Percutaneous Treatment of Saphenous Vein Grafts

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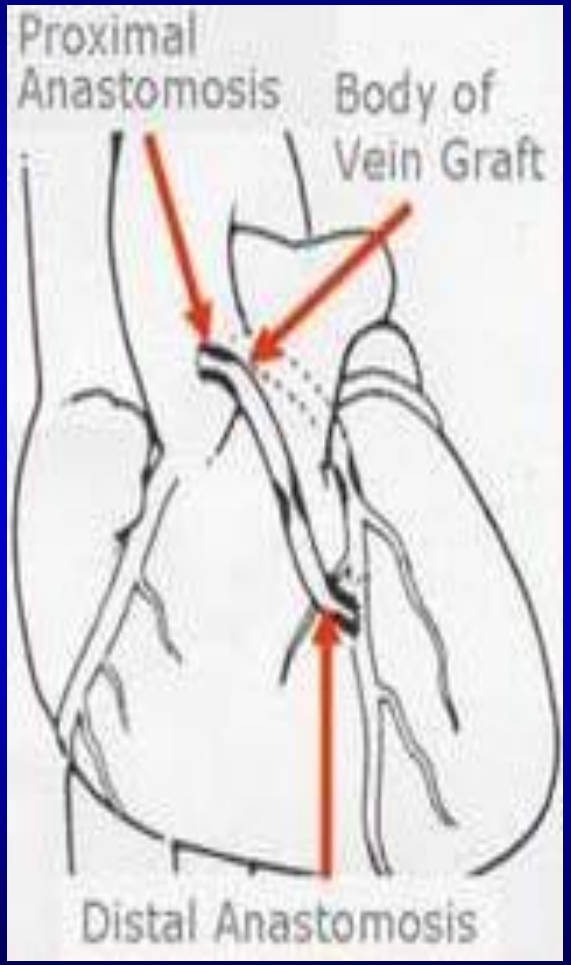
UCLA School of Medicine

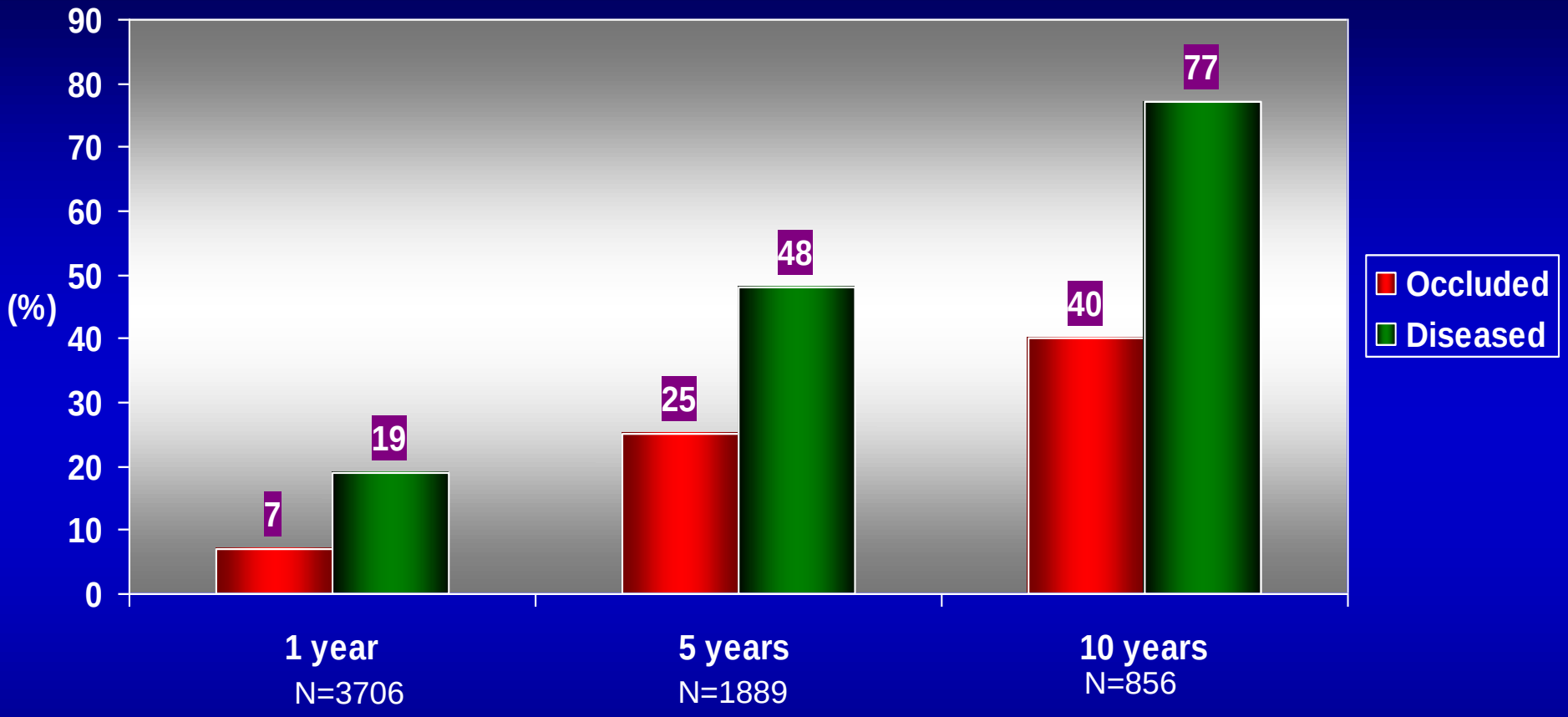
SVG Pathology

- SVGs are not like native coronary arteries
  - 300,000 new CABG/year*
  - 10% of PCI case volume



*MedPar Data

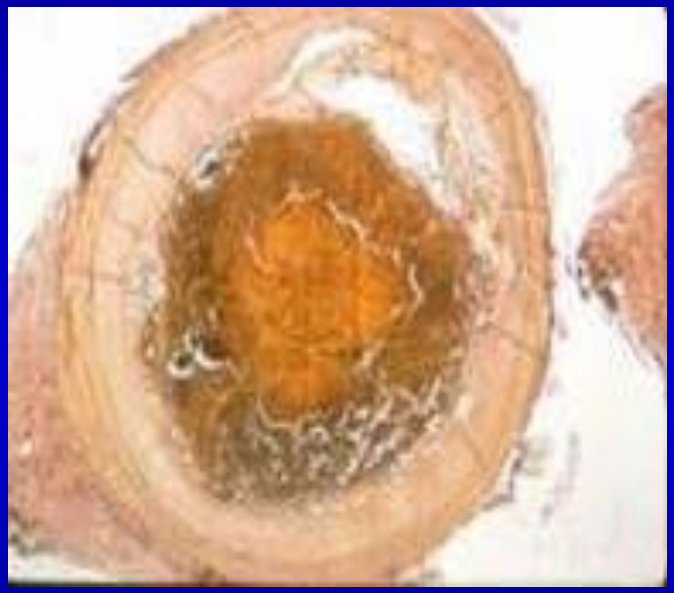
SVG Angiographic Patency



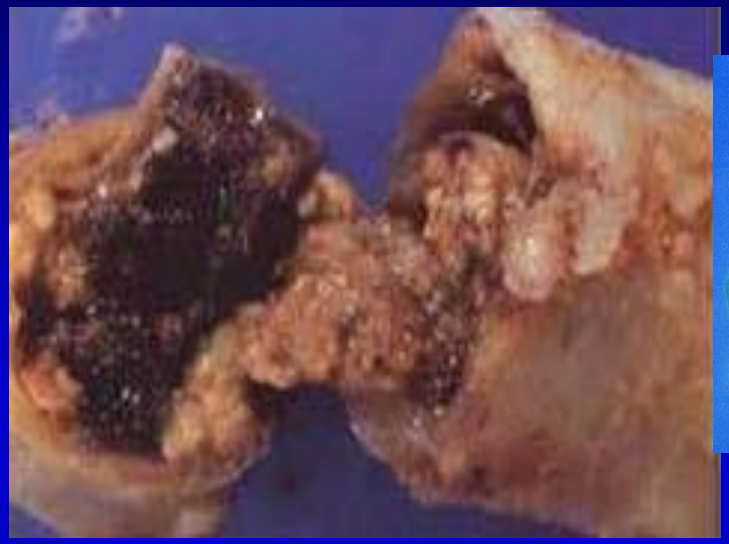
Fitzgibbon et al. JACC 1996;28:616

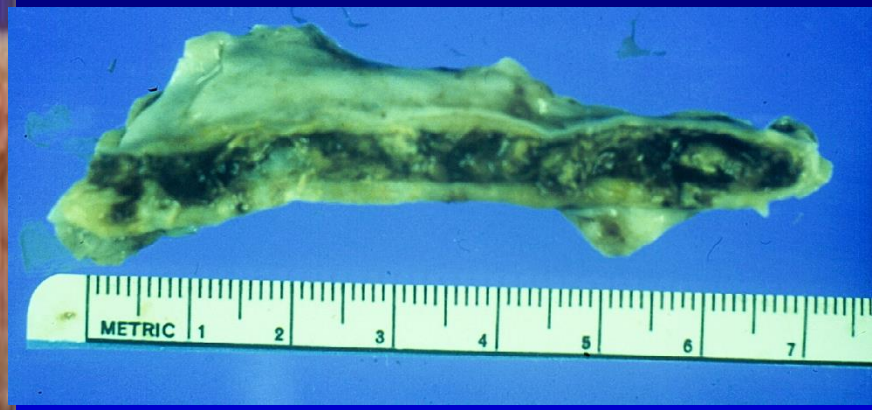
Typical SVG disease progression

- *First month*
  - Thrombosis
  - Intimal hyperplasia
- *1-7 years*
  - Build-up of atherosclerosis with superimposed thrombus
- *7-10 years*
  - Occlusion



SVG Pathology





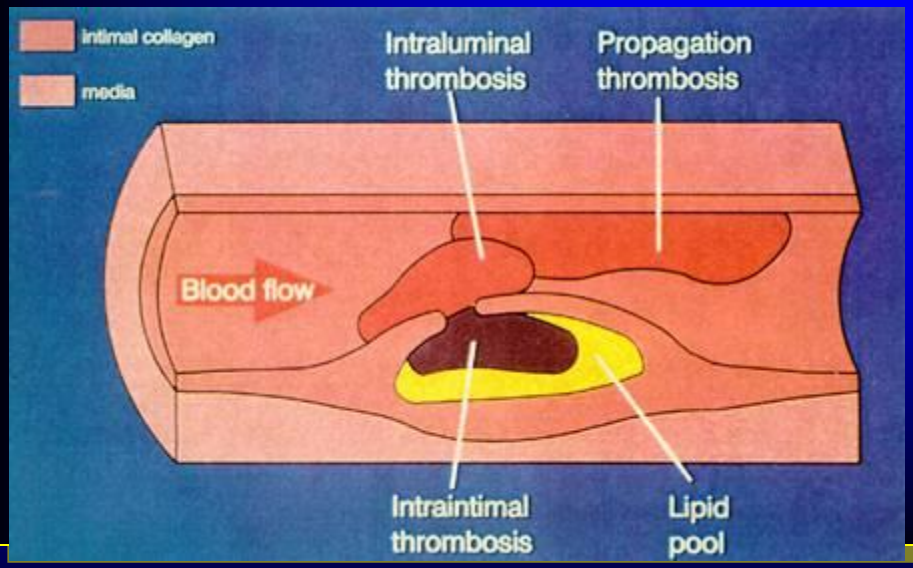
- Friable atheroma and thrombi are bulky and particularly prone to distal embolization during PCI, leading to a significant increase in the risk of death or MI

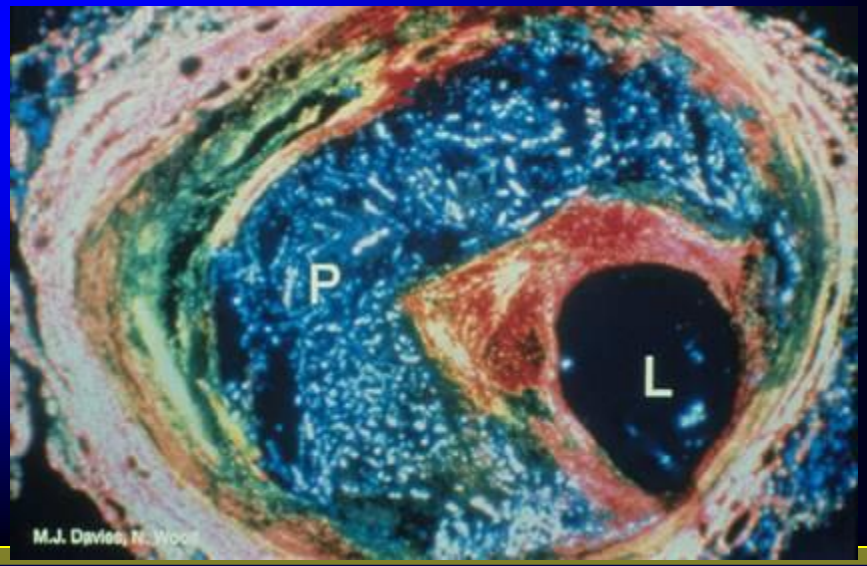
Saphenous Vein Graft PCI

- PCI of degenerated SVG is associated with worse outcomes compared with PCI of native coronaries
  - Acute complications
    - Periprocedural MI
    - No-reflow
  - Long-term
    - Restenosis
- Patients often have comorbid conditions, extensive disease, and LV dysfunction

Microvascular Complications of PCI

- Athero-thromboembolization
- No Reflow
- Myocardial Necrosis

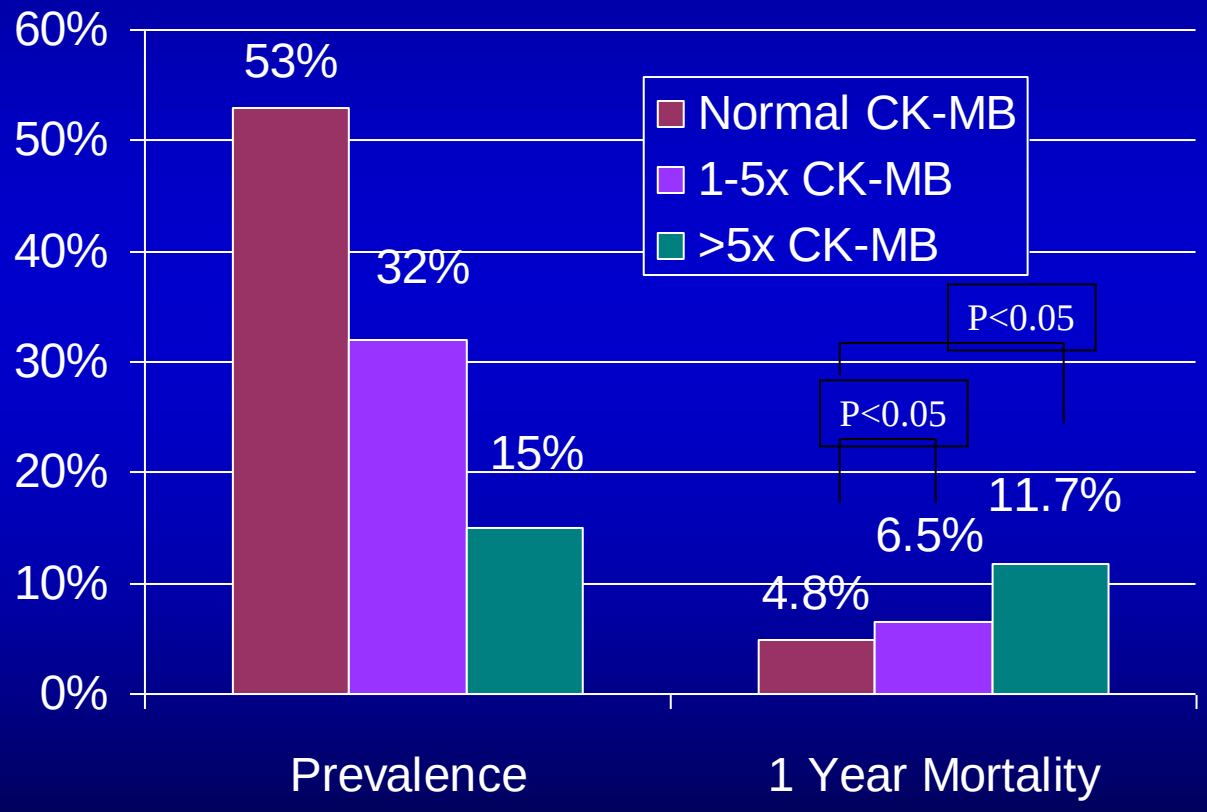




CK-MB Rise in SVG PCI

Rates After Successful SVG Intervention

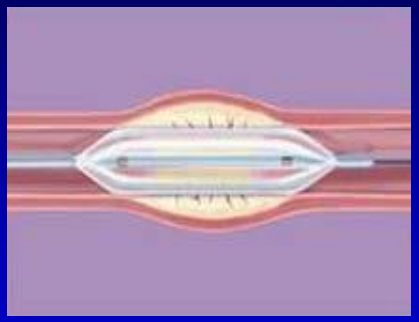
n=1056 consecutive SVG interventions

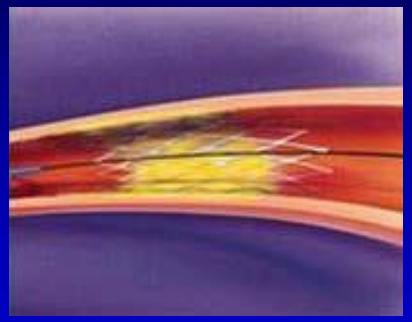


- 47% had CK-MB rise, even after successful PCI
- 15% had major CK-MB rise
- Even minor CK-MB rise related to a significant late mortality increase
- Patients with major CK-MB rise had 2.5x the mortality as those with normal CK-MB

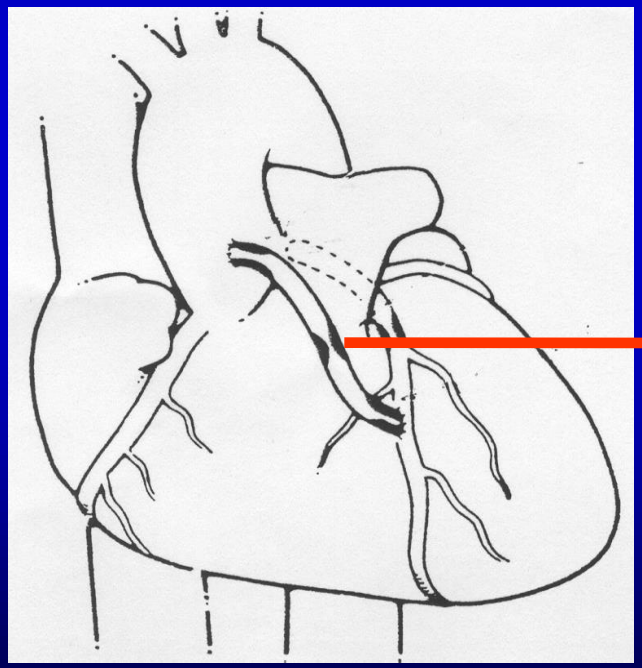
Hong, *et al.,* Circulation. 1999;100:2400-2405.

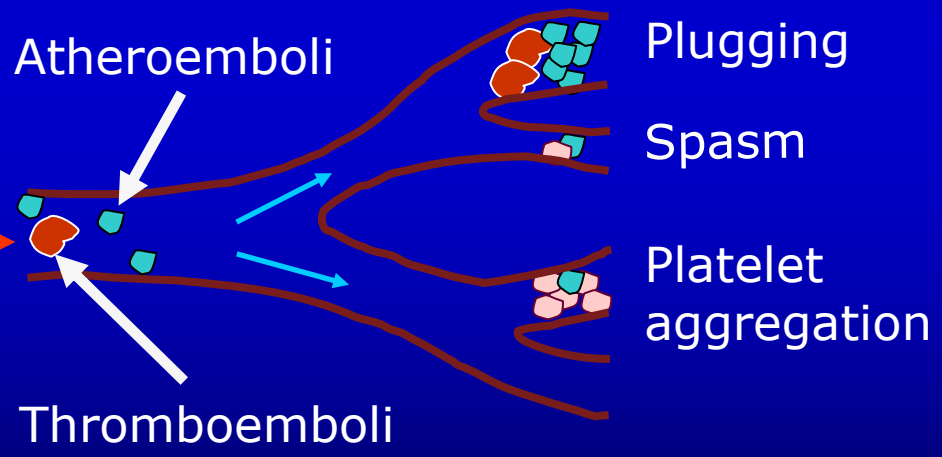
Causes of Microvascular Obstruction





- Distal embolization from PCI causes microvascular obstruction via plugging, with secondary spasm and platelet aggregation





Adapted from Hori M, *et al.*, *Am J Physiol.* 1986;250:H509-518.
Illustration by Boston Scientific Corporation.

No-Reflow Has Lasting Consequences

- Complicates 10–15% of SVG PCI[1]
- 31% rate of AMI[2]
- Increases in-hospital mortality by 10-fold[2]
- Atheroembolization is a key contributor[3]

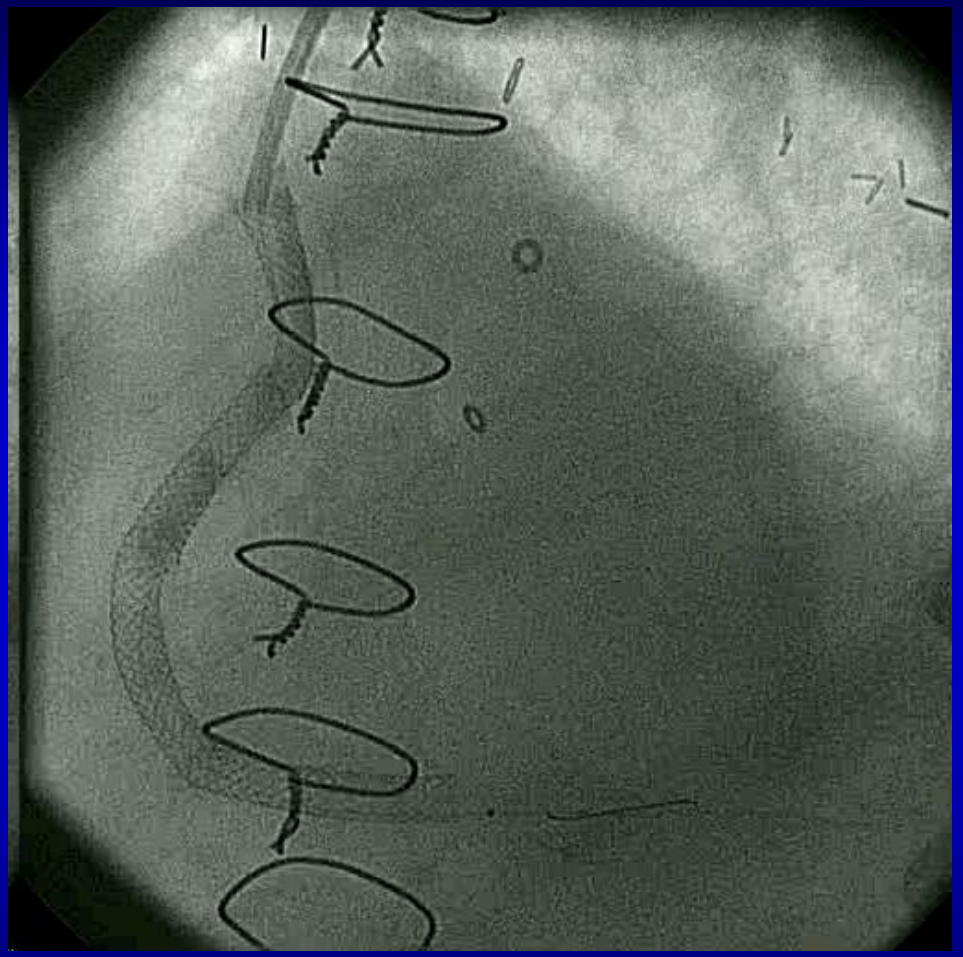


Image courtesy of Dr. Donald S. Baim

1 Sdringola, *et al.,* Cathet Cardiovasc Intervent. 2001
2 *Abbo, et al*., American Journal of Cardiology, 1995.
3 Rezkalla, *et al.,* Circulation. 2002.

STATE-OF-THE-ART PAPER

Saphenous Vein Graft Intervention

State-of-the-Art 2011

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Los Angeles, and Palo Alto, California; Seoul, South Korea; Atlanta, Georgia; New York, New York; Dallas, Texas; Antwerp, Belgium; Washington, D.C.; Munich, Germany; and Boston, Massachusetts

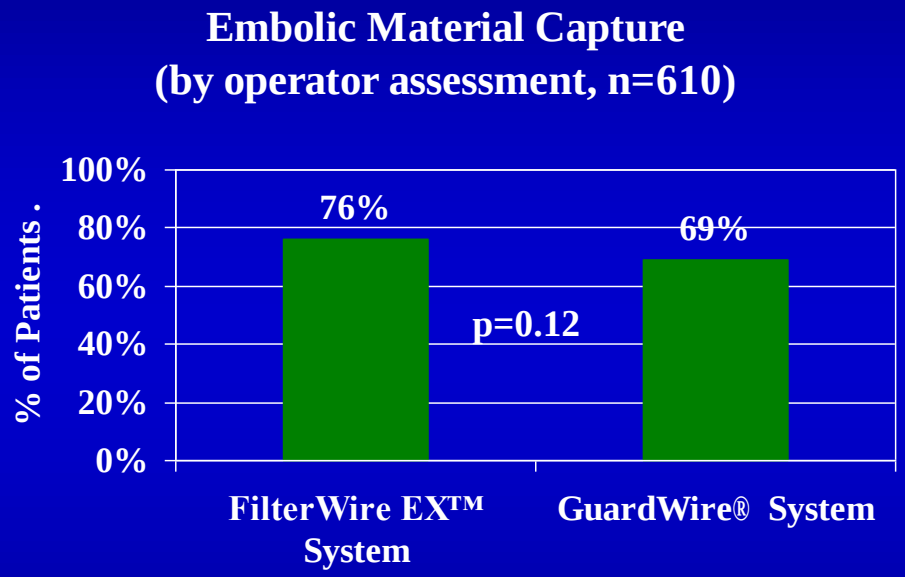
Saphenous vein grafts are commonly used conduits for surgical revascularization of coronary arteries but are associated with poor long-term patency rates. Percutaneous revascularization of saphenous vein grafts is associated with worse clinical outcomes including higher rates of in-stent restenosis, target vessel revascularization, myocardial infarction, and death compared with percutaneous coronary intervention of native coronary arteries. Use of embolic protection devices is a class I indication according to the American College of Cardiology/American Heart Association guidelines to decrease the risk of distal embolization, no-reflow, and periprocedural myocardial infarction. Nonetheless, these devices are underused in clinical practice. Various pharmacological agents are available that may also reduce the risk of or mitigate the consequences of no-reflow. Covered stents do not decrease the rates of periprocedural myocardial infarction and restenosis. Most available evidence supports treatment with drug-eluting stents in this high-risk lesion subset to reduce angiographic and clinical restenosis, although large, randomized trials comparing drug-eluting stents and bare-metal stents are needed. (J Am Coll Cardiol Intv 2011;xx:xxx)

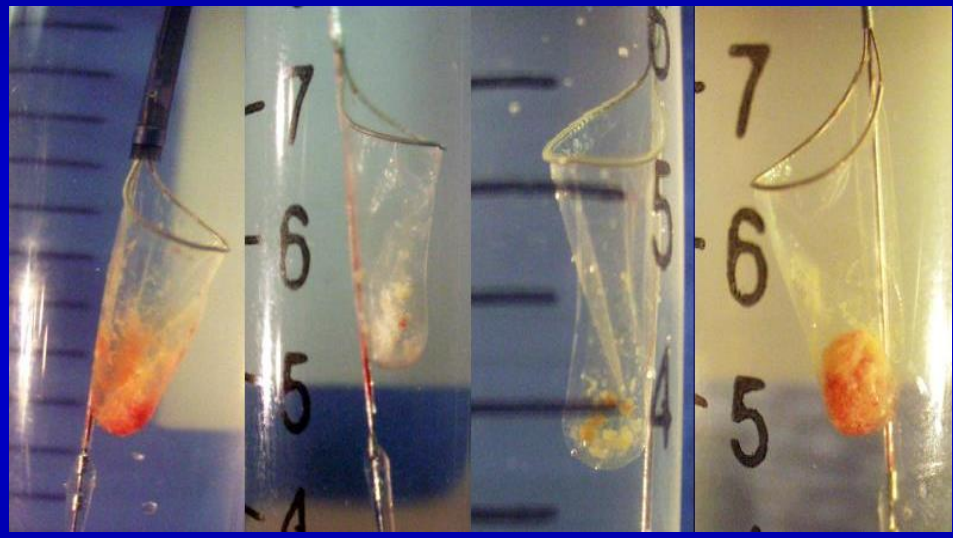
Should embolic protection be used for all SVG Intervention?

Rationale for Embolic Protection

- Embolization is common and is associated with 8-10 fold increase in mortality
- Although risk factors can be identified, embolization cannot be reliably predicted

Material Capture: FIRE Trial



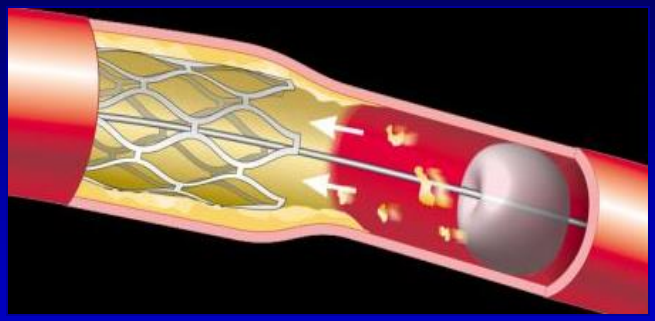


Material capture is common and independent of patient demographics, clinical presentation, and lesion characteristics.

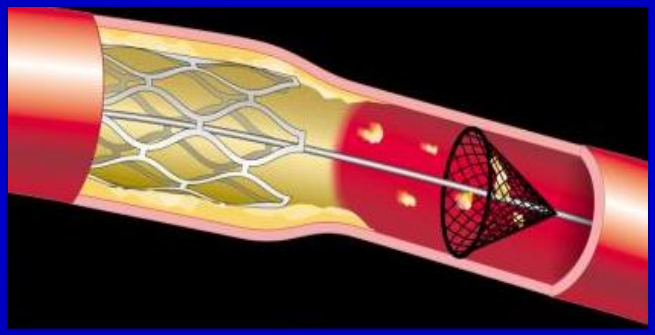
Weisz, et.al. JACC Vol. 43, (suppl A); 72A-73A

Embolic Protection Devices

Distal occlusion + aspiration (Percusurge)



Distal filters



Proximal occlusion + aspiration

Occlusion and Aspiration

Advantage

- Easy to cross lesion
- Captures smaller particles and “humoral” mediators
- Frequently applicable
- Easy device retrieval

Disadvantage

- Difficult to image during stenting
- Balloon injury
- Transient occlusion/ischemia
- May not catch particles near balloon and not get full evacuation
- Can’t cover side branch
- Cumbersome operation

SAFER (Saphenous Vein Graft Angioplasty Free of Emboli Randomized) Trial

801 patients with SVG Disease

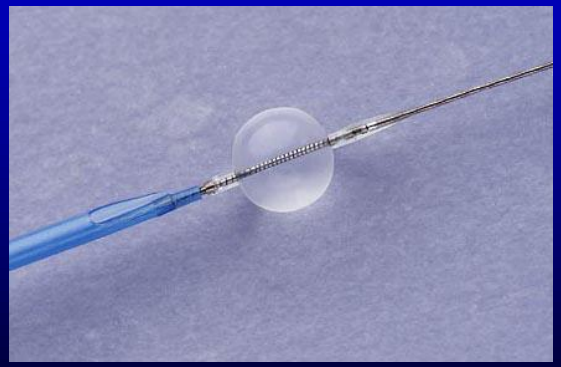
Mean graft age 10.4 yrs (range 7-13)

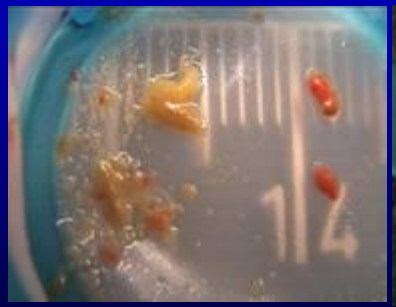
Randomized

GuardWire Plus
n=406

Conventional Guidewire
n=395

Endpoint: 30-day MACE





Baim DS, et al. Circulation 2002

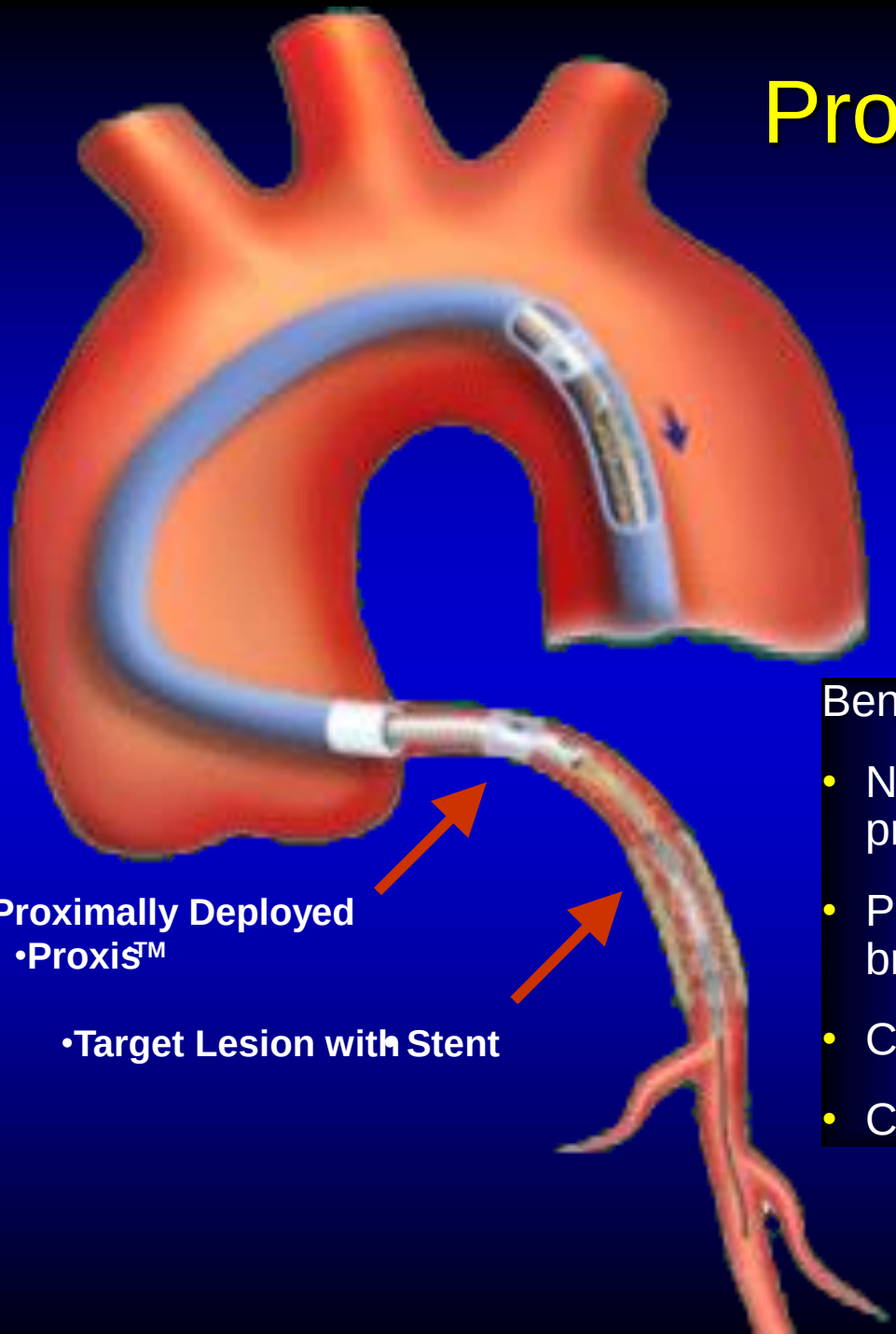
SAFER Trial

*Primary Endpoint

	With protection (n=406)	No protection (n=395)	P-value
***MACE out to 30 days**	9.6%	16.5%	*p=.004*
•All MI	8.6%	14.7%	*p=.008*
•*Q-wave MI*	*1.2%*	*1.3%*	*NS (p=1.00)*
•*Non Q-wave MI*	*7.4%*	*13.7%*	*p=.004*
•Death	1.0%	2.3%	*NS (p=.171)*
•Emergent CABG	0.0%	0.5%	*NS (p=.243)*
•TLR	1.0%	2.0%	*NS (p=.257)*

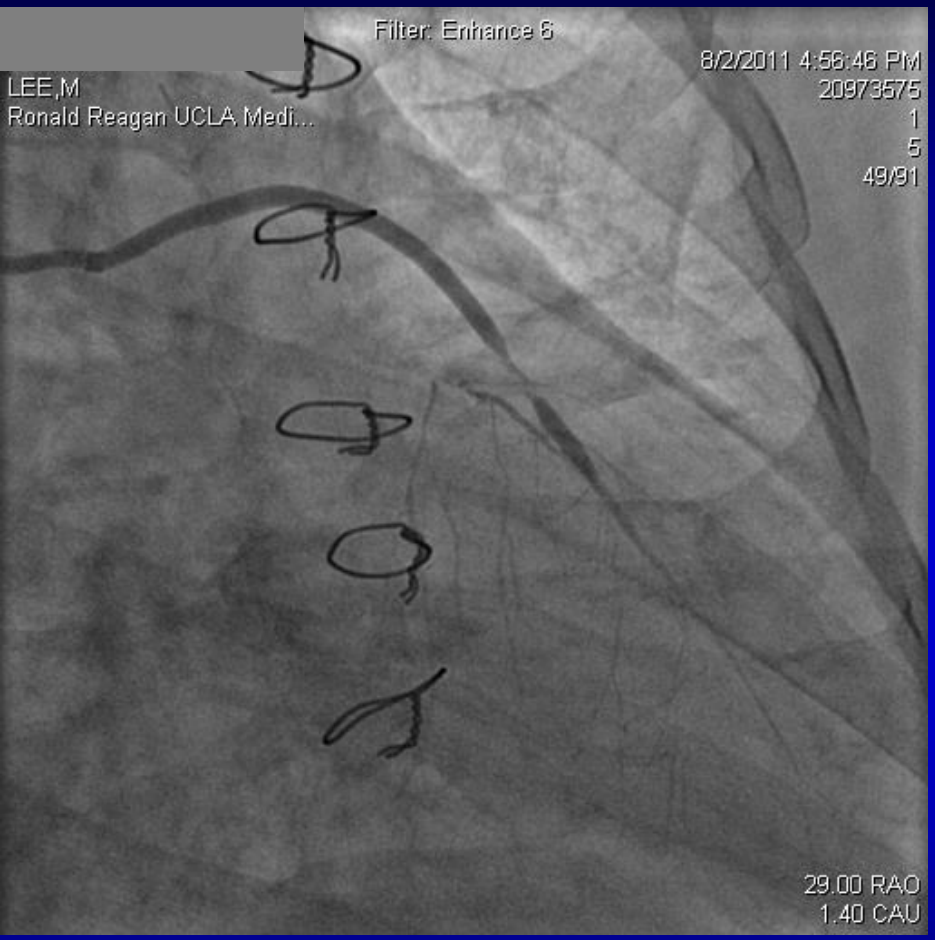
Baim DS, *et.al.,* Circulation. 2002;105:1285-1290.

Proxis



Benefits

- Nothing crosses the lesion prior to protection
- Protection of main vessel and side branches
- Captures large and small particles
- Can handle large embolic loads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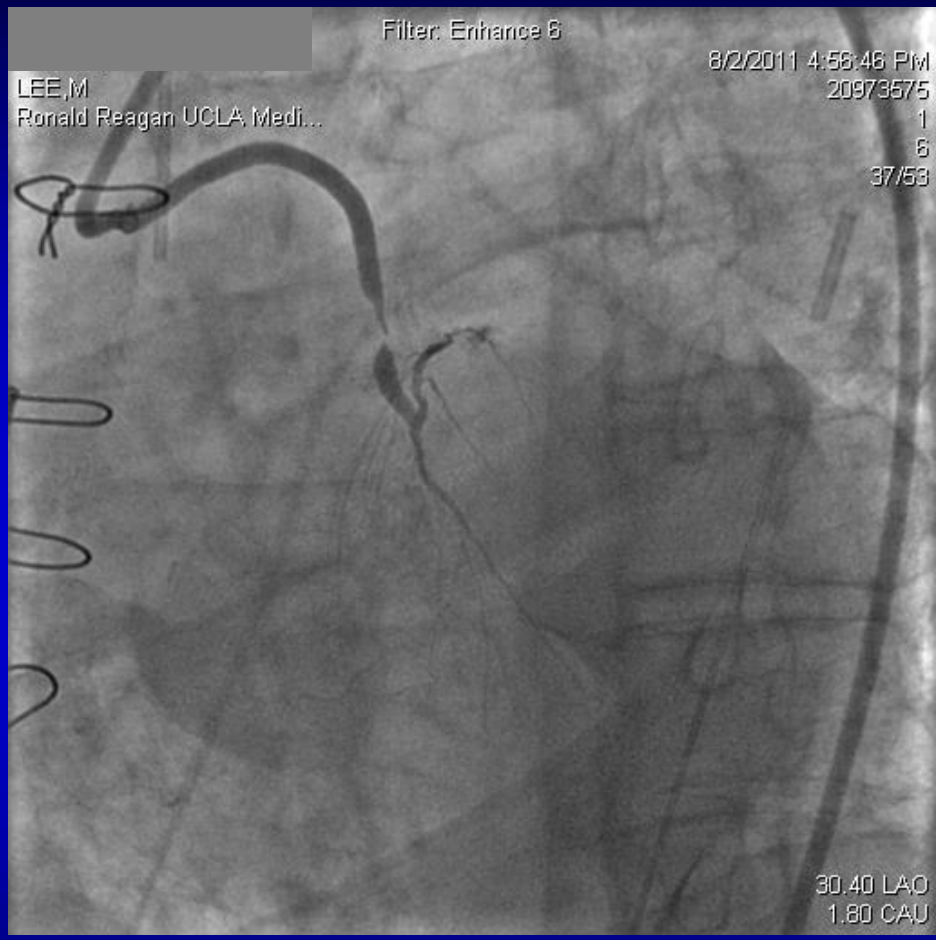
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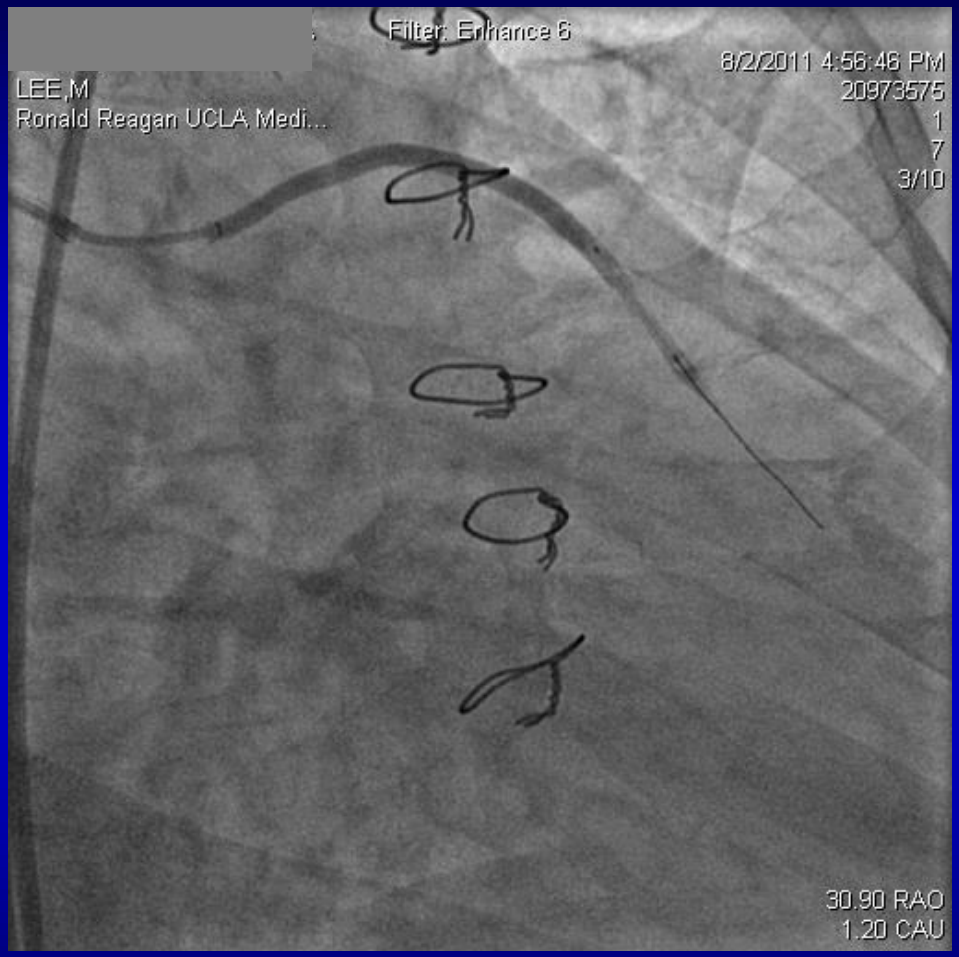
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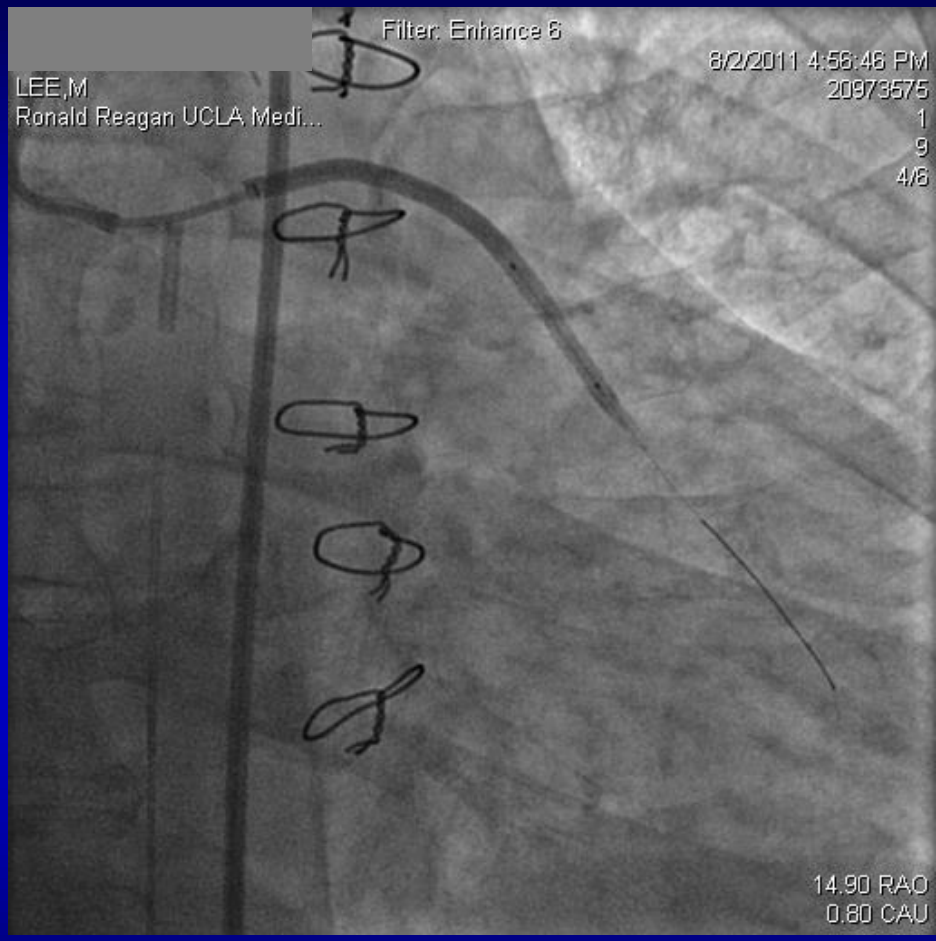
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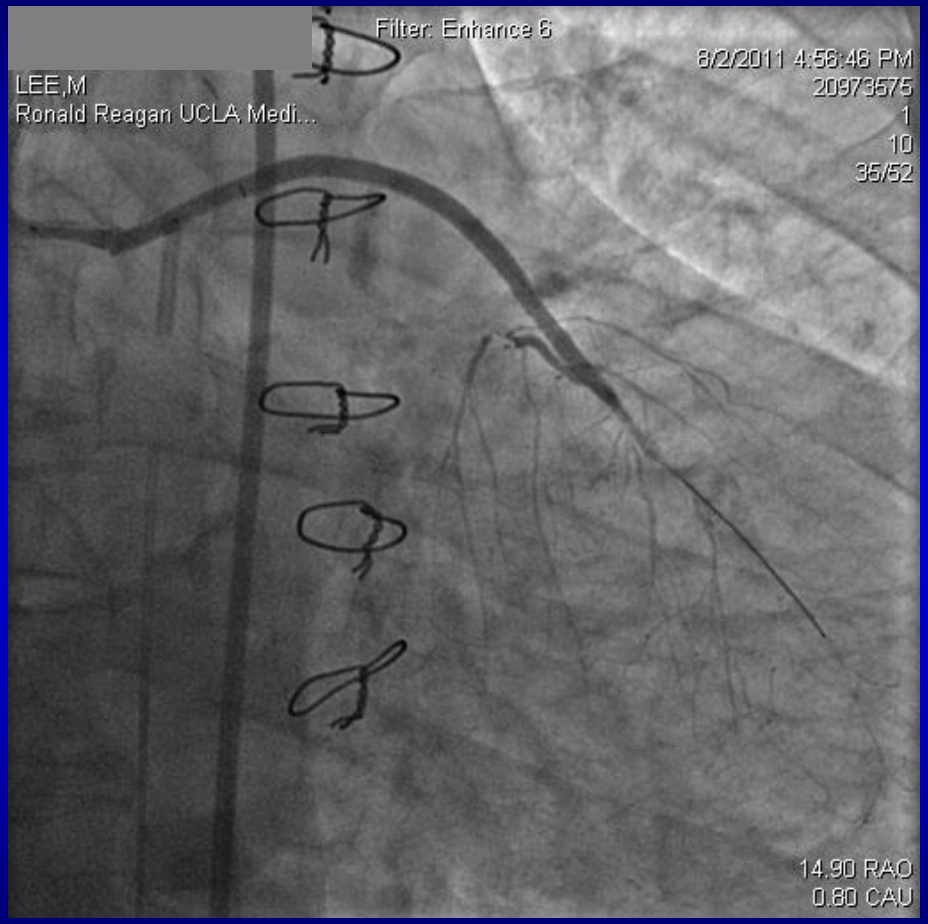
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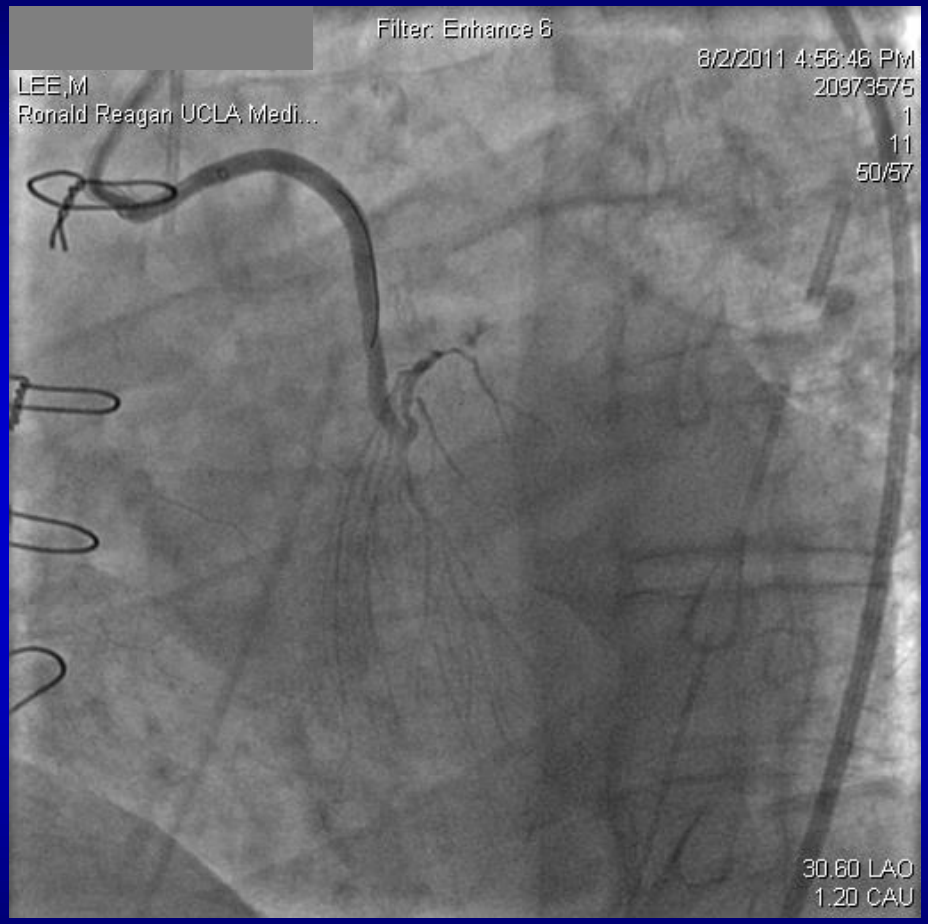
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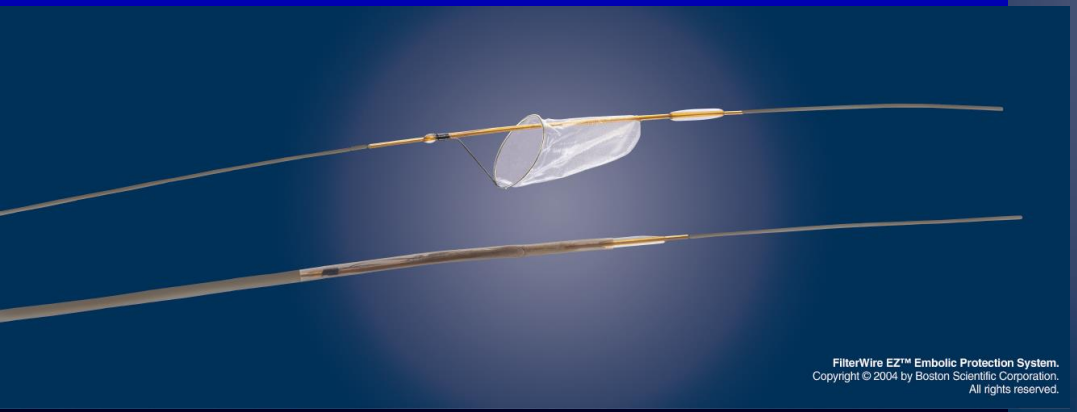
Filters

Advantage

- Maintain Flow
- Visualization during procedure
- Non-ischemic
- Intuitive operation

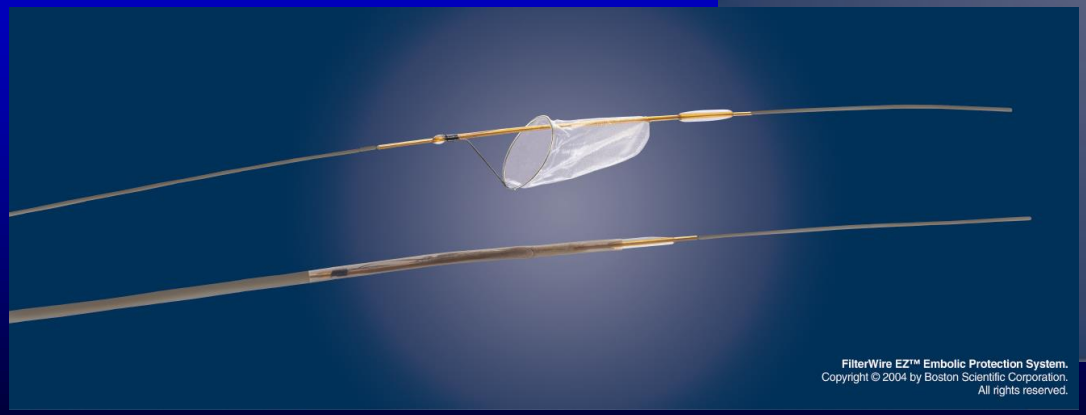
Disadvantage

- May not capture all particles <100 micron
- Does not control secretions of humoral factors

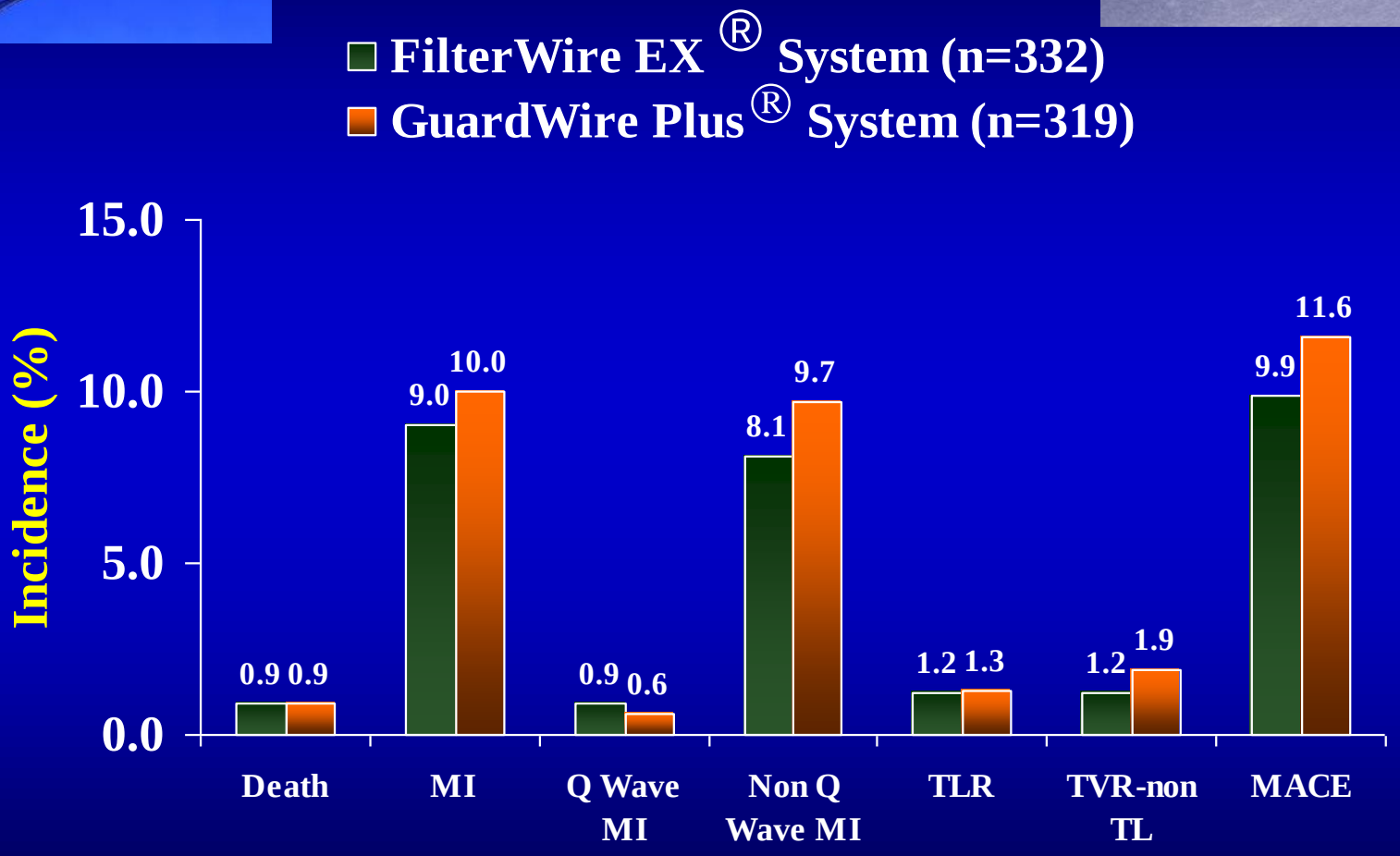


FilterWire EZ™ System*

- Suspension arm conforms filter to curvature
- Improved guidewire
- Pre-loaded
- 3.2F Profile
- Re-designed Delivery Sheath
- Re-tooled nosecone

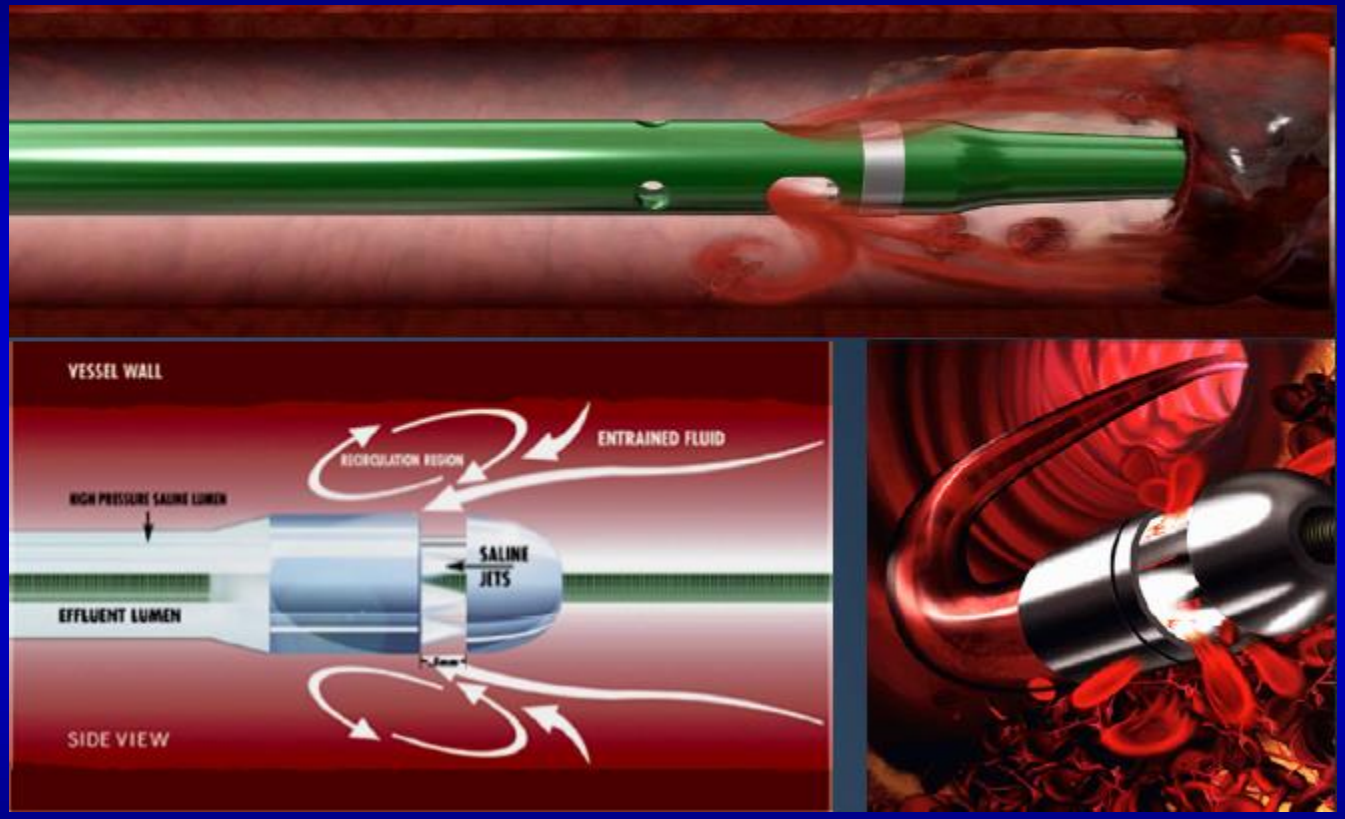


FIRE Trial
30-Day MACE



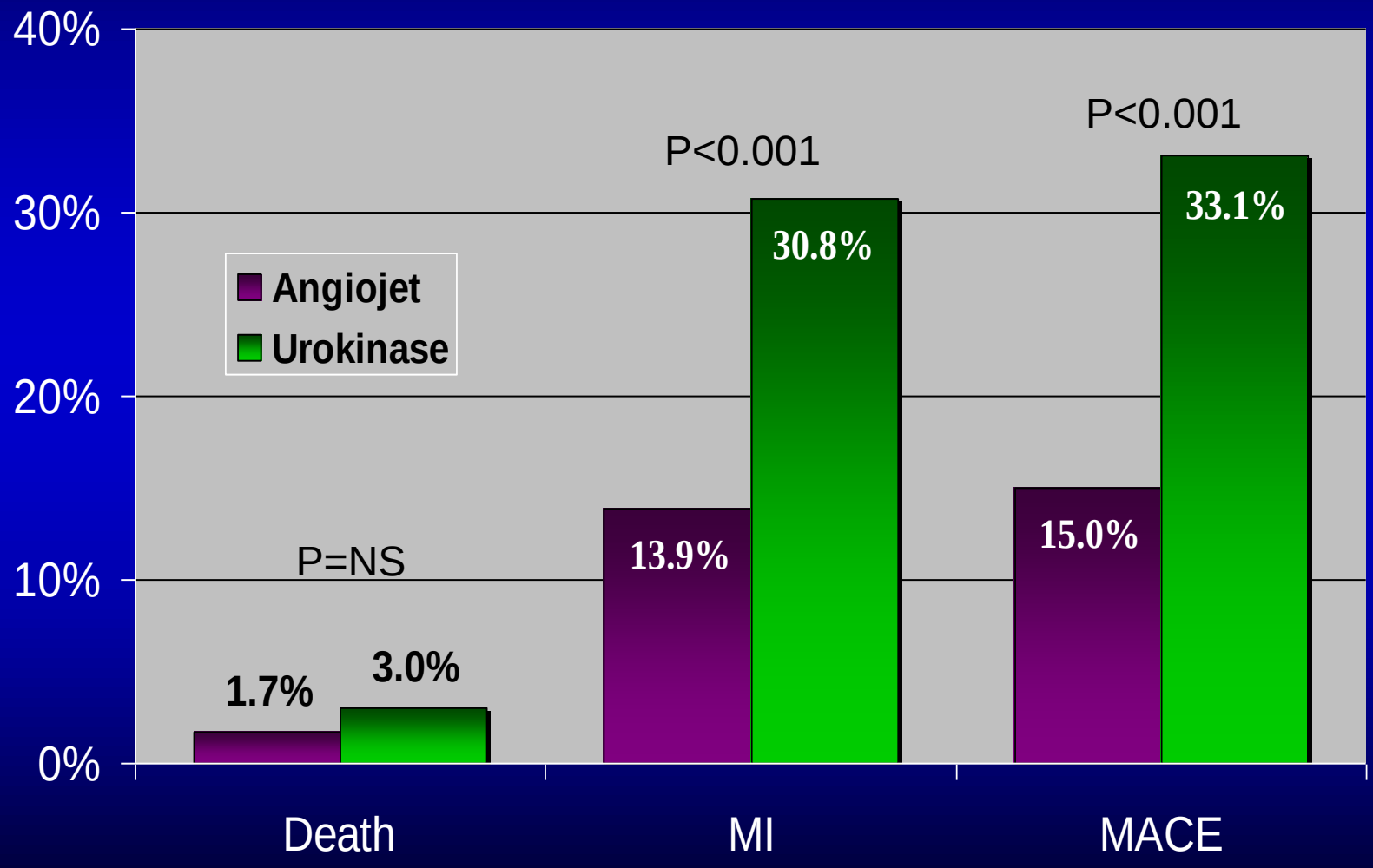
P = 0.0016 (non-inferiority for MACE with 5.5% delta)

Stone et al. Circulation 2003.


VESSEL WALL
RECIRCULATION REGION
ENTRAINED FLUID
HIGH PRESSURE SALINE LUMEN
SALINE JETS
EFFLUENT LUMEN
SIDE VIEW

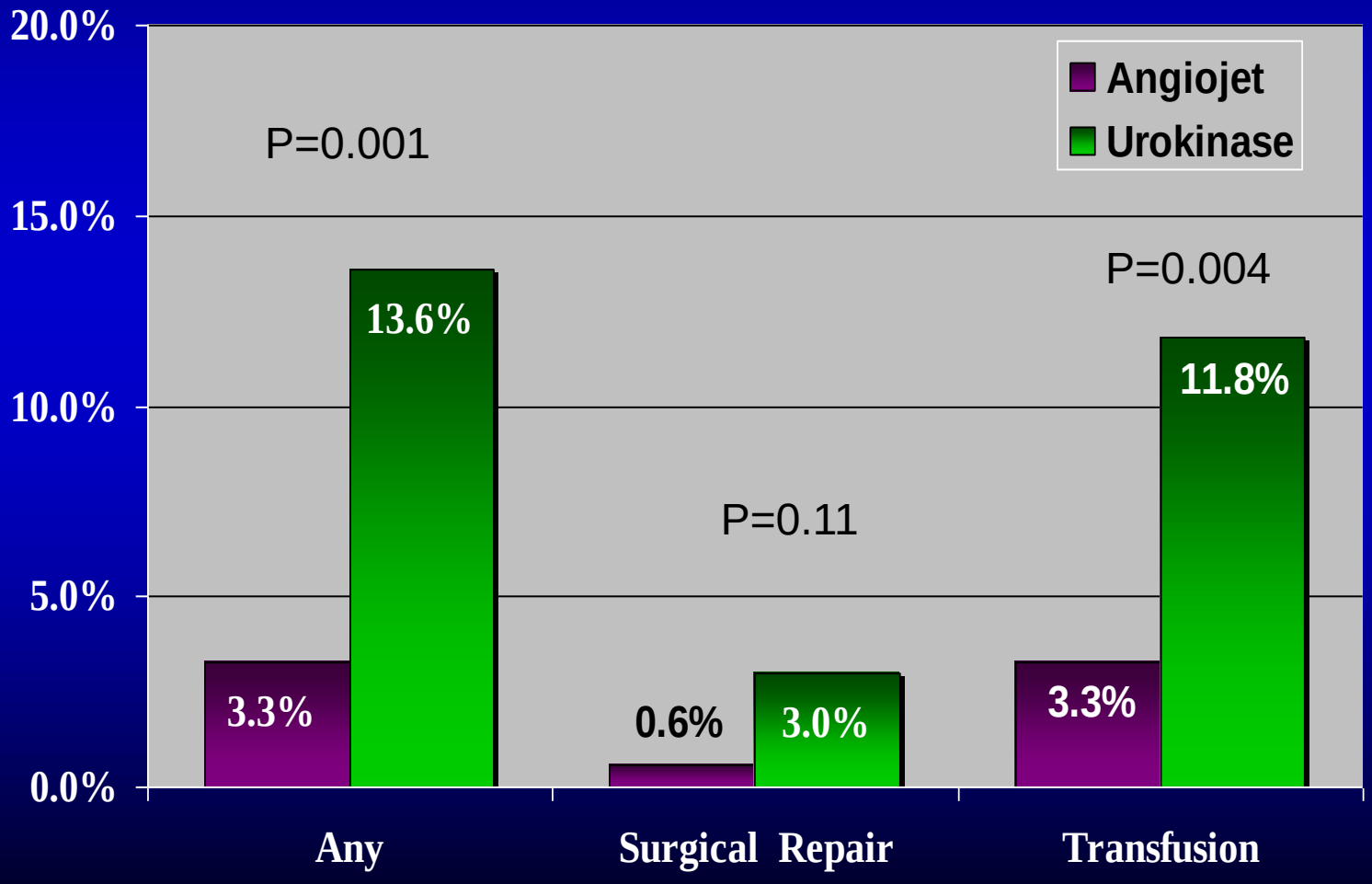
30-Day Clinical Results

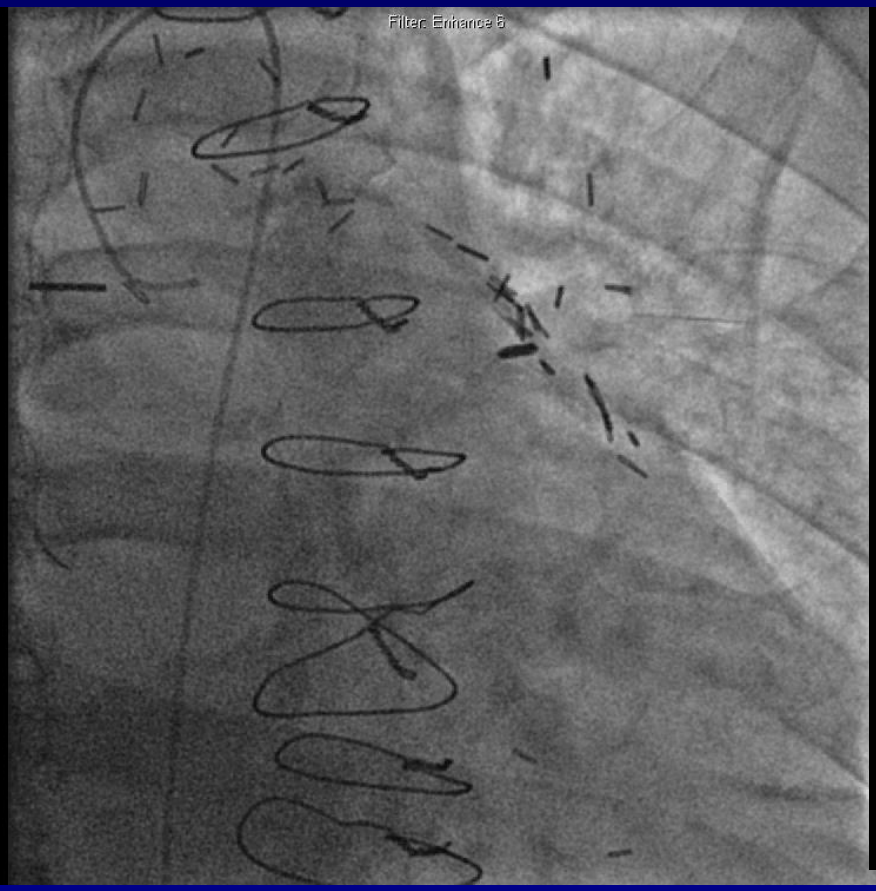
Stopped early (349 vs 500) by DSMB!



VEGAS 2
Trial

Bleeding Complications

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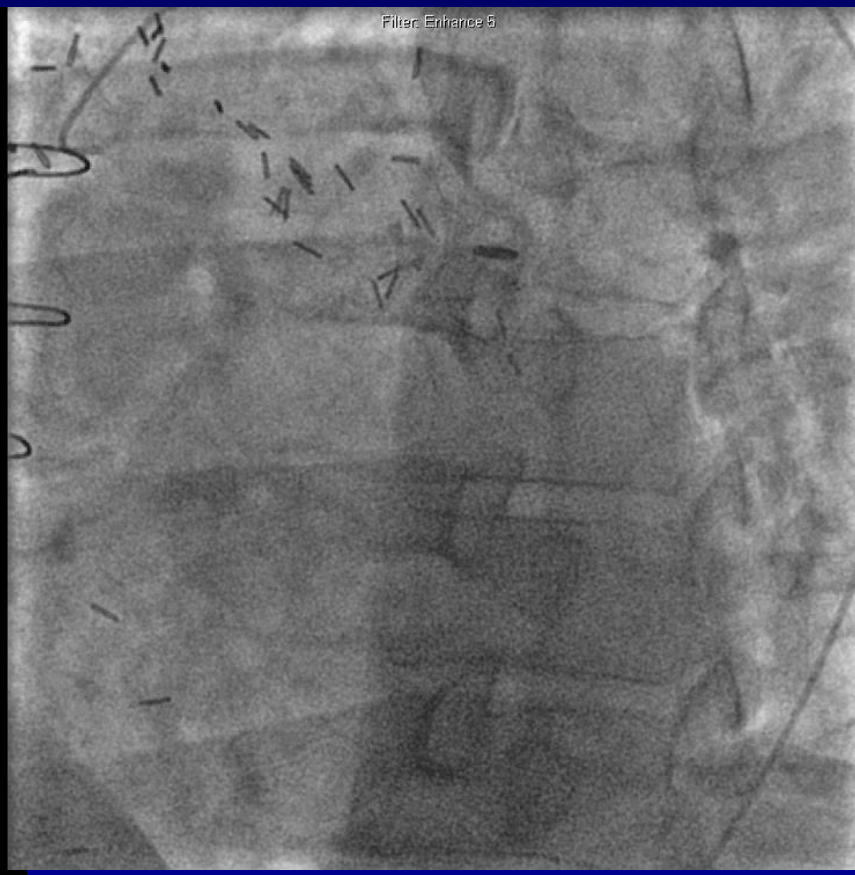
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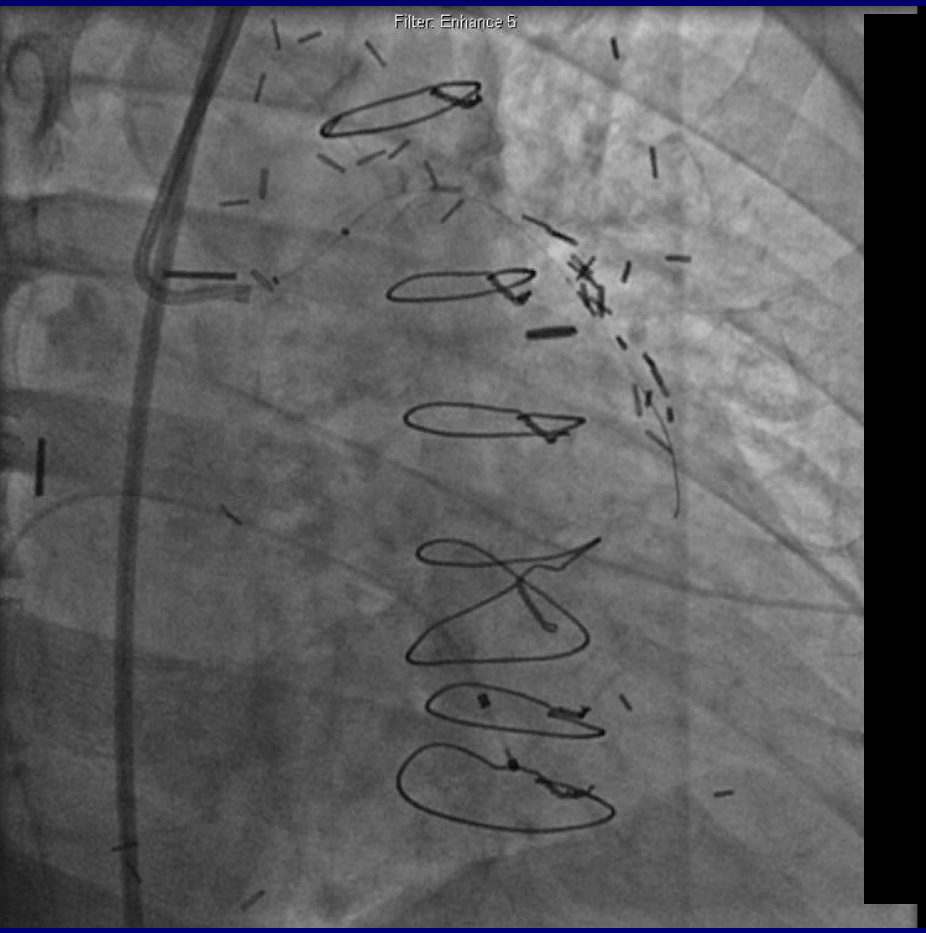
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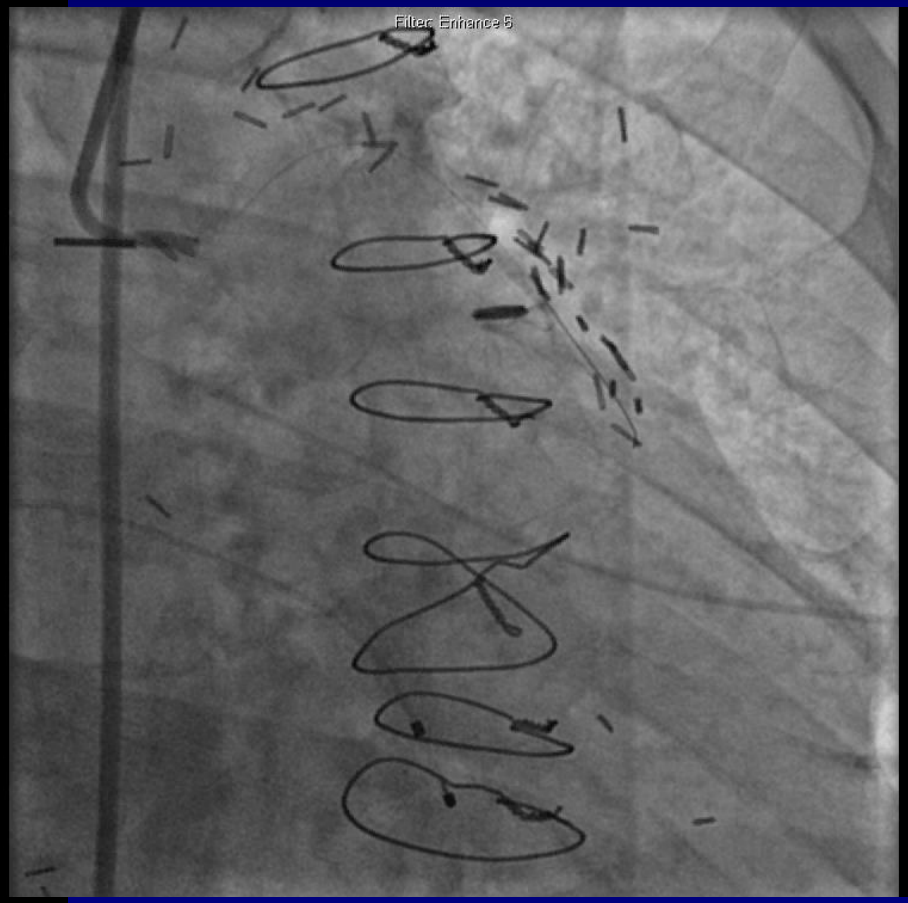
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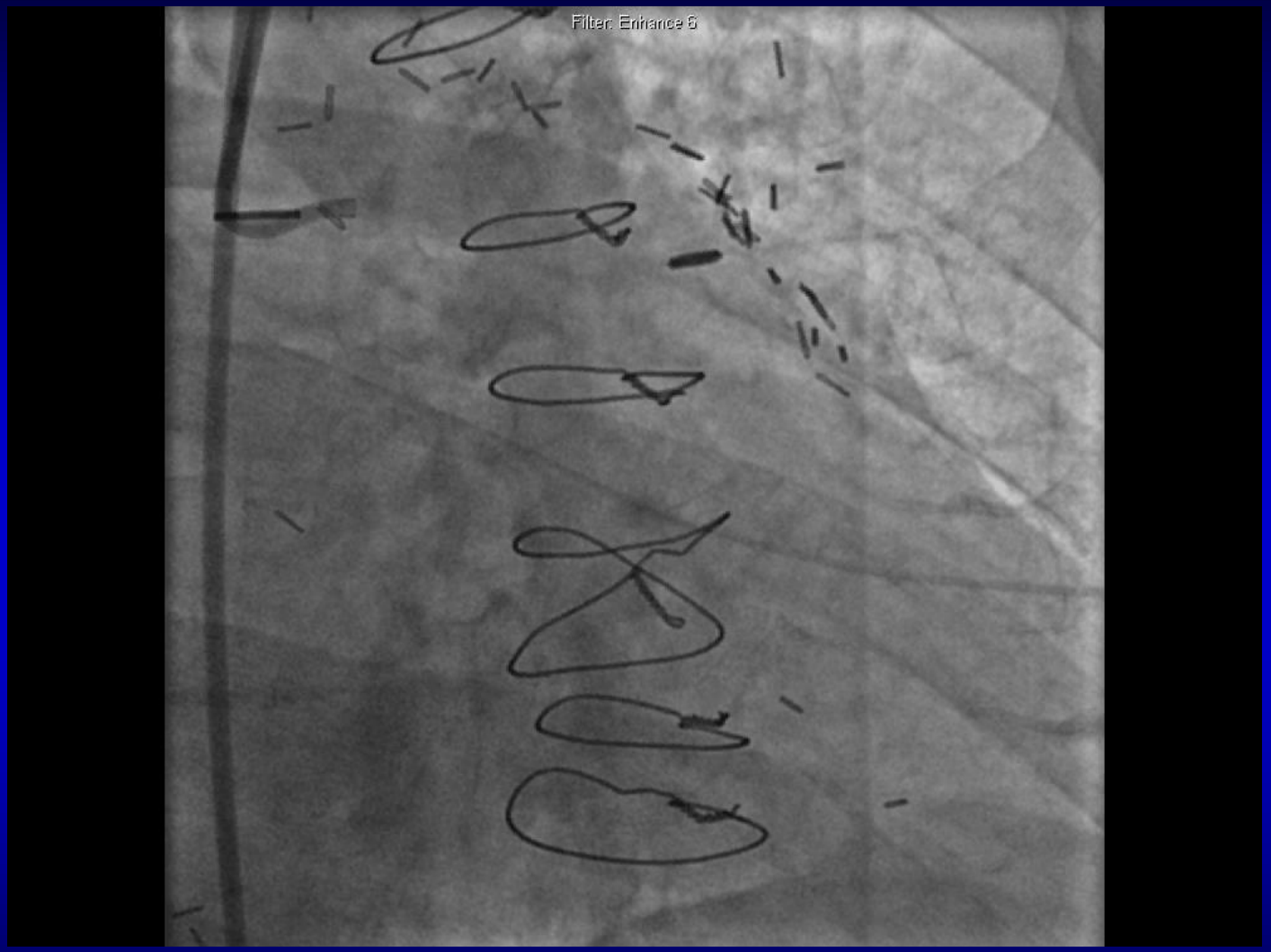
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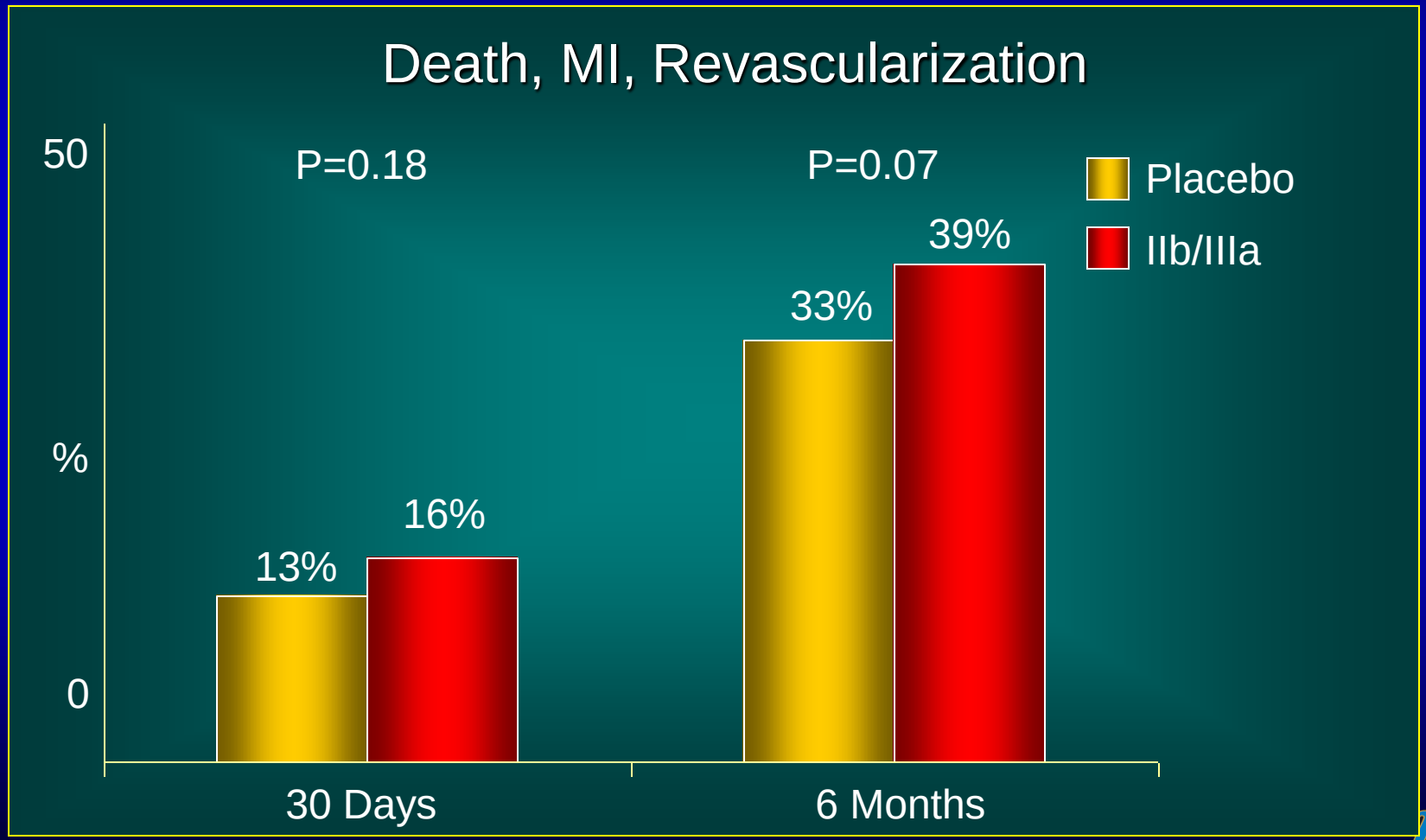
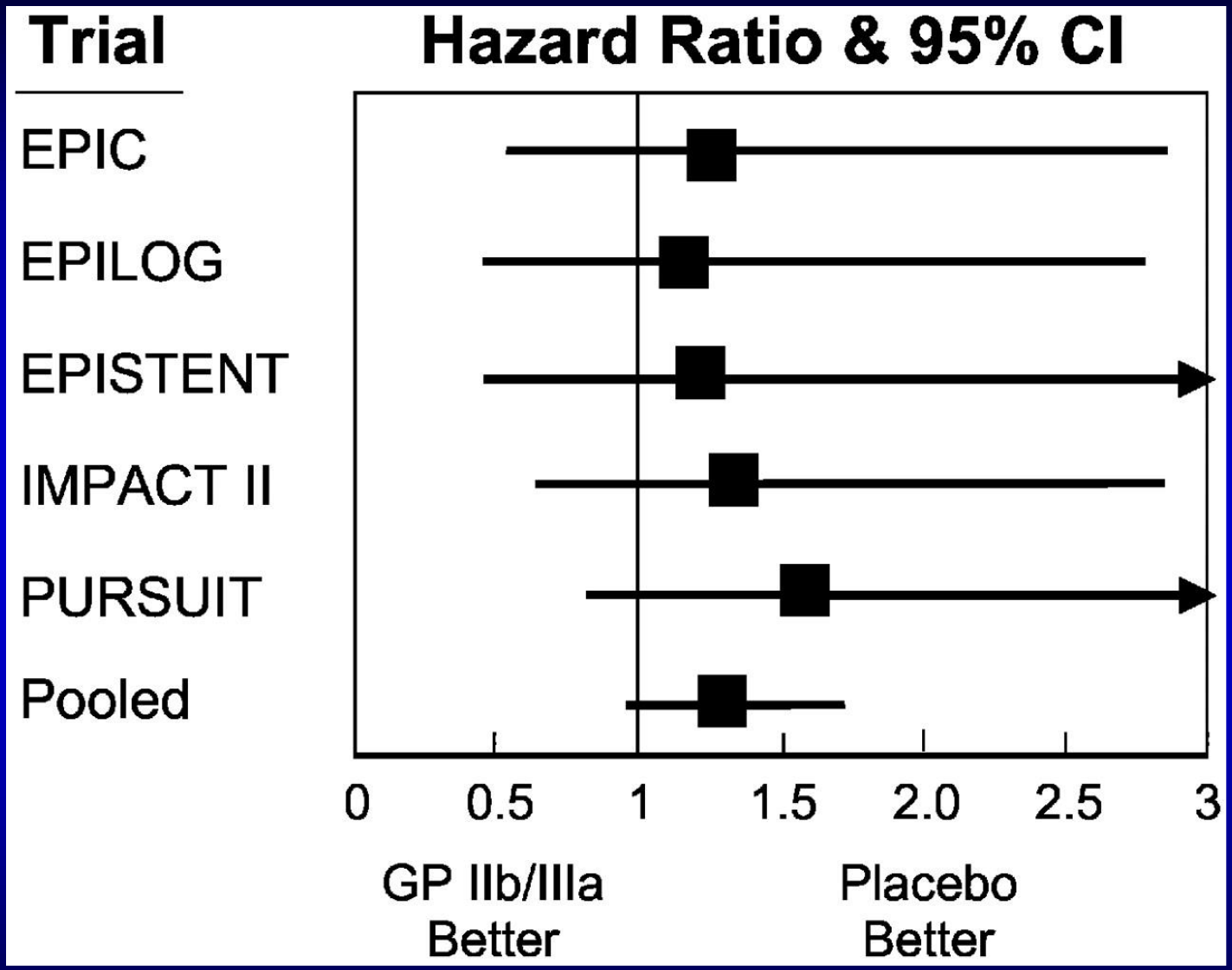
Is there any role of GP IIb/IIIa receptor antagonists in SVG Intervention?

Lack of Benefit of GPIIb/IIIa Inhibitors in SVG PCI

Pooled Analysis of 5 Randomized Trials

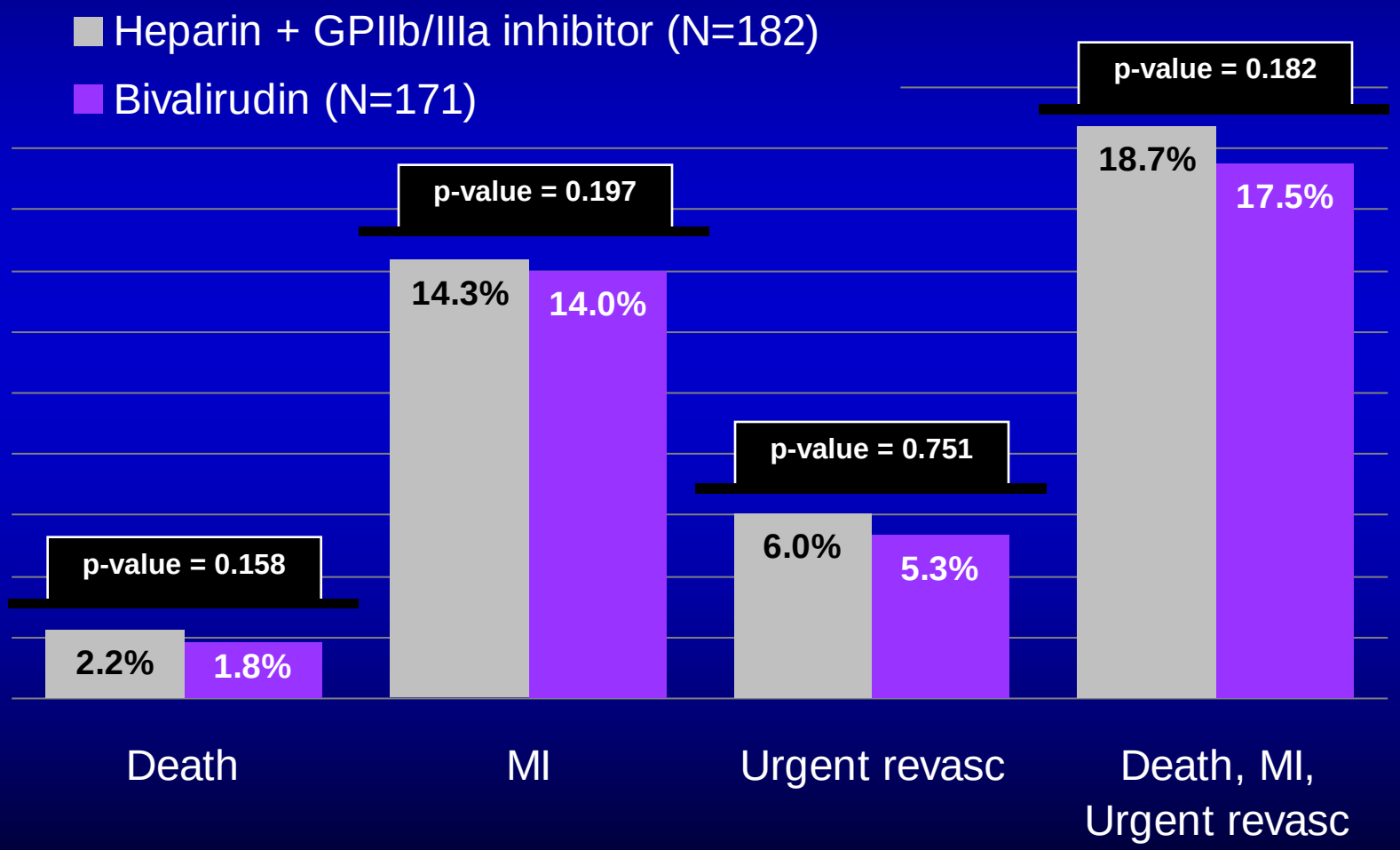


Roffi et al. Circulation 2002



Roffi et al, Circulation 2002;106:3063

SVG Intervention
6-month Follow up



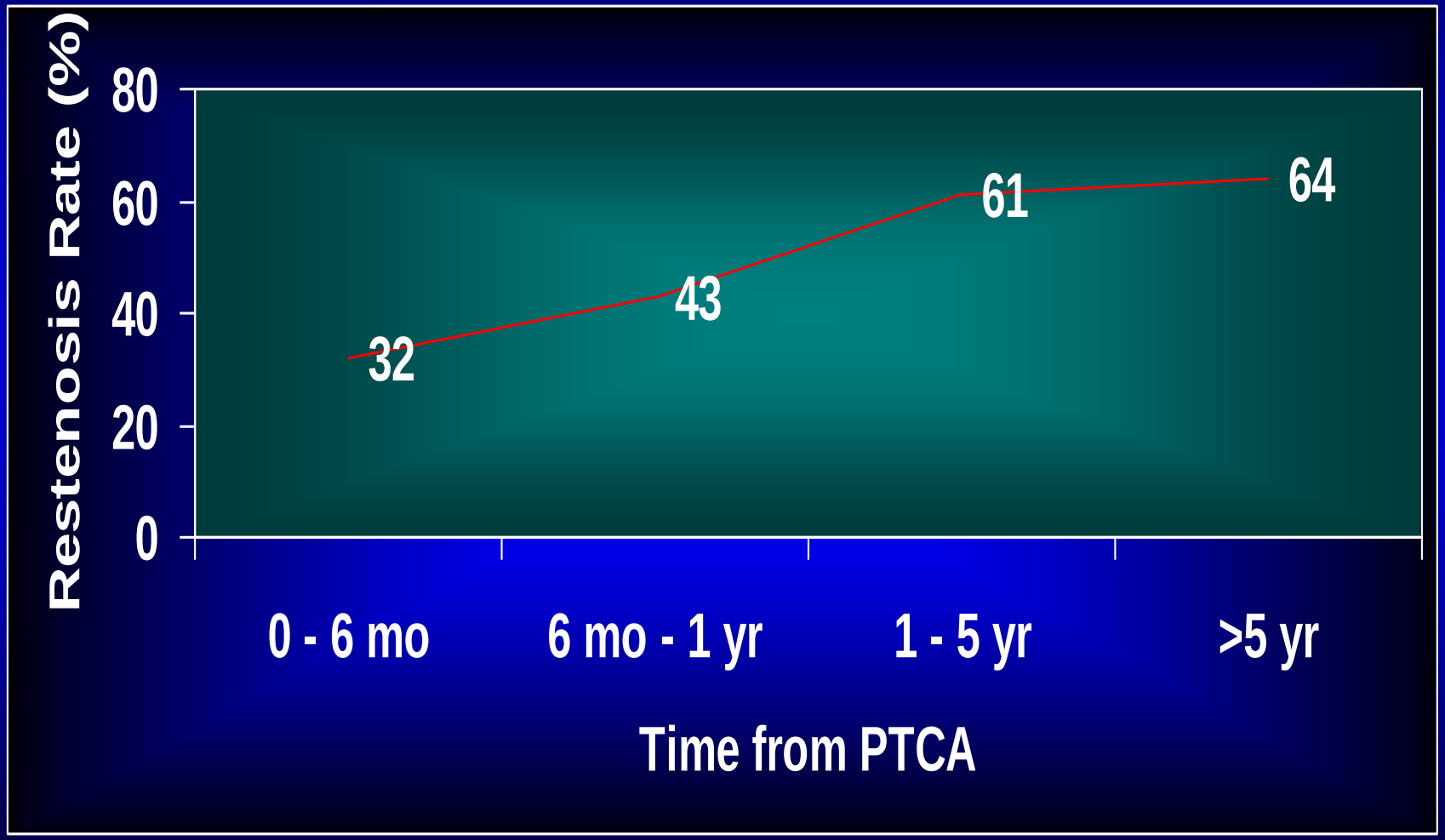
Lincoff AM: TCT 2003

Conclusion

IIbIIIa inhibitors offer NO benefit in SVG intervention

SVG Balloon Angioplasty

Temporal Course of Restenosis



Douglas et al, Circulation 1991.

SAVED (SAphenous Vein De Novo) Trial

215 patients with angina pectoris and/or objective evidence of myocardial ischemia ***and*** de novo lesions in SVG
Vessel diameter: 3.0-5.0 mm

Randomized

PTCA
n=107

Stenting (Palmaz-Schatz)
n=108

Endpoint: 6-month angiographic restenosis

Savage et al. NEJM 1997

SAVED (SAphenous Vein De Novo) Trial

Cumulative Events	PTCA (n=107)	Stent (n=108)	p-value
Procedural Success (%)	**69**	**92**	**<0.001**
Restenosis at 6 months (%)	**46**	**37**	**0.24**
MACE free at 8 months (%)	**58**	**73**	**0.03**
Death at 8 months (%)	**9**	**7**	**0.44**
TLR at 8 months (%)	**26**	**17**	**0.09**

Conclusions:

- Stenting of SVG resulted in superior procedural outcomes, a larger gain in luminal diameter, and a reduction in MACE
- However, there was no benefit in angiographic restenosis

Savage et al. NEJM 1997

DES vs. BMS for SVG Intervention

223 consecutive patients underwent SVG intervention

Non-randomized, single center, retrospective analysis

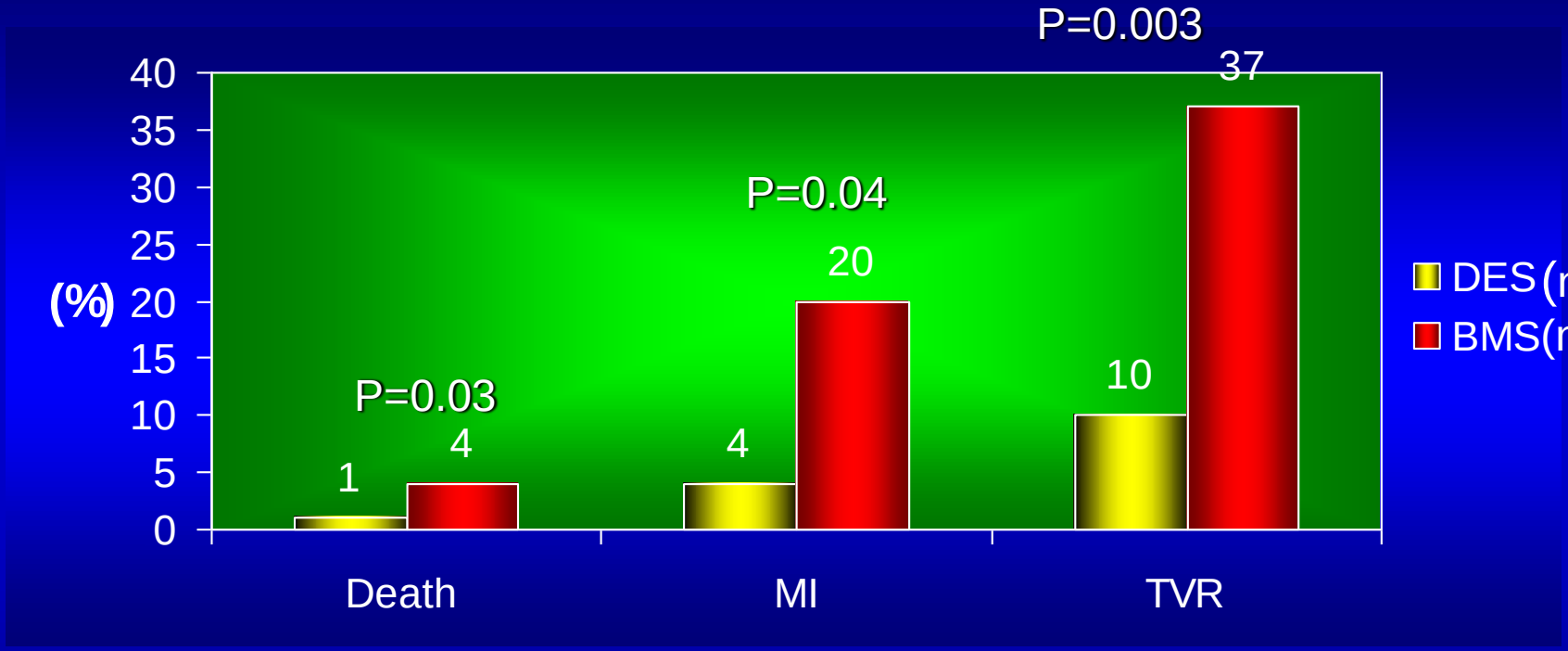
Operator discretion

BMS (201 stents)
n=84 patients

DES (289 stents: 211 SES, 78 PES)
n=139 patients

Lee MS, et al. Catheter Cardiovasc Interv 2005

Clinical Outcomes at 9 Months



Lee MS et al. Cathet Cardiovas Interv 2005.

RRISC Trial

Reduction of Restenosis In Saphenous vein grafts with Cypher stent

75 patients with 96 lesions localized in 80 diseased SVG.
Prospective, randomized, double-blind, non industry sponsored, single center, trial

Randomized

BMS
n=37

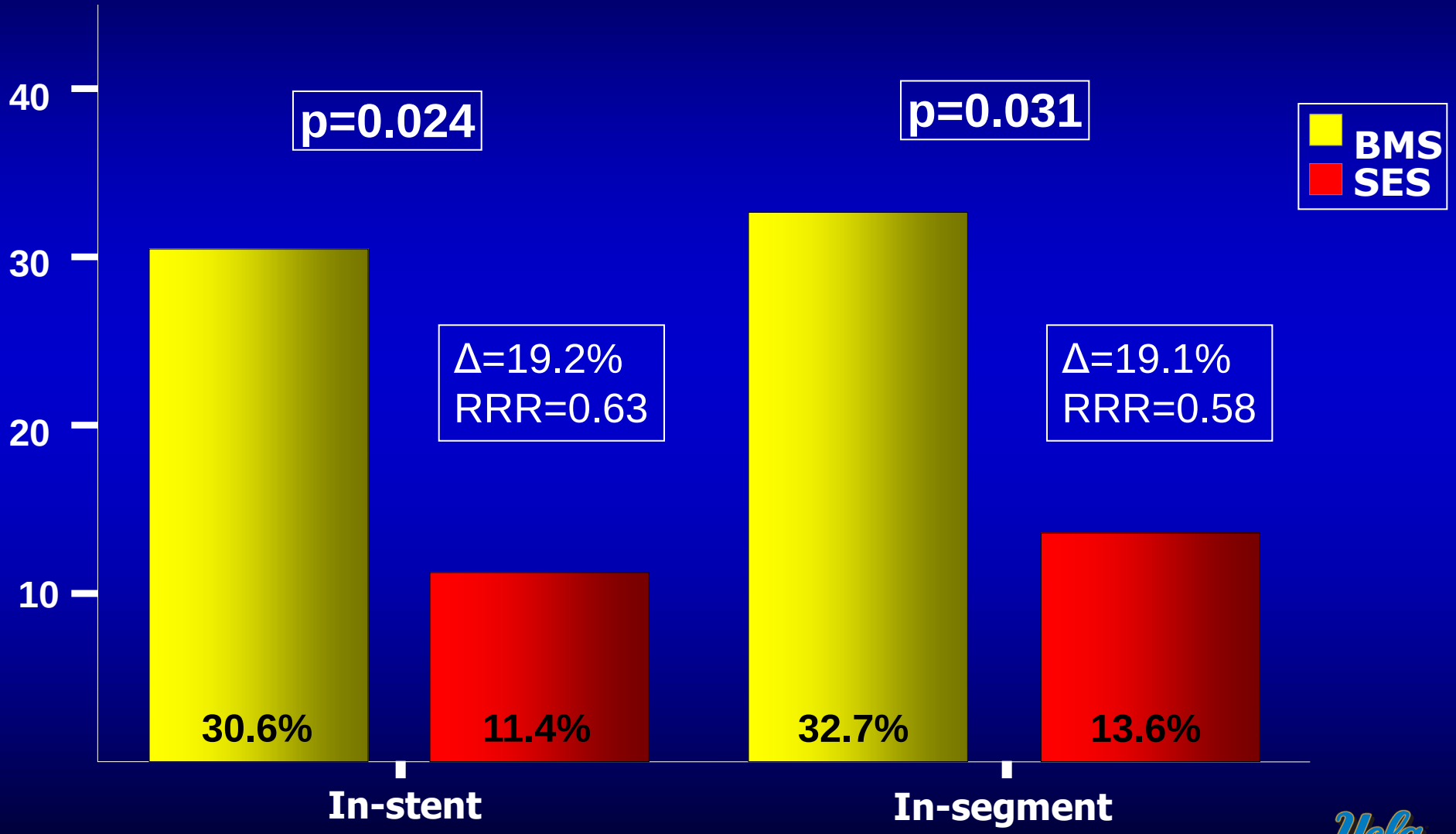
Cypher stent
n=38

Primary endpoint
- -6-month in-stent late loss

Secondary endpoints (all at 6 months follow up):
- -Binary angiographic restenosis (in-stent/in-segment)
- -Clinical events (death, MI, TLR, TVR)

Vermeersch et al. JACC 2006

Binary Restenosis



Vermeersch et al. JACC 2006

6-month MACE

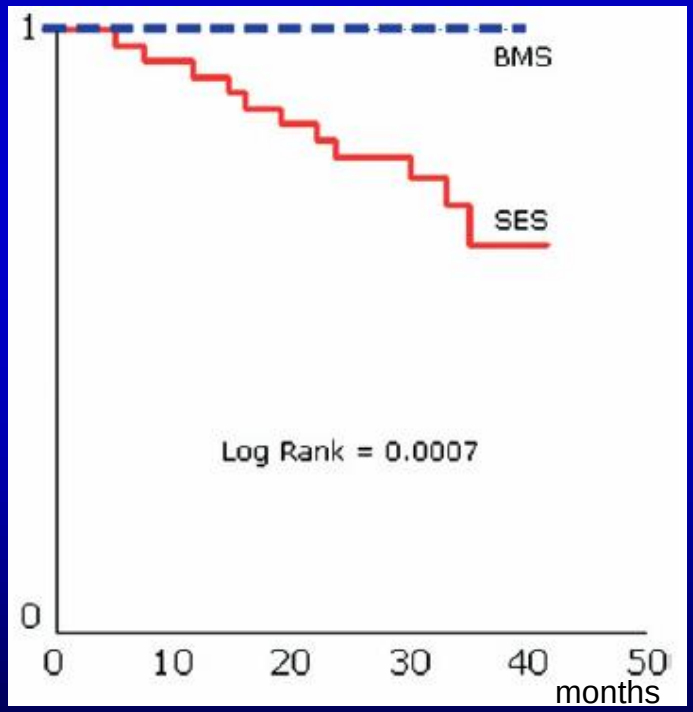
	BMS n=37	SES n=38	P value
In-hospital			
Death	**0**	**0**	
Repeat revascularization	**0**	**0**	
Periprocedural MI	**1 (2.7%)**	**2 (5.3%)**	**0.99**
Between discharge and 6 months			
Death	**0**	**1 (2.6%)**	**0.99**
Myocardial infarction	**0**	**1 (2.6%)**	**0.99**
TLR (per-patient)	**8 (21.6%)**	**2 (5.3%)**	**0.047**
TVR (per-patient)	**10 (27%)**	**2 (5.3%)**	**0.012**
Cumulative 6-month MACE	**11 (29.7%)**	**6 (15.8%)**	**0.15**

Vermeersch et al. JACC 2006

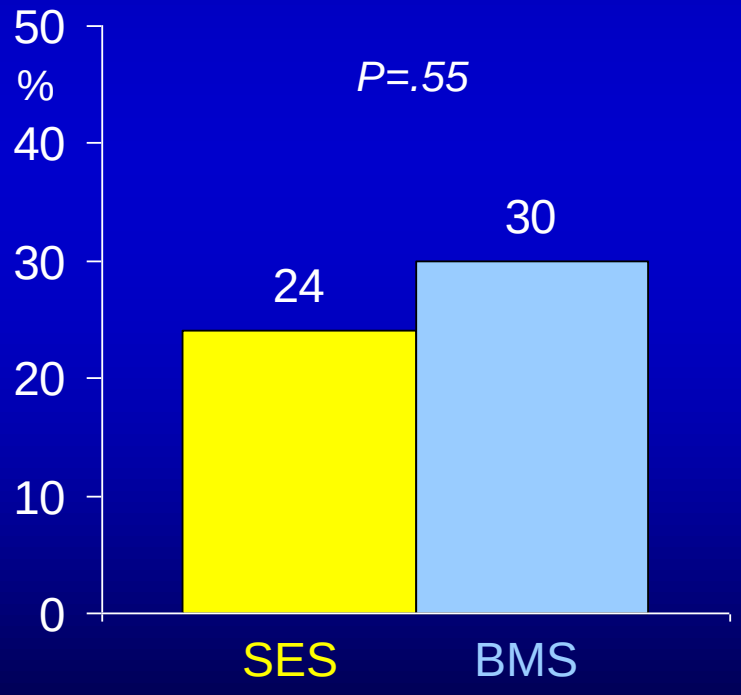
DES vs. BMS in Saphenous Vein Graft Lesions

DELAYED RRISC Trial
N=75

Survival



TLR



Vermeersch et al., JACC 2007

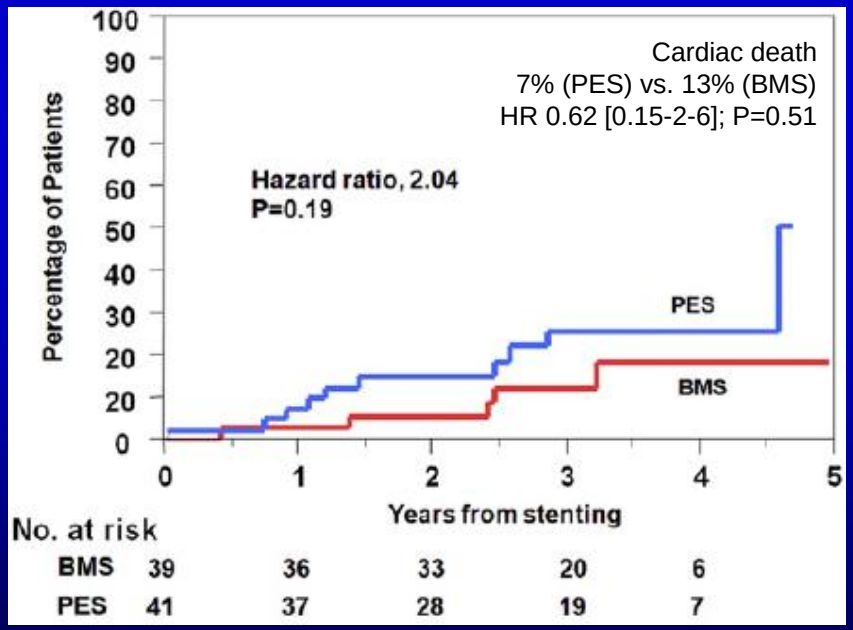
Stent Thrombosis
(ARC criteria)

	BMS n=37	SES n=38	P value
Definite	0	2 (5.2%) 1 fatal at 13 mo 1 non fatal at 30 mo	0.49
Probable	0	0	-
Possible	0	3 (7.9%) 1 sudden death at 7.5 mo 1 sudden death at 11.5 mo 1 sudden death at 35 mo	0.30
Total	0	5 (13.1%)	0.02 Log Rank

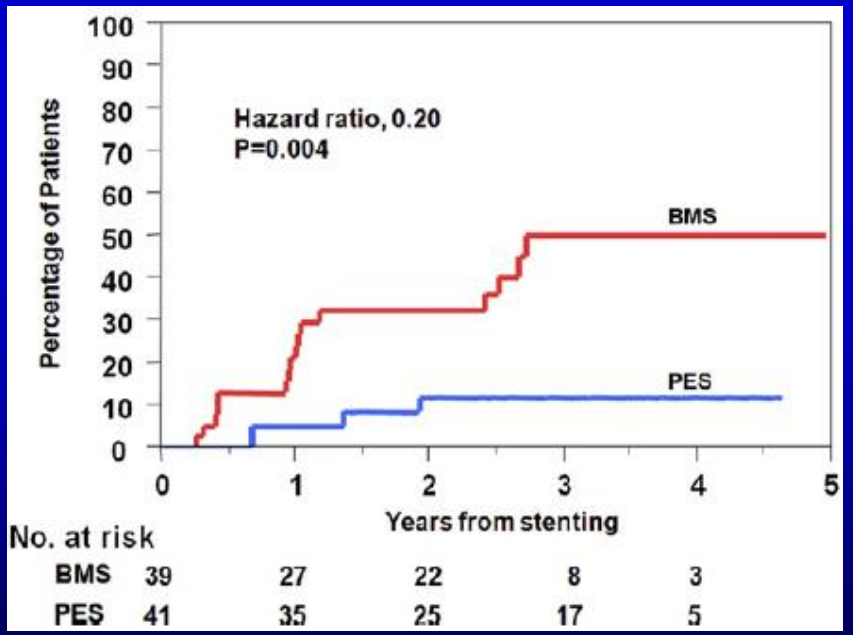
DES vs. BMS in Saphenous Vein Graft Lesions

SOS Trial
N=80

All-cause Death

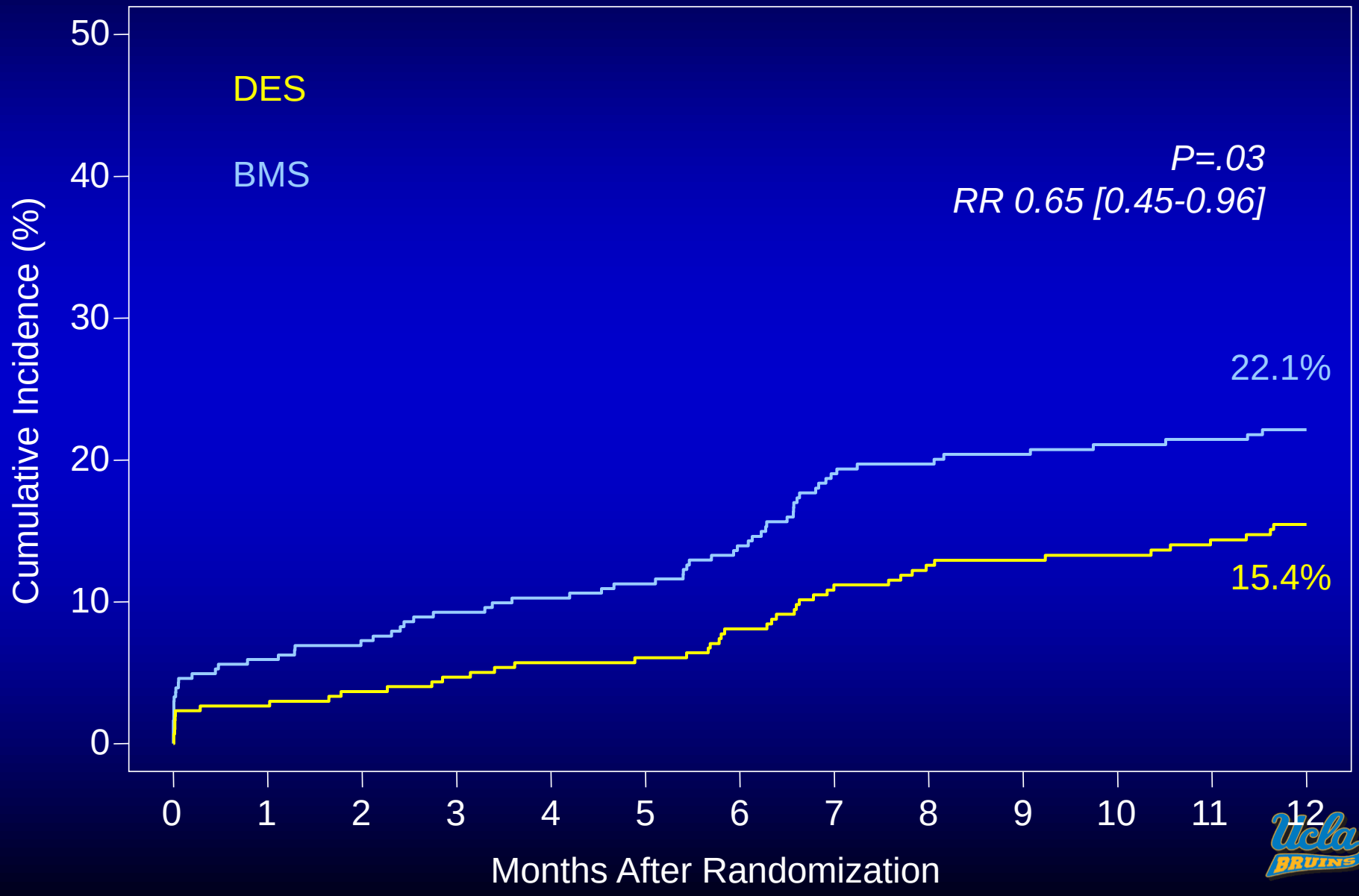


Target Lesion Revascularization



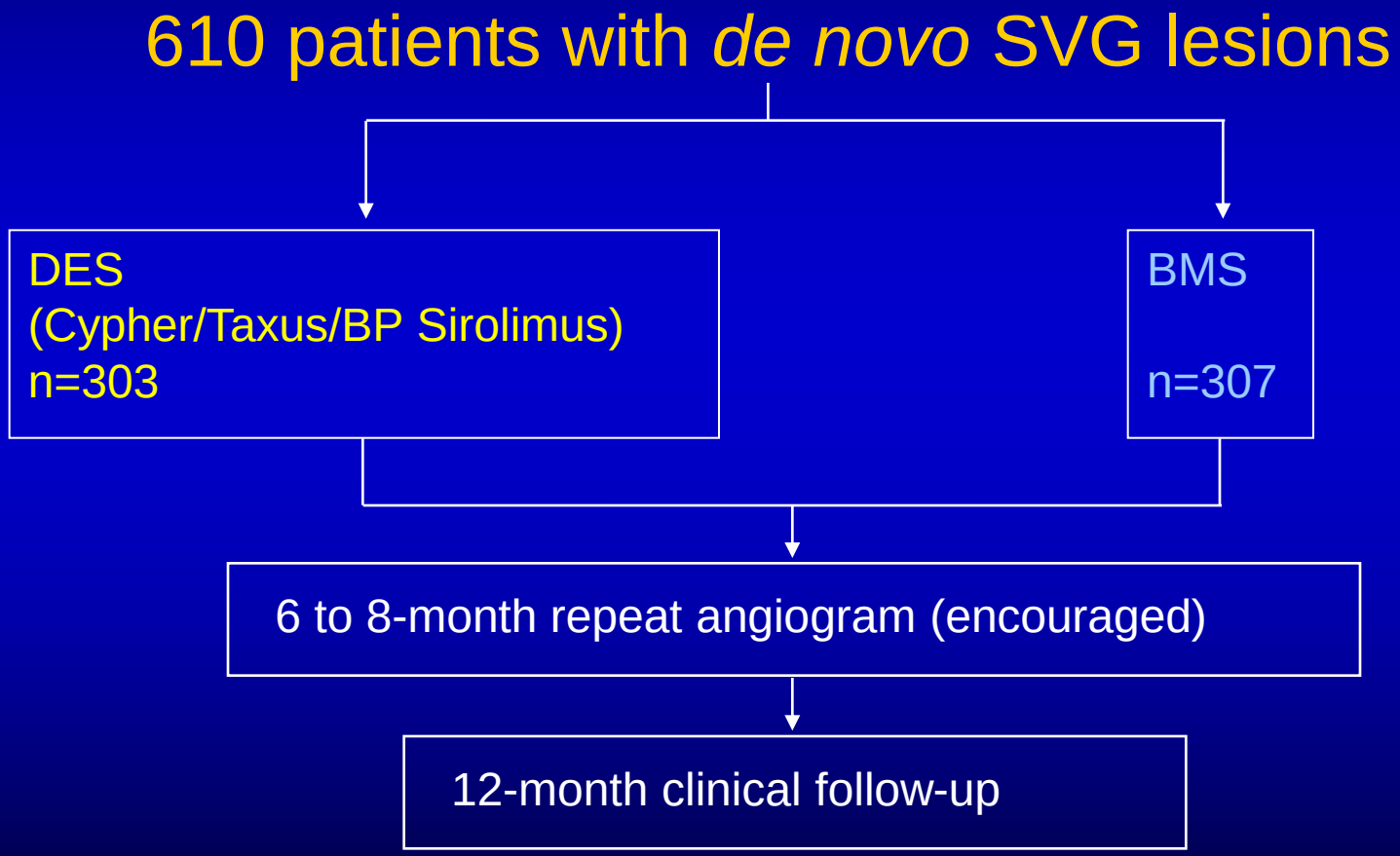
Brilakis et al., JACC Intv 2011

Primary Endpoint: Death/MI/TLR

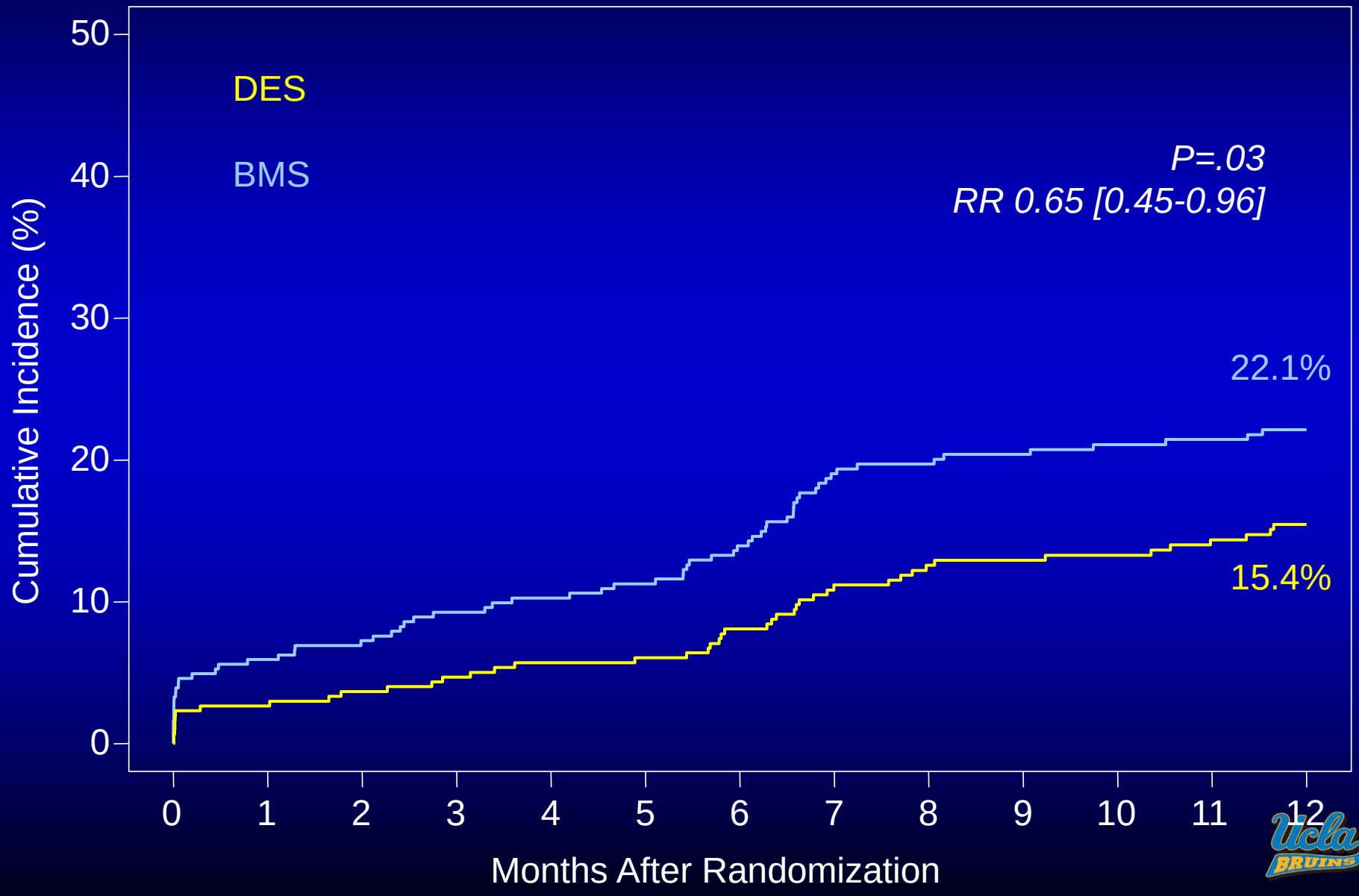


ISAR-CABG

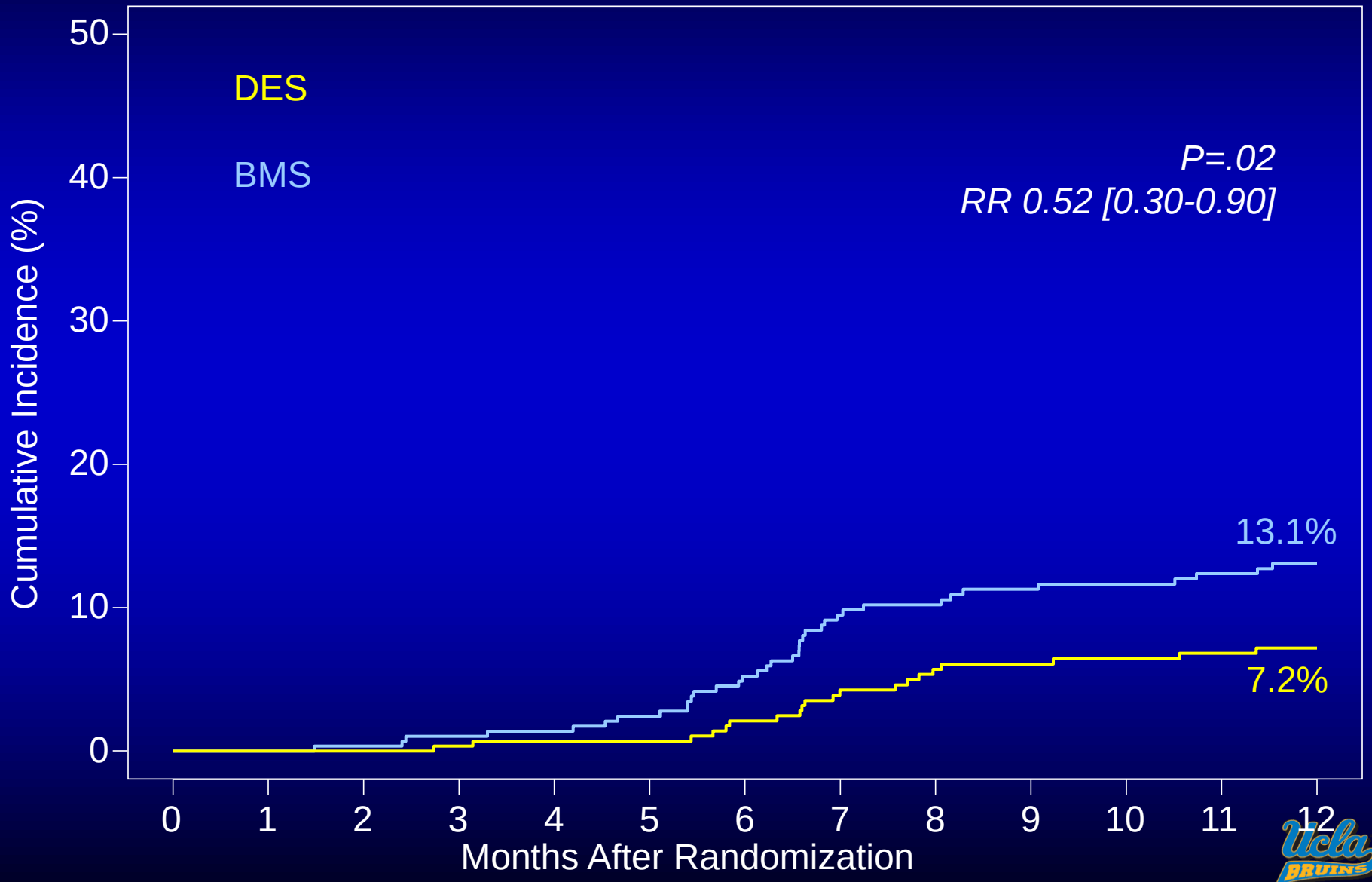
*I*s Drug-Eluting *S*tenting *A*ssociated With Improved *R*esults in *C*oronary *A*rtery *B*ypass *G*rafts?



Primary Endpoint: Death/MI/TLR



Target Lesion Revascularization



Conclusions

- The behavior of SVG disease is substantially different from native CAD-with higher incidence of procedural complications and long-term failure
- Glycoprotein IIb/IIIa antagonists are ineffective in SVG intervention, presumably due to their ineffectiveness against atheroemboli
- Embolic protection in SVG PCI can dramatically reduce 30 day MACE rates and should be used in SVG PCI
- A large randomized trial with long-term follow up is needed to determine if DES is preferred over BMS

Thank You!

Safety and Efficacy of CYPHER® in Saphenous Vein Grafts

Limitations

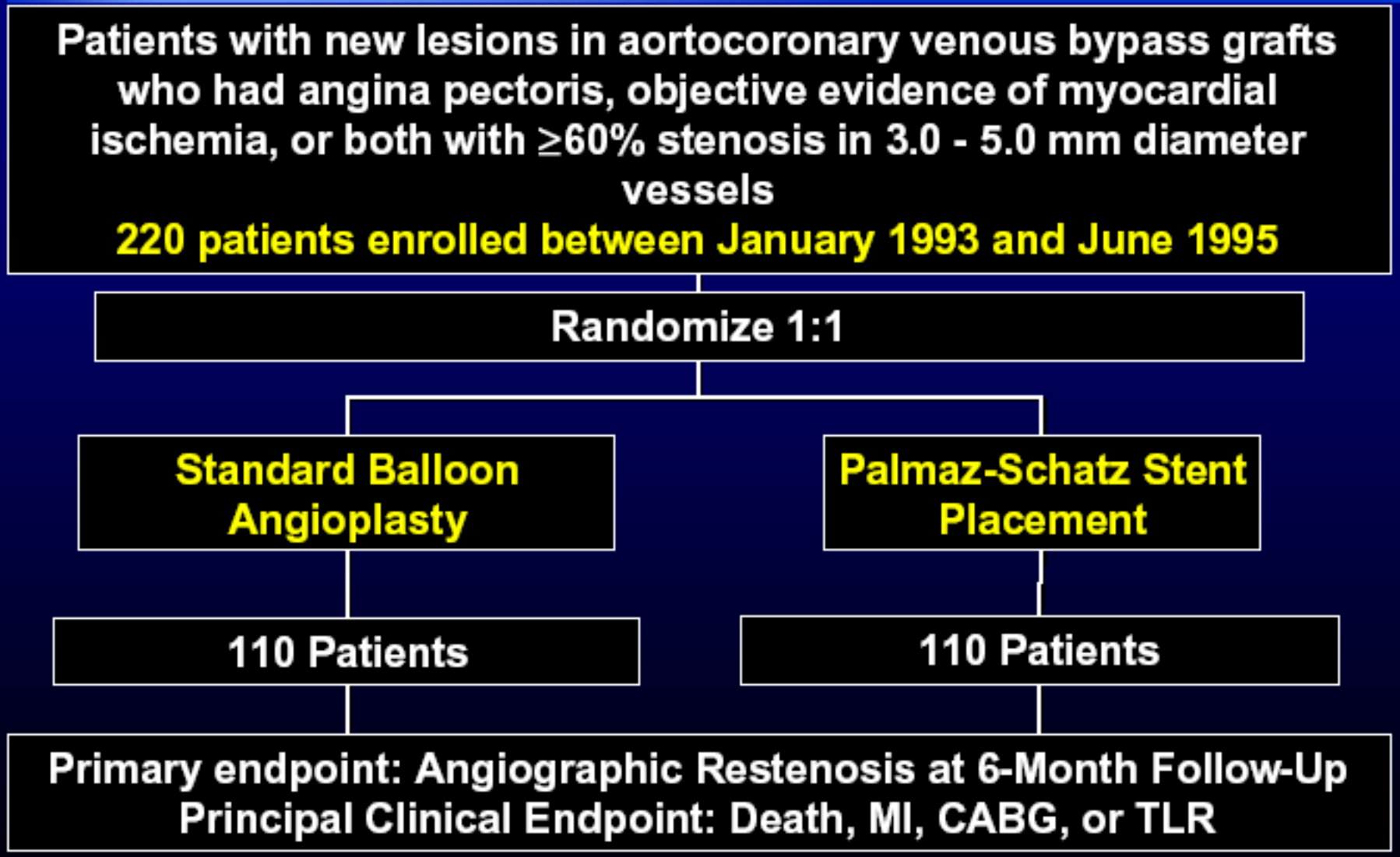
- There have been no large, randomized studies comparing the safety and efficacy of bare-metal stenting vs. CYPHER® stenting for the treatment of saphenous vein grafts
- Event rates reported in these publications reflect anecdotal experience at several high-volume institutions
- Due to the limited data contained in studies evaluating the use of CYPHER® in saphenous vein grafts, these data sets are not adequately powered to evaluate variables with low event rates (such as stent thrombosis)

Background

- Within 10 years of surgery, 50% of all saphenous vein bypass grafts have severe atherosclerotic disease
  - Lawrie GM, et al., *Am J Cardiol* 1976;38:856-62.
  - Hamby RI, et al. *Circulation* 1979;60:901-9.
  - Bourassa MG, et al., *Am J Cardiol* 1984;53:102C-107C.
  - Bourassa MG, et al., *Circulation* 1985; 72:Suppl V:V-71–V-78.
  - Virmani R, et al., *Cardiovasc Clin* 1988;18:41-62.
  - Lytle BW, et al., *J Thorac Cardiovasc Surg* 1985;89: 248-58.
  - FitzGibbon GM, et al., *J Am Coll Cardiol* 1991;17:1075-80.
- Management of these lesions remains problematic, due to the risks of repeated surgery and high rates of restenosis with bare-metal stenting

Savage M., et al., *NEJM* 1997; 337:740-47.
Peykar S., et al., Minerva Cardioangiol 2004; 52: 379-90.

Study Design



Savage M., et al., *NEJM* 1997; 337:740-47.

Exclusion Criteria

- Myocardial infarction within 7 days
- Contraindication to aspirin, dipyridamole, or warfarin
- Ejection fraction < 25%
- Diffuse disease that would require > 2 stents
- Thrombus
- Outflow obstruction of the graft due to distal anastomotic stenosis or poor runoff in the recipient native vessel

Savage M., et al., *NEJM* 1997; 337:740-47.

Safety and Efficacy of Bare-Metal Stents in Saphenous Vein Grafts

Baseline Clinical Characteristics

	Angioplasty (n = 107)	Stent Placement (n = 108)
Age (y)	66 ± 9	66 ± 9
Male (%)	79	82
Hyperlipidemia (%)	64	65
Hypertension (%)	55	61
Diabetes Mellitus (%)	36	23*
Current Smoking (%)	15	17
Prior MI (%)	70	68
Unstable Angina (%)	77	82
LVEF (%)	0.52 ± 0.14	0.53 ± 0.14

* p = 0.05

Savage M., et al., *NEJM* 1997; 337:740-47.

Baseline Anatomical Characteristics

	Angioplasty (n = 107)	Stent Placement (n = 108)
Age of graft (y)	9.4 ± 4.3	10.1 ± 4.2
Distal Anastomoses (%)		
- Single	82	84
- Multiple	18	16
Target Lesion (%)		
- Aortic anastomosis	9	7
- Proximal Third	29	43
- Middle Third	36	29
- Distal Third	21	19
- Coronary anastomosis	5	2
# of Lesions Treated (%)		
- one	83	82
- two	10	14
- three or more	7	4

Savage M., et al., *NEJM* 1997; 337:740-47.

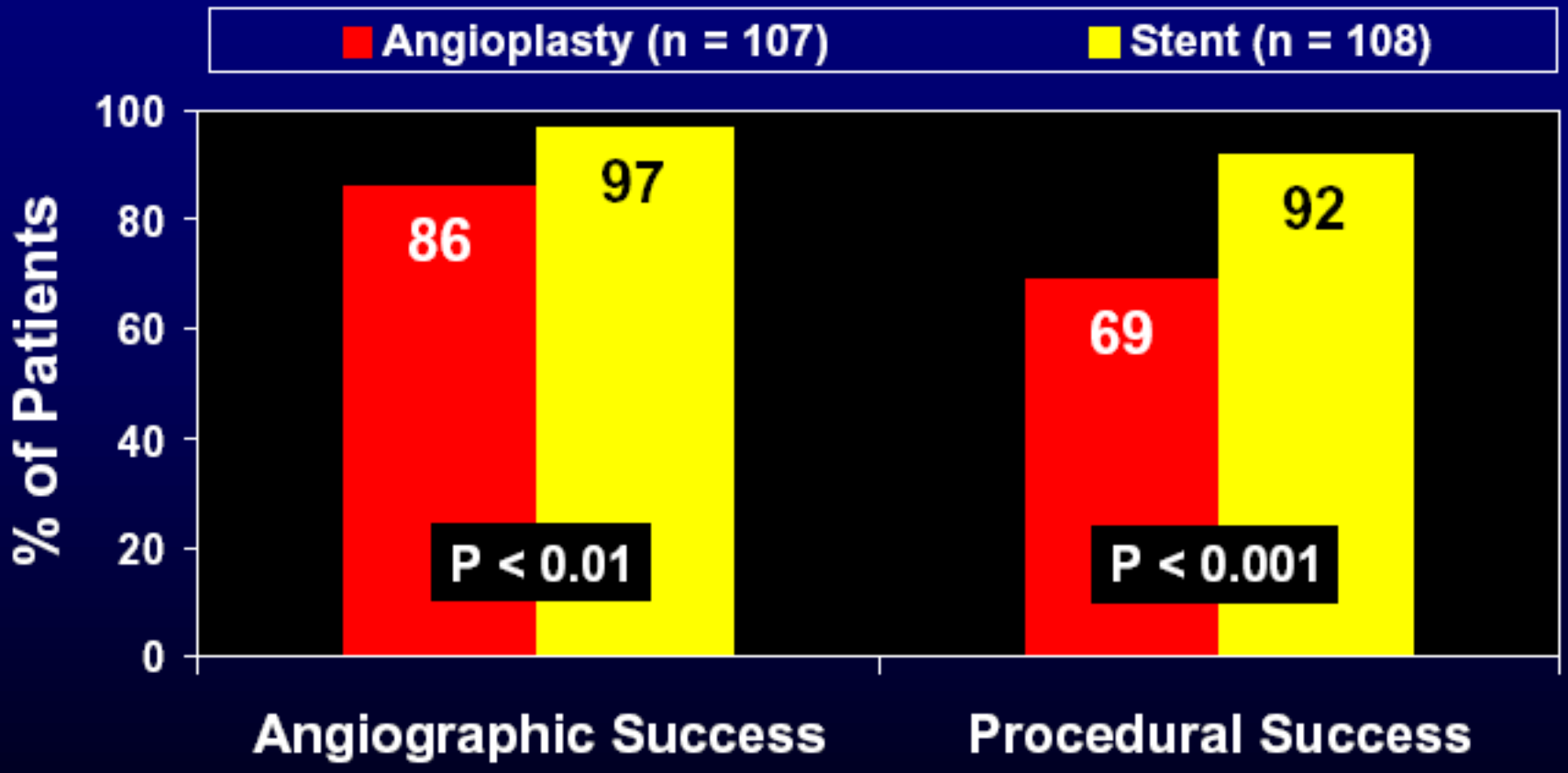
Baseline Lesion Characteristics

	Angioplasty (n = 107)	Stent Placement (n = 108)
Lesion Length, mm	9.8 ± 5.2	9.6 ± 5.4
Diameter Stenosis (%)	71 ± 12	72 ± 12
Eccentricity (%)	82	73
Ulceration (%)	39	35
Lesion Bend > 45° (%)	10	11
Tortuous Graft (%)	39	39

Savage M., et al., *NEJM* 1997; 337:740-47.

Safety and Efficacy of Bare-Metal Stents in Saphenous Vein Grafts

Angiographic and Procedural Success



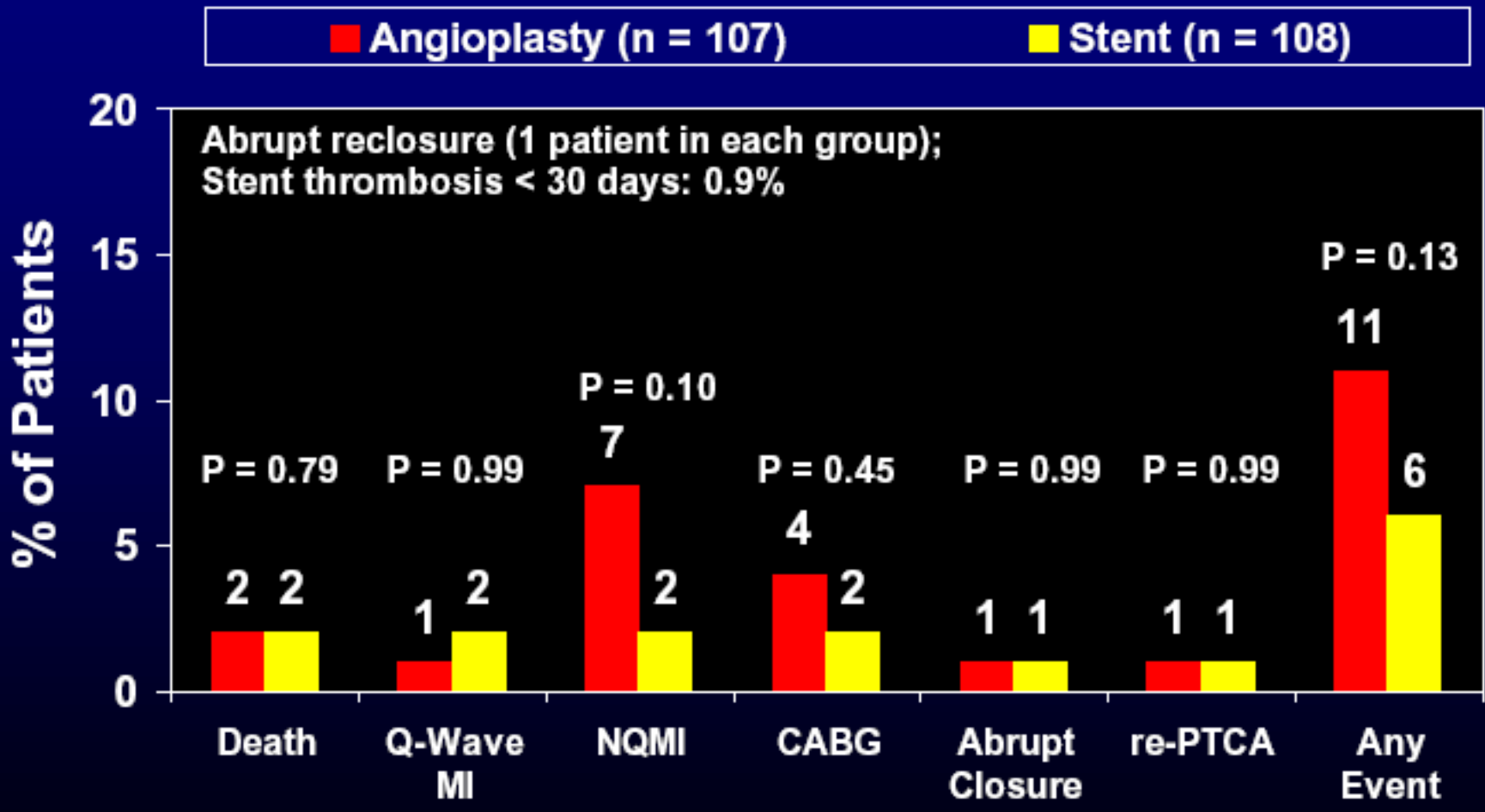
Residual stenosis
≤ 50% post-PCI

Angiographic success without
a major in-hospital complication

Savage M., et al., *NEJM* 1997; 337:740-47.

Safety and Efficacy of Bare-Metal Stents in Saphenous Vein Grafts

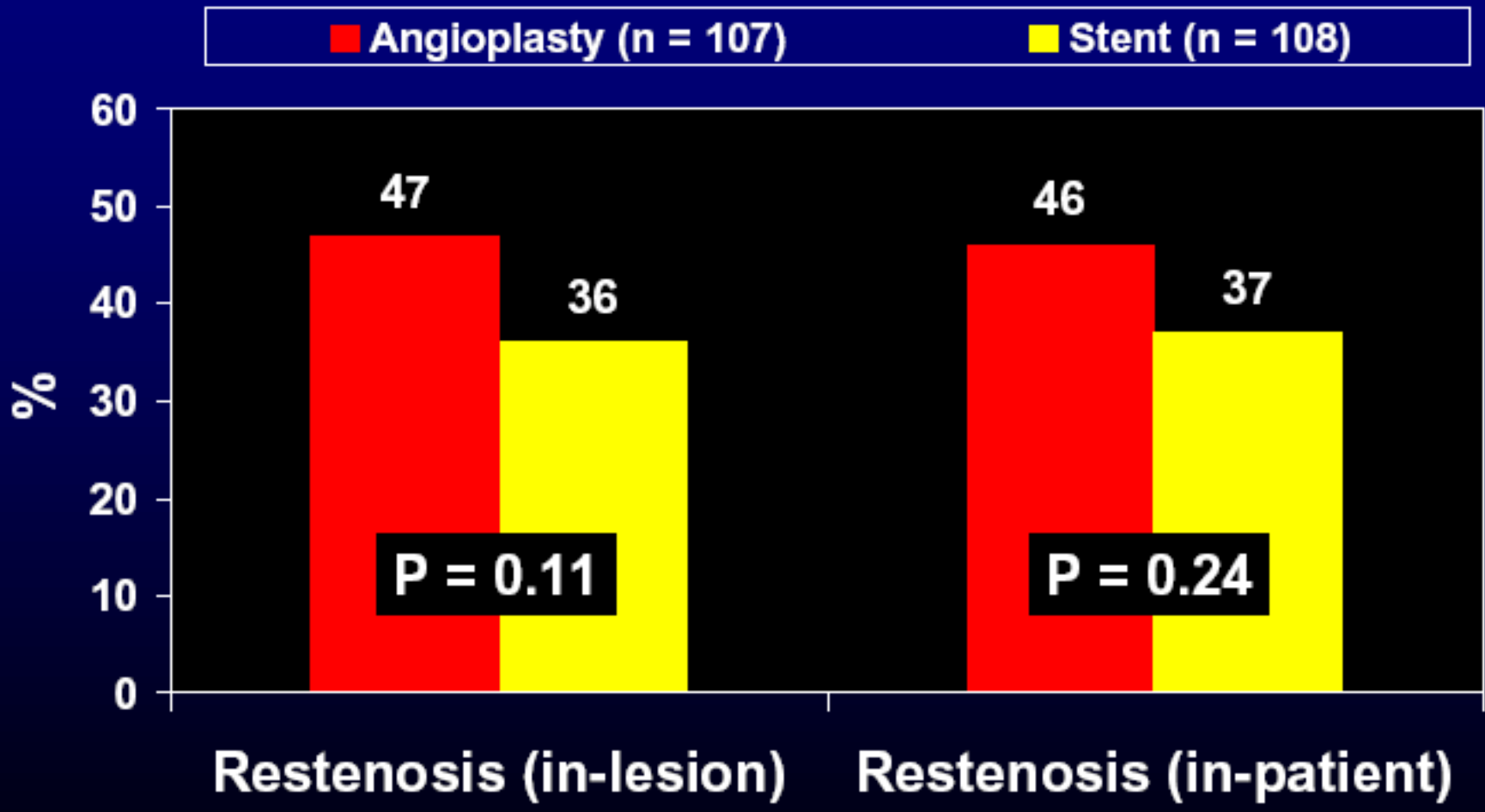
In-Hospital Outcomes



Savage M., et al., *NEJM* 1997; 337:740-47.

Safety and Efficacy of Bare-Metal Stents in Saphenous Vein Grafts

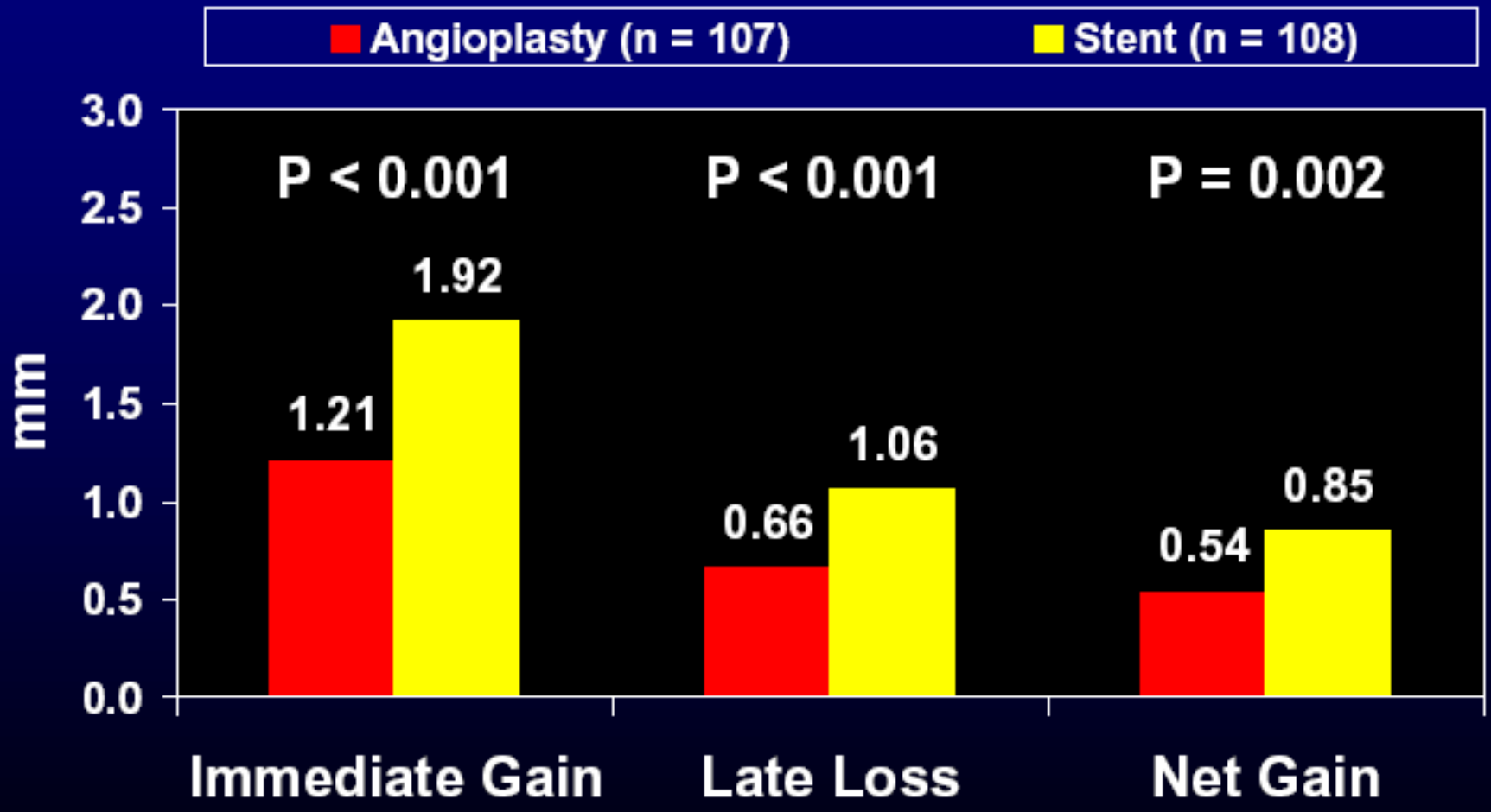
Restenosis at 6-Month Follow-Up



Savage M., et al., *NEJM* 1997; 337:740-47.

Safety and Efficacy of Bare-Metal Stents in Saphenous Vein Grafts

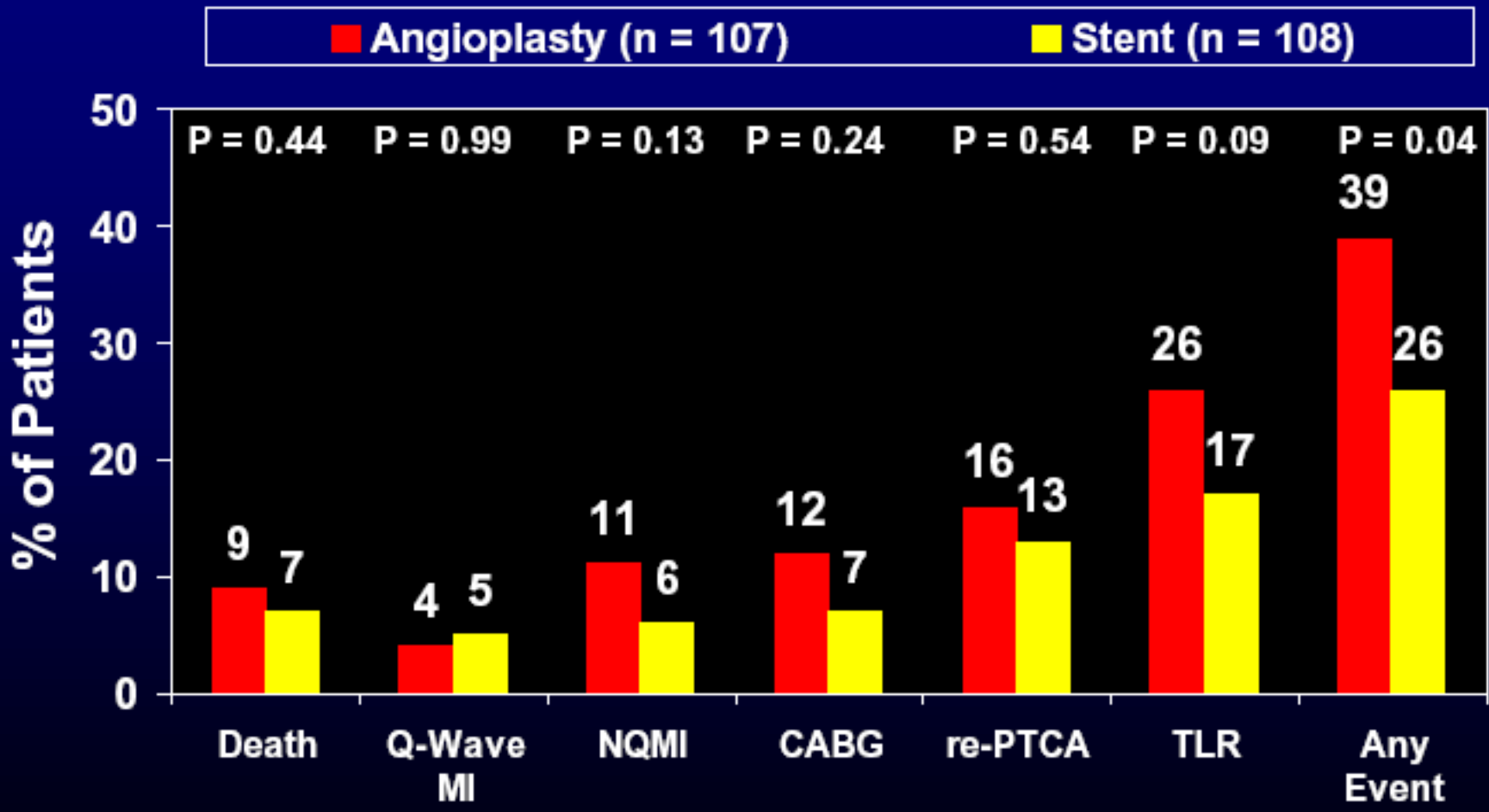
Angiographic Outcomes



Savage M., et al., *NEJM* 1997; 337:740-47.

Safety and Efficacy of Bare-Metal Stents in Saphenous Vein Grafts

MACE Up To 240 Days Post-PCI



Savage M., et al., *NEJM* 1997; 337:740-47.

Conclusions

- As compared with balloon angioplasty, stenting of selected venous bypass-graft lesions resulted in superior procedural outcomes, a larger gain in luminal diameter, and a reduction in major cardiac events
- However, there was no significant benefit in the rate of angiographic restenosis, which was the primary endpoint of the study

Savage M., et al., *NEJM* 1997; 337:740-47.

SAFER: Methods

- 801 SVG patients were randomized to either:
  - Stent placement over a conventional 0.014-inch angioplasty guidewire (n=395)
  - Stent placement over the shaft of the distal protection device (n=406)

- Primary endpoint:
  - Composite of death, myocardial infarction, emergency bypass, or target lesion revascularization by 30 days

Baim D., et al., *Circulation* 2002; 105:1285-90.

SAFER: Inclusion / Exclusion Criteria

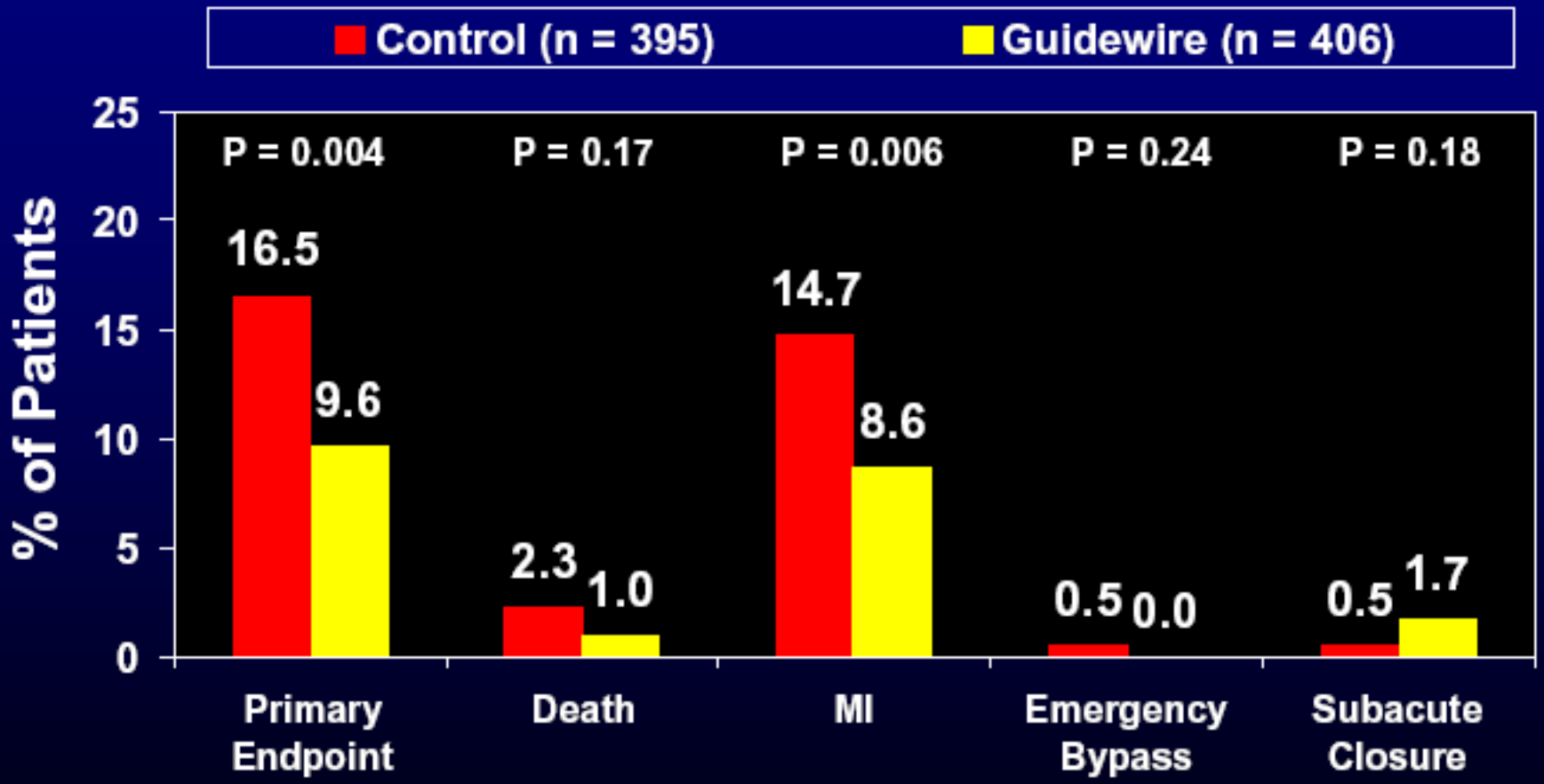
- Inclusion Criteria:
  - History of angina and signs of myocardial ischemia resulting from a ≥ 50% stenosis located in the mid-portion of a saphenous vein graft
  - Reference diameter between 3 and 6 mm

- Major exclusion criteria:
  - Recent myocardial infarction with baseline elevation of CK-MB fraction
  - Ejection fraction ≤ 25%
  - Baseline creatinine > 2.5 mg/dL (unless on long-term hemodialysis),
  - planned use of an atherectomy device

Baim D., et al., *Circulation* 2002; 105:1285-90.

Safety and Efficacy of Bare-Metal Stents in Saphenous Vein Grafts

Clinical Outcomes Through 30 Days



Composite of death, MI, emergency bypass, or TLR

↑ CK-MB ≥ 3x ULN

Baim D., et al., *Circulation* 2002; 105:1285-90.

FIRE: Methods

- 651 SVG patients were randomized to either:
  - filter-based FilterWire EX distal protection device (n=332)
  - GuardWire balloon occlusion and aspiration system (n=319)

- Primary end point:
  - Composite of death, myocardial infarction, or target vessel revascularization by 30 days

Stone G., et al., *Circulation* 2003;108:548-53.

FIRE: Inclusion Criteria

- ≥ 21 years of age
- PCI with planned stenting of ≥ 1 de novo SVG
- Reference vessel diameter between 3.5 - 5.5 mm

Stone G., et al., *Circulation* 2003;108:548-53.

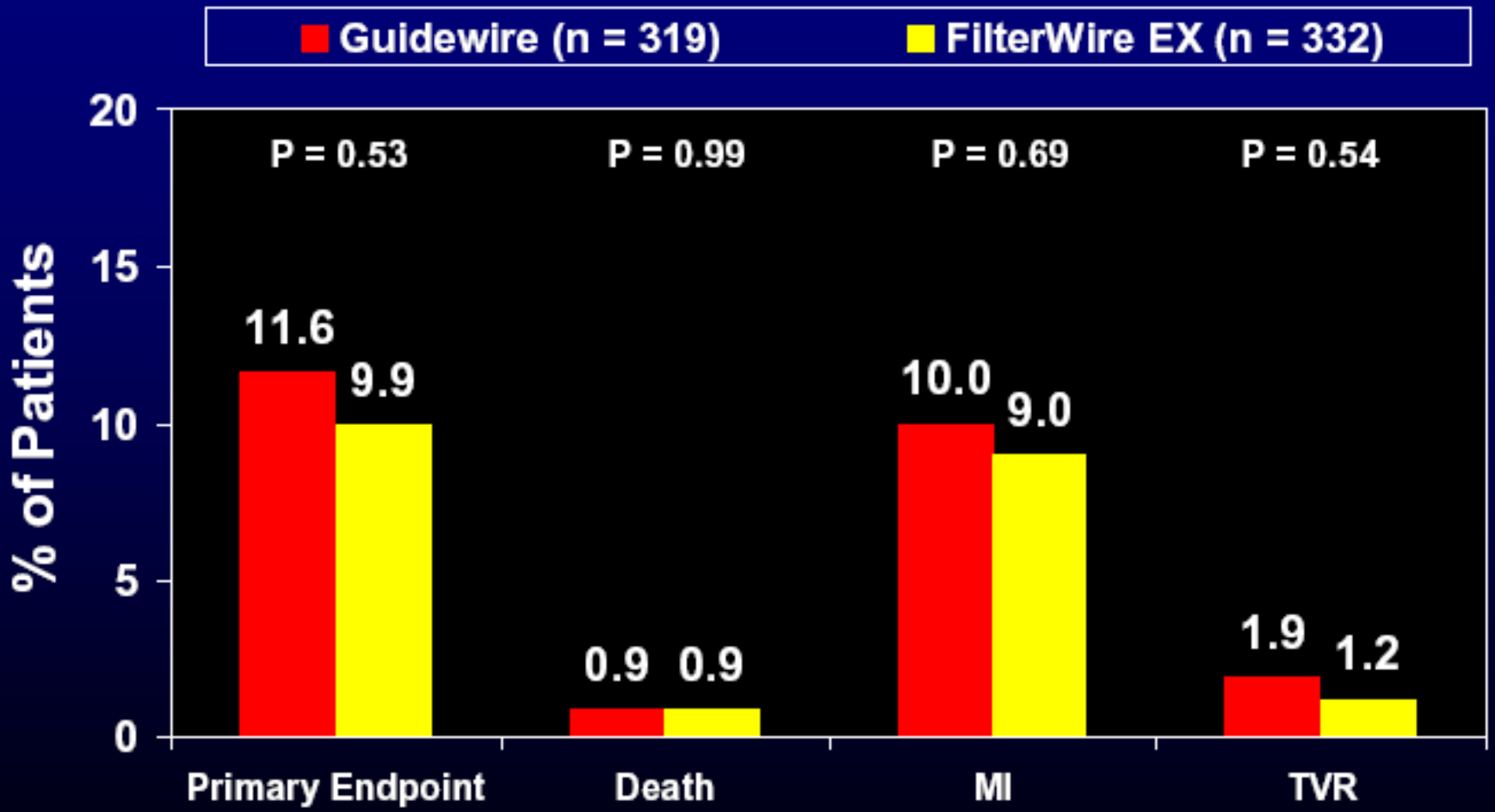
FIRE: Major Exclusion Criteria

- Recent or acute myocardial infarction
- Current elevation of CK-MB enzyme
- Cerebrovascular event within 2 months
- Baseline creatinine > 2.5 mg/dL
- Prior PCI within 30 days
- Planned use of an atherectomy device
- SVG age < 6 months
- True aorto-ostial lesion ≤ 10 mm in length
- TIMI 0 flow
- Lesion within 2.5 cm of the distal anastomosis or 2 cm of relatively straight vessel distal to the lesion not present
- Unprotected Y-limb
- Branch vessel proximal to the study device
- Planned use of laser or atherothrombectomy devices
- Left ventricular ejection fraction < 25%

Stone G., et al., *Circulation* 2003;108:548-53.

Safety and Efficacy of Bare-Metal Stents in Saphenous Vein Grafts

Clinical Outcomes Through 30 Days



Stone G., et al., *Circulation* 2003;108:548-53.

VENESTENT: Aim and Methods

- **Aim:**
  - **Compare acute and long-term angiographic and clinical outcome of balloon angioplasty and elective stenting in de novo lesions in the body of a SVG**

- **Randomization:**
  - **Between August 1996 and December 1998, 150 patients were enrolled at 9 centers, with 165 lesions were randomly assigned to:**
    - **Balloon angioplasty (n = 73)**
    - **Stent implantation (n = 77)**

Hanekamp C., et al., *Catheterization and Cardiovascular Interventions* 2003; 60:452–57.

VENESTENT: Major Inclusion Criteria

- Patients scheduled for PTCA of ≥ 1 de novo lesions in the body of an SVG were included
- Stable or unstable angina were included, except in case of AMI < 3 days prior to PCI
- Presence of one or more SVG lesions
- Good distal runoff
- Ability to accommodate a 2.5– 4.5 mm stent
- Lesion length ≤ 30 mm
- Patients with different levels of stenosis in different grafts were eligible

Hanekamp C., et al., *Catheterization and Cardiovascular Interventions* 2003; 60:452–57.

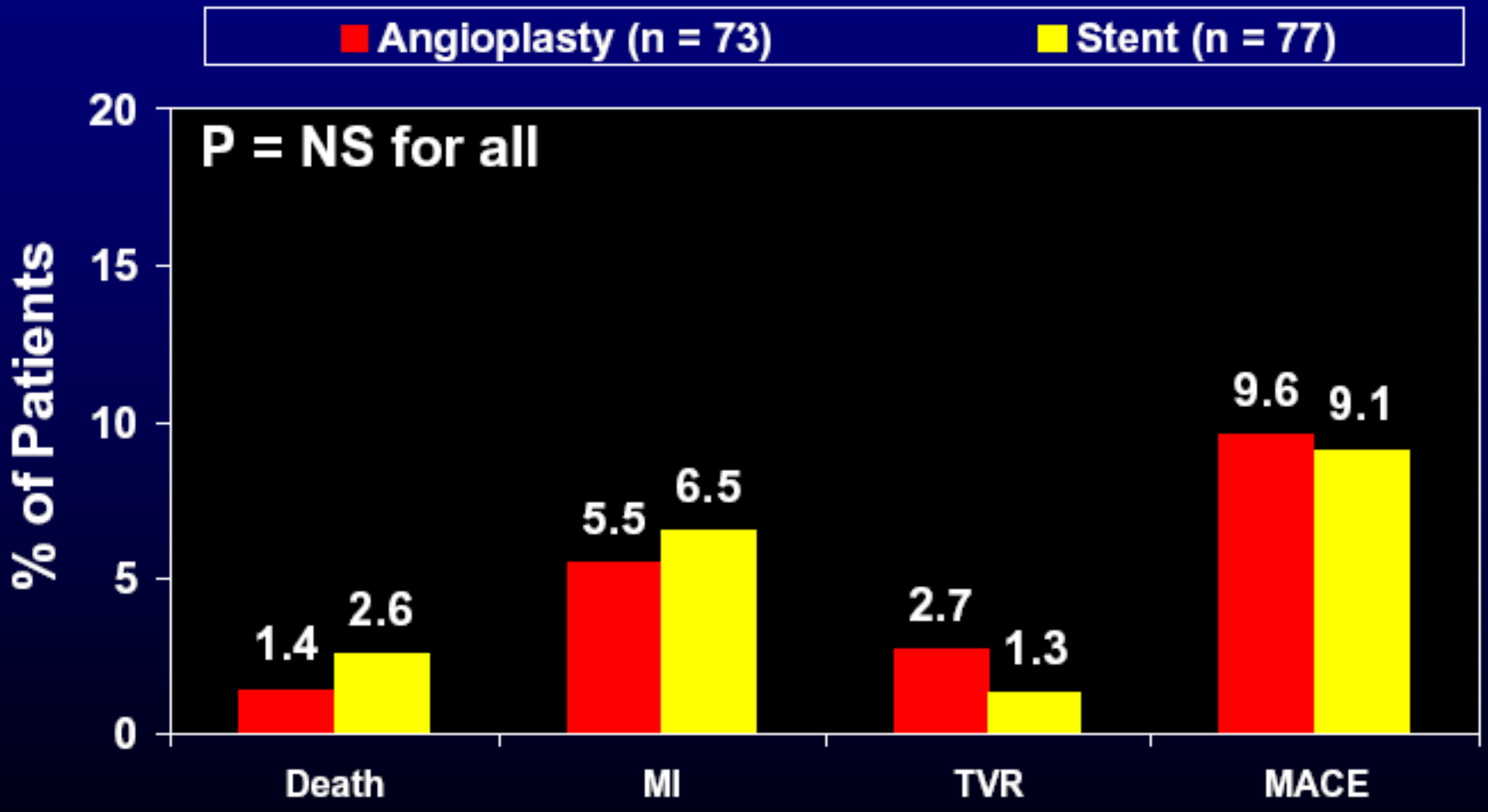
VENESTENT: Major Exclusion Criteria

- Ostial or anastomotic lesions
- Total occlusion of the graft
- Renal failure
- Angiographic evidence of thrombus in the graft
- Use of warfarin
- > 1 stenosis within the same graft

Hanekamp C., et al., *Catheterization and Cardiovascular Interventions* 2003; 60:452–57.

Safety and Efficacy of Bare-Metal Stents in Saphenous Vein Grafts

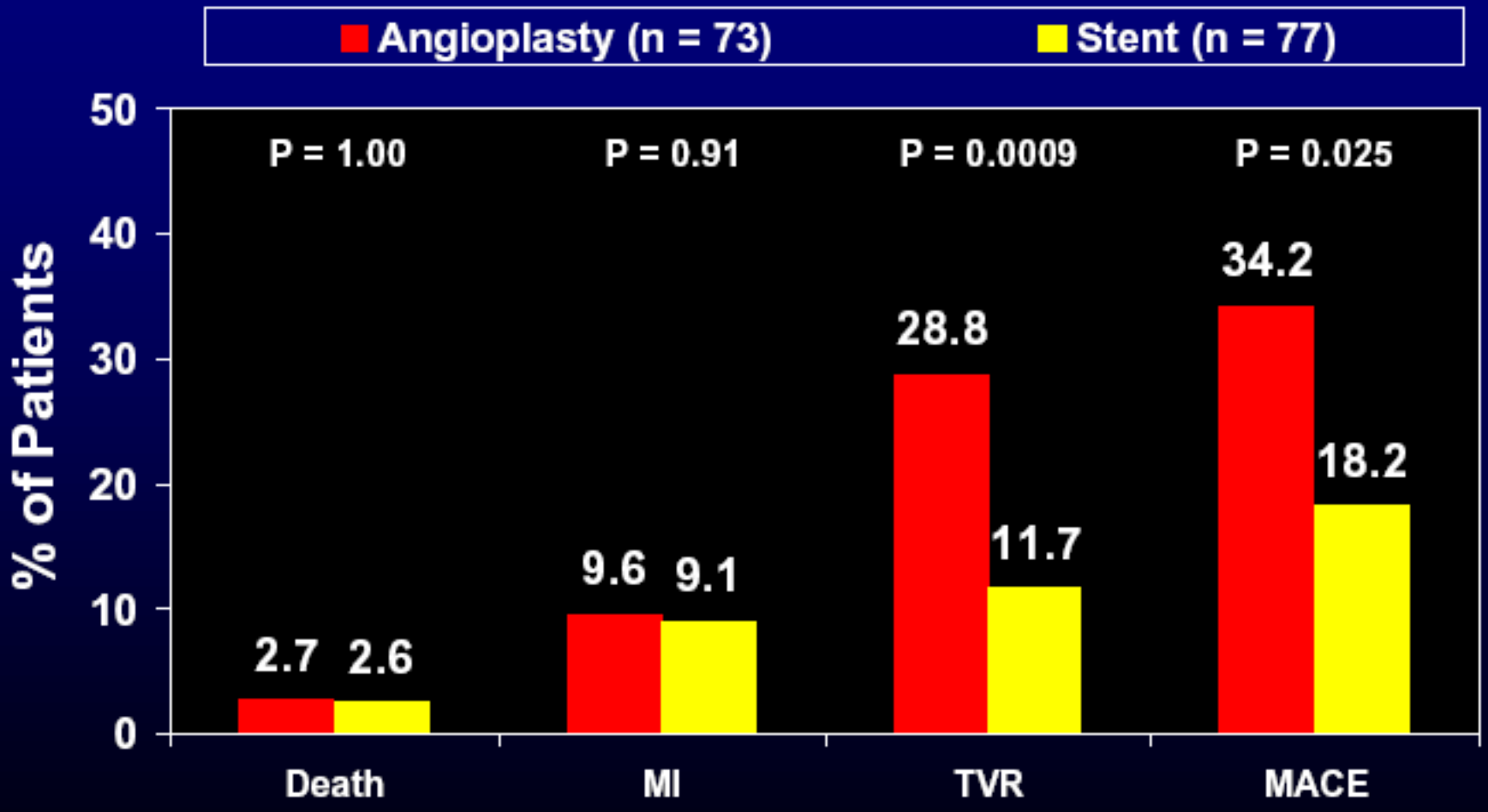
VENESTENT: In-Hospital Events



Hanekamp C., et al., *Catheterization and Cardiovascular Interventions* 2003; 60:452–57.

Safety and Efficacy of Bare-Metal Stents in Saphenous Vein Grafts

VENESTENT: 6-Month Events



Hanekamp C., et al., *Catheterization and Cardiovascular Interventions* 2003; 60:452–57.

Experience with CYPHER® in SVG

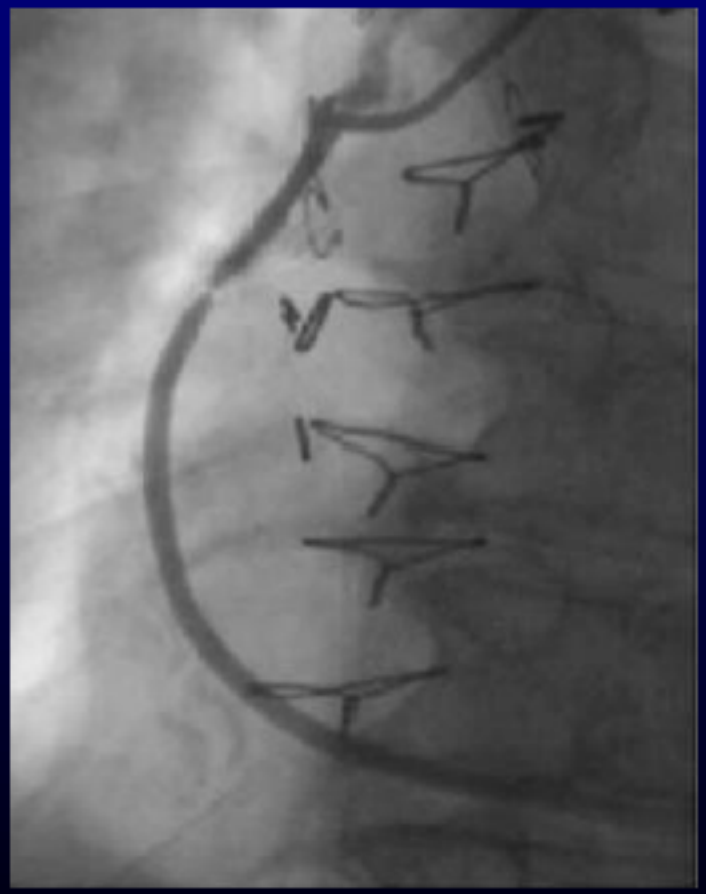
- **Costa M., et al., Cath Lab Digest 2003; 11:20 – 23.**
  - **Case report**
- Costa M., et al., *Catheter Cardiovasc Interv* 2004;61: 368-75.
  - Case report
- Price M., et al., Catheter Cardiovasc Interv 2005;65:208-11.
  - 35 patients treated with CYPHER®
- Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.
  - 61 patients treated with DES
    - 35 patients treated with CYPHER®
  - 89 patients treated with BMS (historical control)
- Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.
  - 19 patients treated with CYPHER®

Case Report: CYPHER® in SVG

- 79-year-old male
- History of hypertension, diabetes mellitus and hypercholesterolemia
- 1980:
  - 4-vessel bypass grafting
- June 2002:
  - Unstable angina
  - Angiography demonstrated 4th case of restenosis in 14 months
    - Patient previously treated with repeat PCI, cutting balloon and brachytherapy
  - Enrolled in compassionate use of CYPHER trial (SECURE)

Costa M., et al., Cath Lab Digest 2003; 11:20 – 23.

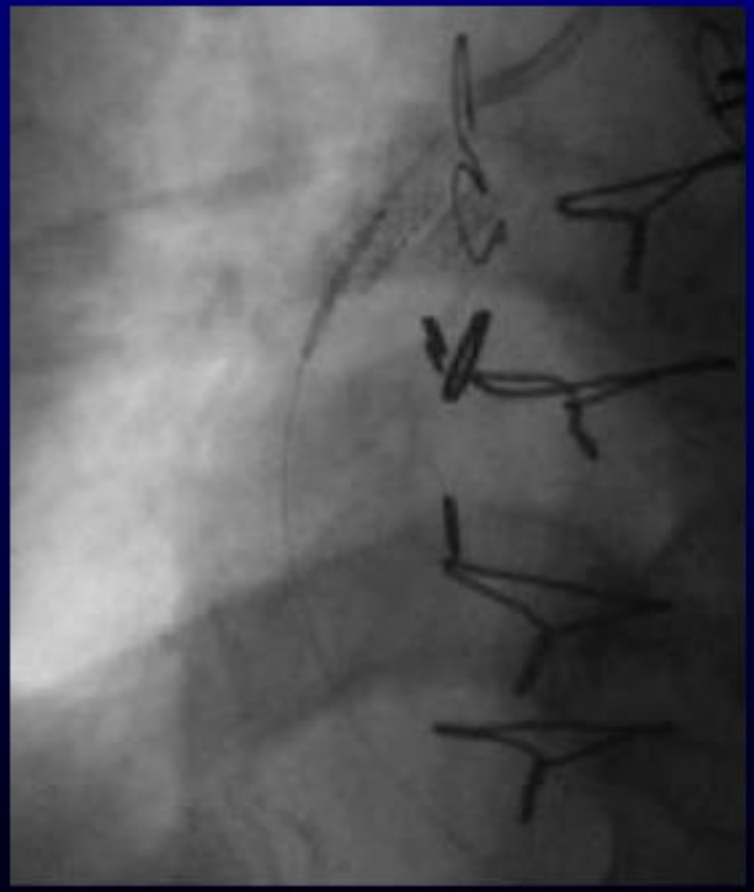
Baseline Angiogram



In-stent restenosis (80% in-stent and distal to the stent edge stenosis) observed in the proximal mid-portion of the SVG to the RCA

Costa M., et al., Cath Lab Digest 2003; 11:20 – 23.

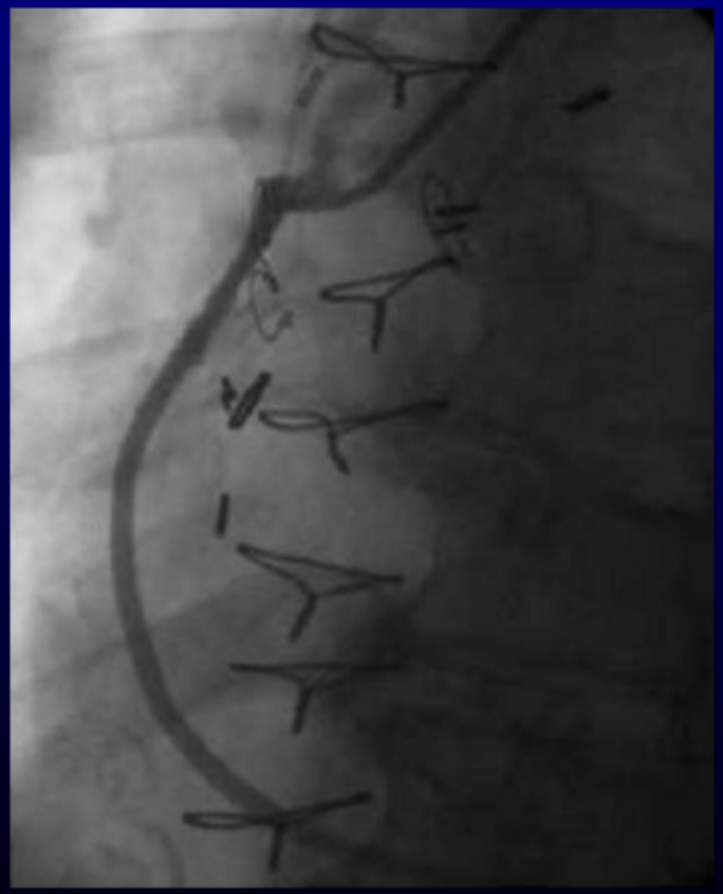
Stent Positioning



Stent positioning and its relationship with anatomical landmarks, such as the edges of the previous stent

Costa M., et al., Cath Lab Digest 2003; 11:20 – 23.

Stent Placement



3.5 x 18 mm CYPHER stent deployed directly (no predilatation)

Inflated up to 16 ATM

Post-PCI IVUS indicated a well-expanded and apposed stent

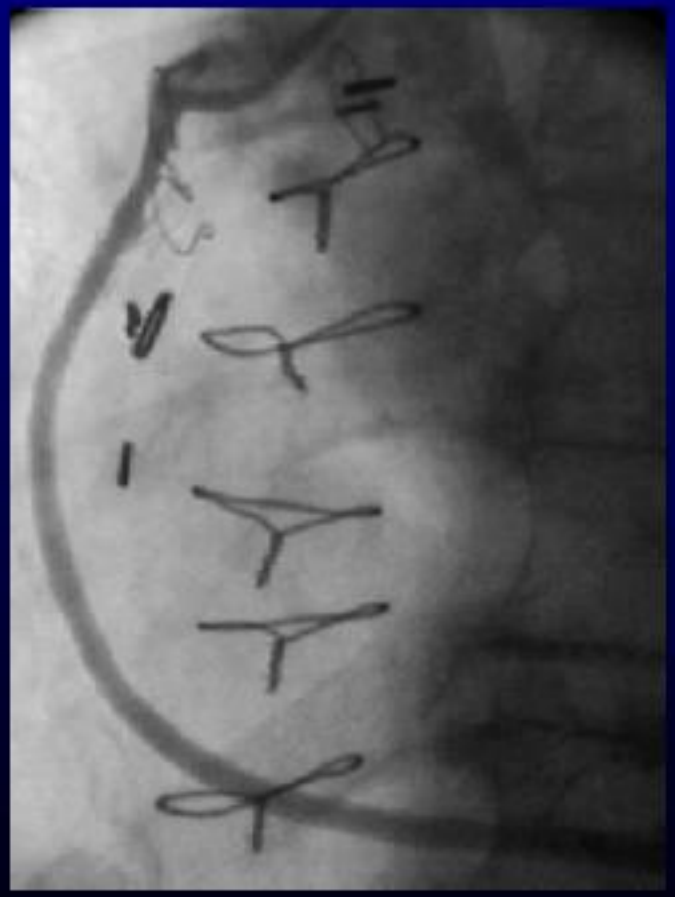
Costa M., et al., Cath Lab Digest 2003; 11:20 – 23.

Clinical Outcome

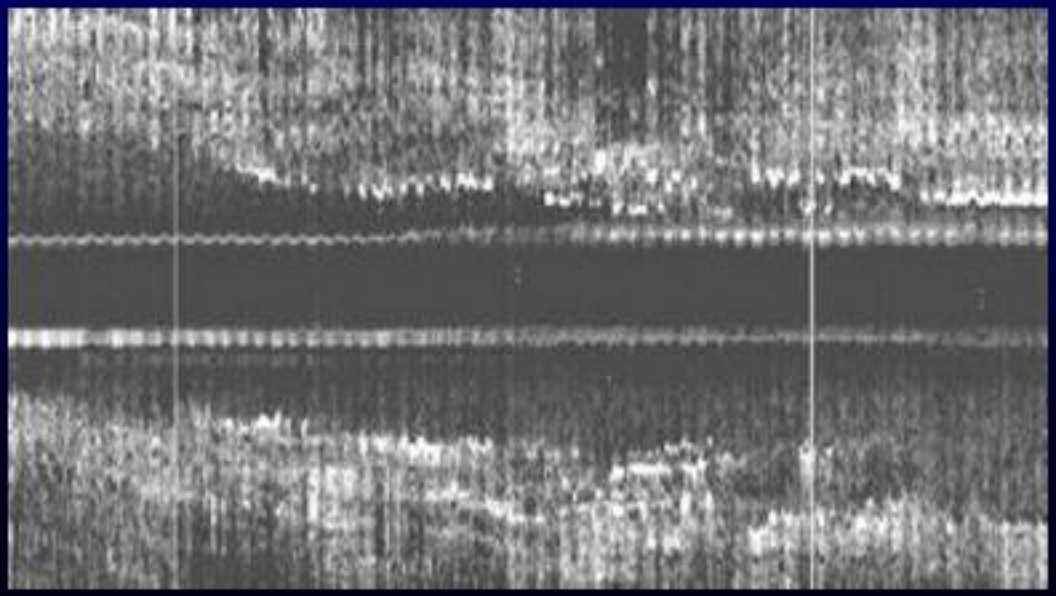
- No elevation in post-procedure cardiac enzymes
- Discharged on clopidogrel 75 mg/day and aspirin 325 mg per day for an indefinite period
- At 8-month follow-up, the patient remained asymptomatic

Costa M., et al., Cath Lab Digest 2003; 11:20 – 23.

8-Month Follow-Up Angiogram



Virtually No Late Loss in the Target Segment by IVUS or Angiography



Costa M., et al., Cath Lab Digest 2003; 11:20 – 23.

Experience with CYPHER® in SVG

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  - 89 patients treated with BMS (historical control)
- Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.
  - 19 patients treated with CYPHER®

Case Report: CYPHER® in SVG

- 74-year-old female
- Recurrent symptoms of unstable angina and a history of previously degenerated saphenous vein grafts
- Repeat angiography:
  - occlusion of the side-to-side anastomosis to obtuse marginal (OM1)
  - diffuse severe ISR of the vein graft to the LAD

Costa M., et al., *Catheter and CV Interven* 2004;61: 368-75.

Compassionate Use: CYPHER® in SVG

- Alternative options to CYPHER ruled-out:
  - 4th CABG:
    - Both mammary arteries were occluded
    - No further venous conduits for harvest
  - Brachytherapy was not an option due to:
    - Vessel size
    - Lesion length (35 mm)
    - Lesion location
- Enrolled in compassionate use of CYPHER trial (SECURE)

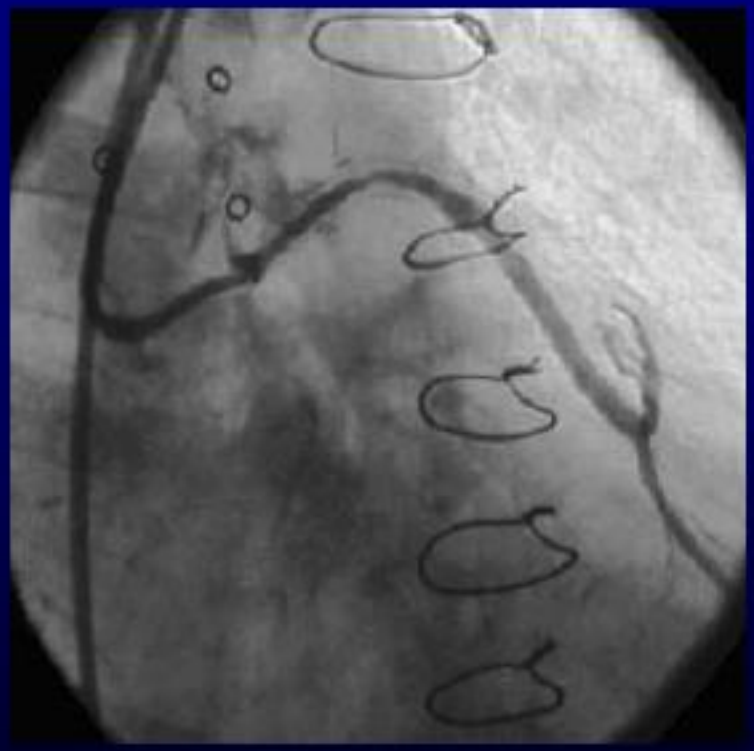
Costa M., et al., *Catheter and CV Interven* 2004;61: 368-75.

Stent Placement

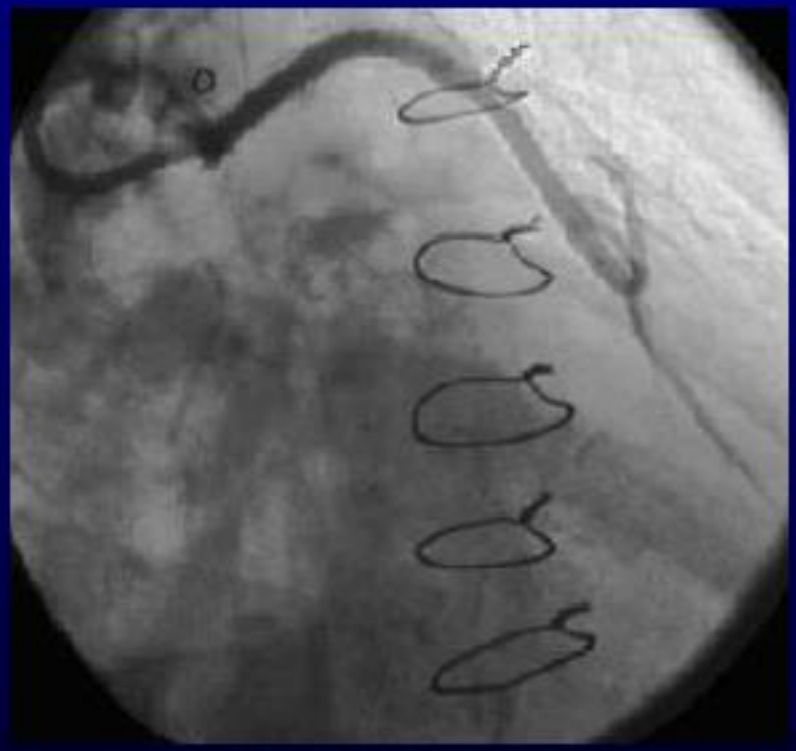
- A distal protection device was deployed
- At 25 atm, two 3.0 x 18 mm CYPHER stents deployed in the mid and proximal/ostial segments of the SVG to LAD
  - overlap of approximately 1 mm
- Post-dilation with a 5.0 x 18 mm noncompliant balloon inflated to 20 atm
- After two runs with the aspiration catheter, the distal protection device was deflated
  - Total occlusion time: 9 minutes

Costa M., et al., *Catheter and CV Interven* 2004;61: 368-75.

Pre- and Post-Stenting Angiograms



Pre-PCI
Diffuse ISR of the Vein Graft to the LAD



Post-PCI:
Widely patent stents with TIMI 3 Flow

Costa M., et al., *Catheter and CV Interven* 2004;61: 368-75.

Clinical Follow-Up

- No elevation in post-PCI cardiac enzymes
- Patient discharged on the next day
- Discharge medications:
  - Ticlopidine 250 mg twice a day for 3 months (clopidogrel allergy)
  - Aspirin 325 mg per day for an indefinite period
- 1-month telephone follow-up:
  - No reports of angina or any other adverse events
- Ticlopidine discontinued at 3 months secondary to gastrointestinal side effects
- No reports of angina at 6 and 9 months

Costa M., et al., *Catheter and CV Interven* 2004;61: 368-75.

Experience with CYPHER® in SVG

- Costa M., et al., Cath Lab Digest 2003; 11:20 – 23.
  - Case report
- Costa M., et al., *Catheter Cardiovasc Interv* 2004;61: 368-75.
  - Case report
- **Price M., et al., Catheter Cardiovasc Interv 2005;65:208-11.**
  - **35 patients treated with CYPHER®**
- Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.
  - 61 patients treated with DES
    - 35 patients treated with CYPHER®
  - 89 patients treated with BMS (historical control)
- Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.
  - 19 patients treated with CYPHER®

Objective

- Evaluate the clinical outcome of patients undergoing sirolimus-eluting stent (SES) implantation for de novo lesions within saphenous vein grafts

Price M., et al., *Catheter Cardiovasc Interven.* 2005;65:208-11.

Methods

- Retrospective analysis of 35 patients with ≥ 6 months follow-up following placement of a CYPHER stent for a de novo saphenous vein graft lesion at Scripps Clinic

- Between May and November 2003, all SVG patients received CYPHER unless:
  - Contraindication to prolonged dual antiplatelet therapy
  - Appropriate-sized CYPHER stent not available
  - ≥ 5 mm stent diameter required

Price M., et al., *Catheter Cardiovasc Interven.* 2005;65:208-11.

Medications

- Medications:
  - Aspirin:
    - Prior to PCI: 325 mg
    - Post-PCI: daily indefinitely
  - Clopidogrel:
    - Post-PCI: 300 mg loading dose in patients not on clopidogrel; continued with 75 mg/d for ≥ 3 months

Price M., et al., *Catheter Cardiovasc Interven.* 2005;65:208-11.

Baseline Characteristics

Variable	Patients Treated with SES for SVG (n=35)
Age, years	69 ± 10
Men (%)	74
Hypertension (%)	80
Hypercholesterolemia (%)	80
Diabetes Mellitus, DM (%)	26
Insulin-Dependent DM (%)	11
Prior MI (%)	51
PVD (%)	20
LVEF < 40% (%)	31

Price M., et al., *Catheter Cardiovasc Interven.* 2005;65:208-11.

Baseline Characteristics

Variable	
Age of bypass graft, years	10.1 ± 6.5
Indication for PCI (%)	
- ACS / STEMI	28
- Stable Angina	72
Target Lesion Location (%)	
- Bypass graft ostium	21
- Graft body	23
- Distal Anastomosis	26
Distal Protection Used (%)	33

Price M., et al., *Catheter Cardiovasc Interven.* 2005;65:208-11.

Procedural Characteristics

Variable	
SES / vessel, n	1.2
Median Stent Length, mm - (range)	18 mm (8-46mm)
Median Stent Diameter, mm - Ostium - Body - Distal Anastomosis	 3.5 mm 3.5 mm 2.5 mm
Distal Protection (%)	33
Balloon Post-Dilation (%)	43%
Max Balloon Post-Dilation (%) - ≥ 0.5 mm larger than stent - ≥ 1.0 mm larger than stent	 8 lesions 3 lesions

Price M., et al., *Catheter Cardiovasc Interven.* 2005;65:208-11.

In-Hospital Outcomes

- Angiographic Success: 100%
- Death: 0%
- Thrombosis: 0%
- Non-Q-Wave MI: 11%
- TVR: 0%

Price M., et al., *Catheter Cardiovasc Interven.* 2005;65:208-11.

Out-of-Hospital Outcomes

	n=35
• All Cause Death:	5.7% (n=2)
• Cardiac Death:	2.9% (n=1)
- presumed ST 6 days post-PCI	
• Stent Thrombosis:	2.9% (n=1)
• Myocardial Infarction:	11.4% (n=4)
• TVR:	5.7% (n=2)
• MACE:	20.0% (n=7)

Mean follow-up: 7.5 ± 2.2 months

Clopidogrel Use at Follow-Up: 84%

- average length of clopidogrel: 6.5 ± 2.2 months

Price M., et al., *Catheter Cardiovasc Interven.* 2005;65:208-11.

Limitations

- Retrospective nonrandomized study
- Small sample size
- Rate of angiographic restenosis could not be assessed since angiographic follow-up was not mandated

Price M., et al., *Catheter Cardiovasc Interven.* 2005;65:208-11.

Conclusions

- In this study, the treatment of saphenous vein graft lesions with the CYPHER stent was associated with a low rate of clinically driven TVR
- 11% rate of peri-procedural MI
  - Consistent with recent reported outcomes for SVG intervention

Baim D., et al., *Circulation* 2002; 105:1285-90.

Stone G., et al., *Circulation* 2003;108:548-53.

Price M., et al., *Catheter Cardiovasc Interven.* 2005;65:208-11.

Experience with CYPHER® in SVG

- Costa M., et al., Cath Lab Digest 2003; 11:20 – 23.
  - Case report
- Costa M., et al., *Catheter Cardiovasc Interv* 2004;61: 368-75.
  - Case report
- Price M., et al., Catheter Cardiovasc Interv 2005;65:208-11.
  - 35 patients treated with CYPHER®
- **Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.**
  - **61 patients treated with DES**
    - **35 patients treated with CYPHER®**
  - **89 patients treated with BMS (historical control)**
- Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.
  - 19 patients treated with CYPHER®

Objective

- Evaluate clinical and angiographic outcomes of drug-eluting stent (DES) implantation in saphenous vein graft (SVG) lesions

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Methods

- Between March 2002 and March 2004, 61 consecutive patients (69 lesions) underwent drug-eluting stent placement in SVG
- A control group included 89 consecutive patients (120 lesions) who underwent BMS placement in in SVG lesions during the 24 months prior to the introduction of DES
- Exclusion Criteria:
  - AMI < 1 week prior to PCI
  - implantation of a covered stent
  - brachytherapy

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Medications

- All patients pretreated with aspirin and either ticlopidine or clopidogrel (300 mg loading dose in patients not pretreated)
- IV UFH (100 IU/kg)
  - maintain ACT between 250 and 300 seconds
- GP IIb/IIIa inhibitor:
  - Physician Discretion
- Discharge:
  - Aspirin: Indefinitely
  - Thienopyridine:
    - ≥ 6 months in SES group
    - ≥ 1 month in BMS group

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Baseline Characteristics

	Bare-Metal Stent (n = 89)	DES (n = 61)	P-value
Age (y)	67 ± 8	67 ± 8	0.85
Male (%)	88.8	83.6	0.46
Family History of CAD (%)	27.0	37.7	0.21
Hypercholesterolemia (%)	49.4	65.6	0.07
Hypertension (%)	53.9	60.7	0.50
Diabetes Mellitus (%)	15.7	19.7	0.66
Prior MI (%)	62.9	59.0	0.73
Age of SVG (years)	9.2 ± 4.8	9.7 ± 5.6	0.58
Unstable angina (%)	40.4	29.5	0.23
Multivessel Disease (%)	100	96.7	0.32
LVEF (%)	48.7 ± 10.4	50.6 ± 8.1	0.24

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Lesion Characteristics

	Bare-Metal Stent (n = 120)	DES (n = 69)	P-value
Lesion Location (%)			0.46
- Ostial	15.0	18.8	
- Proximal	28.3	31.9	
- Mid	22.5	26.1	
- Distal and Anastomotic	34.2	23.2	
Restenotic Lesions	6.7	34.8	<0.001
Total Occlusion	3.3	4.3	0.71
Calcium	5.0	8.7	0.36
Thrombus	21.7	13.0	0.18

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Procedural Characteristics

	Bare-Metal Stent (n = 120)	DES (n = 69)	P-value
Stents / Lesion, n	1.08 ± 0.30	1.20 ± 0.61	0.050
Length of Stent / Lesion, mm	20.4 ± 8.8	29.4 ± 19.8	< 0.001
Max Balloon Diameter, mm	3.83 ± 0.58	3.35 ± 0.39	< 0.001
Max Balloon Inf Pressure, atm	15.1 ± 3.5	17.7 ± 3.9	< 0.001
No Reflow (%)	1.1	0	1.0
Distal Protection Devices (%)	22.5	31.1	0.26
GP IIb/IIIa Inhibitors (%)	21.3	14.8	0.40
Sirolimus-eluting stent (%)	-	n = 35	
Paclitaxel-eluting stent (%)	-	n = 26	

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

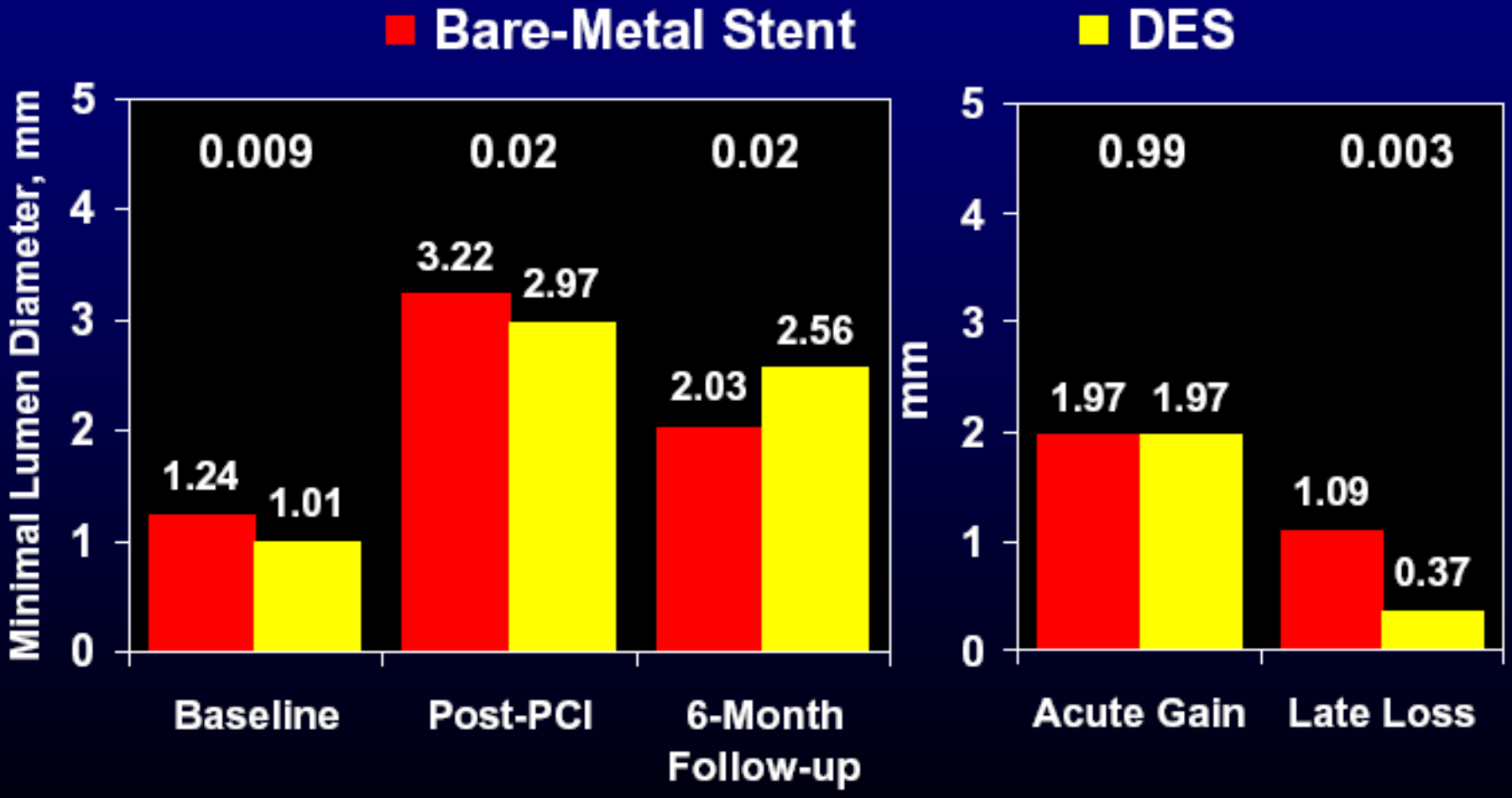
Outcomes

SES / vessel, n	1.2
Median Stent Length, mm	18 mm
- (range)	(8-46mm)
Median Stent Diameter, mm	
- Ostium	3.5 mm
- Body	3.5 mm
- Distal Anastomosis	2.5 mm
Distal Protection (%)	33
Balloon Post-Dilation (%)	43%
Max Balloon Post-Dilation (%)	
- ≥ 0.5 mm larger than stent	8 lesions
- ≥ 1.0 mm larger than stent	3 lesions

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Angiographic Outcomes

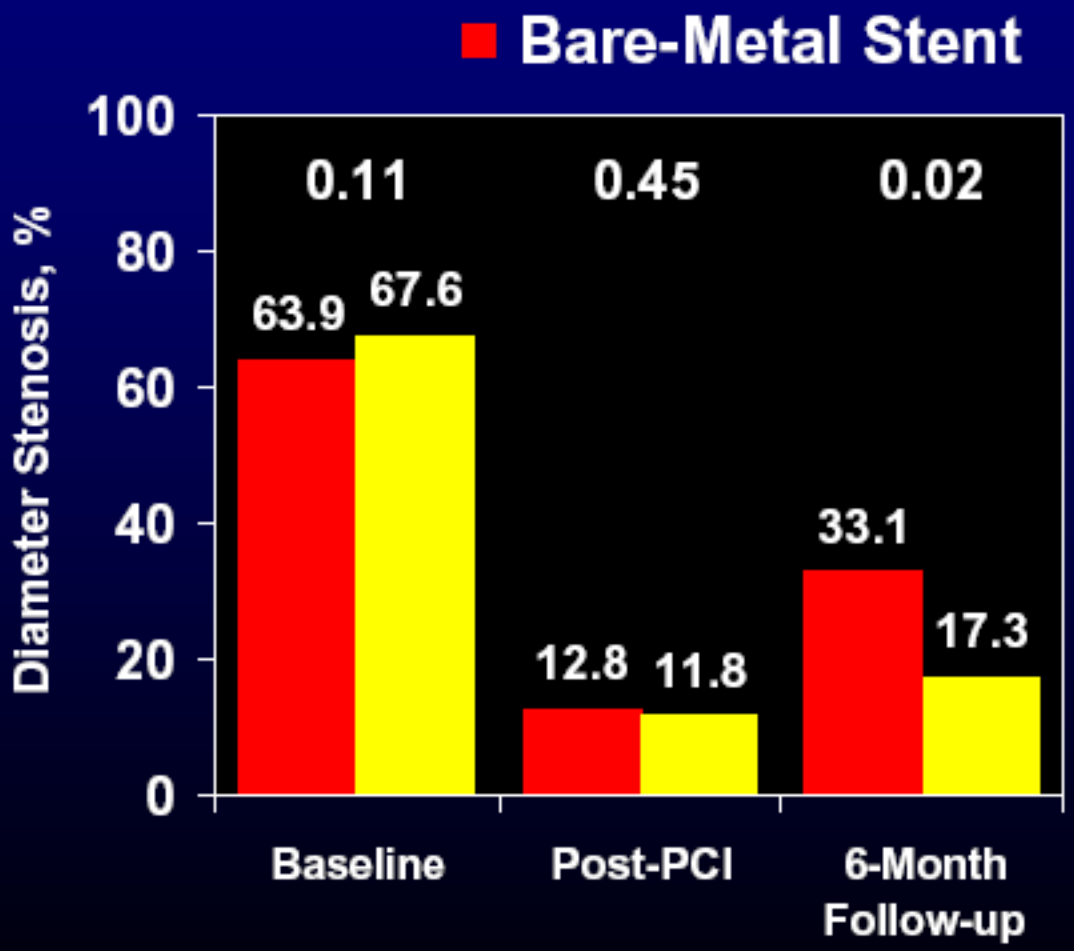
Minimal Lumen Diameter, Acute Gain, and Late Loss

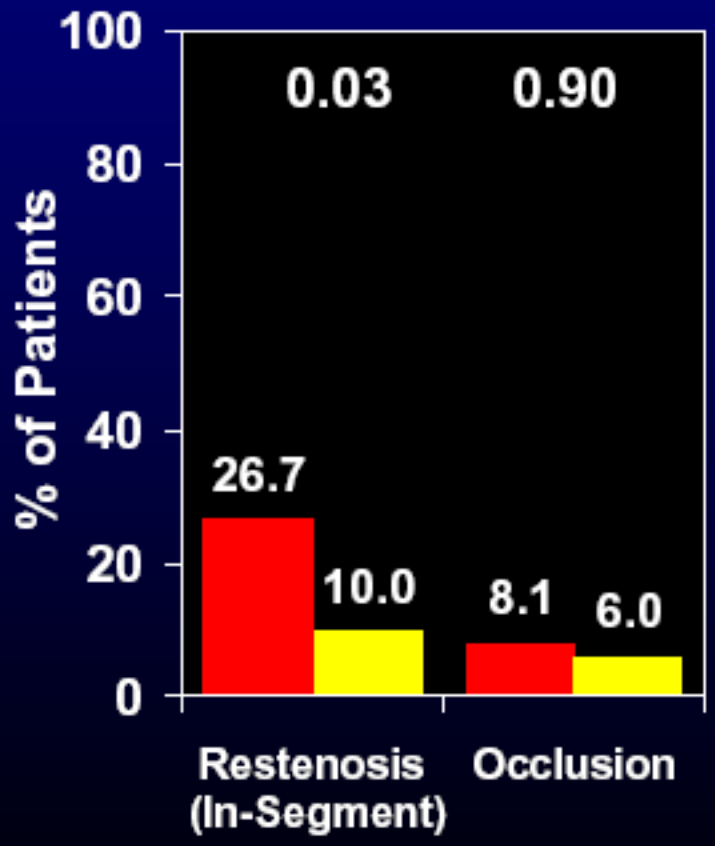


Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Angiographic Outcomes

Minimal Lumen Diameter, mm

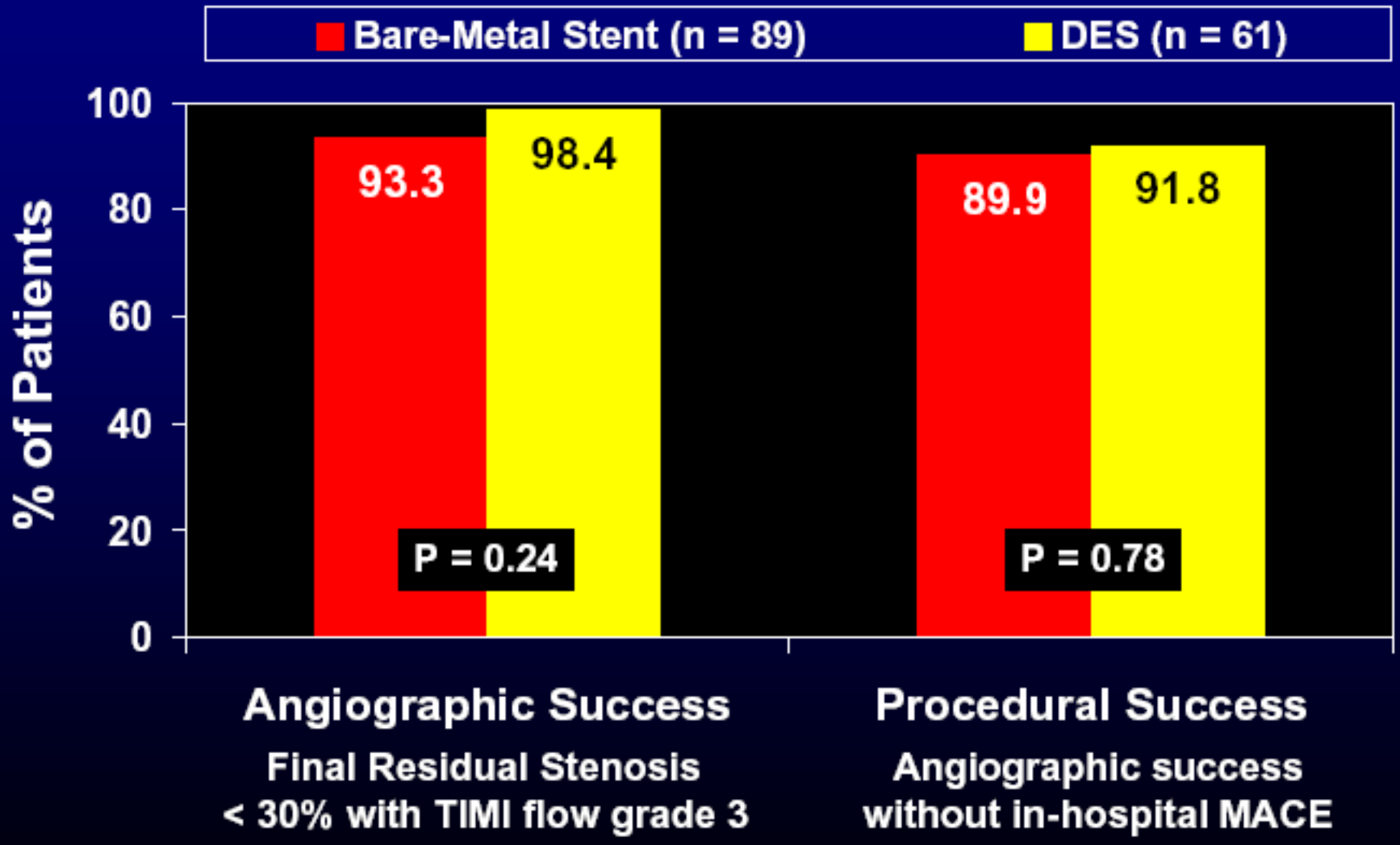




Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Safety and Efficacy of CYPHER in Saphenous Vein Grafts

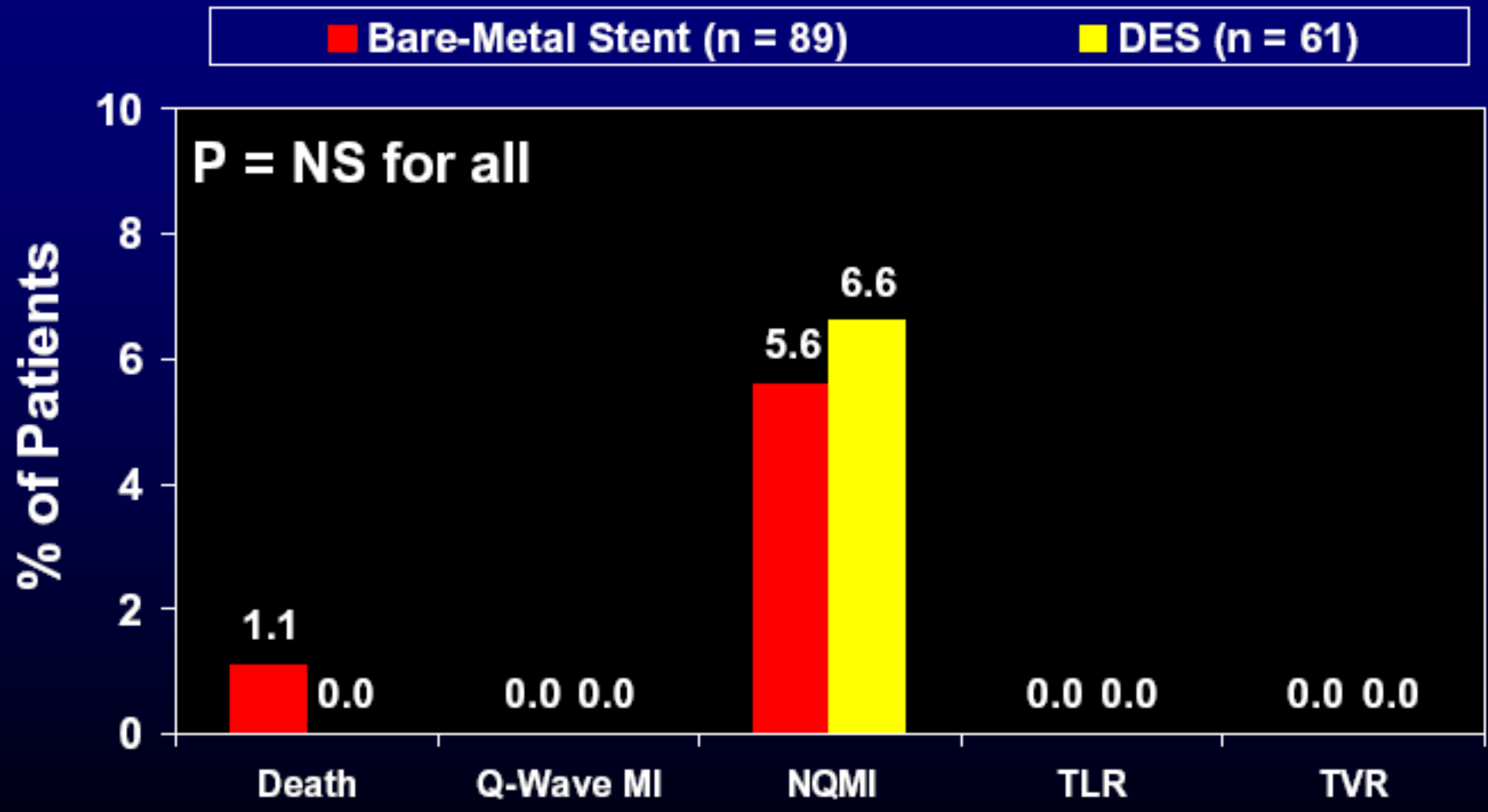
Angiographic and Procedural Success



Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Safety and Efficacy of CYPHER in Saphenous Vein Grafts

In-Hospital Outcomes

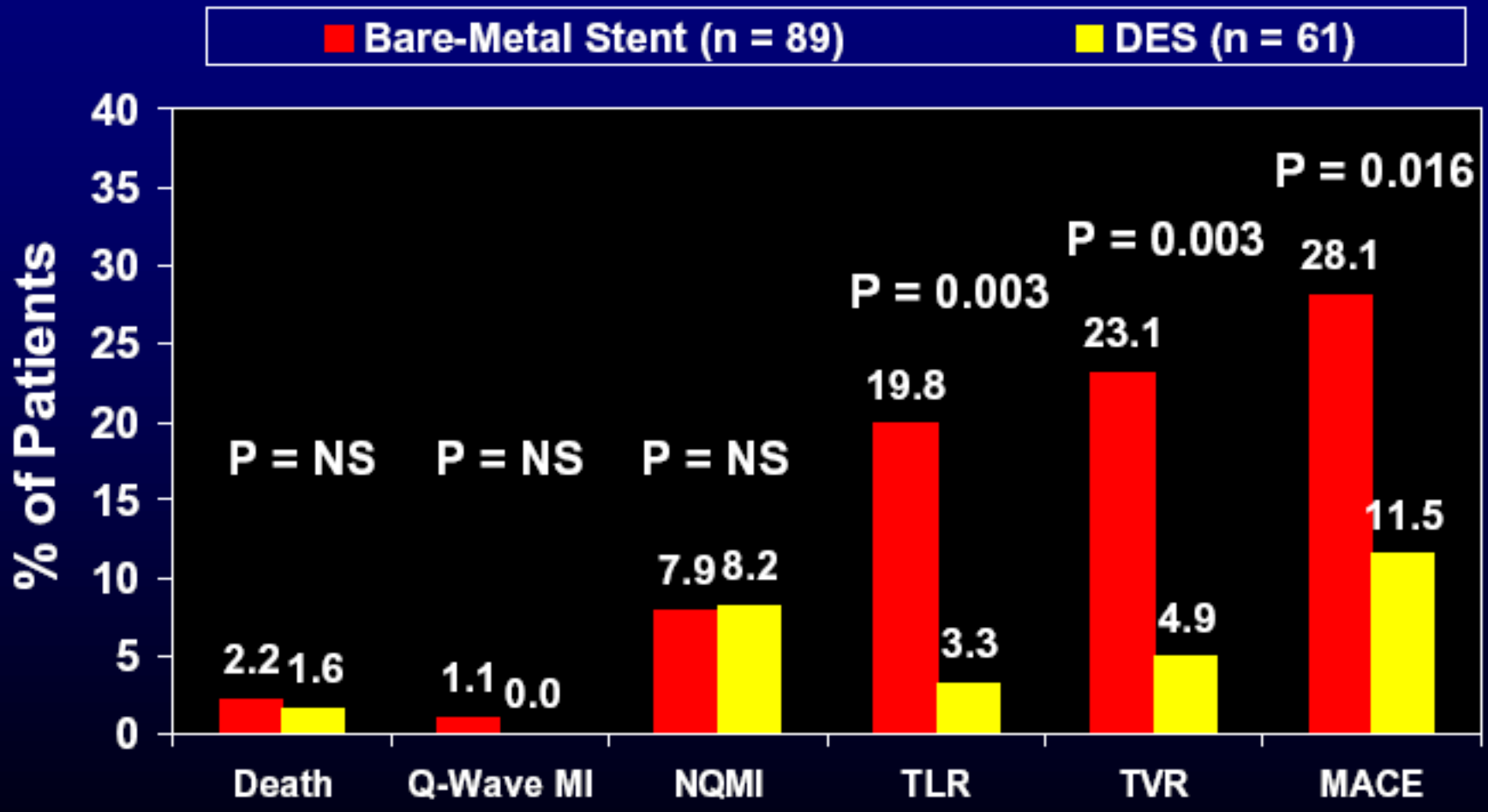


No reports of stent thrombosis

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Safety and Efficacy of CYPHER in Saphenous Vein Grafts

Outcomes Through 6 Months



No reports of stent thrombosis

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Limitations

- Retrospective study
- 2 different types of drug-eluting stents used
- Incomplete angiographic follow-up
  - 69% BMS and 71% DES
- Clinical follow-up only through 7 months

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Conclusions

- This report represents a large cohort of patients treated on SVG by DES implantation with complete clinical follow-up
- DES placement in SVG lesions appears feasible with a high procedural success rate
- Compared to the BMS historical group, the DES group was associated with a significant reduction in restenosis, TLR, and 6-Month MACE

Ge L., et al., *J Am Coll Cardiol* 2005;45:989-94.

Experience with CYPHER® in SVG

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  - Case report
- Costa M., et al., *Catheter Cardiovasc Interv* 2004;61: 368-75.
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    - 35 patients treated with CYPHER®
  - 89 patients treated with BMS (historical control)
- Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.
  - 19 patients treated with CYPHER®

Methods

- RESEARCH (Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital) was a single-center registry in which CYPHER was the device of choice for all percutaneous coronary interventions, per hospital policy

- 19 patients with de novo lesions in a SVG with a RVD of < 3.0 mm were enrolled

- Primary Endpoint:
  - Death, MI, or Repeat TVR

Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.

Baseline Characteristics

	CYPHER (n = 19)
Age (y)	67
Male (%)	84
Current Smoker (%)	11
Previous Smoker (%)	42
Diabetes Mellitus (%)	11
Hypertension (%)	53
Hypercholesterolemia (%)	79
Previous MI (%)	58
Previous PCI (%)	42
Presentation (%):	
- Stable Angina	68
- ACS	32

Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.

Medications / Distal Protection Devices

- Clopidogrel: 300 mg loading dose followed by 75 mg/daily for 6 months
- Aspirin: indefinite
- GP IIb/IIIa Inhibitors (42%) and distal protection devices (32%) were at physician's discretion

Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.

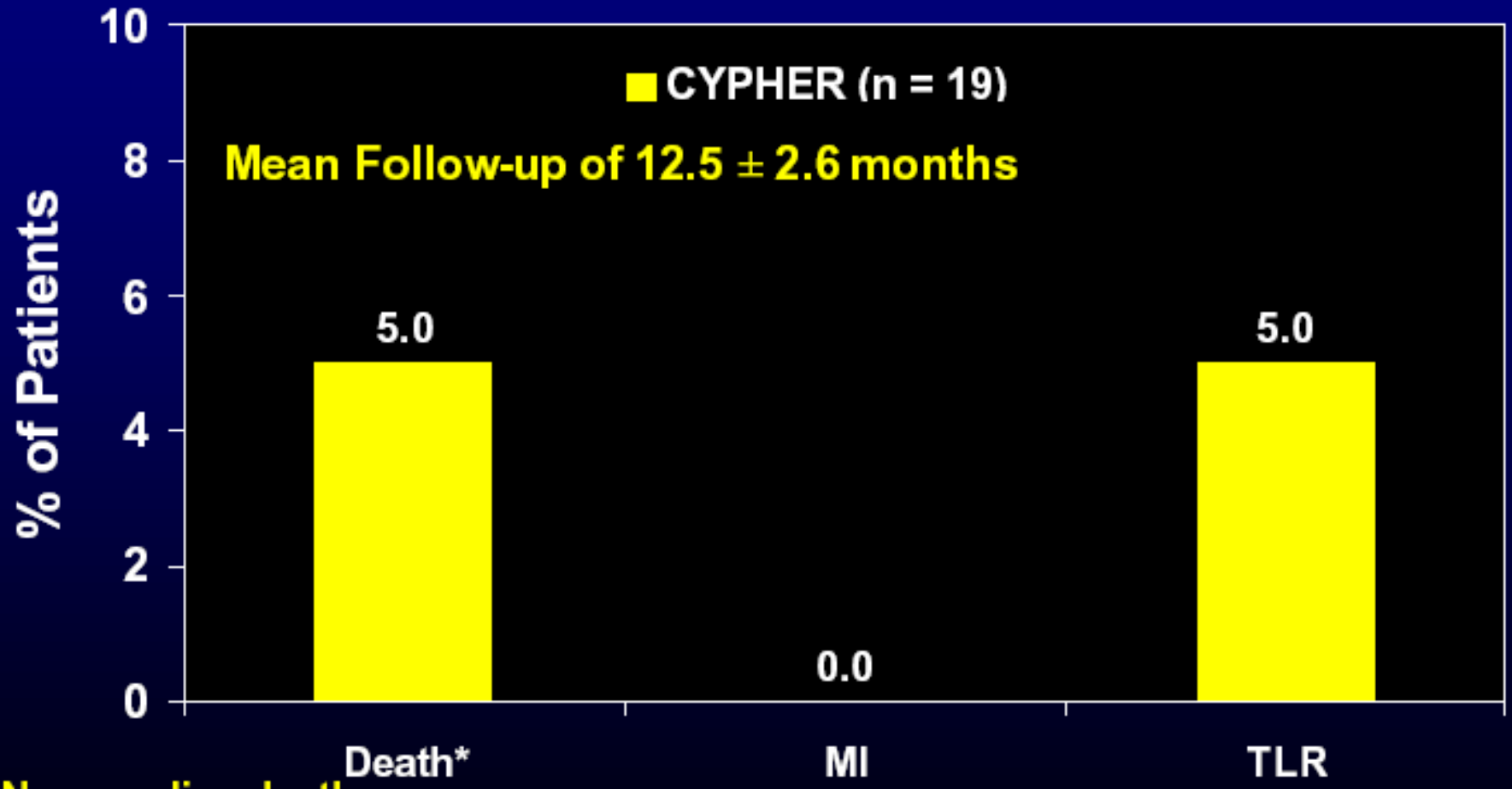
In-Hospital Outcomes

- Major adverse cardiac events (MACE):
  - 11%, related to 2 patients with a peri-procedural AMI
    - 1 Non-Q-wave MI and 1 Q-wave MI
  - Distal protection device was not used in either case

Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.

Safety and Efficacy of CYPHER in Saphenous Vein Grafts

Out-of-Hospital Outcomes at Follow-Up



Non-cardiac death;
F/U indicated widely patent graft with no evidence of restenosis

Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.

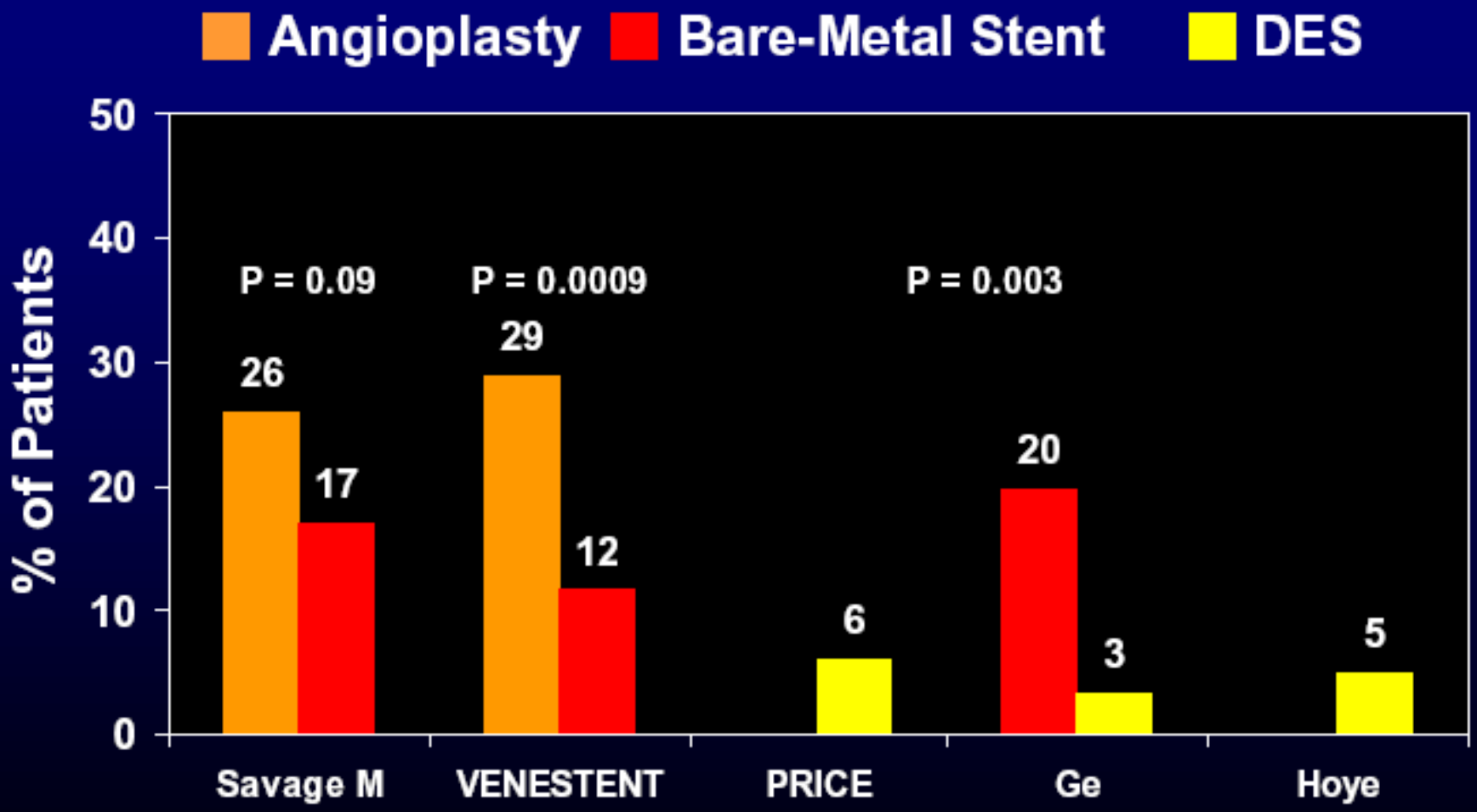
Conclusions

- Utilizing SES for PCI of degenerate SVGs is associated with a low rate of TVR
- Increased utilization of distal protection devices might reduce the periprocedural AMI rate

Hoye A., et al., *J Invas Cardiol* 2004; 16:230-33.

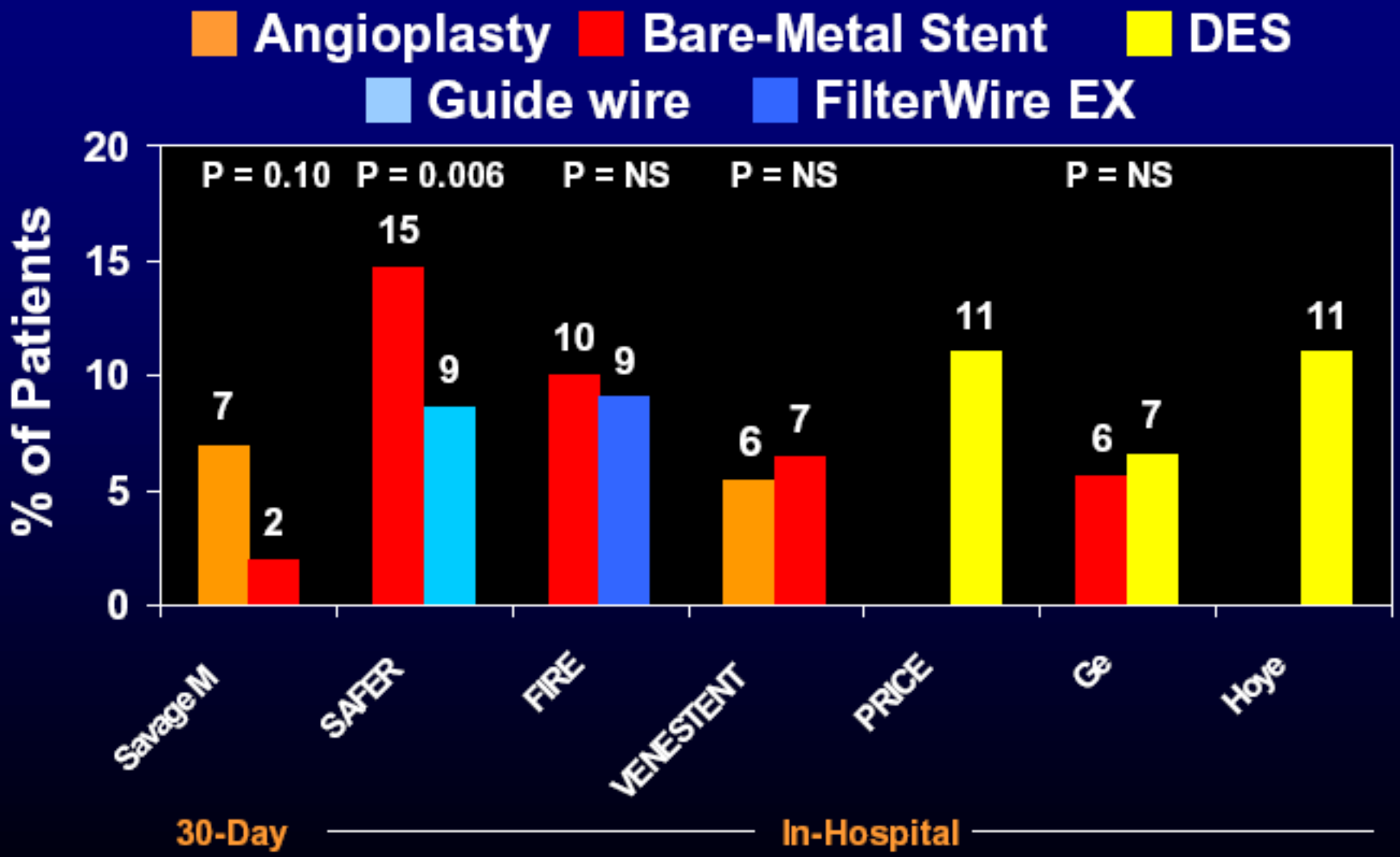
Safety and Efficacy of CYPHER in Saphenous Vein Grafts

6-Month TLR



Safety and Efficacy of CYPHER in Saphenous Vein Grafts

Myocardial Infarction



Summary

- Saphenous Vein Graft (SVG) stenting is associated with increased adverse event rates
- Compared to historical data with bare-metal stents, SVG stenting with CYPHER® appears relatively safe and feasible with lower rates of restenosis and TLR
  - Rates of myocardial infarction appear to be within the range seen with bare-metal stents