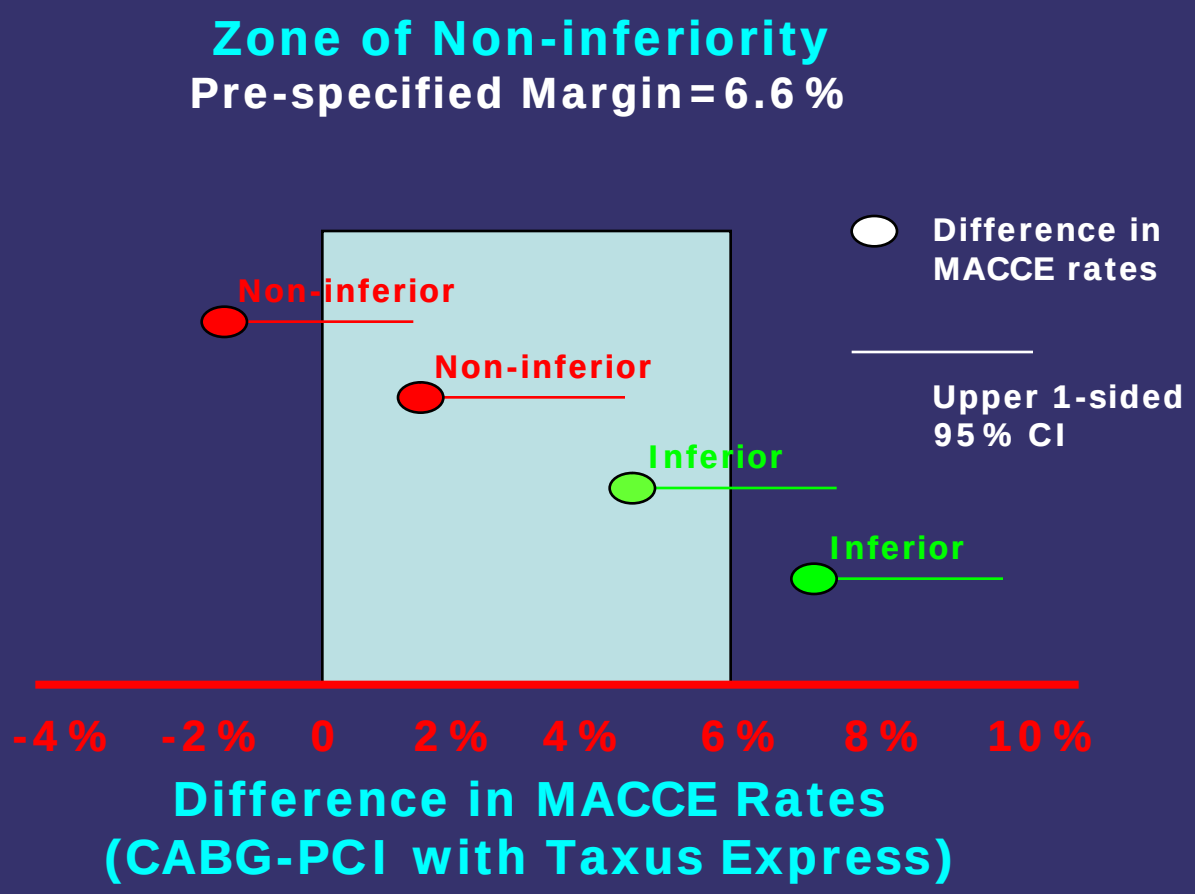




Hannan, et al. N Engl J Med 2008;358:331-41

Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) Trial

Conducted at 62 European sites and 23 sites in the US, SYNTAX randomized 1800 patients to either CABG (n=897) or PCI (n=903) with the Taxus DES, with a primary end point of 12-month major adverse cardiac and cerebrovascular events (MACCE), defined as all-cause death, cerebrovascular event, MI, and repeat revascularization (PCI and/or CABG).



Ong, et al. Am Heart J 2006;151:1194-204
Piaggio, et al. JAMA 2006;295:1152-60

Main Results from SYNTAX Randomized Trial

End point	CABG (%)	DES (%)	p
MACCE	12.1	19.8	0.0015
Death/MI/stroke	7.7	7.6	0.98
Revascularization	5.9	13.7	<0.0001
Stroke	2.2	0.6	0.003
MI	3.2	4.8	0.11
All-cause death	3.5	4.3	0.37

Serruys PW et al. European Society of Cardiology Congress 2008; September 1, 2008; Munich, Germany.

Patrick W Serruys : “People shouldn't leave the room thinking that PCI is inferior just because it did not pass the test for noninferiority. It's basically up to the patient to assess the different risks.”

Friedrich W Mohr : “We did not meet the noninferiority test, so that says that CABG is the treatment of choice—that's clear from those data. And I didn't expect to see that at one year”.

HeartWire September 1, 2008

CARDIA: Stents vs. CABG in Diabetics

CARDIA trial was designed to demonstrate noninferiority of PCI to CABG, in diabetic patients with multivessel disease. CARDIA fell short of its planned recruitment, enrolling only 510 patients out of the intended 600, meaning that the noninferiority parameters set for the trial were not reached due to insufficient power.

12-mo events	CABG	PCI	Odds ratio (95% CI)	p
Death/MI/stroke	10.2	11.6	1.15 (0.65–2.03)	0.63
Stroke	2.5	0.4	0.16 (0.02–1.33)	0.09
Revascularization	2.0	9.9	5.31 (2.0–14.11)	0.001

Kapur A. European Society of Cardiology Congress 2008;September 1, 2008; Munich, Germany.

Anatomy of Left Main Stenosis

- Left main stem stenosis occurs as an isolated lesion in only 6% to 9% of patients, whereas over 70% to 80% of patients also have multivessel CAD.

- Most LMS stenoses (40% to 94%) occur in the distal segment of the artery and extend into the proximal coronary arteries.

- Morphologically, around one-half of LMS lesions have significant calcification.

Cardiovasc Surg 2003;11:497–505
Catheter Cardiovasc Interv 2006;68:357– 62

Revascularization for Unprotected Left Main Stem Coronary Artery Stenosis

CABG in Left Main Stenosis

Author (Ref. #) (Year)	Year of Surgery	n	Mortality (%)			
			Hospital	30-Day	1-Year	2-Year
Jonsson et al. (31) (2006)	1970 to 1999	1,888	2.7	—	—	—
Lu et al. (30) (2006) (2005)	1997 to 2003	1,197	2.8	3	5	6
Keogh and Kinsman (16) (2003)	2003	5,003	3	—	—	—
Dewey et al. (29) (2006) (2001)	1998 to 1999	728	—	4.2	—	—
Yeatman et al. (28) (2006) (2001)	1996 to 2000	387	2.4	—	—	5
Ellis et al. (27) (2006) (1998)	1990 to 1995	1,585	2.3	—	—	—
Weighted average	—	10,788	2.8	—	—	—

BMS in Left Main Stenosis

Author (Ref. #)	Sites	n	% Eligible	Stent	In-Hospital to 30-Day		1- to 2-Year Follow-Up	
					Mortality	Revascularization	Mortality	Revascularization
Keeley et al. (34)	1	54	—	100%	5%	20%	31%	15%
Silvestri et al. (35): high risk	1	47	—	100%	9%	—	11%	15%
Silvestri et al. (35): low risk	1	93	—	100%	0%	—	3%	21%
Tan et al. (36): all	25	279	—	85%	14%	—	24%	34%
Tan et al. (36): low risk	25	89	—	85%	3.4%	—	3.4%	31%
Black et al. (37)	1	92	—	100%	4%	—	6.5%	16%
Takagi et al. (38)	1	63	—	58%	0%	10%	16%	31%
Park et al. (39)	4	270	—	100%	0%	4%	7%	29%
Brueren et al. (40)	1	71	—	64%	1%	4%	10%	25%
Kelley et al. (41)	3	97	—	100%	9%	—	28%	20%
Weighted average	38	1,155			6%	3%	17%	29%

Taggart, et al. J Am Coll Cardiol 2008;51:885–92

DES in Left Main Stem Stenosis

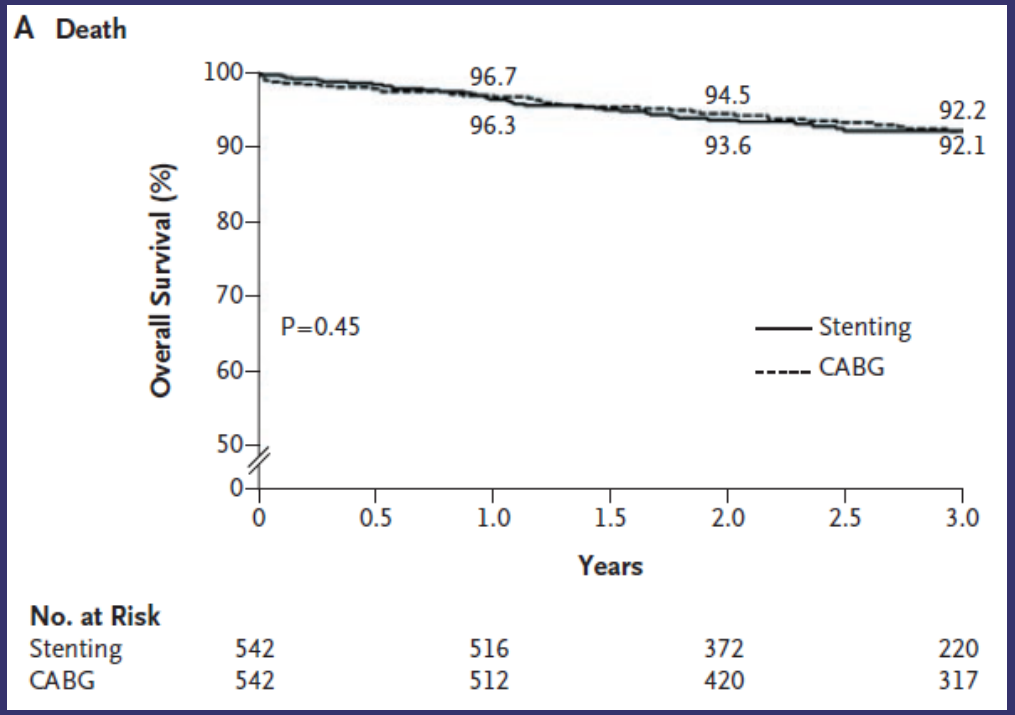
Author (Ref. #)	n	Ostial	Mid	Distal/ Bifurcation	CAD (%)	EF	30-Day Death (%)	30-Day MI (%)	30-Day TLR (%)	Follow-Up, Months	Death (%)	MI (%)	TLR/TVR (%)	Angiography When (Months)	Angiography (%)	Restenosis (%)
De Lezo et al. (17)	52	13	25	42	37	57	0	4	0	12	0	0	2	6	67	6
Valgimigli et al. (19)*	130			72	85	41	10	4	0	18	14	4	6	8	85	9
Price et al. (20)	50	—	—	94	?	>40	0	8	6	9	10	2	38	9	96	42
Chieffo et al. (21)	107			82	?	52	0	9	0	12	3	1	20	<12	85	
Lee et al. (23)	50	42	20	60	66	51	2	0	0	6	4		7	6	42	?
Kim et al. (22)*	116	23	6	100	76	60	0	6	0	18	0	0	5	6	85	11
Palmerini et al. (24)	94	17	3	80	100	52	3.2	4.5	1	14	13.4	8.3	20	14	66	20
Weighted average	599						2.4	6	2.1%	11	7	1.6	13%			21%

Taggart, et al. J Am Coll Cardiol 2008;51:885–92

Stents vs. CABG for Left Main Coronary Artery Disease

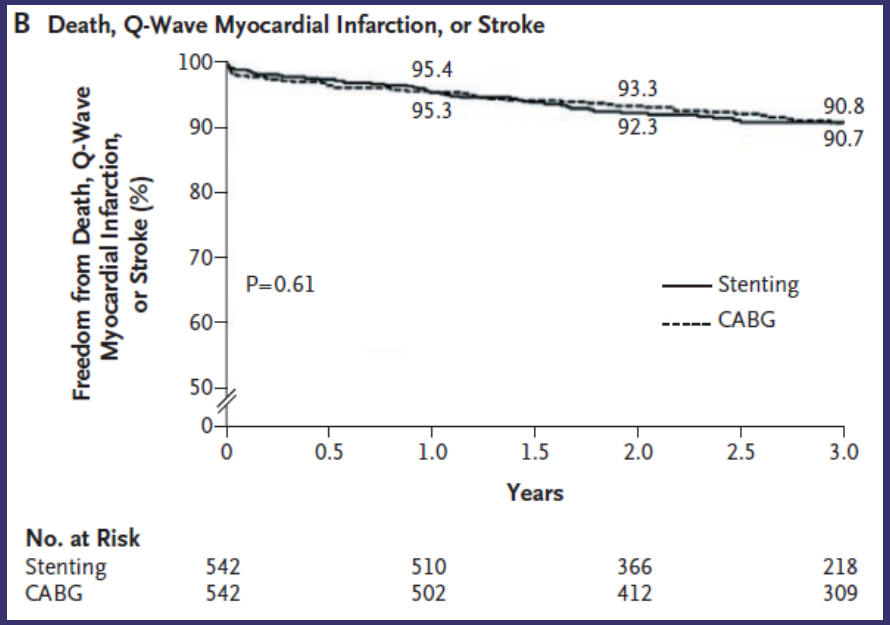
We evaluated 1102 patients with unprotected left main coronary artery disease who underwent stent implantation and 1138 patients who underwent CABG in Korea between January 2000 and June 2006.

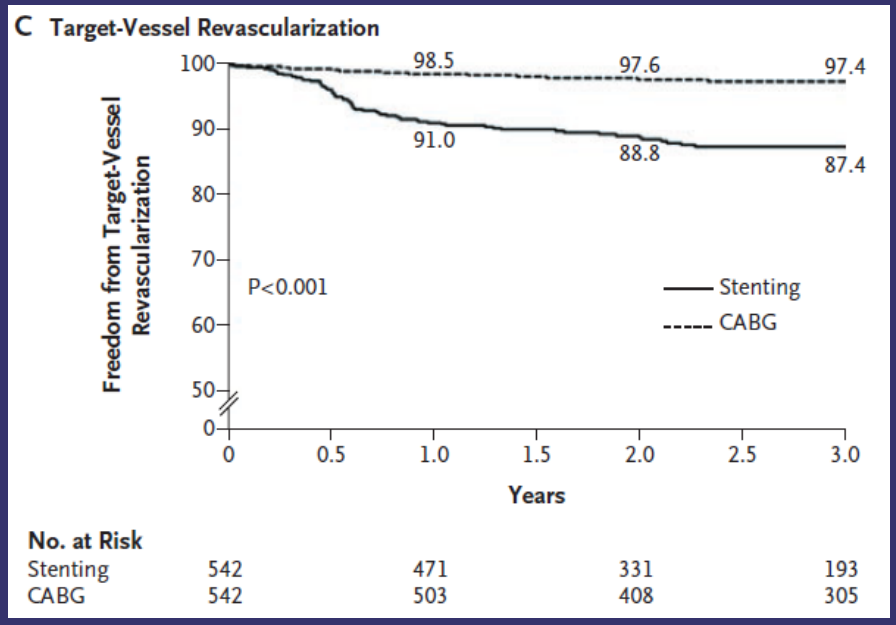
Variable	Stent Group (N=1102)	CABG Group (N=1138)	P Value
Angiographic characteristics			
Involved location (% of patients)			0.04
Ostium, midshaft, or both	50.6	46.2	
Distal bifurcation	49.4	53.8	
Extent of diseased vessel (% of patients)			<0.001
Left main only	25.2	6.2	
Left main plus single-vessel disease	24.0	10.5	
Left main plus double-vessel disease	26.0	26.3	
Left main plus triple-vessel disease	24.8	57.0	
Right coronary artery disease (% of patients)	35.9	70.7	<0.001
Restenotic lesion (% of patients)	2.9	1.2	0.005
Ejection fraction (%)			<0.001
Median	62	60	
Interquartile range	57–67	52–66	



Seung, et al. N Engl J Med 2008;358:1781-92

Stents vs. CABG for Left Main Coronary Artery Disease





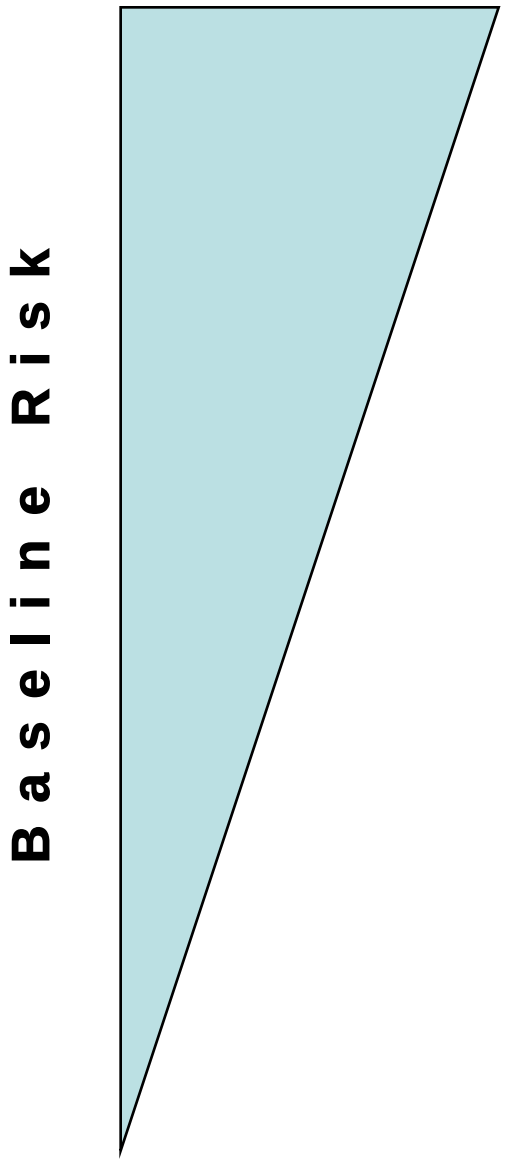
Outcome	Overall Cohort (N=542 pairs)		Wave 1 (N=207 pairs)		Wave 2 (N=396 pairs)	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Death	1.18 (0.77–1.80)	0.45	1.04 (0.59–1.83)	0.90	1.36 (0.80–2.30)	0.26
Composite outcome of death, Q-wave myocardial infarction, or stroke	1.10 (0.75–1.62)	0.61	0.86 (0.50–1.49)	0.59	1.40 (0.88–2.22)	0.15
Target-vessel revascularization	4.76 (2.80–8.11)	<0.001	10.70 (3.80–29.90)	<0.001	5.96 (2.51–14.10)	<0.001

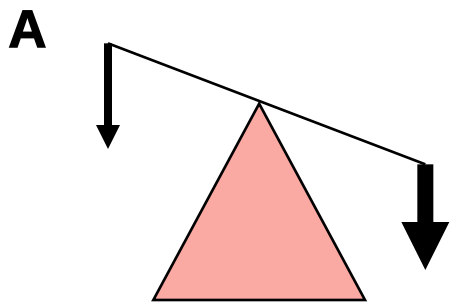
* CABG denotes coronary-artery bypass grafting. Wave 1 shows comparisons between bare-metal stents and CABG, and Wave 2 shows comparisons between drug-eluting stents and CABG. Hazard ratios are for the stenting group as compared with the CABG group.

Seung, et al. N Engl J Med 2008;358:1781-92

PCI Still Inferior but Approaching CABG Effectiveness. Why?

Baseline Risk: A Major Determinant of the Effectiveness of an Intervention !!





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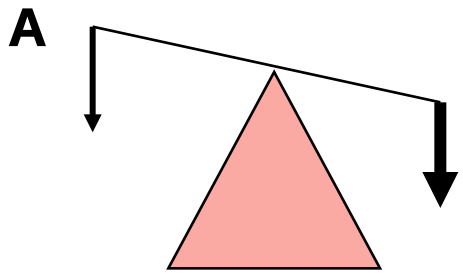

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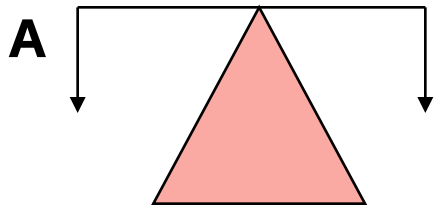
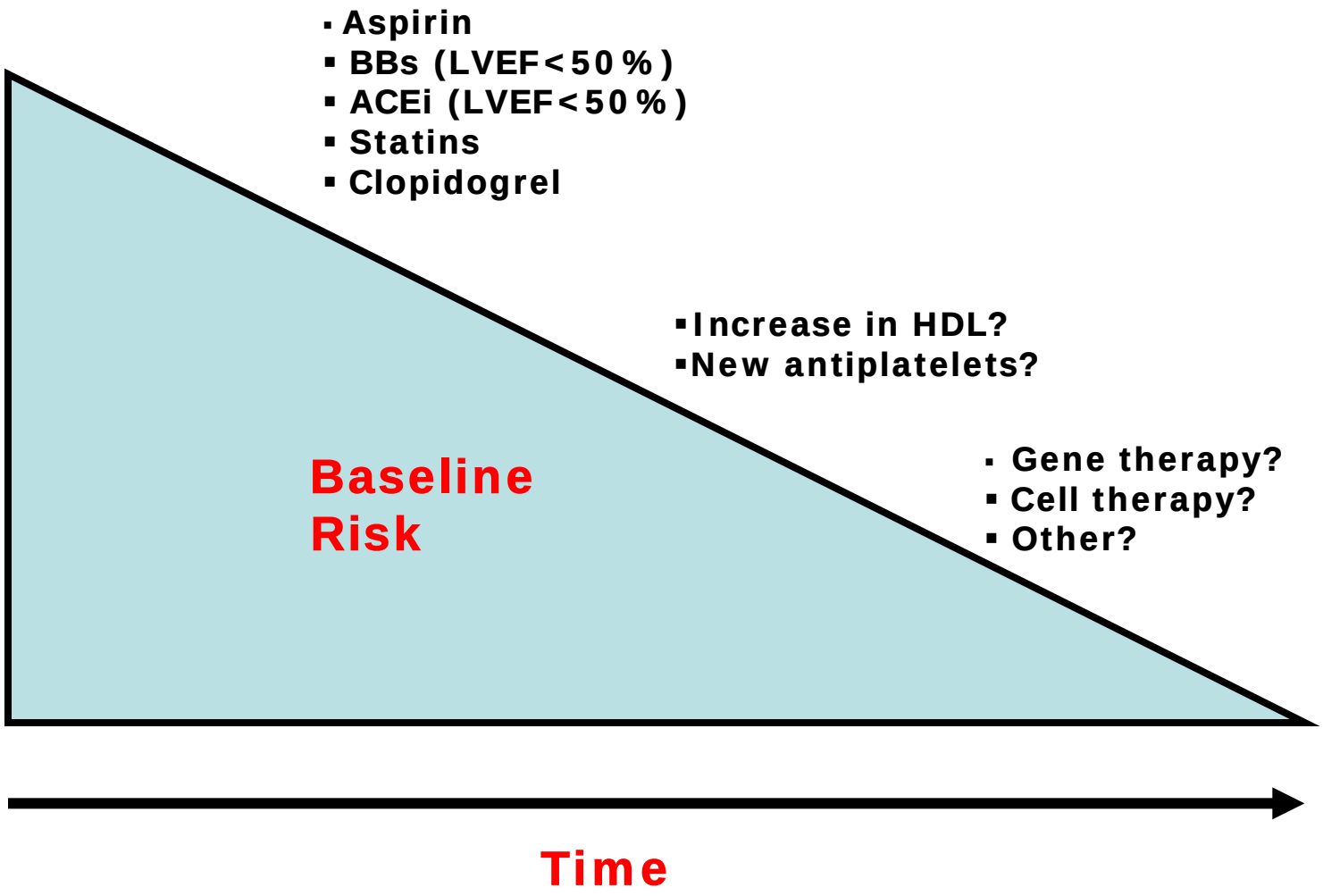


B = A

Effects of Medical Management on Baseline Risk in CAD



Symptomatic / Ischemic CAD:Prognosis

- Swedish low-dose aspirin trial (**SAPAT**; 2035 patients; median follow-up 4.2 years). ***Cardiac death rate of 0.9% per year***.
  Lancet 1992;12;340:1421-5

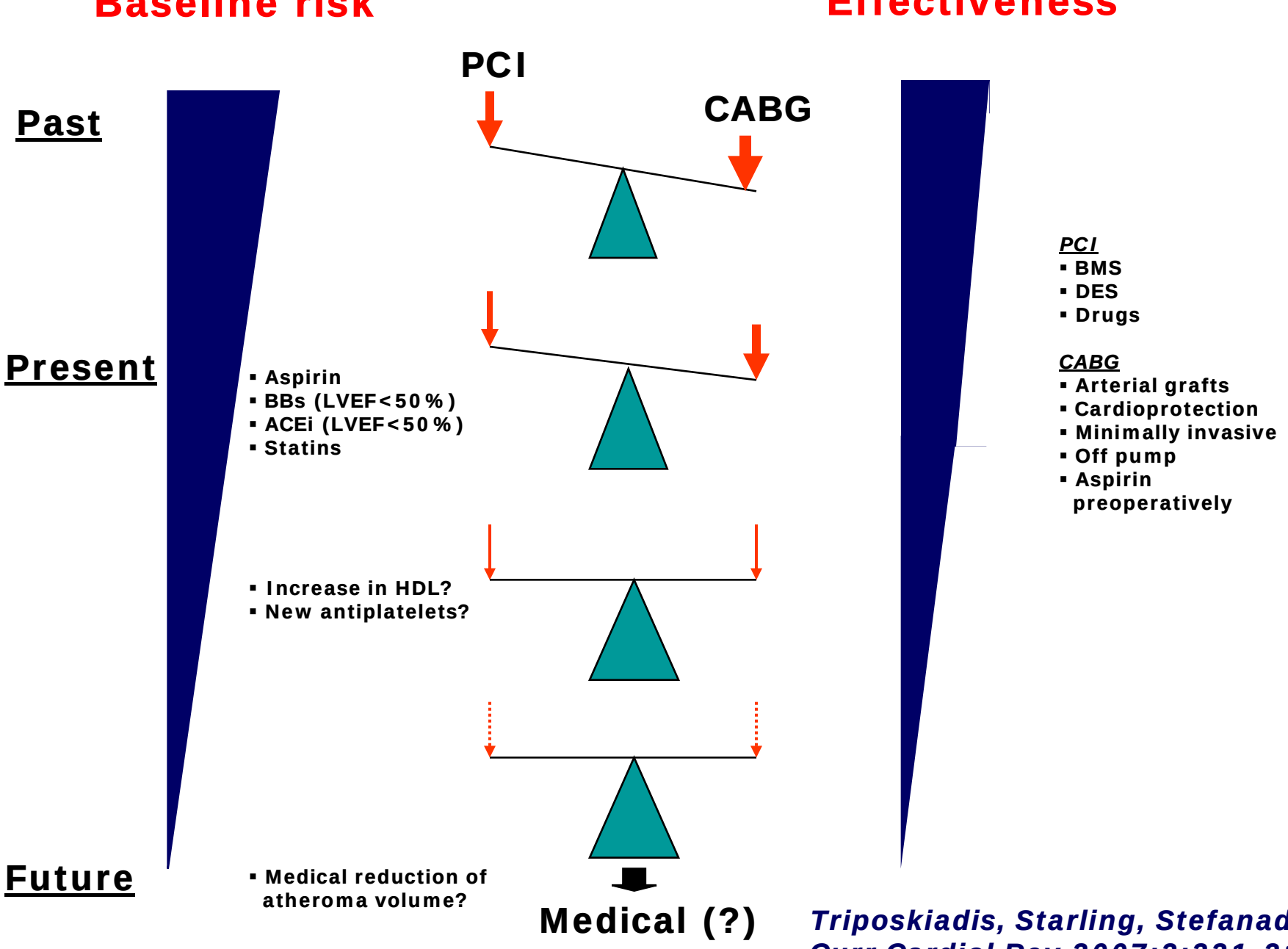
- Total Ischaemic Burden European Trial (**TIBET**; 682 patients; 2 years) ***Cardiac death rate of 1% per year among patients with a positive exercise test***.
  Eur Heart J 1996;17:96-103

- Angina Prognosis Study In Stockholm (**APSIS**;809 patients; 3.4 years) ***Cardiac death rate of 1.2% per year***.
  Eur Heart J 1996;17:76-89

- **ACTION** trial. ***Cardiovascular mortality rate of 0.9% per year.***
  Lancet 2004;364:849-57

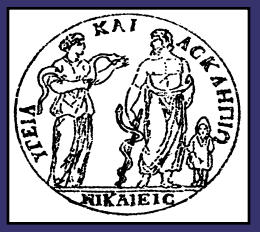
- **Jabbour, et al** (693 patients; 4.6 years) ***Cardiac death rate 0.8 per year***.
  Am J Cardiol 2004; 93: 294-99

- ***Rates of non-fatal myocardial infarction ranged from 1.0% (APSIS) to 2.6% (TIBET) per year***.



Triposkiadis, Starling, Stefanadis
Curr Cardiol Rev 2007;3:221-31

Management of Chronic Stable Angina: Lessons from the Randomized Trials



…….When revascularization is considered for the treatment of multivessel CAD, the selection of PTCA or CABG depends on the coronary anatomy, LV function, need for complete revascularization, and patient preference. In high-risk patients who have left main coronary artery disease or three-vessel coronary artery disease with impaired LV function, current data support surgical revascularization as the treatment of choice to achieve complete revascularization…….

Solomon and Gersh. Ann Intern Med 1998;128:216-223

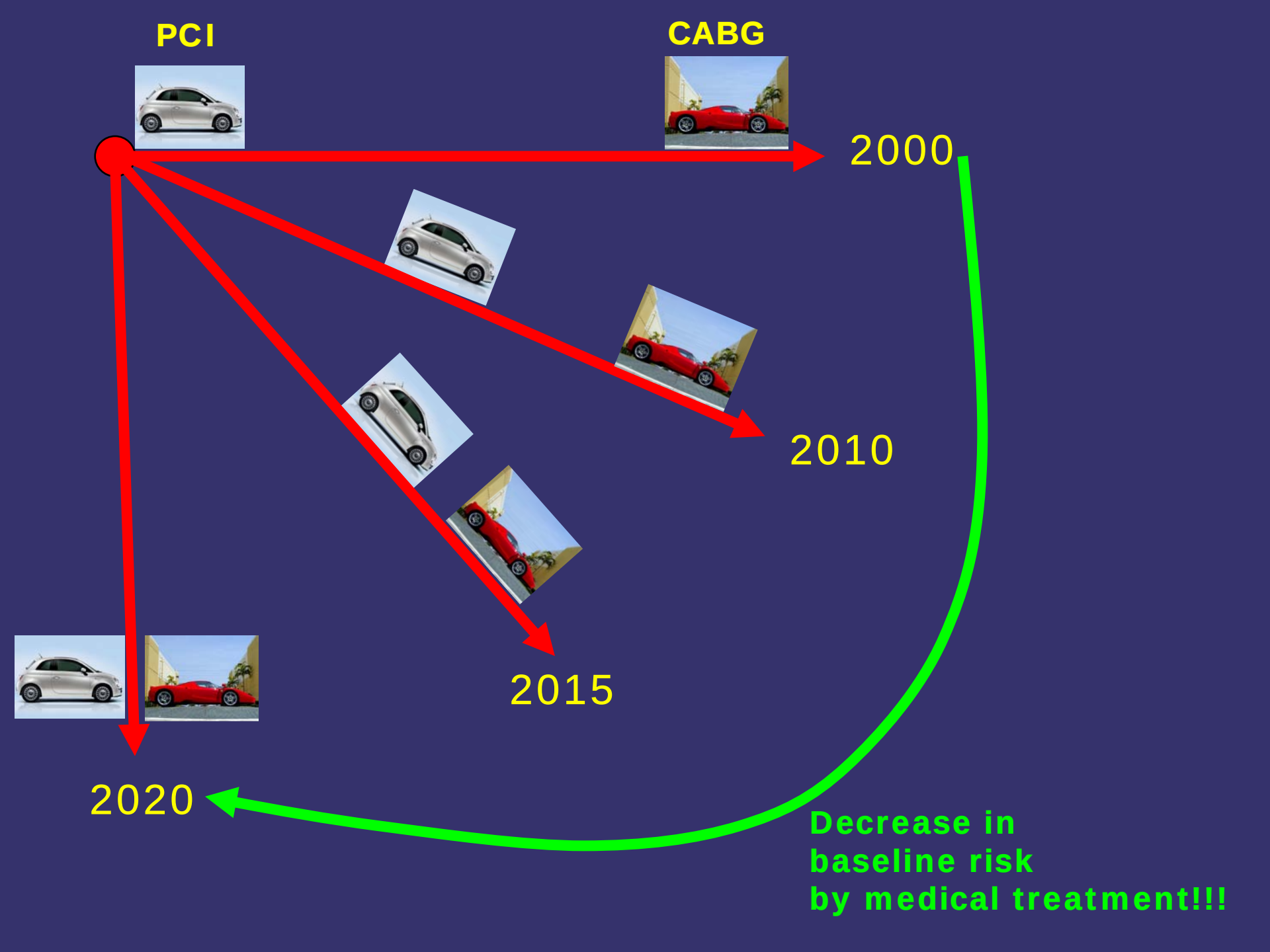
+

" It's basically up to the patient to assess the different risks."

PCI

?

CABG


PCI
CABG
2000
2010
2015
2020
Decrease in
baseline risk
by medical treatment!!!

ENDEAVOR III: Clinical events at two years

Event	Endeavor, n=313 (%)	Cypher, n=112 (%)	p
All death	1.6	4.5	0.14
Q-wave MI	0	0	—
Non-Q-wave MI	0.6	3.6	0.04
Stent thrombosis	0	0	—
TLR	7.0	4.5	0.50
MACE	9.3	11.6	0.47

Leon M. American College of Cardiology 2007 Scientific Sessions; March 24-27, 2007; New Orleans, LA.

Two-year follow-up from the **ENDEAVOR III** trial suggests that the Endeavor zotarolimus-eluting stent may be equivalent to the sirolimus-eluting Cypher stent, in terms of clinical end points. Rates of major adverse cardiac events (MACE) and target lesion revascularizations (TLR) at two years were not statistically different for the two drug-eluting stents (DES), although fewer patients randomized to the Endeavor experienced periprocedural non-Q-wave MI, a difference that was maintained over the two years of follow-up. ***HeartWireApril 4, 2007***

ENDEAVOR IV: Nine- and 12-month clinical results

End point	Endeavor (%)	Taxus (%)	p
9-mo TVF	6.6	7.2	<0.001*
12-mo TVF	7.7	9.4	0.267
9-mo TVR	5.4	4.9	0.728
12-mo TVR	6.3	6.7	0.753

Leon M. TCT 2007; October 20-25, 2007; Washington, DC.

ENDEAVOR IV: Eight-month angiographic follow-up

End point	Endeavor	Taxus	p
% diameter stenosis, in-stent	26	16	<0.001
% diameter stenosis, in-segment	32	26	0.004
Late loss, in-stent (mm)	0.67	0.42	<0.001
Late loss, in-segment (mm)	0.36	0.23	0.023

Leon M. TCT 2007; October 20-25, 2007; Washington, DC.

Endeavor vs Cypher SORT-OUT III: Efficacy and Safety End Points at Nine Months

End point	Hazard ratio (95% CI)
All-cause mortality	1.45 (0.75–2.79)
Cardiac mortality	2.17 (0.75–6.24)
MI	3.47 (1.14–10.5)
Definite stent thrombosis	4.62 (1.33–16.1)
Target lesion revascularization	4.19 (2.10–8.35)
Clinically significant restenosis	6.59 (2.57–16.9)

Lassen JF. TCT 2008; October 12-17, 2008; Washington, DC.

Endeavor vs Cypher in the Western Denmark Heart Registry

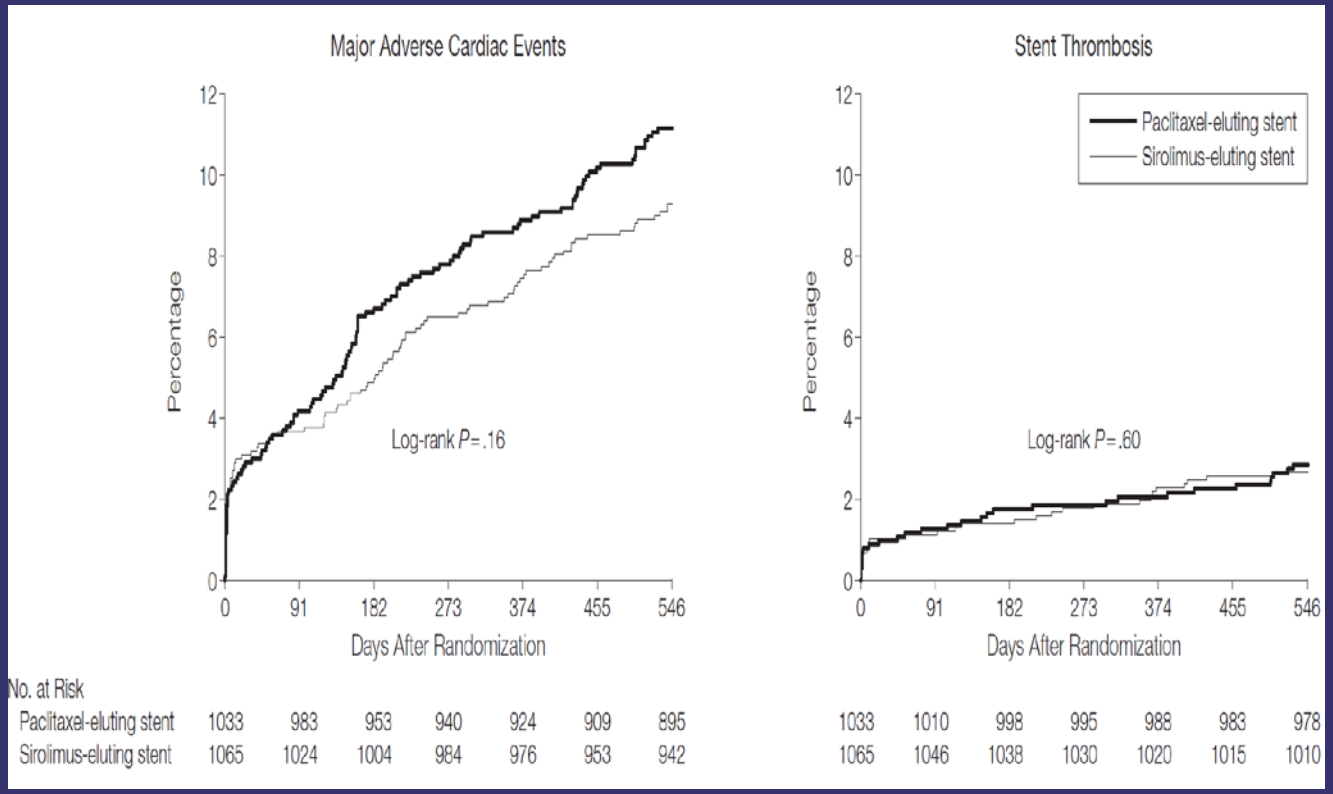
End point	Hazard ratio (95% CI)
All-cause mortality	1.34 (1.04–1.71)
Cardiac mortality	1.83 (0.99–3.41)
MI >28 days	1.01 (0.88–1.16)
Definite stent thrombosis	1.78 (1.06–3.00)
Target lesion revascularization	2.39 (1.82–3.13)
In-segment restenosis (lesion)	2.44 (1.76–3.37)

Thuesen L. TCT 2008; October 12-17, 2008; Washington, DC.

Comparison of Paclitaxel- and Sirolimus-Eluting Stents in Everyday Clinical Practice

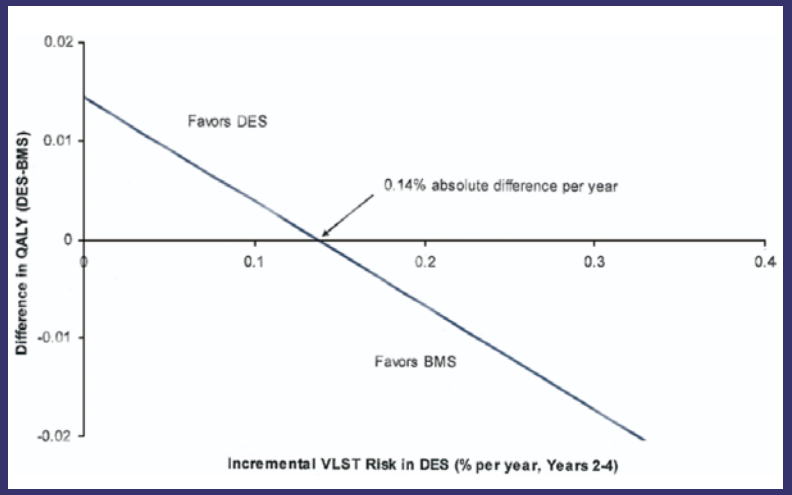
The SORT OUT II Randomized Trial

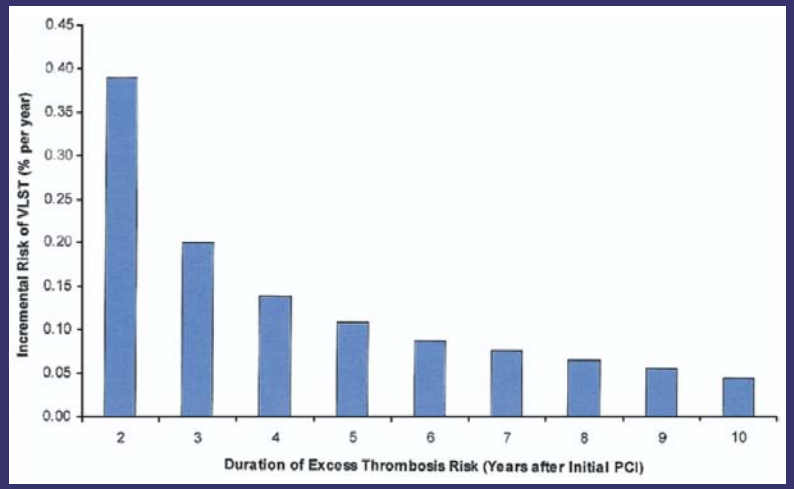
Randomized, blinded trial conducted August 2004 to January 2006 at 5 university hospitals in Denmark. Patients were 2098 men and women (mean [SD] age, 63.6 [10.8] years) treated with percutaneous coronary intervention (PCI) and randomized to receive either sirolimus-eluting (n = 1065) or paclitaxel-eluting (n = 1033) stents. Indications for PCI included ST-segment elevation myocardial infarction (STEMI), non-STEMI or unstable angina pectoris, and stable angina.

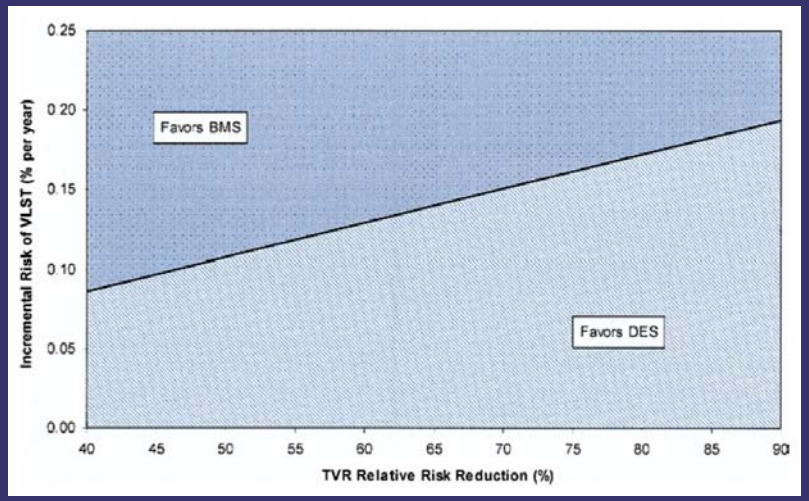


Galløe , et al. JAMA 2008;299:409-416

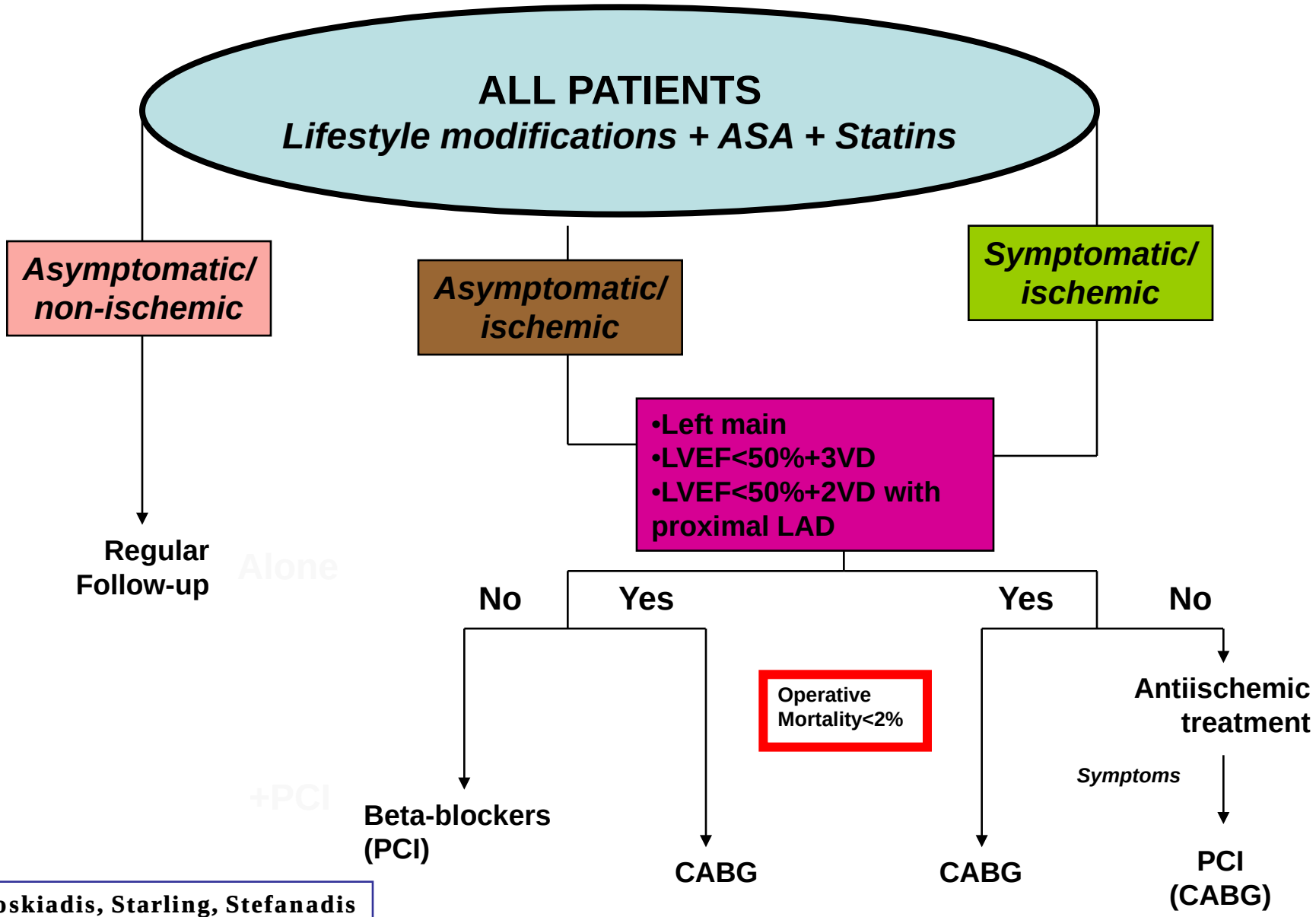
Balancing the Risks of Restenosis and Stent Thrombosis in BMS vs. DES





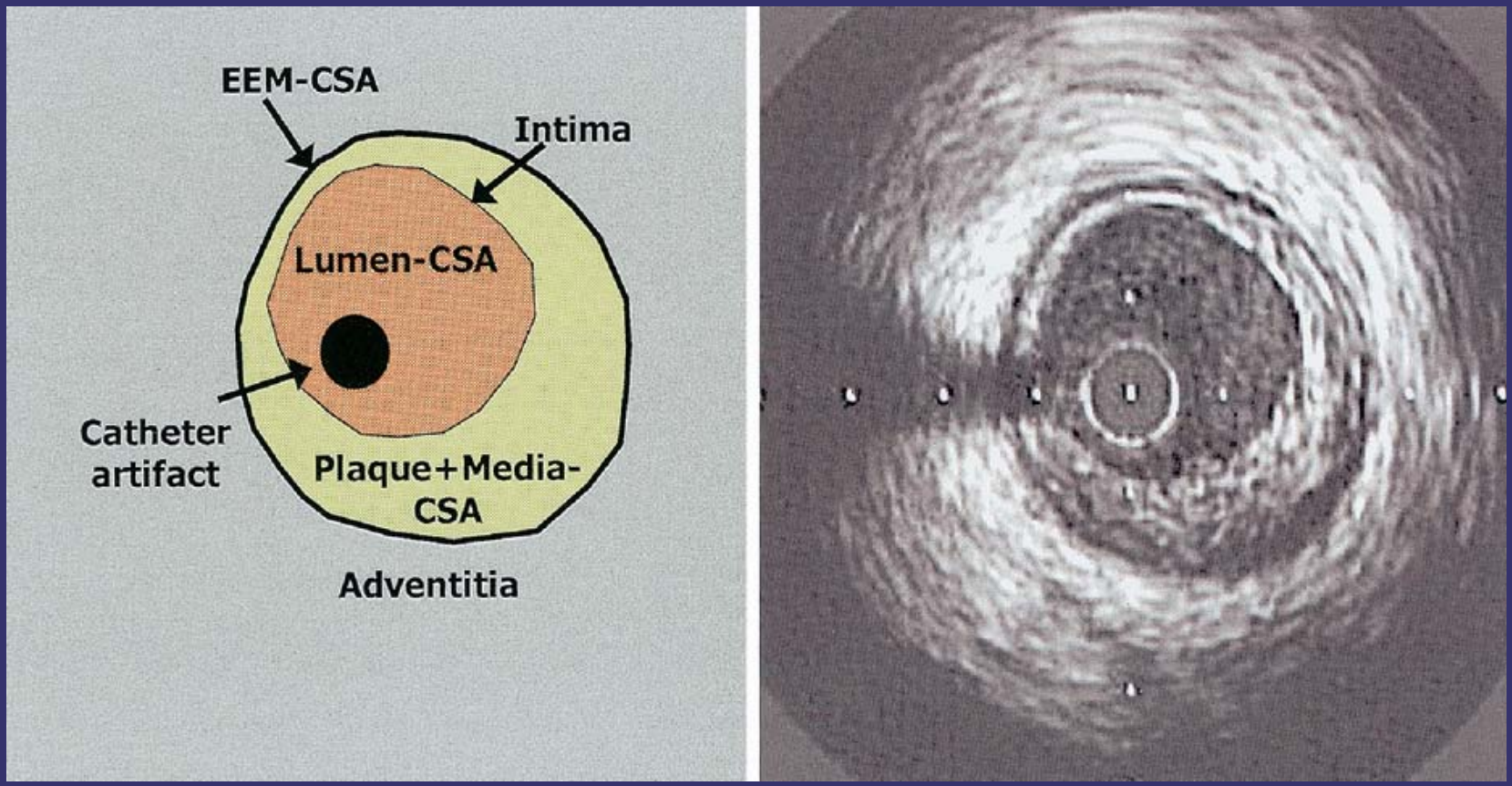


Garg, et al. JACC 2008;51:1844–53



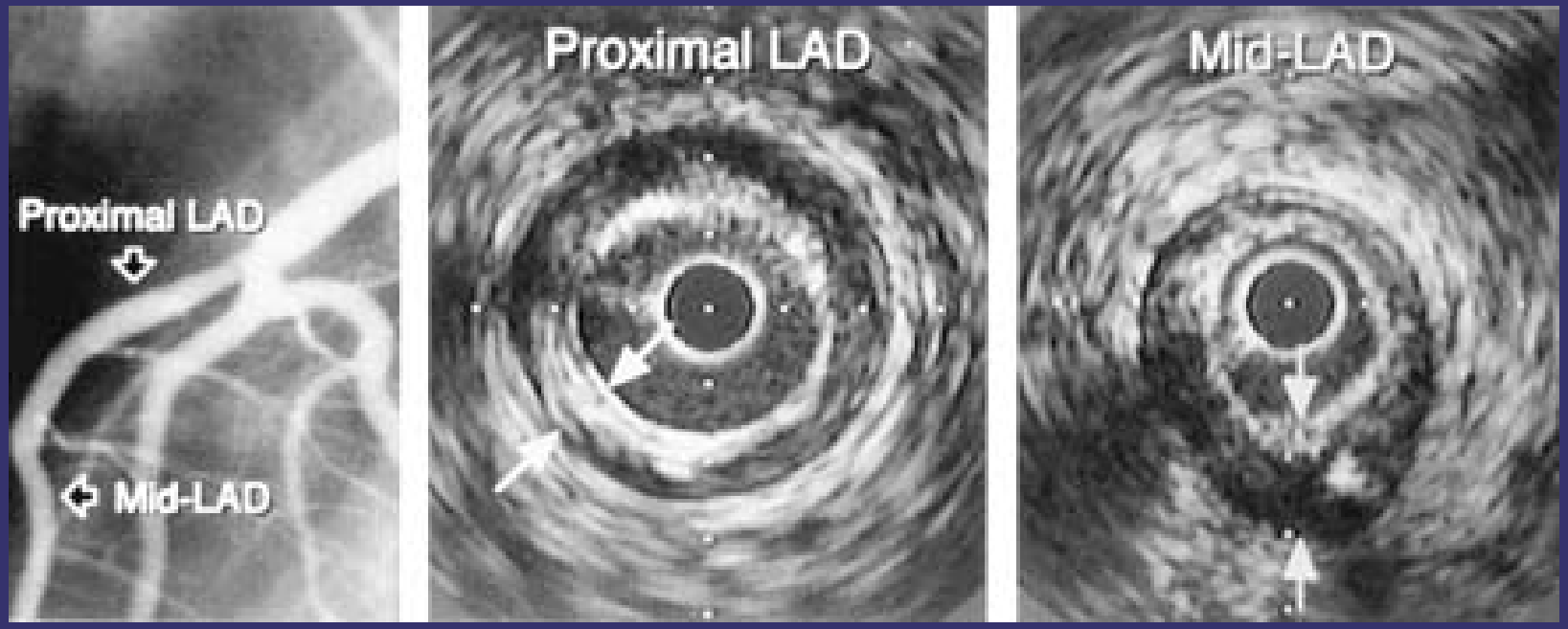
Triposkiadis, Starling, Stefanadis
Curr Cardiol Rev 2007, in press

IVUS Cross-Sectional Image of an Atherosclerotic Human Coronary Artery



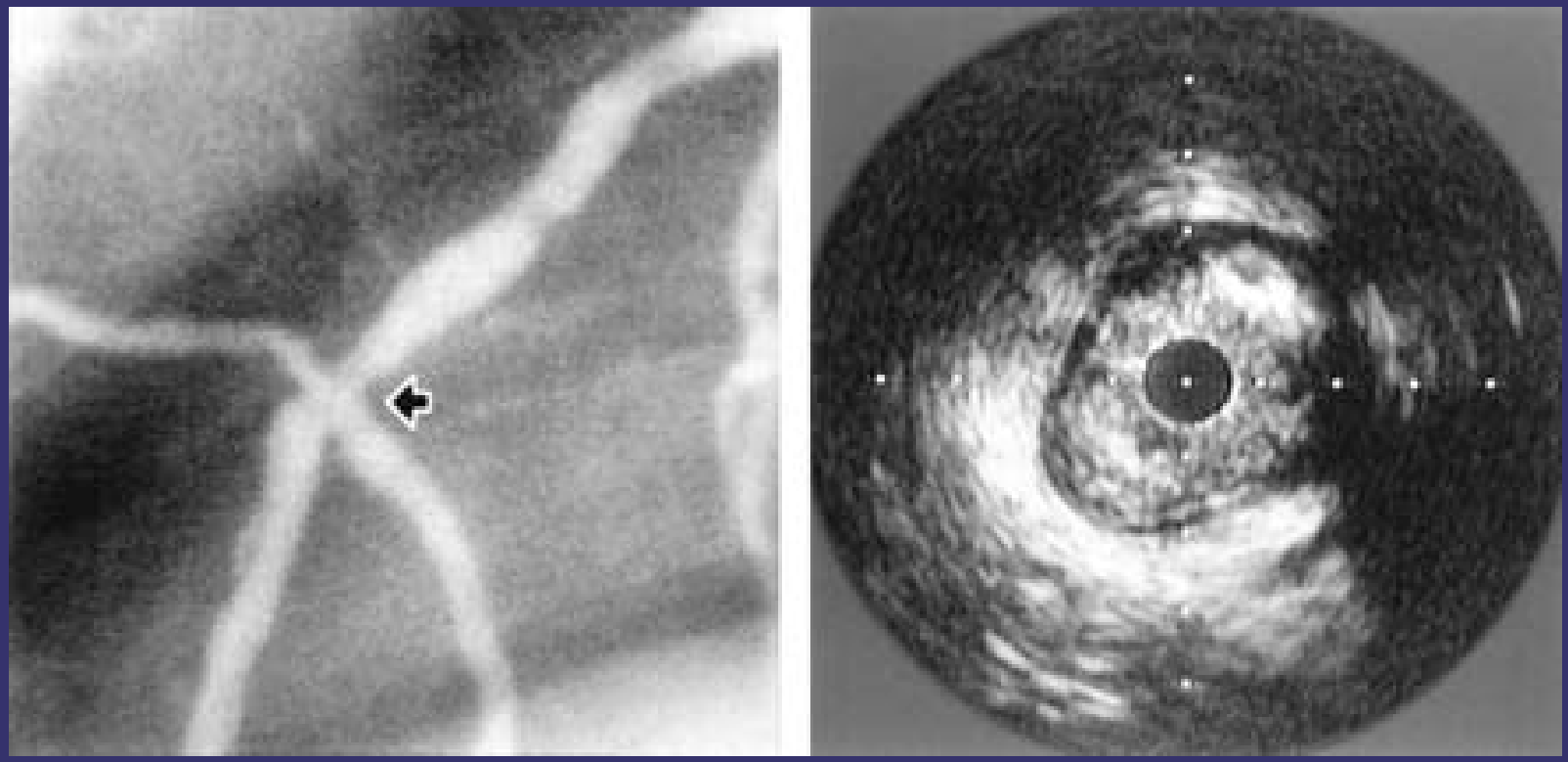
J Am Coll Cardiol 2007;49;925-932

Concealment of Severe Coronary Disease by Diffuse Concentric Involvement



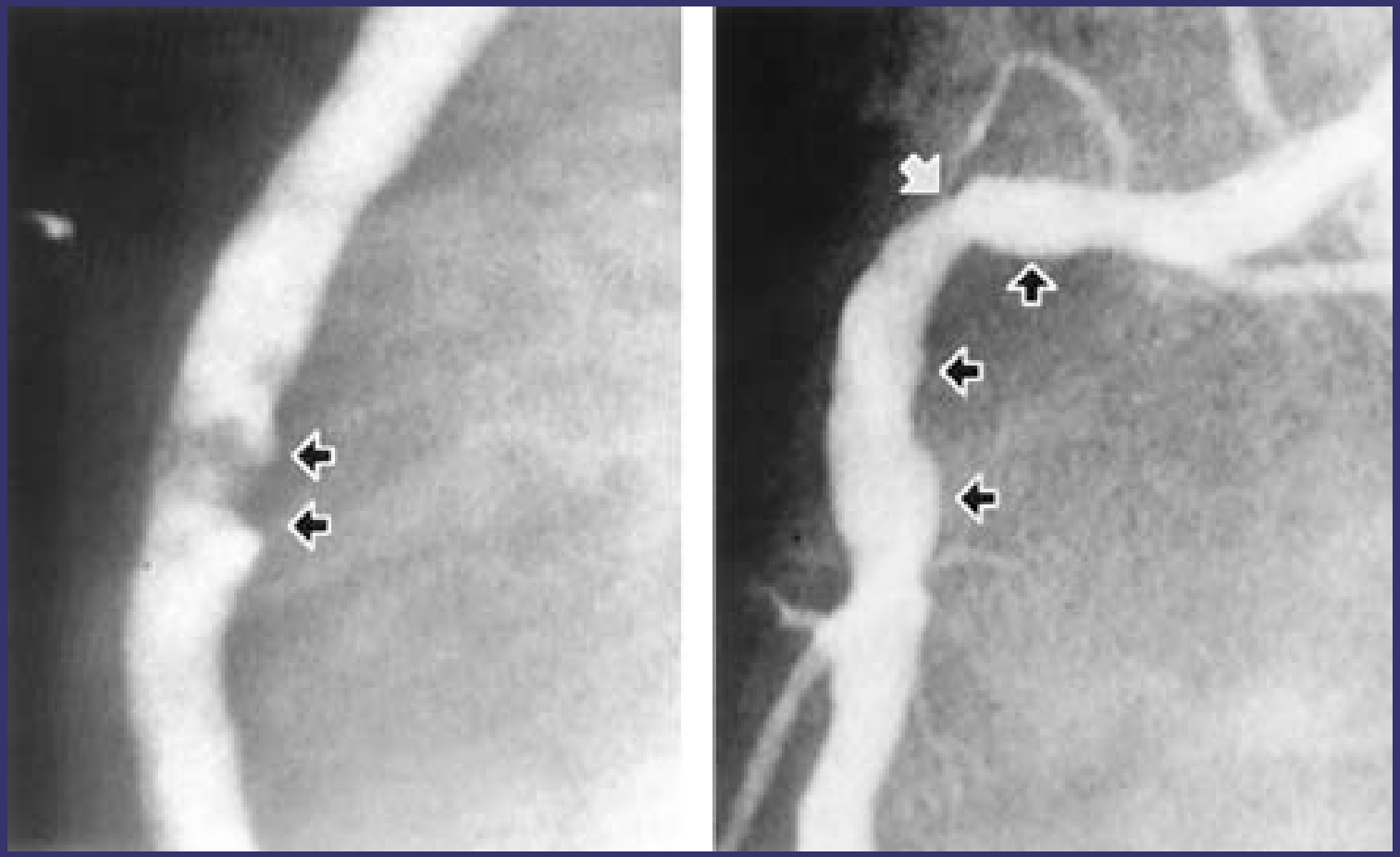
Circulation 1995;92:2333-2342

Concealment of Atherosclerosis by a Coronary Bifurcation



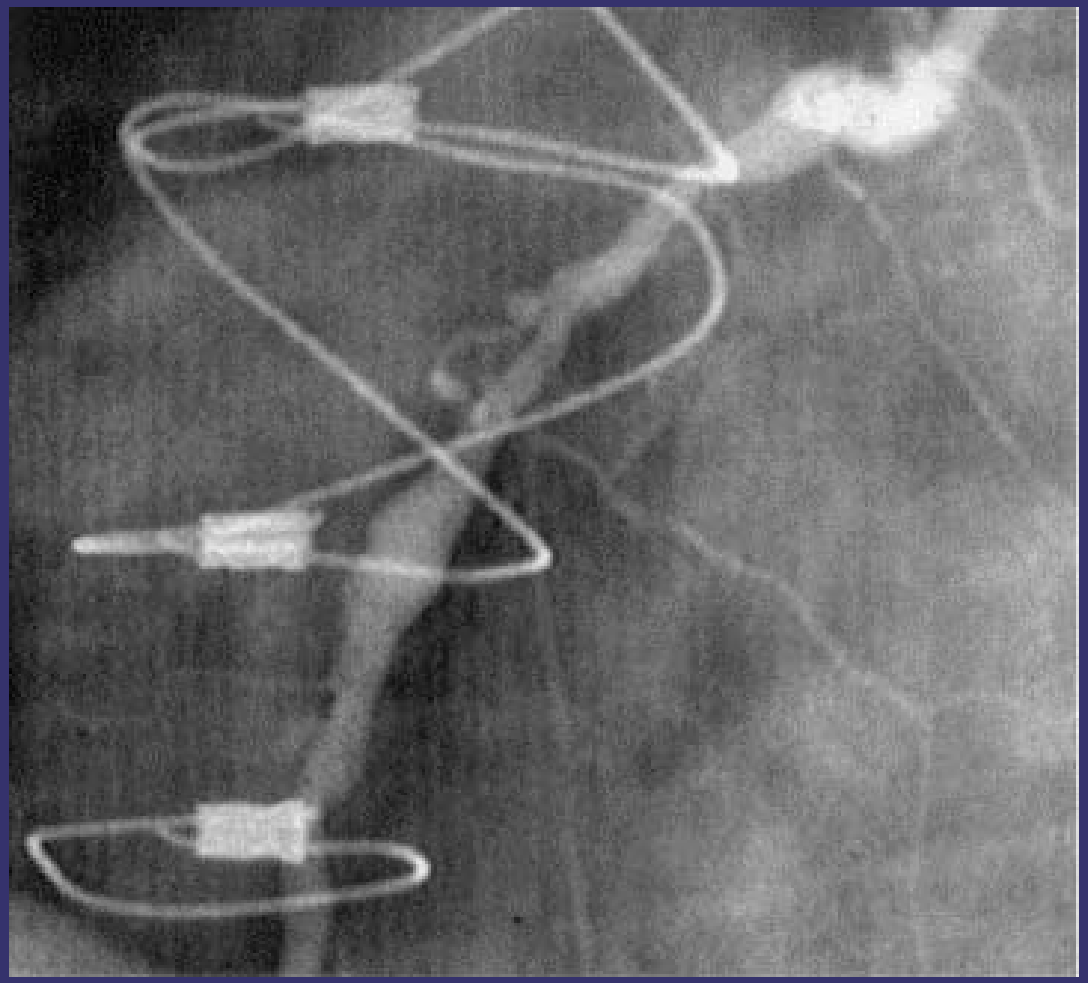
Circulation 1995;92:2333-2342

Angiograms Difficult to Evaluate by Quantitative Angiography



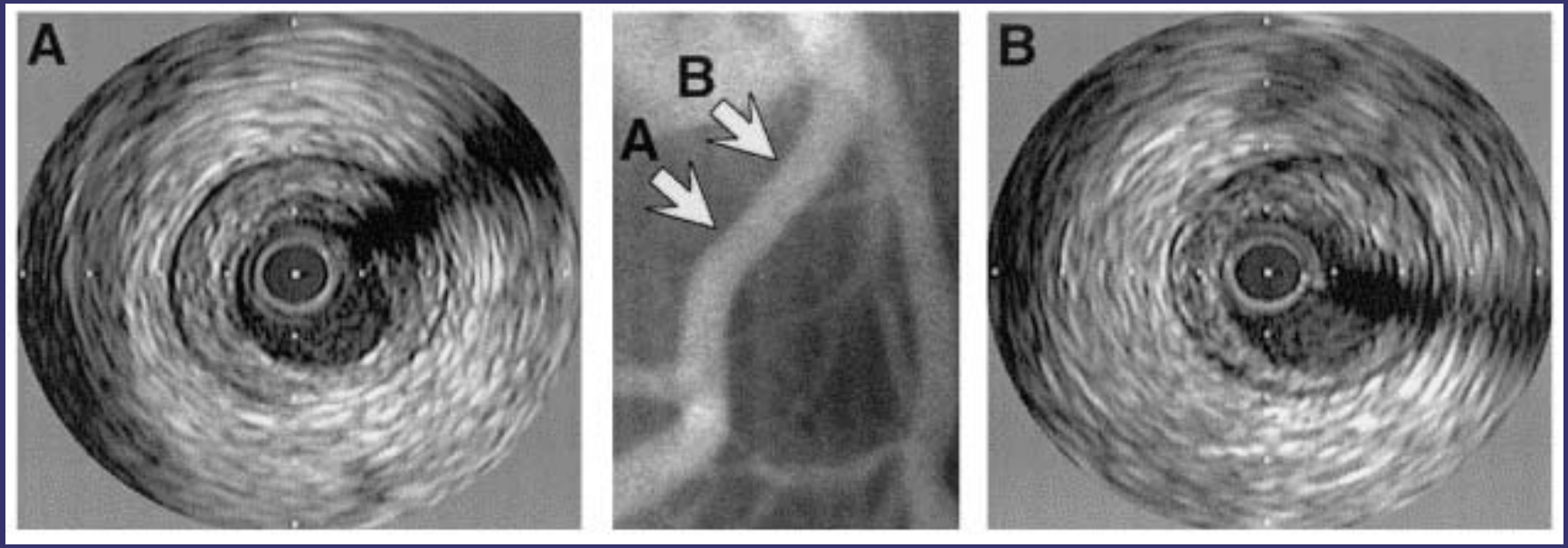
Circulation 1995;92:2333-2342

Angiogram of Complex Lesion of RCA: Which Segment is Normal?



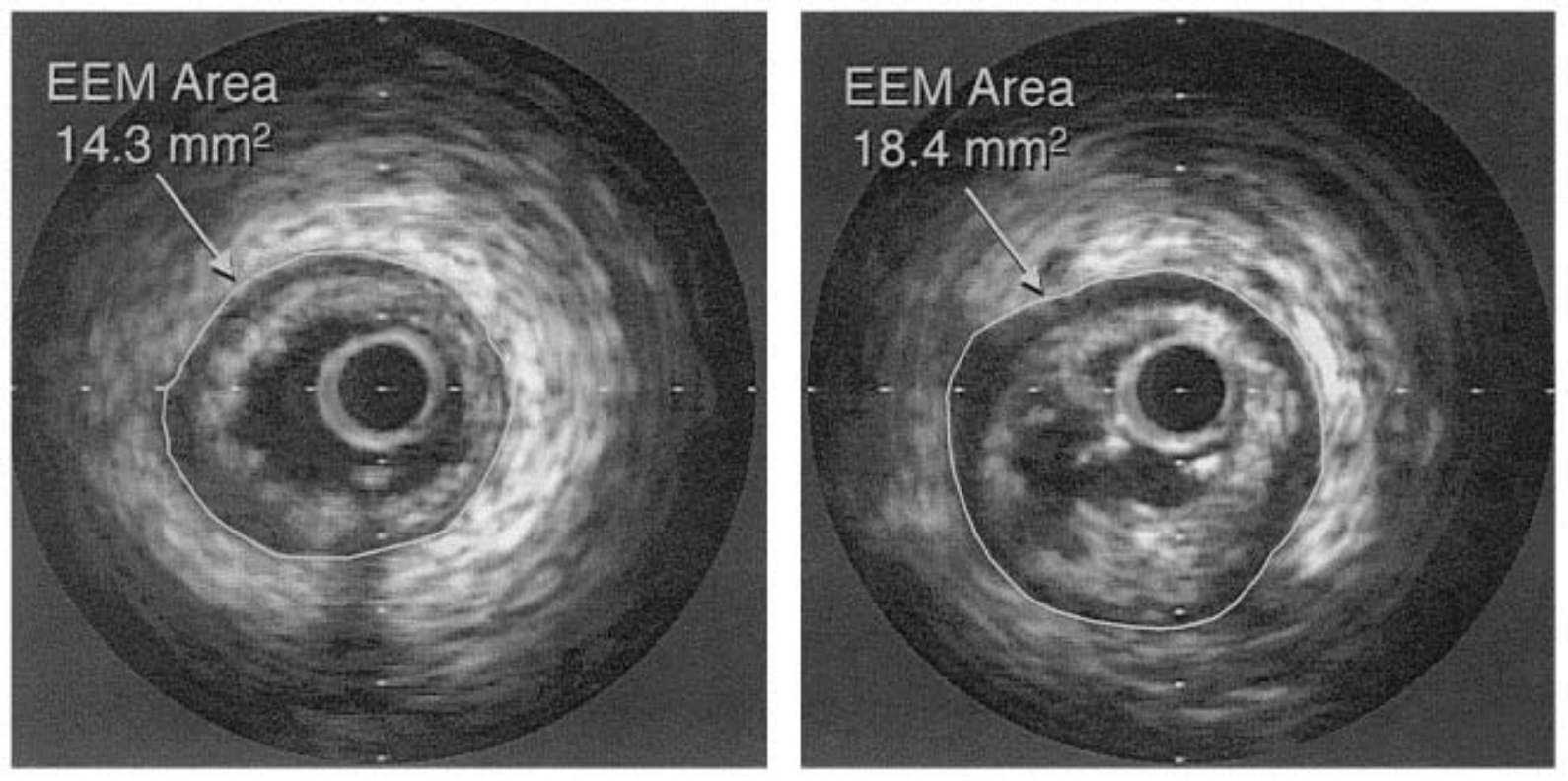
J Am Coll Cardiol 2003;41:103S–112S

Diffuse Disease Masquerading as a Normal Artery



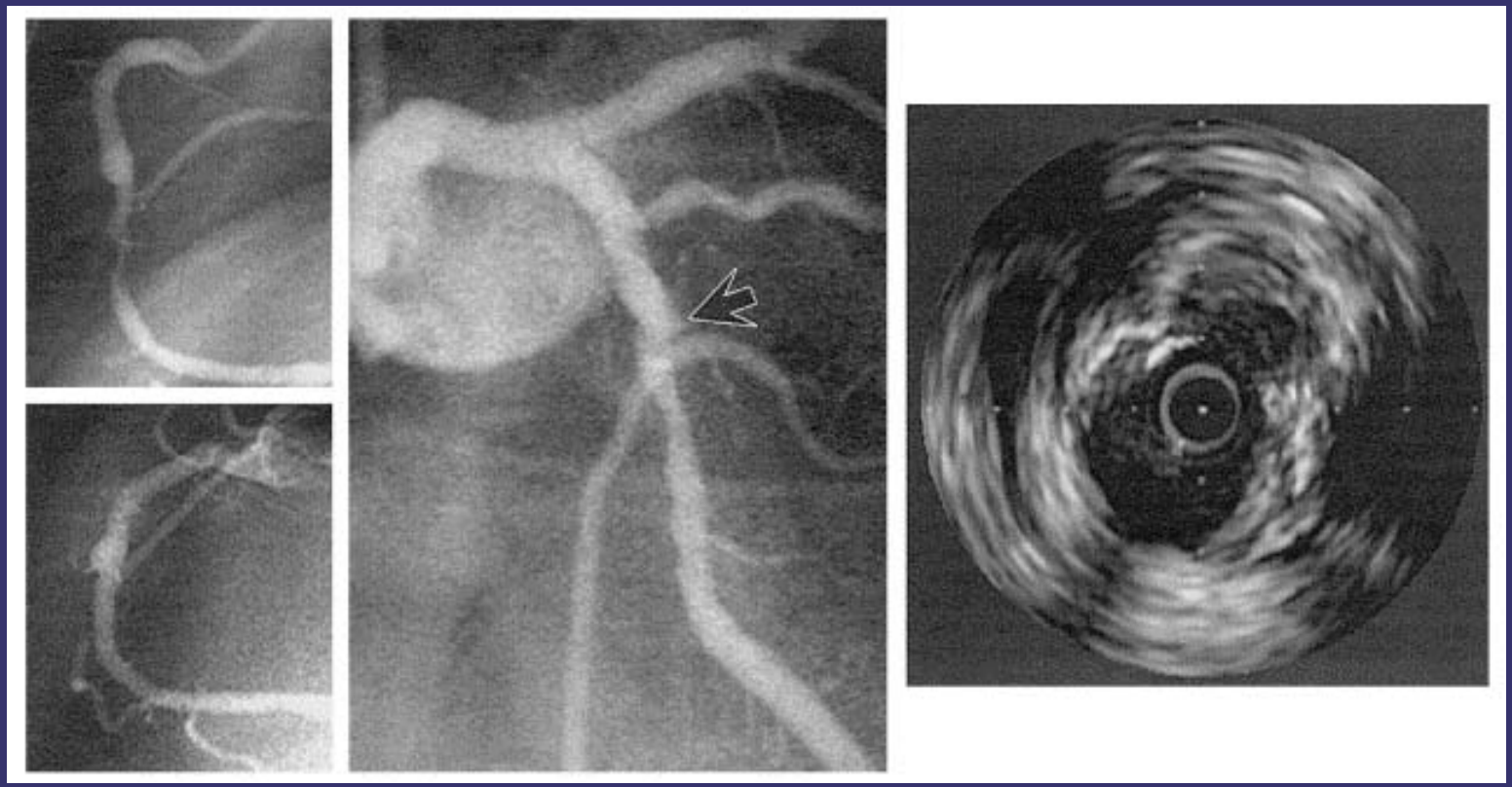
J Am Coll Cardiol 2003;41:103S–112S

Positive Remodeling in a Ruptured Plaque



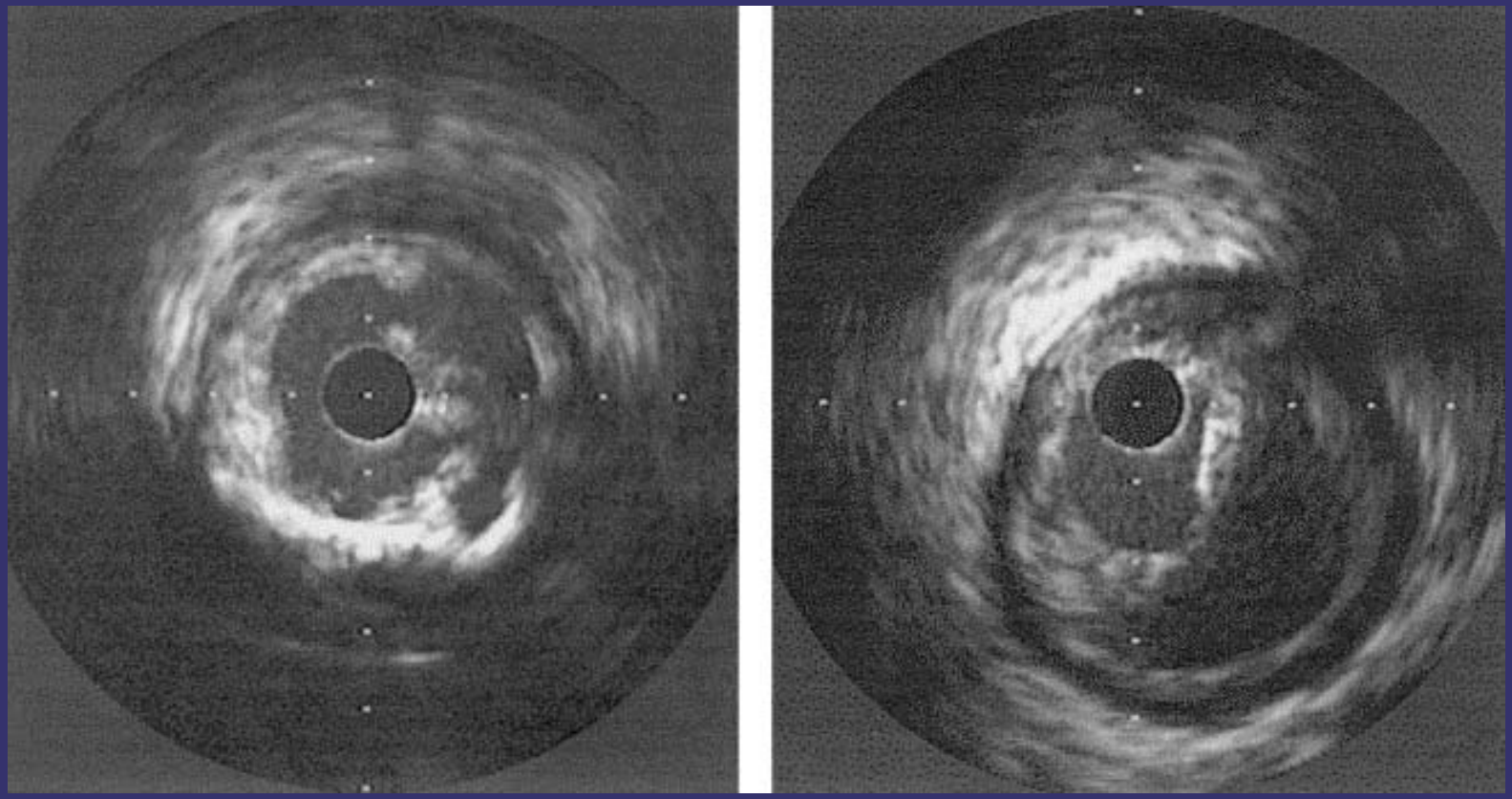
J Am Coll Cardiol 2003;41:103S–112S

The Non-Stenotic Lesion as Culprit



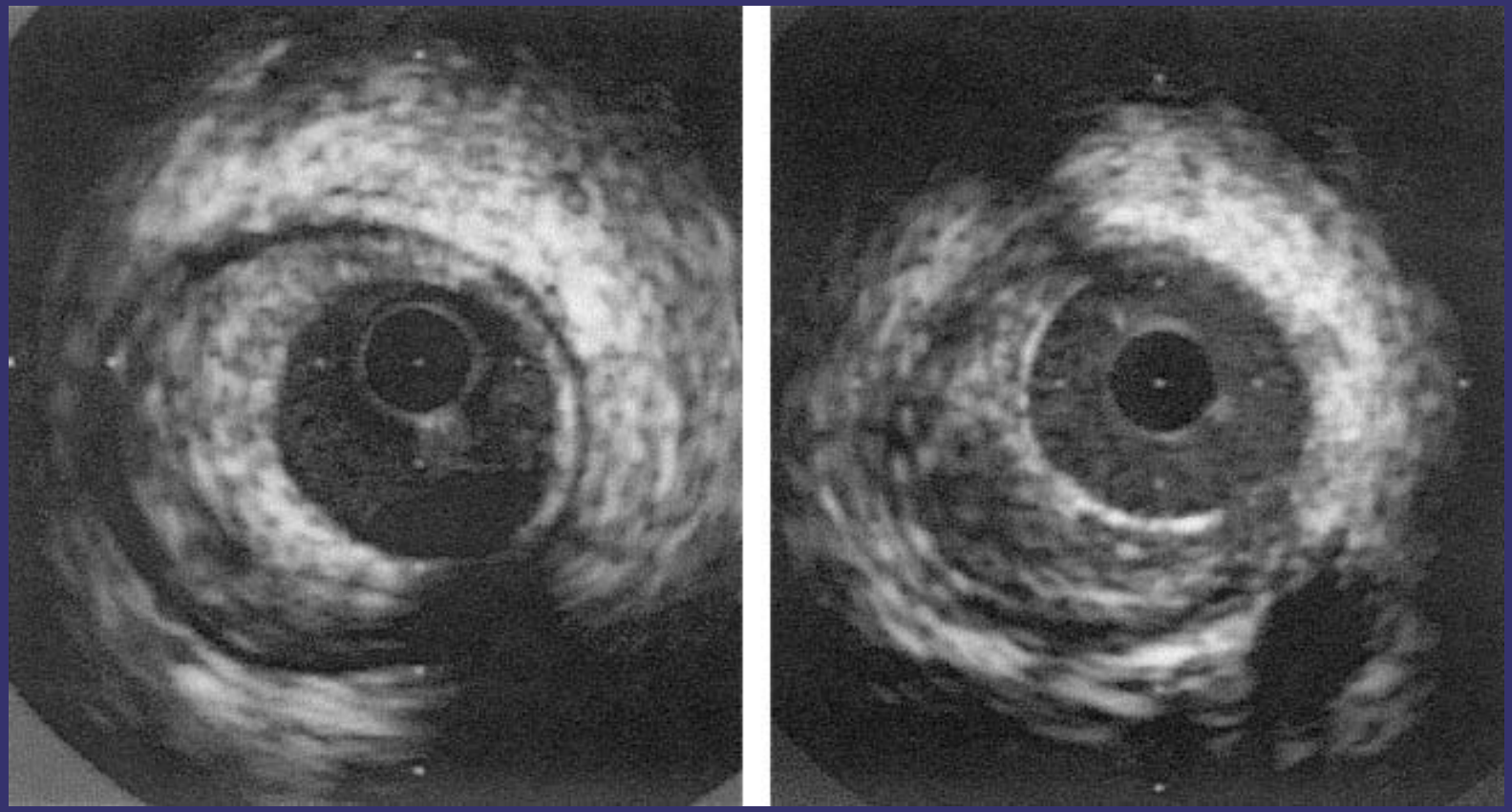
J Am Coll Cardiol 2003;41:103S–112S

Plaque Rupture by IVUS



J Am Coll Cardiol 2003;41:103S–112S

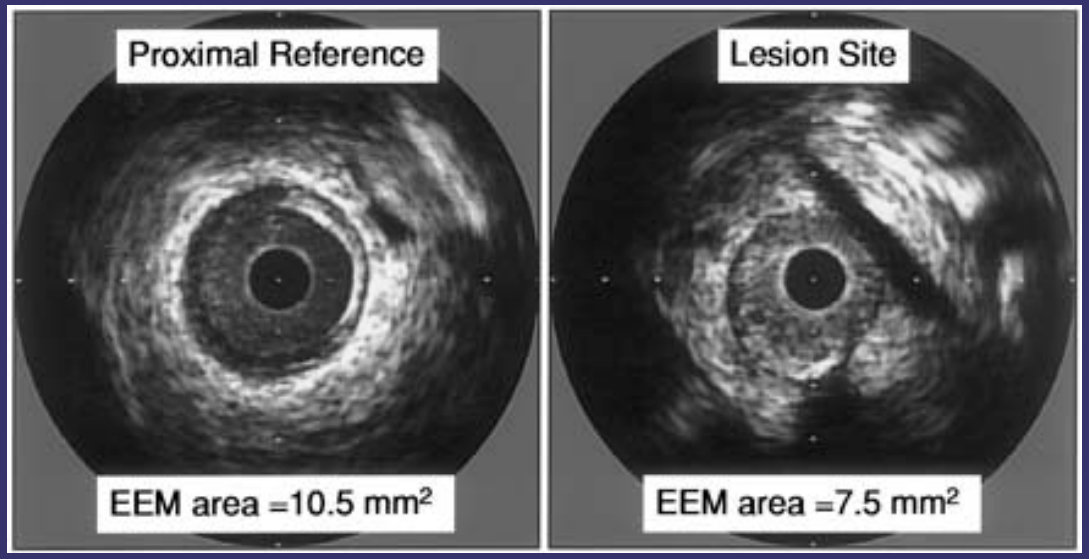
Stable and Vulnerable Coronary Atheromata



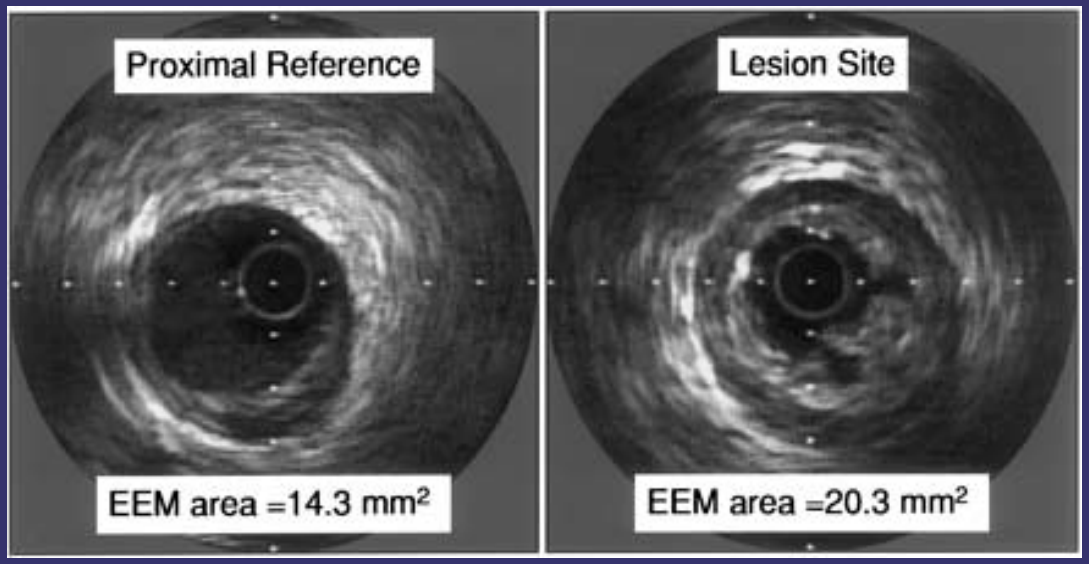
J Am Coll Cardiol 2003;41:103S–112S

Remodeling and Clinical Presentation

Stable clinical presentation



Unstable clinical presentation



Circulation 2002; 101:598-603

Narrative Review: Drug-Eluting Stents for the Management of Restenosis: A Critical Appraisal of the Evidence

Roderick Tung, MD; Sanjay Kaul, MD; George A. Diamond, MD; and Prediman K. Shah, MD

Overestimation of clinical benefit with drug-eluting stent

- Inferior performance of suboptimal thick-strut control bare metal stent (a "straw man")
- Protocol-mandated angiography bias ("oculostenotic" reflex)
- Failure of angiographic surrogate outcomes to consistently translate into clinical benefit
- Attenuation of restenosis benefit in high-risk cohorts

Underestimation of costs of drug-eluting stent

- High cost of drug-eluting stent (3- to 4-fold higher than that of bare metal stent)
- Underestimation of stent utilization rates in clinical trials compared with clinical practice
- Overestimation of restenosis benefit with drug-eluting stent in clinical trials
- Underestimation of duration and cost of antiplatelet therapy in clinical trials

Underestimation of risk for stent thrombosis with drug-eluting stent

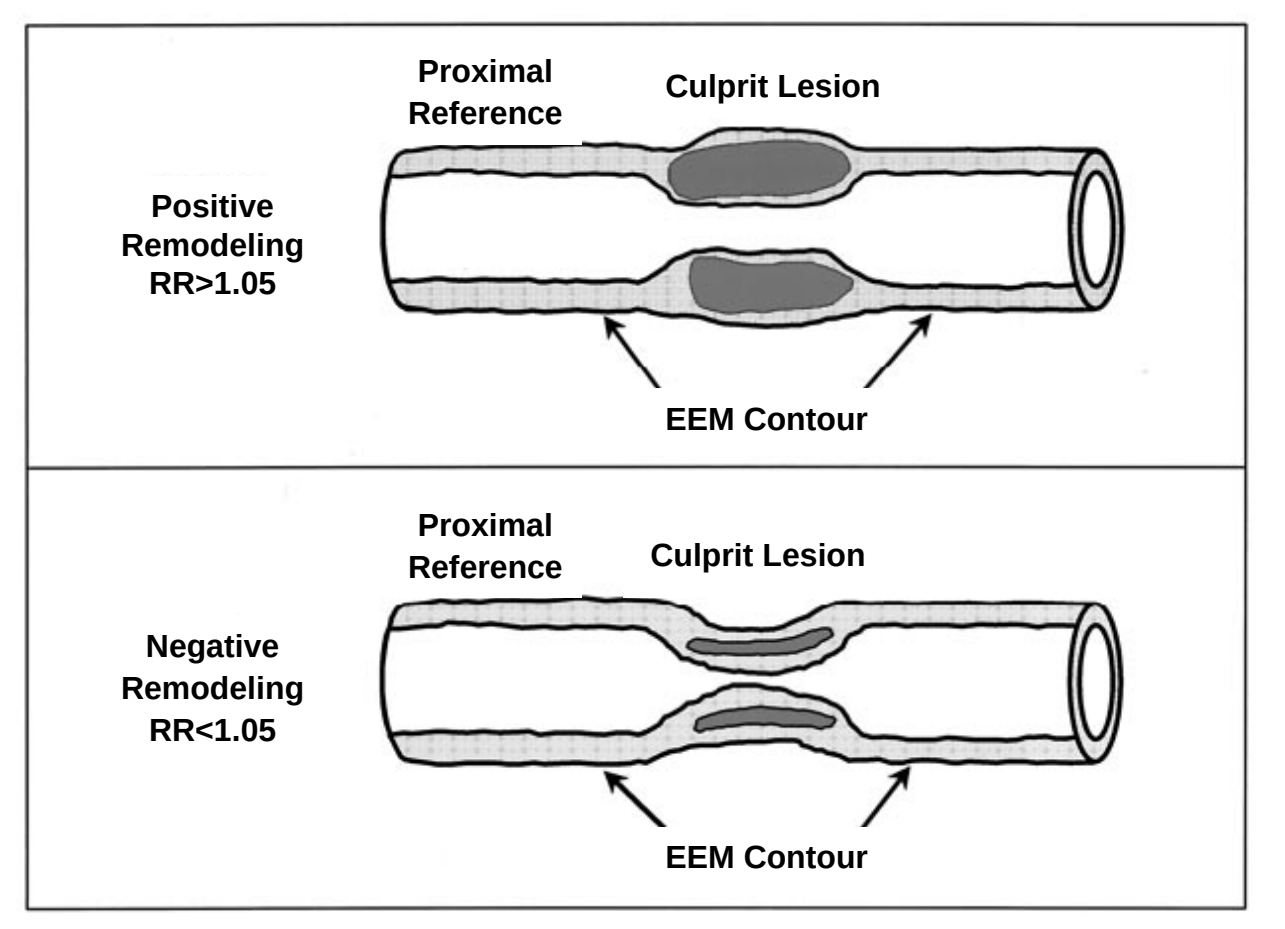
- Increased risk for stent thrombosis in current clinical practice settings (2- to 3-fold more than that in clinical trial data)
- Unacceptably high complication rate of death or myocardial infarction associated with stent thrombosis (approximately 50%)
- Prolonged dual antiplatelet therapy required for preventing stent thrombosis
- Optimal time of interruption of antiplatelet therapy or type of short-term "bridging" therapy during elective procedures unknown

Overreliance on "soft" rather than "hard" outcomes

- Benefit driven primarily by "soft" outcome of target vessel revascularization (the most prevalent component of the composite end point)
- Numeric trends in wrong or neutral direction in "hard" outcomes of death or myocardial infarction
- Questionable validity of composite end point (dissimilar clinical importance, frequency, and therapeutic responsiveness of the individual components)
- No statistically significant difference in weighted end point analysis

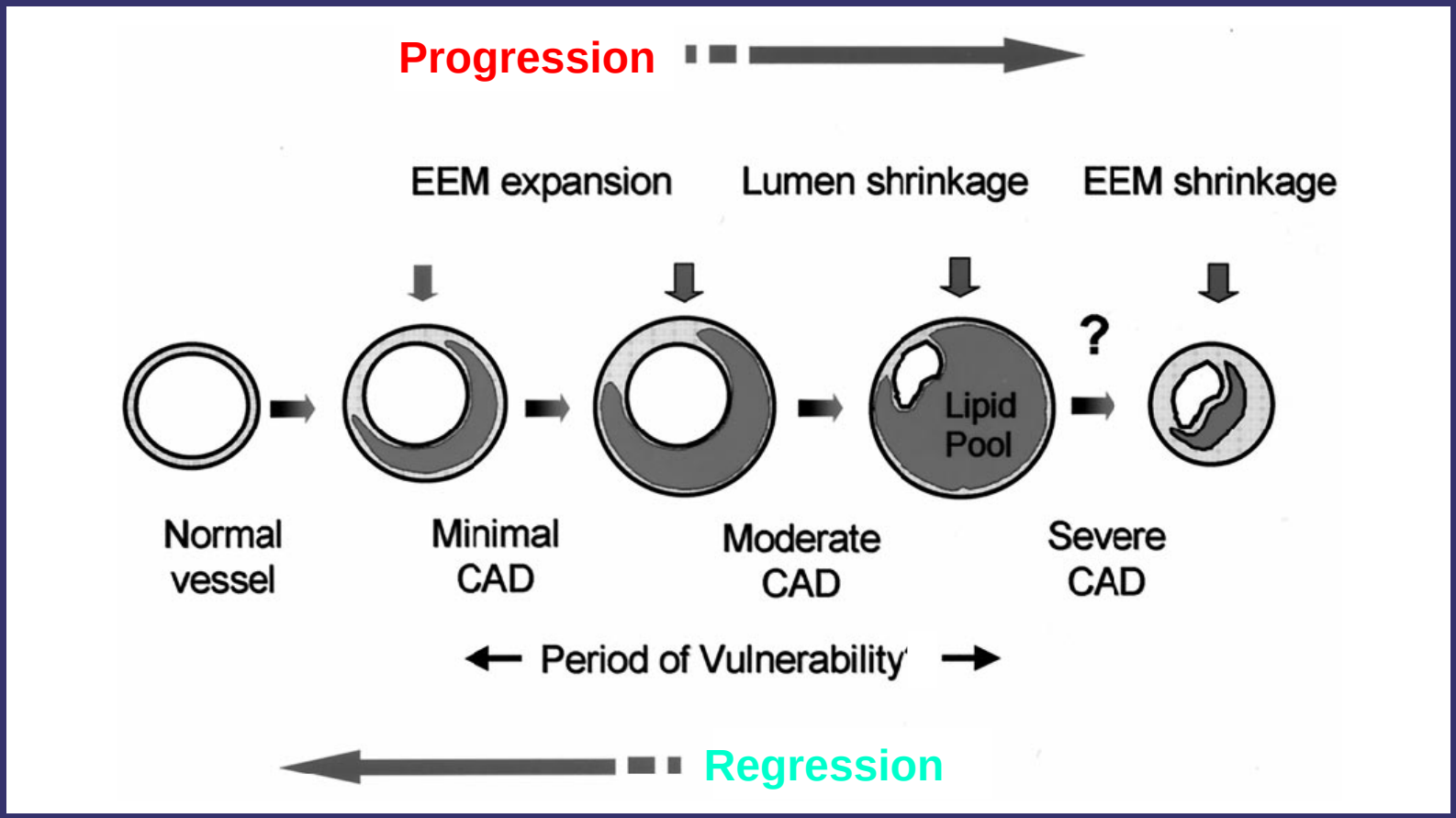
Ann Intern Med 2006;144:913-919

Positive and Negative Arterial Remodeling



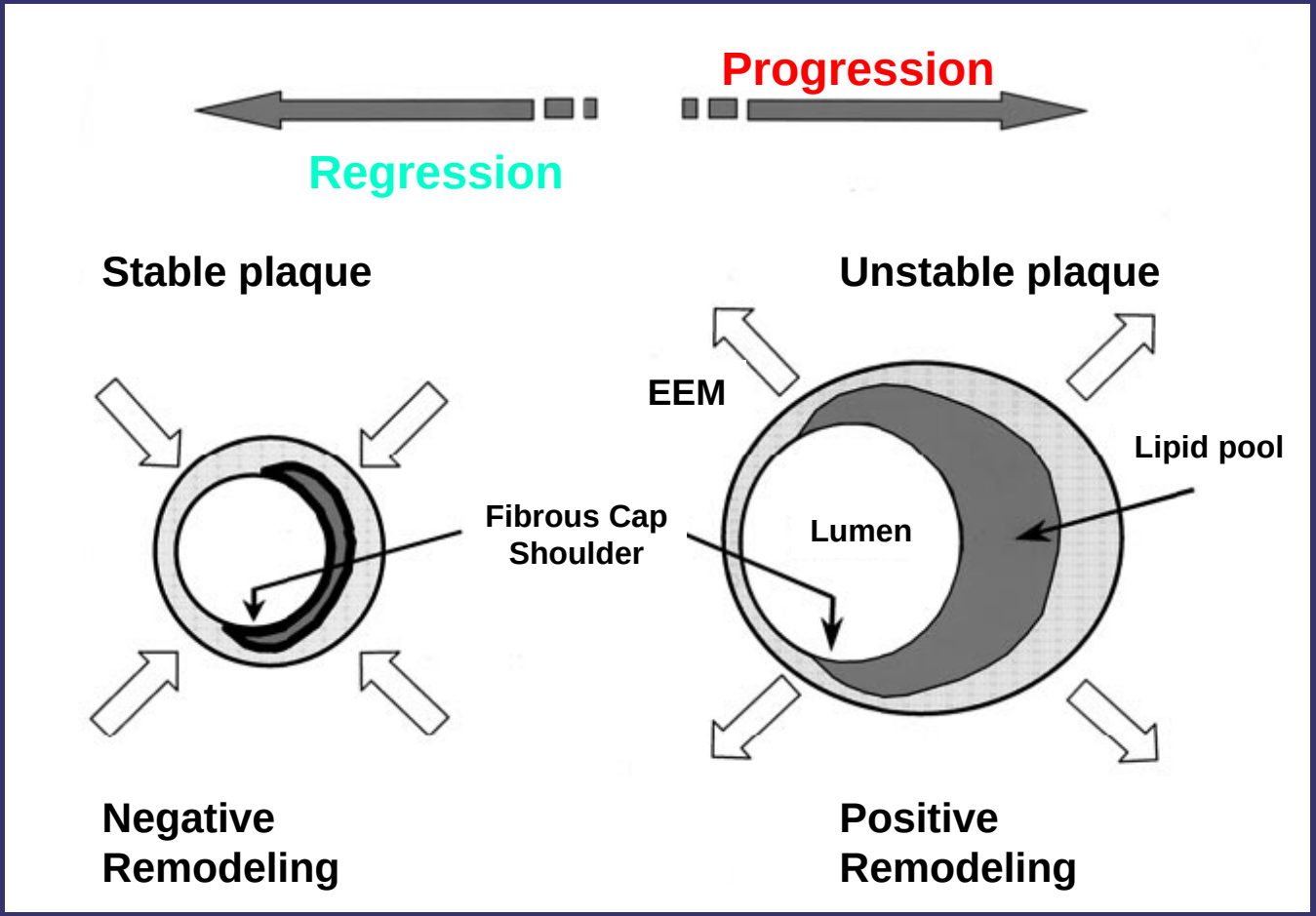
J Am Coll Cardiol 2001;38;297-306

Plaque Accumulation in Coronary Arteries is Associated with Compensatory Changes in Vessel Size



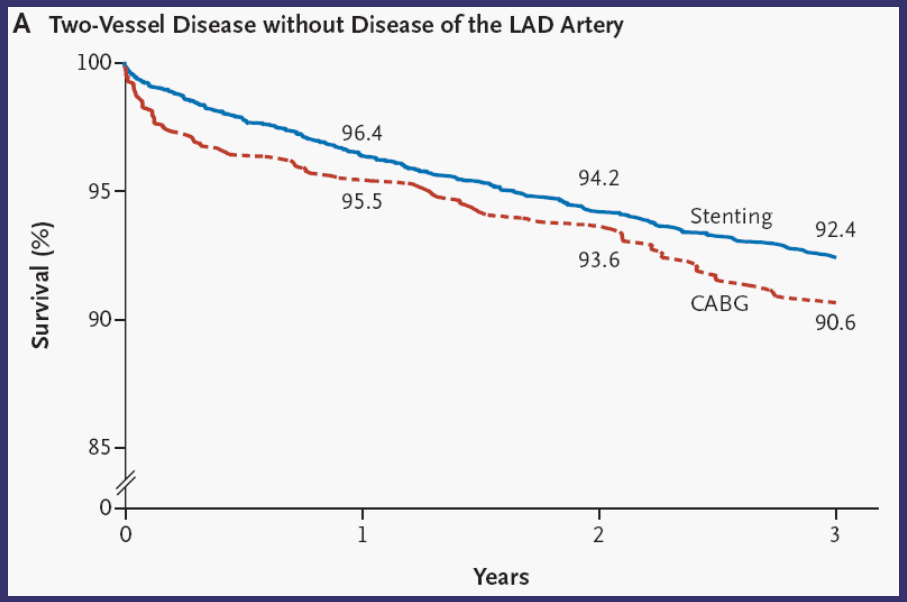
J Am Coll Cardiol 2001;38;297-306

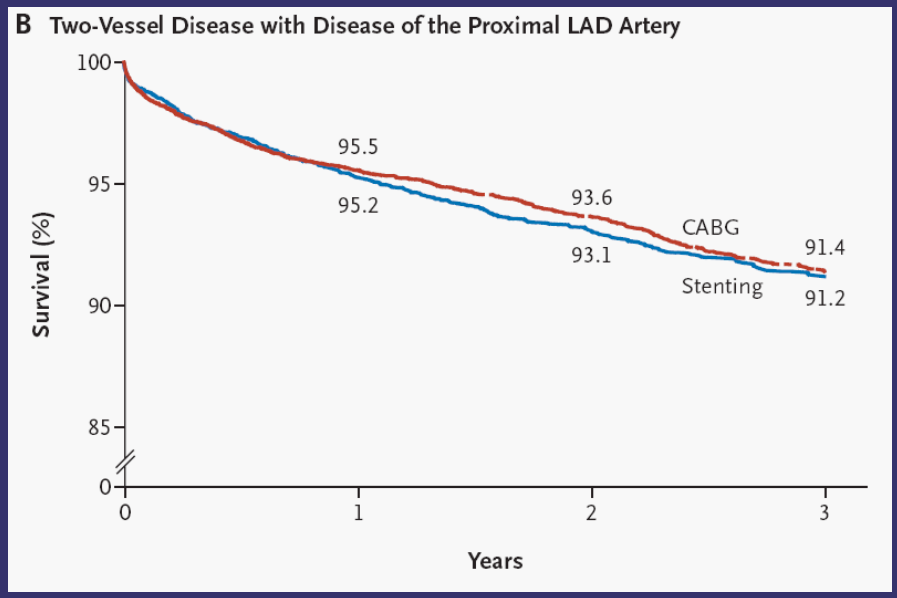
Direction of Remodeling and Temporal Development of Plaques

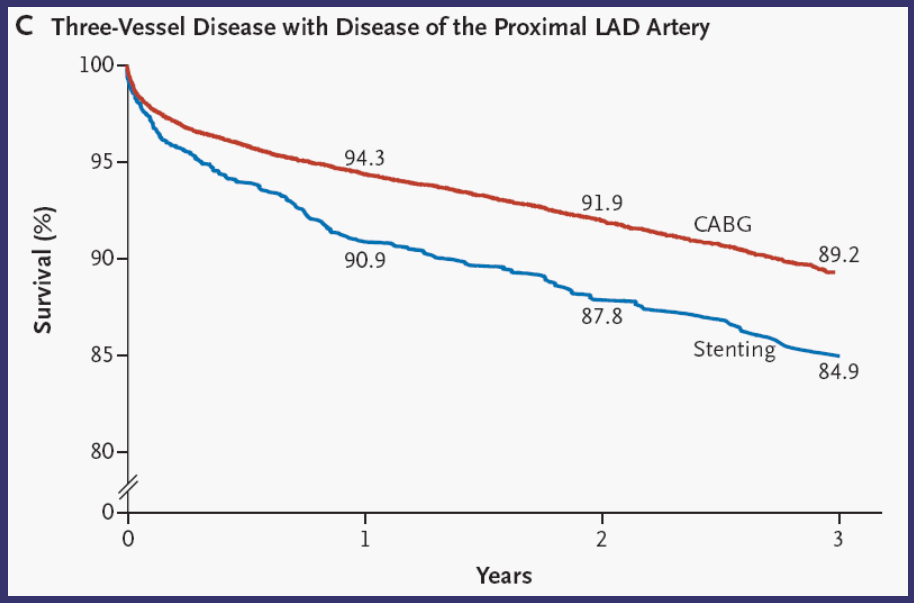


J Am Coll Cardiol 2001;38;297-306

New York Registries







N Engl J Med 2005;352:2174-83

Beyond Restenosis

Five-Year Clinical Outcomes From Second-Generation Coronary Stent Trials

Donald E. Cutlip, MD; Amit G. Chhabra, MBBS, MPH; Donald S. Baim, MD; Manish S. Chauhan, MD; Sachin Marulkar, MBBS, MPH; Joseph Massaro, PhD; Ameet Bakhai, MD; David J. Cohen, MD, MSc; Richard E. Kuntz, MD, MSc; Kalon K.L. Ho, MD, MSc

Background—In the first year after coronary stent implantation, clinical failures are driven mainly by procedural complications and restenosis, but the subsequent relative contributions of restenosis and disease progression to late failures are less clear.

Methods and Results—We observed 1228 patients for 5 years after the implantation of stents as part of pivotal second-generation coronary stent trials. Clinical events of death, myocardial infarction, repeat revascularization, and repeat hospitalization for acute coronary syndrome or congestive heart failure were attributed to the index stented (target) lesion or other distinct sites (either in the target or other coronary vessels) and further classified as procedural, restenosis, or nonrestenosis. During the first year the hazard rate was 18.3% for target-lesion events and 12.4% for events unrelated to the target lesion. After the first year the average annual hazard rate was 1.7% for target-lesion events and 6.3% for nontarget-lesion events. By the fifth year, restenosis events occurred in 20.3% of patients, whereas 30-day procedural complications or later nonrestenosis events occurred in 37.9%, including 11.4% who also experienced a restenosis event, for a combined cumulative event rate of 46.4%. Diabetes mellitus and multivessel disease were independently associated with increased risk for both restenosis and nonrestenosis events.

Conclusion—In a low-risk clinical trial population, the clinical outcome beyond 1 year after stenting is determined by a high rate of events related to disease progression in segments other than the stented lesion, which itself remains relatively stable. (***Circulation***. 2004;110:1226-1230.)

	Year 1		Years 2–5			
End Point	Failures	HR	Failures	HR	Average Annualized HR	Cumulative Failures, n (%)
Composite	321	26.1	221	25.3	7.2	542 (46.4)
All-cause death	11	0.9	78	6.9	1.9	89 (8.2)
Cardiac death	9	0.7	44	3.9	1.0	53 (5.0)
MI or ACS	104	8.5	76	7.4	2.0	180 (15.9)
TLR	146	12.0	57	5.7	1.5	203 (17.5)
TVR (excluding TLR)	40	3.2	47	4.5	1.2	87 (7.6)
Total TVR	185	15.1	86	8.9	2.4	270 (23.4)
Non-TVR	109	8.9	133	12.8	3.5	242 (21.7)
CHF	2	0.2	17	1.5	0.4	19 (1.5)

HR indicates hazard rate, which is the probability of event within a given interval if survived before interval free of event. Cumulative event rates were determined using survival analysis estimates at 5 years.

Baseline Risk vs. Effectiveness Of Intervention