Drug-Eluting Stent for SVG lesions: Useful or Deleterious ?

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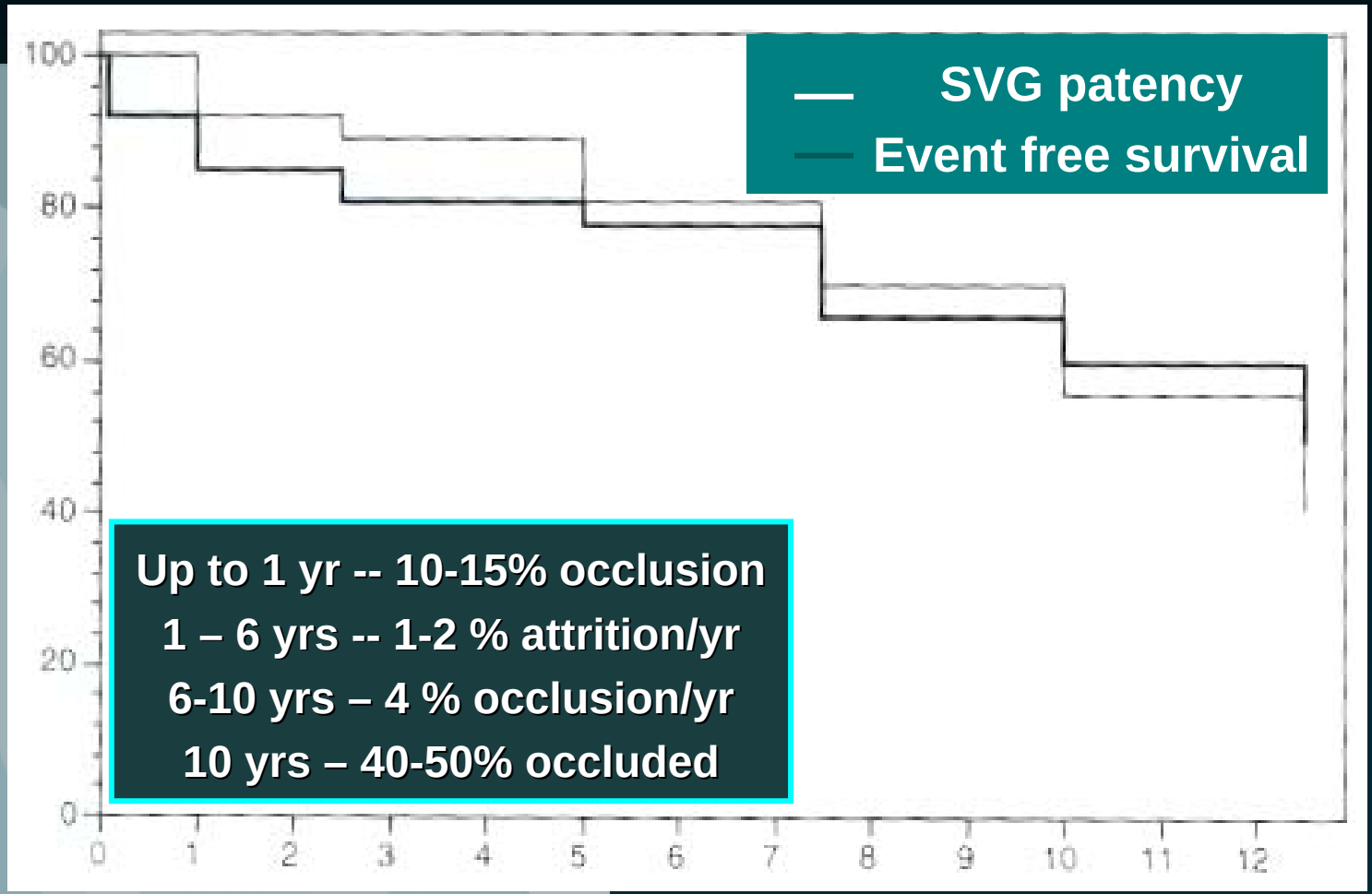
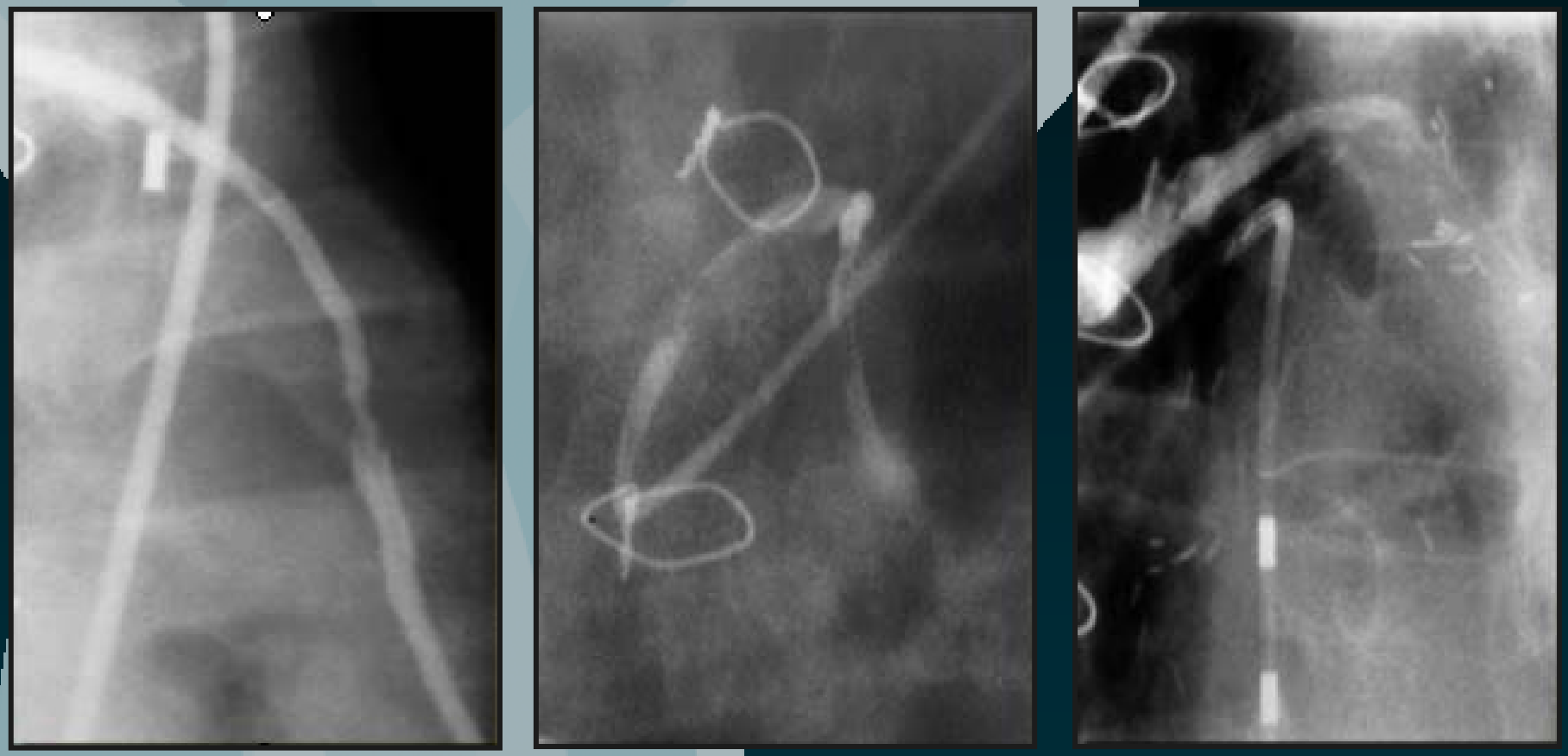
Natural History of SVG



Motwani JG, Topol EJ. Circulation 1998;97:916-31

SVG Intervention

The Problem : Diffusely Diseased SVGs



Treatment Options for Diseased SVGs

- *Re-do CABG Surgery:*
  - Mortality 6 – 8 %
  - Risk of death 3 – 5 x greater than initial procedure
- *PCI:*
  - *Historically* peri-procedural complications high & long-term outcome suboptimal
  - Treat the native vessel

Higher In-hospital Mortality In PCI for SVG

15,331 consecutive pts between 1994 & 1996

		In-hospital Mortality			
	% pts	Death	OR	CI (95%)	P value
Native	94.3	1.0 %	1.0		
SVG	5.7	3.0 %	3.0	2.0 –4.7	< 0.001

O' Conor GT et al. JACC 1999;34:681

Why is SVG PCI unlike Native Vessel Intervention ??

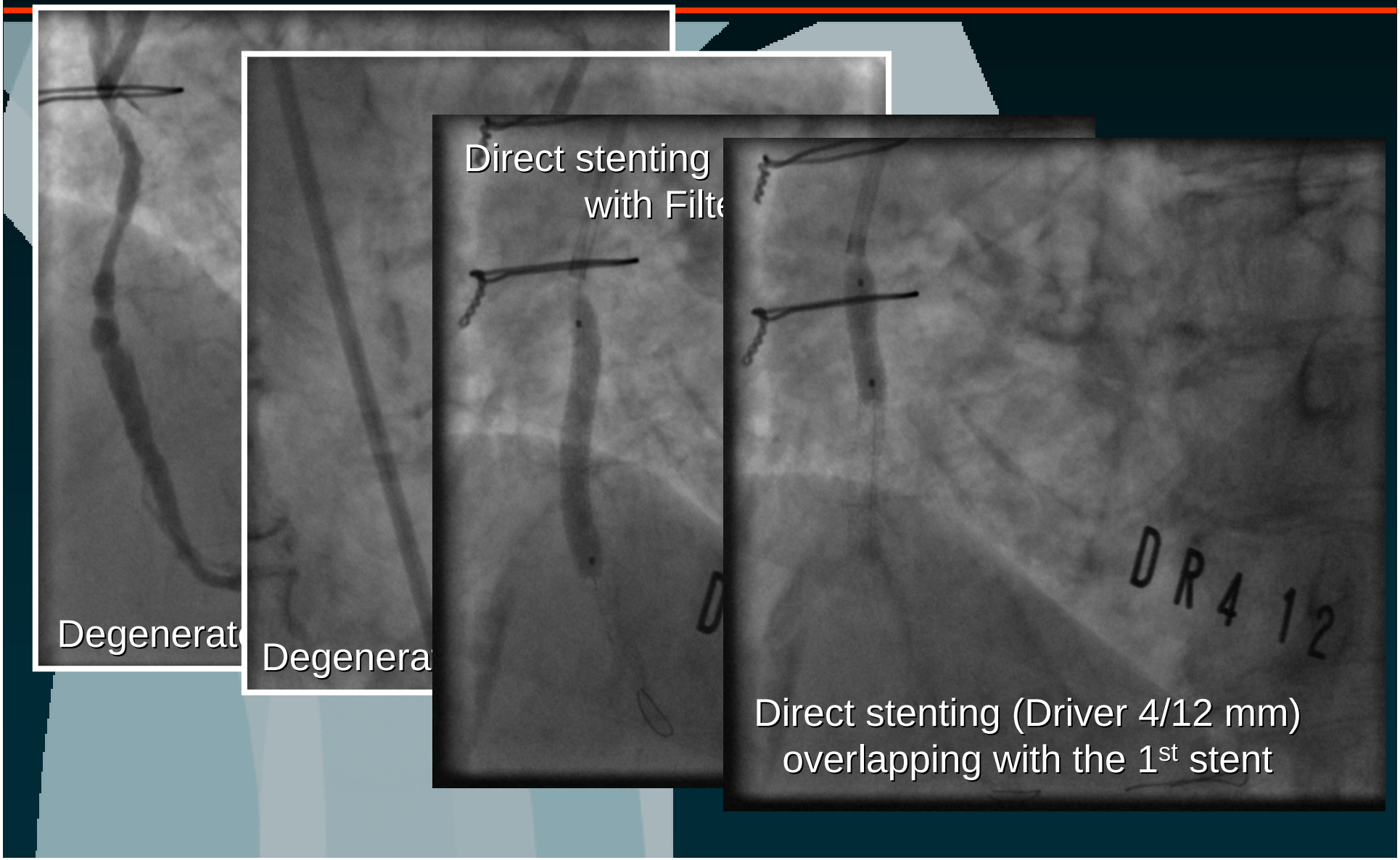
Reason	PCI Solution	Result
Patient population sicker	--	--
Friable atheroma / ↑ embolic risk	Protection devices	↓ periprocedural MI from 16% to 8%
High target vessel failure	Stent	**BMS** also have a high restenosis rate when placed in SVG (12–37% in most studies).

Is DES the logical solution to the high rate of in-stent restenosis with BMS ?

Technical problems with DES placement:
geographical miss, plaque prolapse, progression of nontarget lesions could mitigate the clinical benefit.

Bryan AJ, Curr Opin Cardiol 1994;9:641–9;
Depre C, cs Am J Clin Pathol1998;110:378–84;Van Beusekom H, cs. J Am Coll Cardiol 1993;21:45–54.

Case 1: SVG-RCA treated with stenting & Filter EZ wire



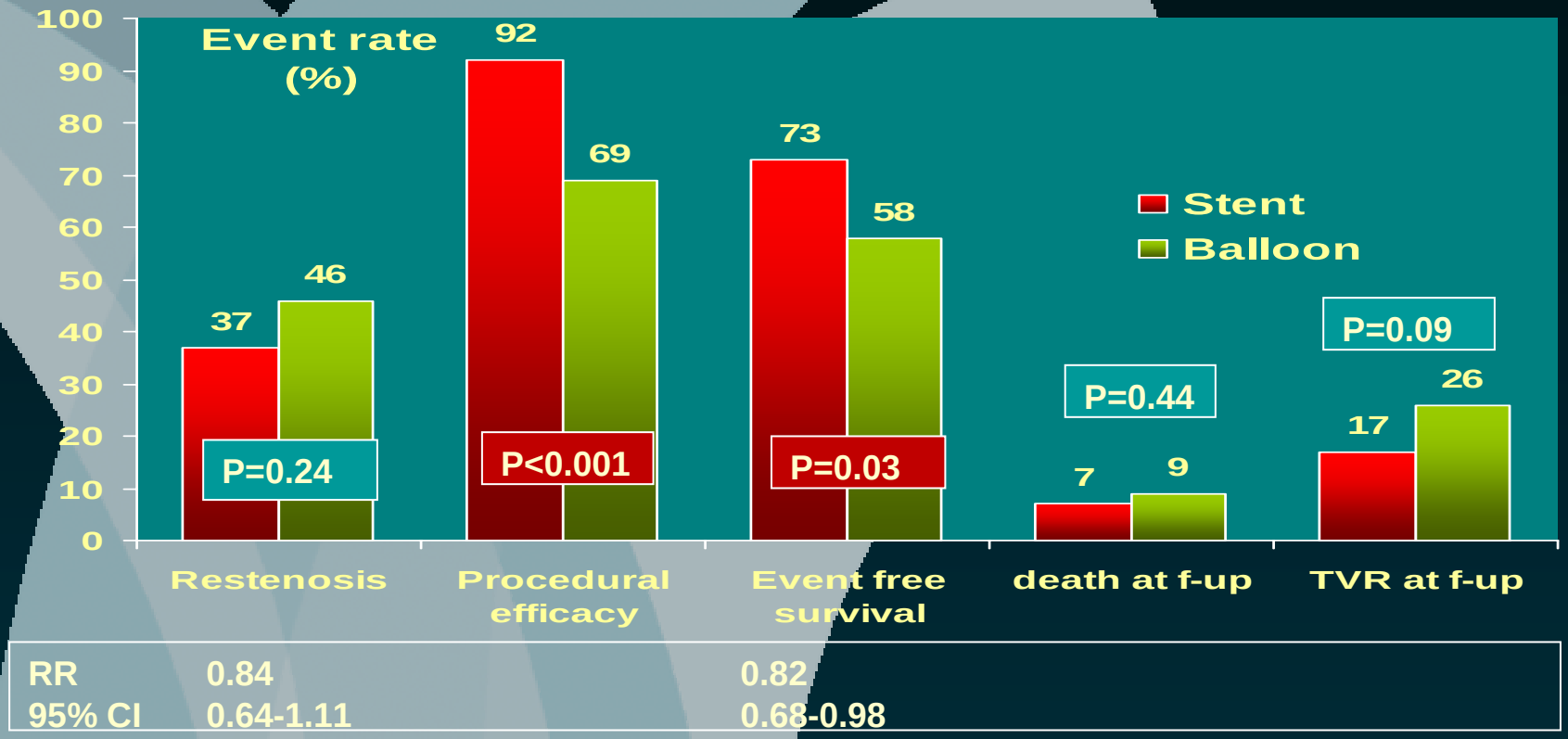
Distal Protection Device: When ?

- Not required:
  - Lesions of proximal or distal anastomosis
  - Lesions of distal native vessel beyond distal anastomosis
  - In-stent restenosis
  - Lesions of the body of the graft:
    - Young graft
    - Low degeneration score
    - Short lesion
    - Single stent
    - No visible thrombus
    - Moderate diameter stenosis

- Required:
  - Old graft
  - Degenerated
  - Long lesion
  - ≥ 2 stents
  - Thrombus
  - High grade stenosis

Fajadet J, 2004

Stenting (BMS) vs Balloon Angioplasty for Venous Coronary Bypass Stenosis (SAVED Trial)

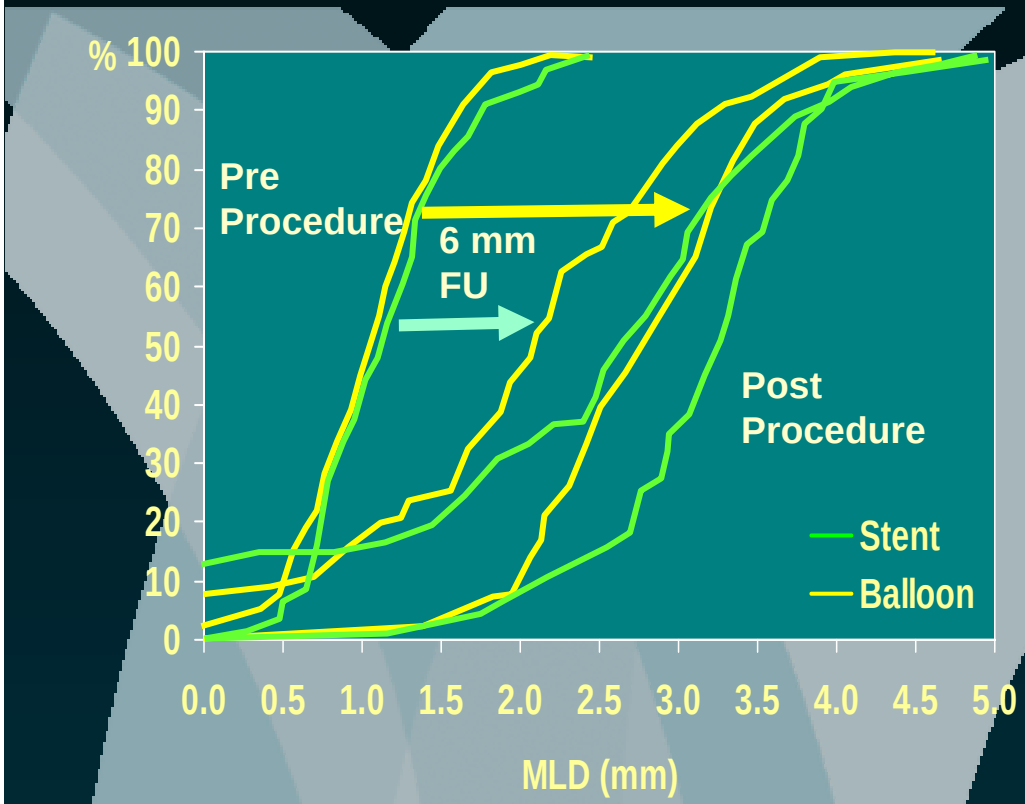


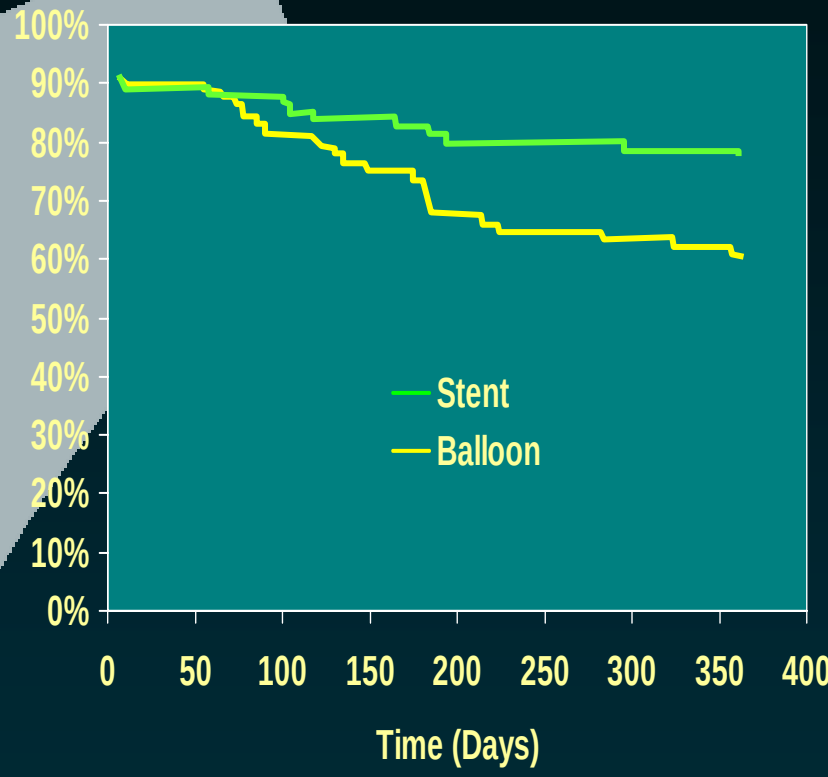
Stenting (BMS) of selected SVG lesion resulted in:

- superior procedural outcomes & a reduction in cardiac event at f-up.
- no significant benefit in the rate of angiographic restenosis (primary end-point)

Savage, et al. N Eng J Med 1997;337:740-747

Balloon Angioplasty & Elective Stent (BMS) Implantation in Venous Bypass Grafts: The Venestent Study



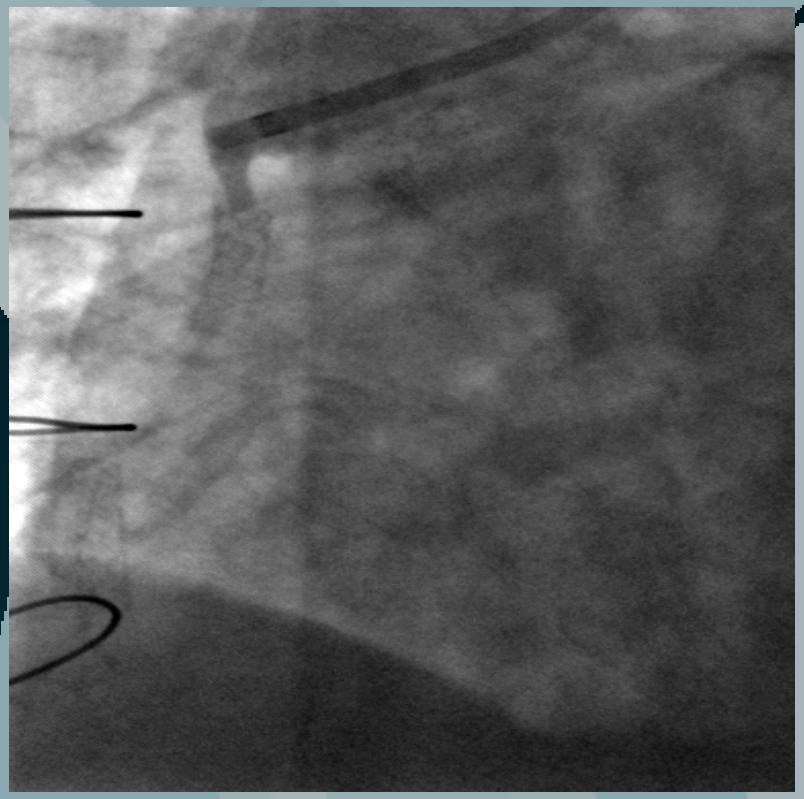


Compared to balloon angioplasty, elective stent implantation (BMS) in de novo SVG lesions is associated with:

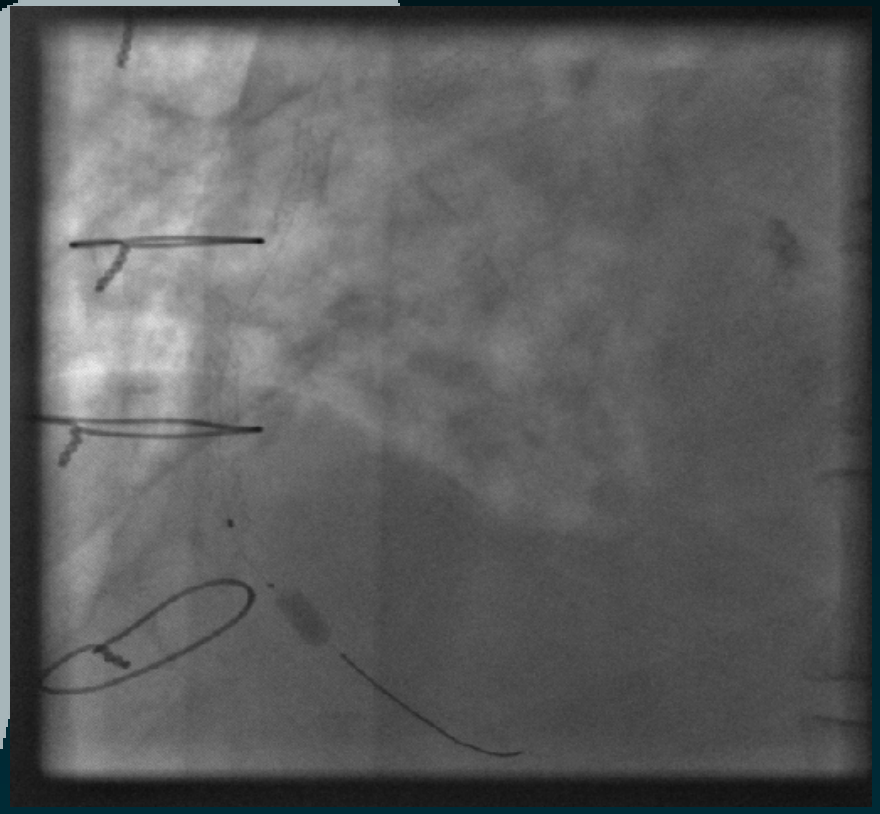
- a significantly lower TVR rate
- a significantly higher event-free survival at 1-yr f-up

Hanekamp CEE., et al. Cathet Cardiovasc Intervent: 2003;60:452–457

Case 2: ACS, occluded SVG-RCA, Treated with DES & PercuSurge GuardWire



Baseline: occluded SVG-RCA (proximal to 2 previously implanted stents, 2 yrs before)



PercuSurge, aspiration, then predilatation followed by stenting

TVR Rates in Retrospective Studies Comparing BMS vs. DES in SVG Lesions

Author (year)	Mean FU (months)	Event type	BMS (n)	BMS Event rate(%)	DES (n)	DES Event rate (%)	P	Angiographic FU (%)
Ge (2005)	6	TVR	89	**23.5**	61	**4.9**	**0.003**	70%
Lee (2006)	9.1±2.1	TVR	84	**37**	139	**10**	**0.035**	30% DES, 67% BMS
Chu (2006)	12	MACE*	57	**18**	48	**21**	**0.84**	No routine FU angio
Hoffman (2007)	6	TLR*	60	**22**	60	**6**	**0.04**	79% DES, 85% BMS
Wohrle (2007)	12	TVR	26	**34.6**	13	**7.7**	**0.12**	100%
Ellis (2007)	12	TVR	175	**11.8**	175	**6.8**	**0.14**	No routine FU angio
Minutello (2007)	20	TVR	50	**36**	59	**15.3**	**0.03**	No routine FU angio
Applegate (2007)	6	TVR	37	**21.6**	38	**5.3**	**0.047**	100%
Applegate (2007)	32 (26.5-36)	TVR	37	**38**	38	**34**	**0.74**	100%
Bansal (2008)	33	TVR	72	**38**	37	**35**	**0.47**	No routine FU angio

*No detailed information on TVR was available for these studies.

Modified after Brilakis ES et al. Cathet Cardiovasc Interv 2008;72:815-818

The Strategic Transcatheter Evaluation of New Therapies (STENT) Group

	DES (n=418)	BMS (n=281)	p
Lesion length (mm)	18.0	16.2	0.1
Vessel diameter (mm)	3.4	3.7	< 0.0001
Stent length (mm)	23.7	22.1	0.007
Distal location (%)	16	8	0.0007
Distal emboli (%)	0.4	3.3	0.003
Acute closures (%)	0.4	2.1	0.04
Death (%)	5.0	6.8	0.41
MI (%)	4.3	8.2	0.005
TVR (%)	5.7	8.5	0.17
SAT (%)	0.5	1.4	0.23
MACE (%)	12.7	20.3	0.008

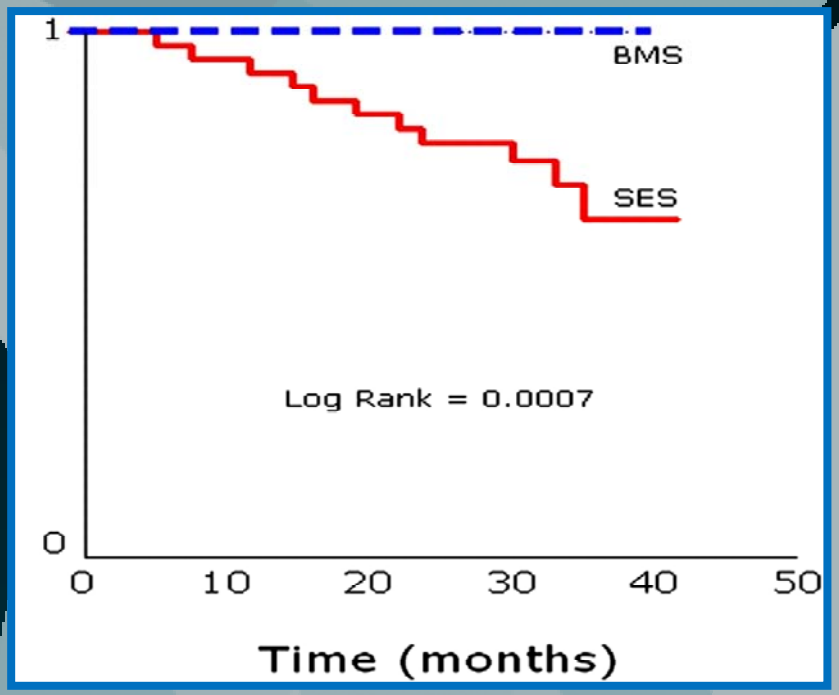
Adjusted proportional HR for MACE 0.61 (95% CI 0.40, 0.91, p=0.0157) favoring DES.
The individual adjusted HR for MI (0.55, 95% CI 0.28, 1.10, p=0.0919)
& TVR (0.60, 95% CI 0.33, 1.11, p=0.1031)

No consistent superior benefits for the use of DES in SVGs

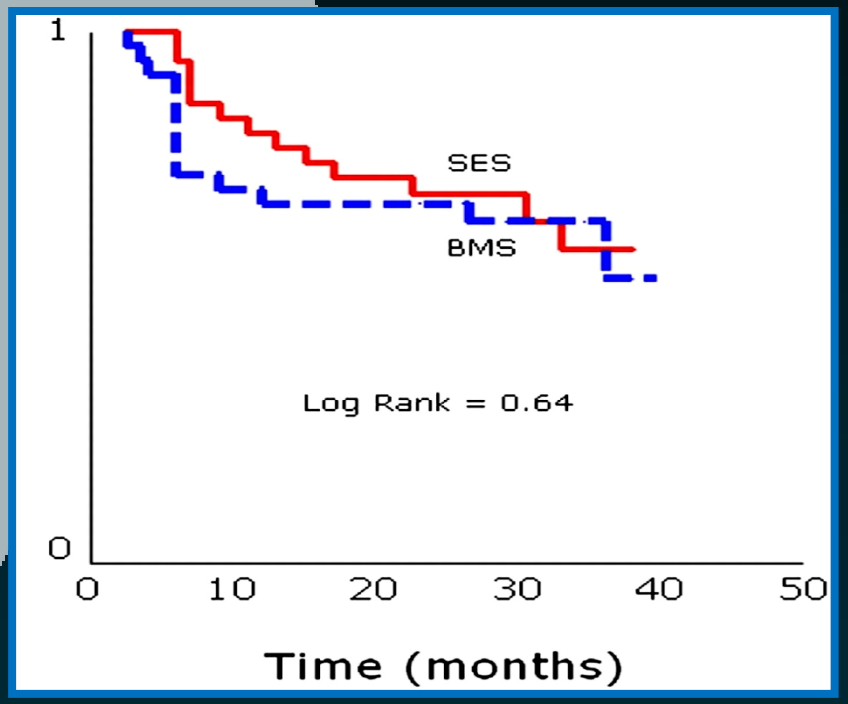
Wilson BH, cs. J Am Coll Cardiol 2007;49 (Suppl B):41B

Sirolimus-Eluting Stenting* in Diseased SVGs:

The Reduction of Restenosis In SVGs with Cypher (Delayed- RRISC) Trial



Increased Mortality



Delayed TVR

- Pts treated with SES showed a significant increase in total mortality; & the benefit of SES in terms of reduced TVR shown at 6 months was lost at long-term f-up

* Off –Label Use; N= 75 pts with 96 SVG lesions

Vermeersch, P. et al. J Am Coll Cardiol 2007;50:261-267

Sirolimus-Eluting Stenting* in Diseased SVGs:
The Reduction of Restenosis In SVGs with Cypher (Delayed- RRISC) Trial

- After a median follow-up of 32 months:
  - 11 deaths occurred in the group receiving SES (29%), but none occurred in the group receiving BMS ($p < 0.001$).
  - 3 deaths were sudden & 1 was caused by stent thrombosis

- Although the findings added to concerns about the long-term safety of DES, the 75-patient study was:
  - Small, not prospectively designed to show a mortality difference.
  - Analysis is post-hoc
  - Some pts may have premature antiplatelet discontinuation

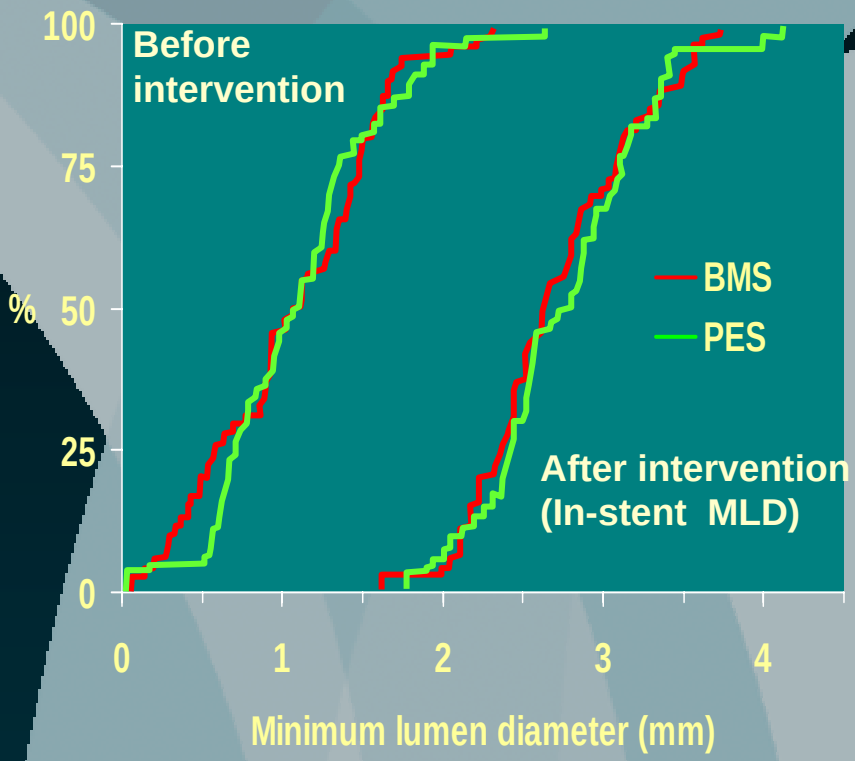
* Off –Label Use; N= 75 pts with 96 SVG lesions

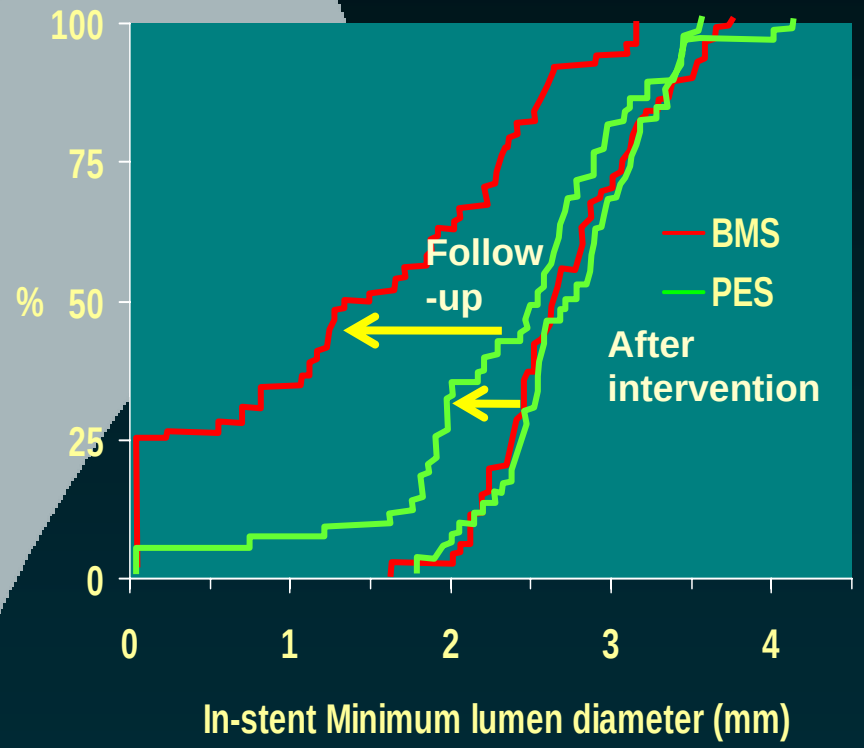
Vermeersch, P. et al. J Am Coll Cardiol 2007;50:261-267

The Stenting Of Saphenous Vein Grafts (SOS) Trial:

In-Stent MLD Cumulative Frequency

Distributions in the BMS & PES Groups





- Angiographic restenosis was 51% in the BMS group vs. 9% in the PES group ($p < .0001$, RR 0.18, 95% CI 0.07-0.48)

* Off –Label Use; N= 80 pts with 112 SVG lesions in 88 SVGs

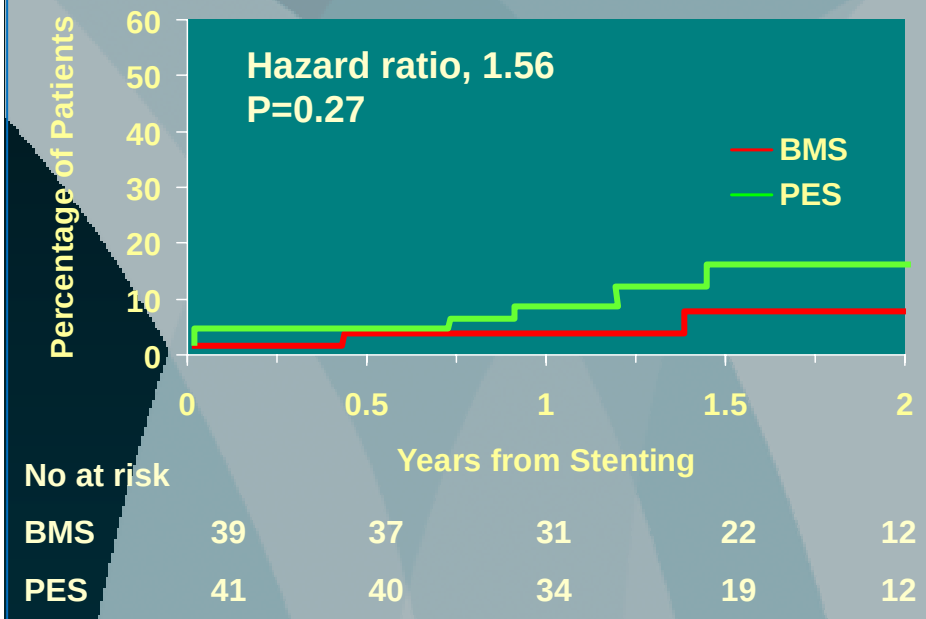
Brilakis E.S., et al. J am Coll Cardiol 2009;53:919-28

The Stenting Of Saphenous Vein Grafts (SOS) Trial:

Death from Any Cause & Myocardial Infarction

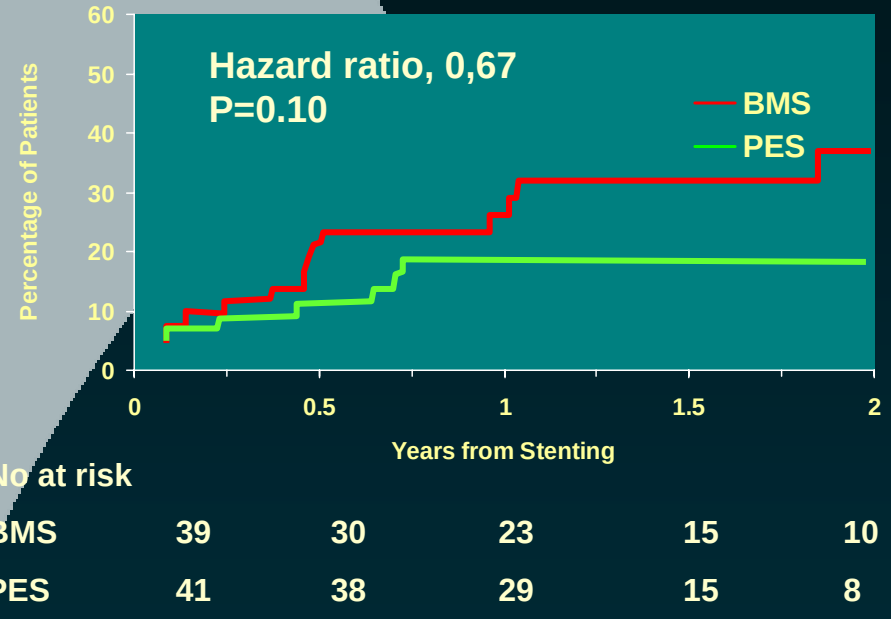
Distributions in the BMS & PES Groups

Death from any cause



No at risk					
BMS	39	37	31	22	12
PES	41	40	34	19	12

Myocardial infarction



No at risk					
BMS	39	30	23	15	10
PES	41	38	29	15	8

- No difference in overall mortality was found between the study groups
- A trend for lower incidence of myocardial infarctions was seen in the Paclitaxel-Eluting Stent (PES) group

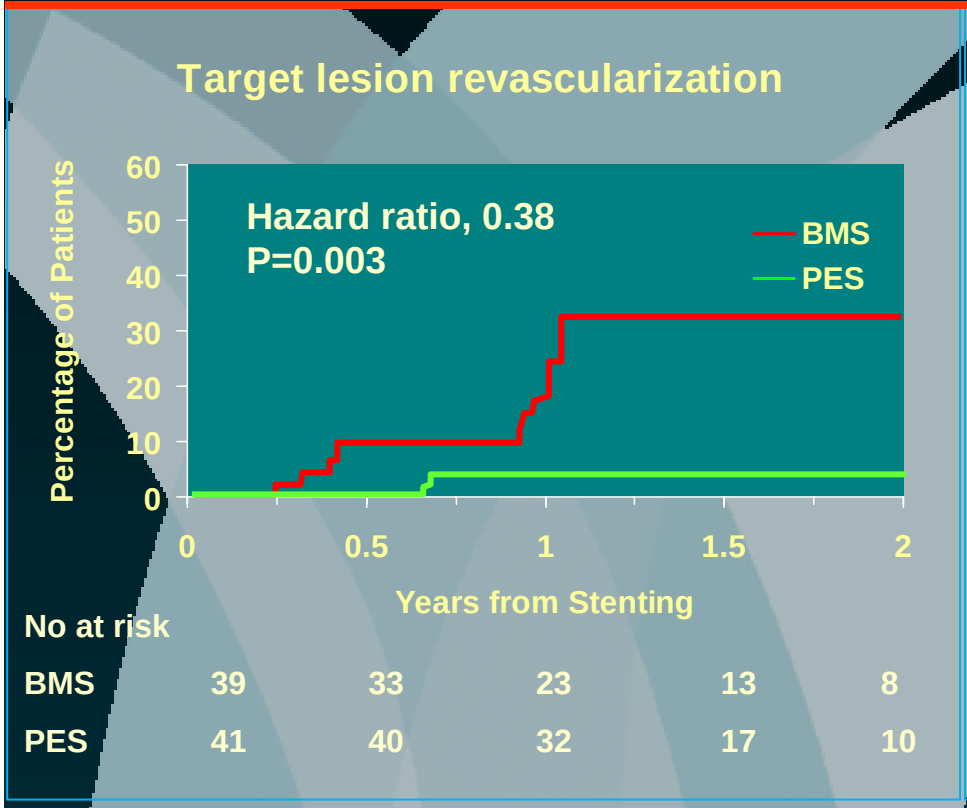
* Off –Label Use; N= 80 pts with 112 SVG lesions in 88 SVGs

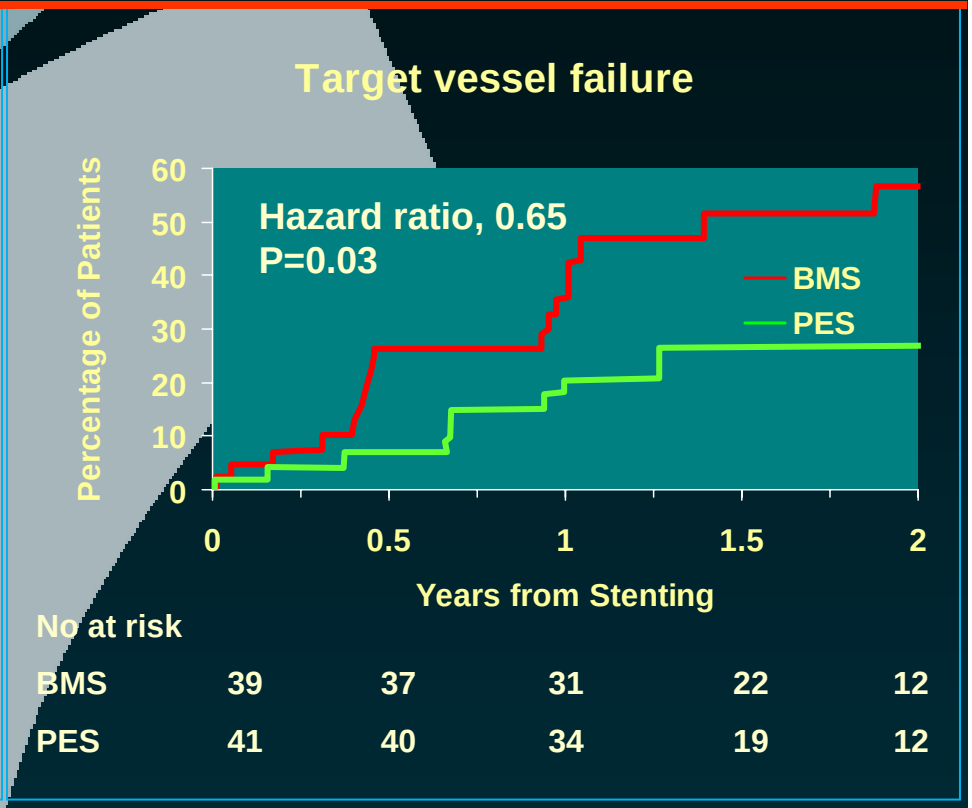
Brilakis E.S., et al. J am Coll Cardiol 2009;53:919-28

The Stenting Of Saphenous Vein Grafts (SOS) Trial:

Target Lesion Revascularization & Target Vessel Failure

Distributions in the BMS & PES Groups



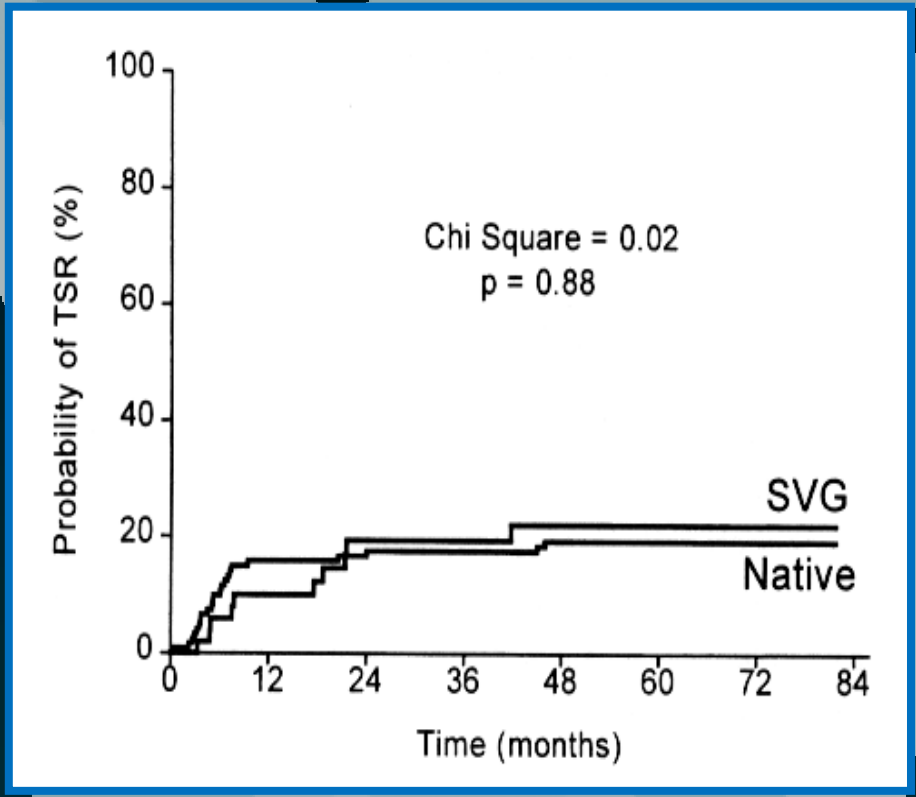


- The incidence of TLR & TVF and composite end point of cardiac death, myocardial infarction & TVR, was significantly lower in the PES group than the BMS group

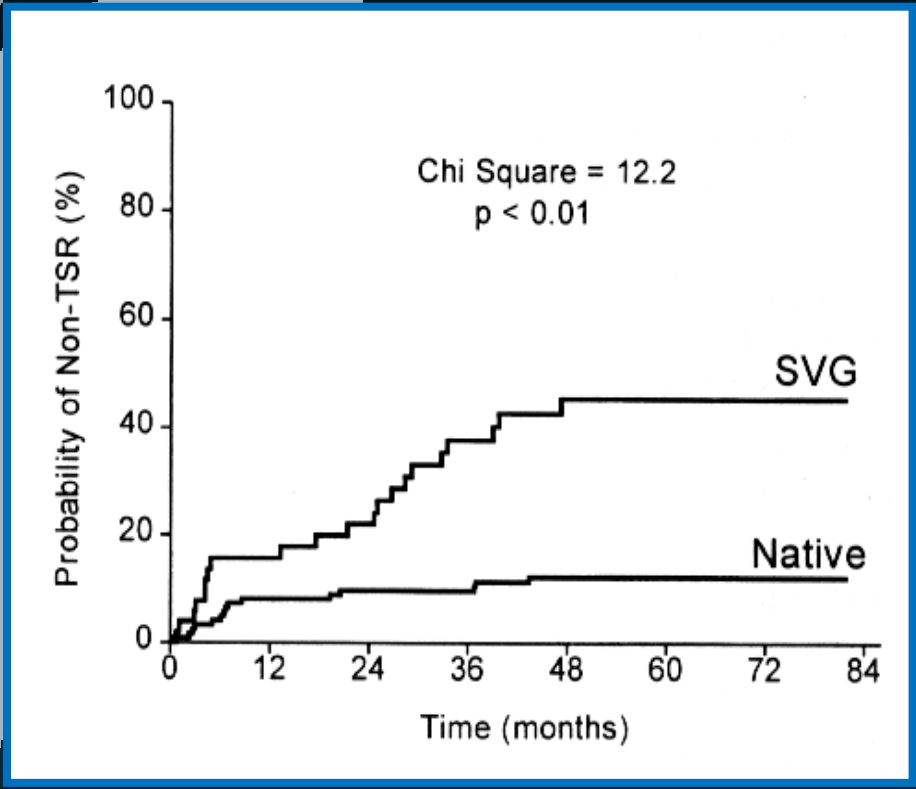
* Off –Label Use; N= 80 pts with 112 SVG lesions in 88 SVGs

Brilakis E.S., et al. J am Coll Cardiol 2009;53:919-28

SVG failure post-PCI often occurs at Non-Target Sites



Target Sites Restenosis



Non-Target Sites Restenosis

Ellis SG, cs.. Am J Cardiol 1997;79:1460–4.

Incidence of Early (30-day) Stent Thrombosis in Vein Graft Intervention: AMEthyst Study

- 786 pts undergoing SVG stenting:
  - 60.2% (n=473) received DES (41.7% Taxus, n=195 & 58.3% Cypher, n=273)
  - 39.8% (n=313) received BMS.

- Compared to BMS pts, DES pts had:
  - lower GP 2b/3a receptor inhibitor use (35.5% vs. 51.1%, p<0.001),
  - smaller ref. vessel diameter (3.02 mm vs. 3.61 mm, p<0.001) &
  - lower plaque volume (94.4 mm3 vs. 131.3 mm3, p<0.001).

- **Early stent thrombosis:**
  - for all pts was 0.5%.
  - No differences between DES & BMS pts, either prior to (0.4% vs. 0.7%, OR 0.65, p=0.67) or after adjustment (adjusted OR 1.10, p=0.93).
  - No differences between Taxus & Cypher, either prior to (0.5% vs. 0.4%, OR 1.37, p=0.83) or after adjustment (adjusted OR 0.22, p=0.58).

Srihari S. Naidu, cs. J Am Coll Cardiol 2009;53:A83 (abstr)

Use of DES in SVG Lesions:
What does the EBM tell us?

- DES produce better primary angiographic end points (lower early risk of restenosis) than BMS
- This does not mean that DES will always:
  - produce better clinical outcomes,
  - achieve better angiographic outcomes for all pts with SVG lesions, or
  - even achieve the same angiographic outcomes at different times after stent implantation.
- Whether there is a problem of "catch-up phenomenon" & increased risk of very late stent thrombosis which may drive late events is still unknown.
- Noise due to late target vessel, non-target lesion disease progression

Use of DES in SVG Lesions:
What should we do?

- "First do no harm!"
  - Use embolic protection regardless of BMS or DES
- *Target vessel revascularization* in SVGs usually due to progression of disease, rather than target lesion failure
- The decision to use DES for SVG lesions remains multifaceted & depends on such factors as graft size, predicted adherence to prolonged dual antiplatelet therapy & the increasingly dominant role of patient preference.
- Be reminded that prolonged dual antiplatelet therapy for both BMS & DES is necessary
- Use DES only in patients who can tolerate prolonged dual antiplatelet therapy

Use of DES in SVG Lesions:
What do we need?

- Current evidence is based on small, largely retrospective data & only 2 small, prospective trials with only short-term follow-up
- To date, the data was underpowered to detect differences in clinical outcomes
- Large, RCTs with longer follow-up are needed