

# **Counterpoint: When is PCI an Acceptable or Preferred Alternative**

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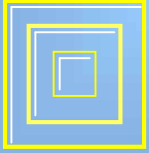
**Disclosures:**

**Cordis, Boston, Medtronic:**

**Research Grants**

**Consultant**

**Speakers Bureau**



**Why do cardiovascular surgeons  
get so much respect?**



**The elite cardiac surgeon:**

**--Good looking**

**--Average ht 6'3"**

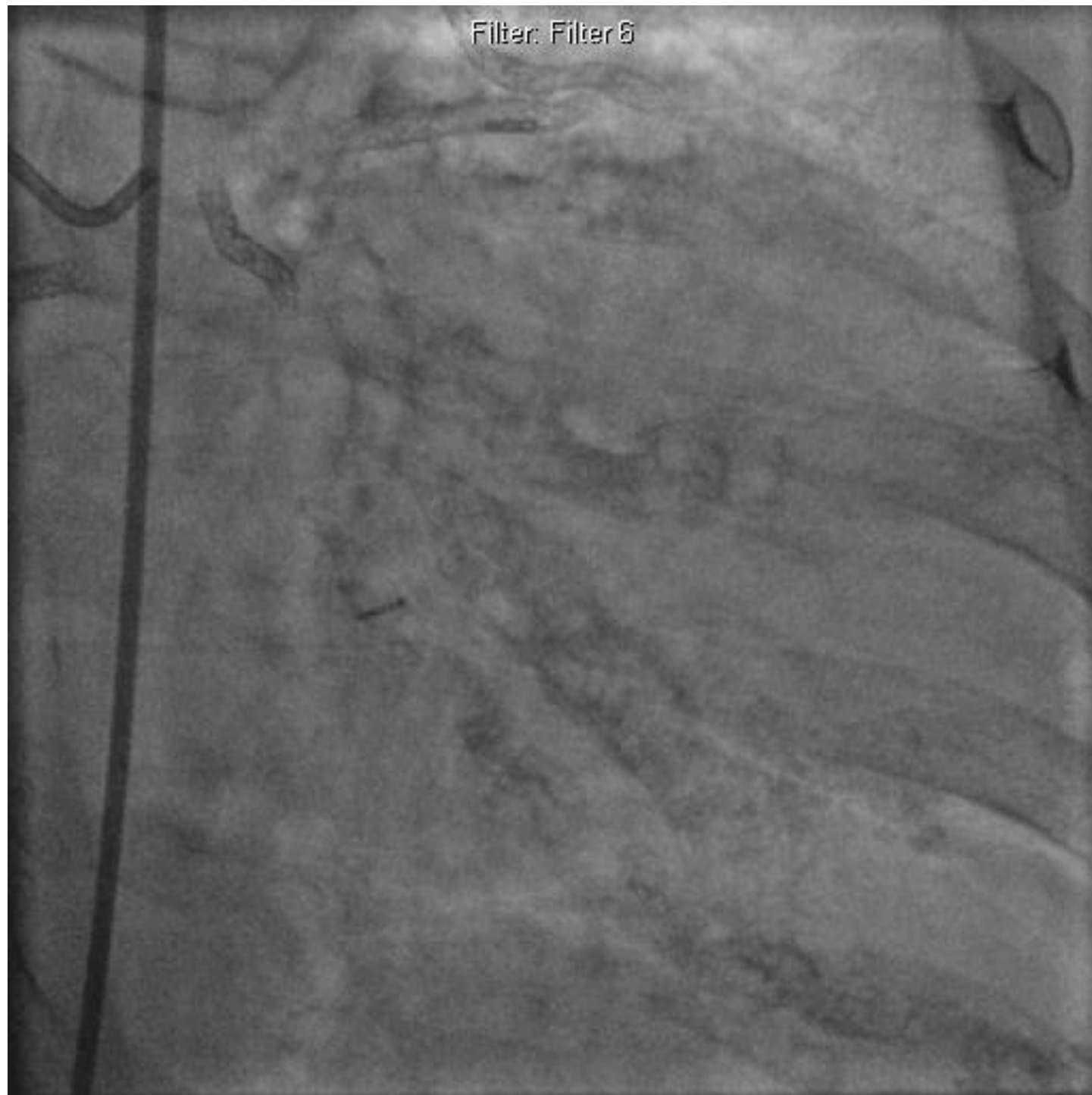


**The basic interventionalist**

**--A little "hunched over"**

**--Average ht 5'7 and...1/2"**

Filter: Filter 8



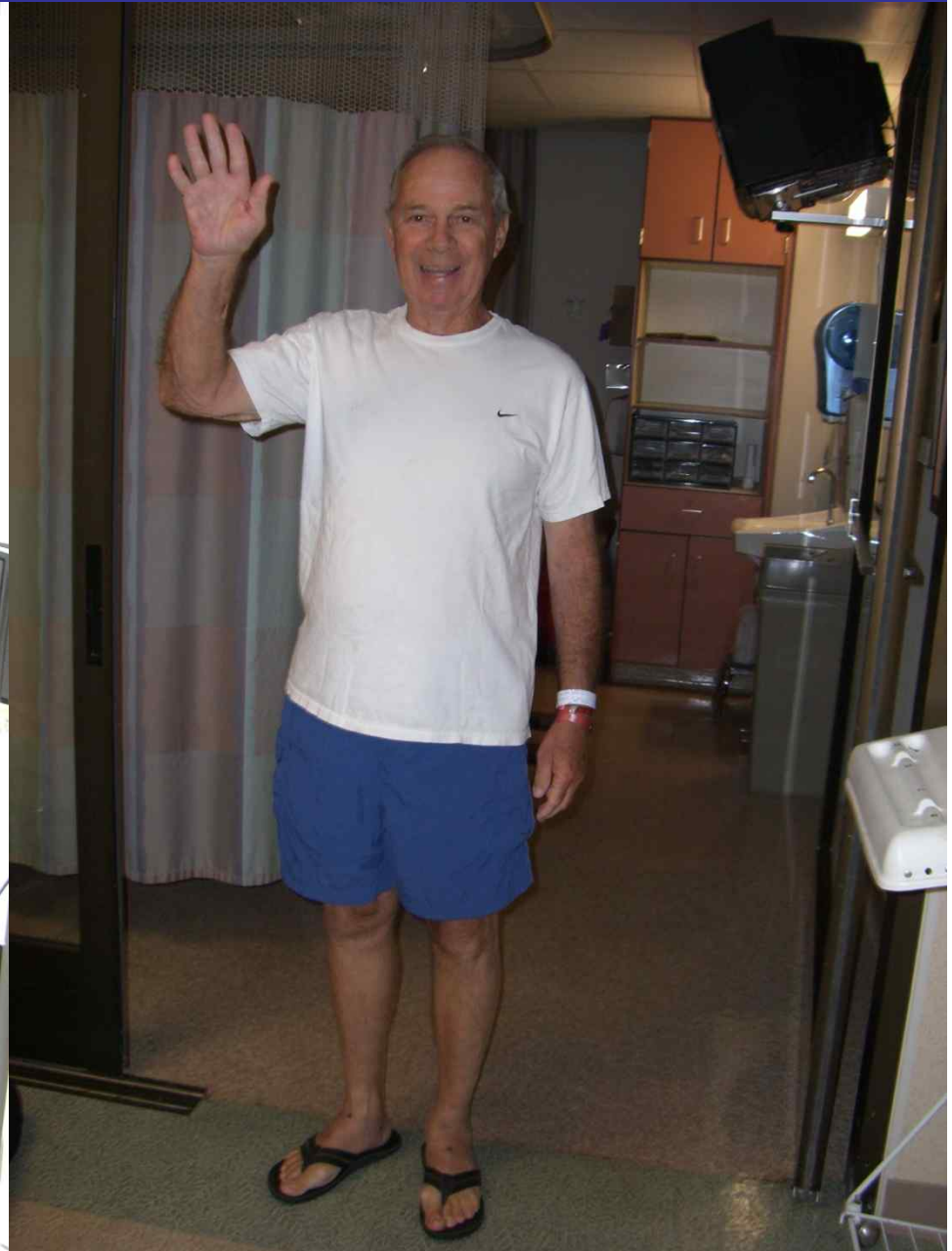
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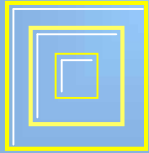


**POD #1 after multi vessel revascularization: *OLD* technology**



**POD #1 after multi vessel revascularization: *NEW* technology**





## The Interventionalist's View of Bypass Surgery

**What do I like about bypass surgery?**

- **Left internal mammary**

**What do I dislike about bypass surgery?**

- **Morbidity of the procedure**
- **Saphenous vein grafts**
- **Acceleration of underlying native coronary disease**

## 2 Impact of increased shear stress on native disease progression

*G. Karthikeyan / International Jou*

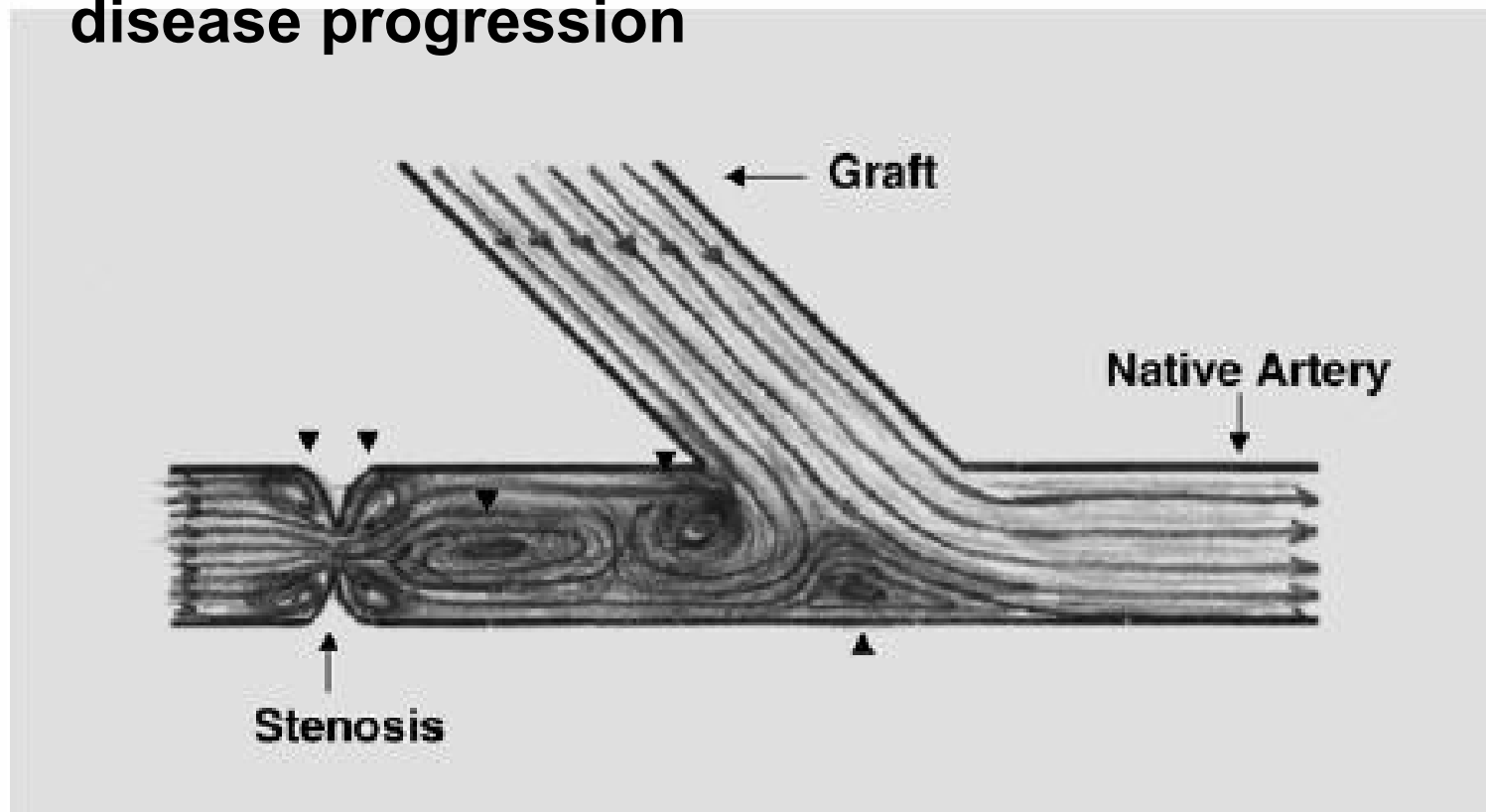
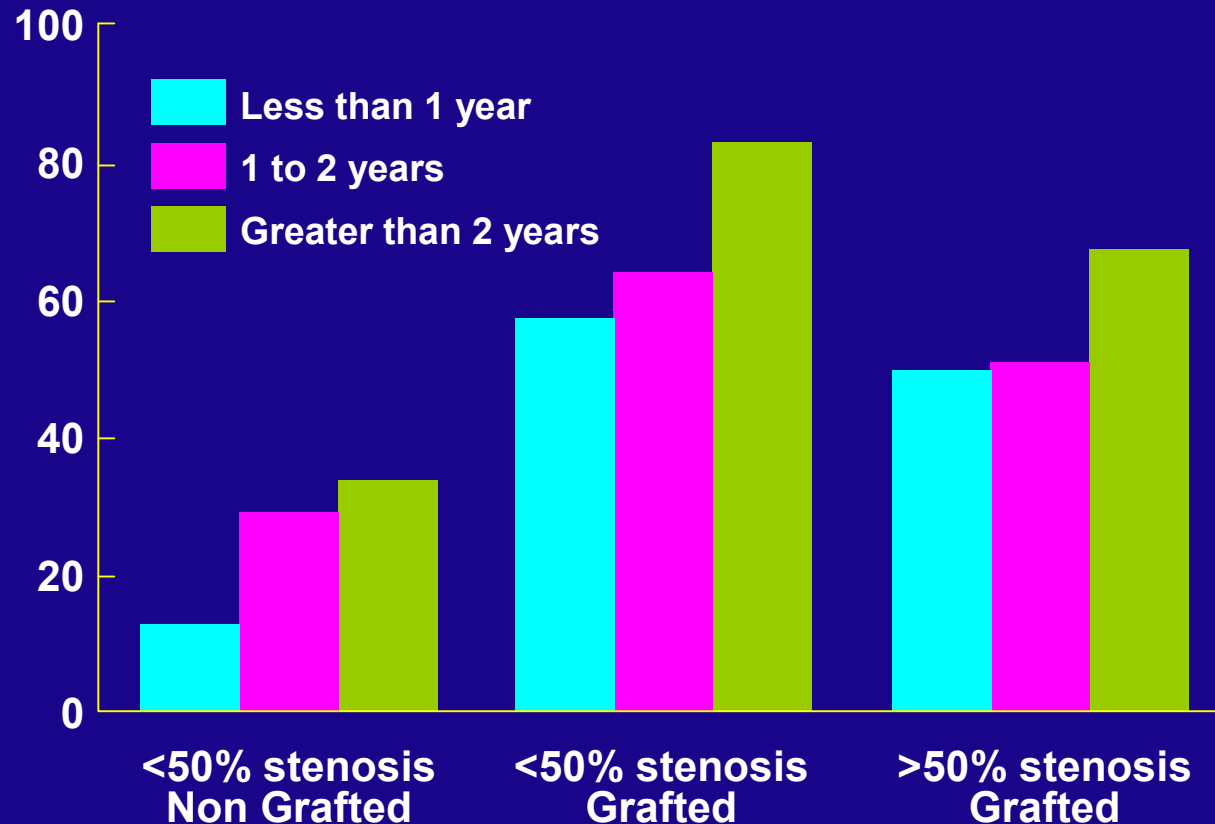


Fig. 1. Schematic representation flow patterns highlighting regions where eddies, vortices, flow separations and bidirectional flow (arrow heads) can potentially occur. The extent, severity and location of these abnormalities can vary depending upon several factors including, the relative flows across the stenosis in the native artery and the graft.



# Percent of Native Arteries with Progression

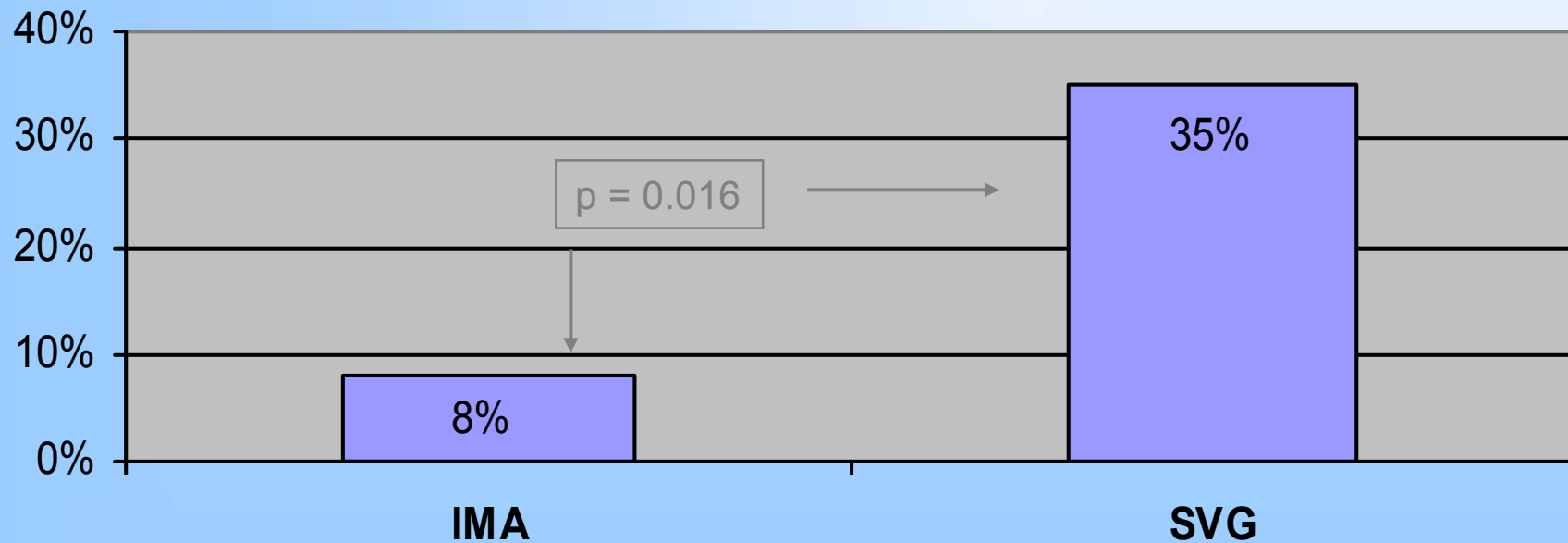
----- Cosgrove et al. Cleveland Clinic; J Thorac and Cardiovasc Surg 82:520-530, 1981



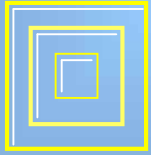
Progression (> 20% decrease in MLD) of atherosclerosis in native vessels was accelerated by vein grafts and occurred in over 50% of native vessels within 2 years of surgery

## Effect of Coronary Artery Bypass Grafting on Native Coronary Artery Stenosis

----Hamada, Y. et al. Journal of Cardiovascular Surgery 2001; 42: 159-164



**35% of native coronaries bypassed with a vein graft progressed to total occlusion by 5 month angiography**

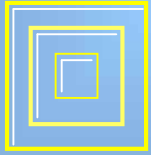


# Risk Factors for Acceleration of Coronary Disease

- **Smoking**
- **LDL cholesterol**
- **Obesity**
- **Sedentary life style**
- **Bypass surgery**
  - especially saphenous vein graft implantation

**The most frequently implanted surgical graft in the U.S. is still a saphenous vein...  
and after a few years, it's not a pretty site!**





# 2008 Isolated CABG Data: Society of Thoracic Surgeons STS

- **158,750 patients with isolated CABG**
  - LIMA = 89.6%
  - Bilateral IMA = 4.2%
  - Radial artery = 6.4%

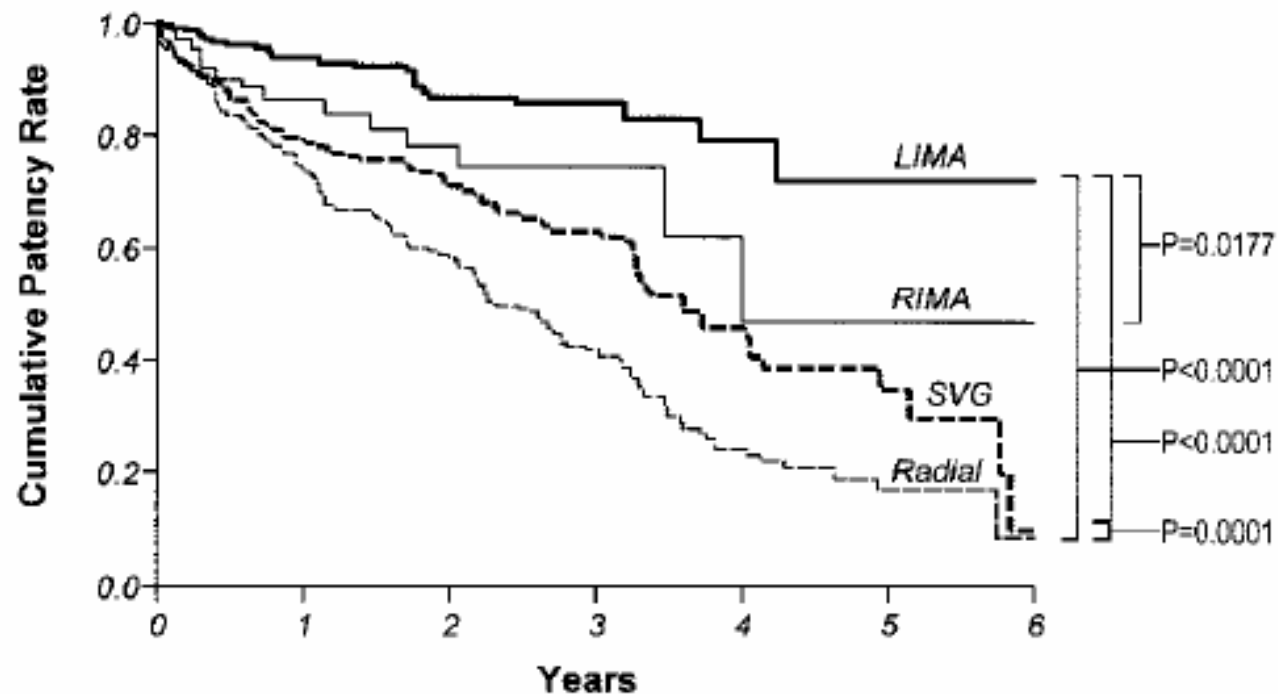
**---- 2008 STS database**

**Bilateral IMA = 27.6%**

**---- SYNTAX**

**By 5 years, vein graft patency was less than 40%. It was even worse for radial artery conduits and not much better for RIMAs!**

**----Khot UN et al. Cleveland Clinic, Circulation. 2004;109:2086-91.**



Numbers at Risk:

LIMA	265	146	89	38	17	3	0
RIMA	75	37	22	10	4	0	0
SVG	267	157	114	63	27	7	0
Radial	392	220	136	64	24	8	0

**Cumulative patency (<70% stenosis) by type of graft**

# Efficacy and Safety of Edifoligide, an E2F Transcription Factor Decoy, for Prevention of Vein Graft Failure Following Coronary Artery Bypass Graft Surgery

## PREVENT IV: A Randomized Controlled Trial

### PREVENT IV Investigators\*

**C**ORONARY ARTERY BYPASS GRAFT (CABG) surgery is one of the most common surgical procedures performed in the United States.<sup>1</sup> In appropriately selected patients, CABG surgery results in improved survival, relief of angina, and

**Context** Coronary artery bypass graft (CABG) surgery with autologous vein grafting is commonly performed. Progressive neointimal hyperplasia, however, contributes to considerable vein graft failure. Edifoligide is an oligonucleotide decoy that binds to and inhibits E2F transcription factors and thus may prevent neointimal hyperplasia and vein graft failure.

**Objective** To assess the efficacy and safety of pretreating vein grafts with edifoligide for patients undergoing CABG surgery.

**Design, Setting, and Participants** A phase 3 randomized, double-blind, placebo-controlled trial of 2014 patients undergoing primary CABG surgery with at least 2 planned

**A contemporary study (2002-2003), 73% received statins, 90% received aspirin!**

periprosthetic leakage as an adaptive response to the increased pressure and shear forces of arterial circulation. Hyperplasia results from proliferation and migration of vascular smooth muscle cells, which release cytokines that degrade the surrounding matrix and contribute to an inflammatory and highly atherogenic environment.<sup>16</sup> The E2F

the edifoligide group vs 121 (6.1%) of 1998 patients in the placebo group; hazard ratio, 0.83 [95% CI, 0.64-1.08];  $P=.16$ ).

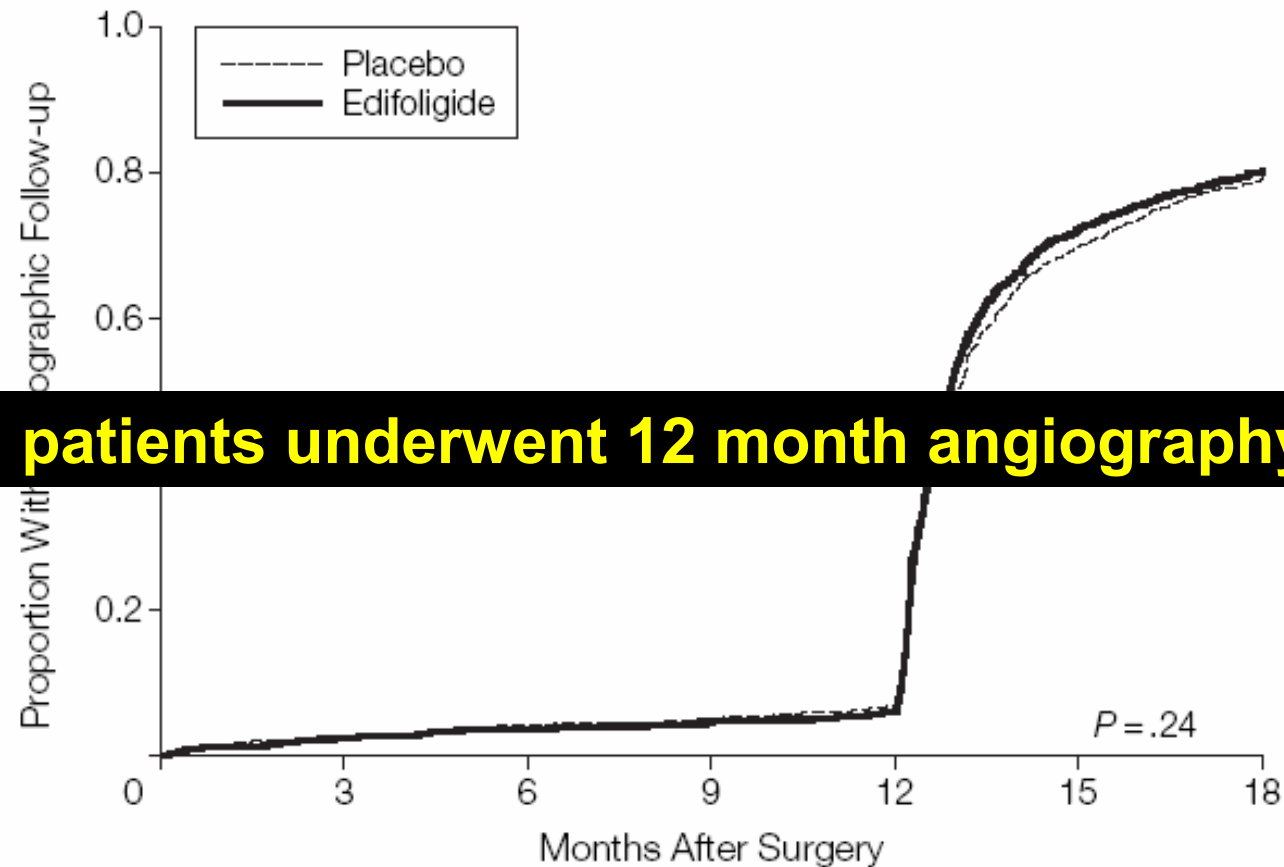
**Conclusions** Failure of at least 1 vein graft is quite common within 12 to 18 months after CABG surgery. Edifoligide is no more effective than placebo in preventing these events. Longer-term follow-up and additional research are needed to determine whether edifoligide has delayed beneficial effects, to understand the mechanisms and clinical consequences of vein graft failure, and to improve the durability of CABG surgery.

**Clinical Trial Registration** ClinicalTrials.gov Identifier: NCT00042081.

JAMA. 2005;294:2446-2454

www.jama.com

**Figure 2.** Kaplan-Meier Curves for Angiographic Follow-up



**1,820 (81%) patients underwent 12 month angiography**

No. at Risk	0	3	6	9	12	15	18
Placebo	1203	1169	1152	1141	1120	364	251
Edifoligide	1197	1166	1152	1141	1125	333	239



**Table 3.** Angiographic Results\*

Event	No./Total (%)		OR (95% CI)	P Value
	Edifoligide	Placebo		
Per patient				
Vein graft failure	436/965 (45.2)	442/955 (46.3)	0.96 (0.80-1.14)	.66
Vein graft occlusion	403/964 (41.8)	397/951 (41.7)	1.00 (0.84-1.20)	.97
Per vein graft				
Vein graft failure	650/2303 (28.5)	671/2254 (29.7)	0.94 (0.80-1.10)	.44
Vein graft occlusion	601/2295 (26.1)	597/2242 (26.5)	0.98 (0.83-1.15)	.83
Internal thoracic artery graft failure	69/809 (8.5)	60/784 (7.6)	1.12 (0.78-1.61)	.53

Abbreviations: CI, confidence interval; OR, odds ratio.

\*Data were available for 1920 of the 2400 angiographic cohort patients. Per vein graft percentages are adjusted for inpatient correlation.

**By 12 months ¼ of SVG's are occluded; 40% of patients had at least one occluded SVG**

**At 1 year ITA failure was less frequent than SVG failure 8% Vs 29%**

# Vein graft failure profoundly increased death, MI and revascularization

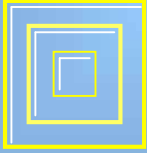
**Table 5.** Clinical Event in Patients by Vein Graft Failure Status

Type of Event	No./Total (%) of Patients	
	Vein Graft Failure (n = 878)	No Vein Graft Failure (n = 1042)
Perioperative MI in CABG surgery	118 (13.4)	71 (6.8)
Death or MI*	122 (13.9)	9 (0.9)
Death, MI,* or revascularization	228 (26.0)	19 (1.8)

Abbreviations: CABG, coronary artery bypass graft; MI, myocardial infarction.

\*Not including perioperative MI in CABG surgery.

**Saphenous vein graft failure**  
**+ Native disease acceleration**  
**= A very difficult day for the**  
**Interventional cardiologist!**

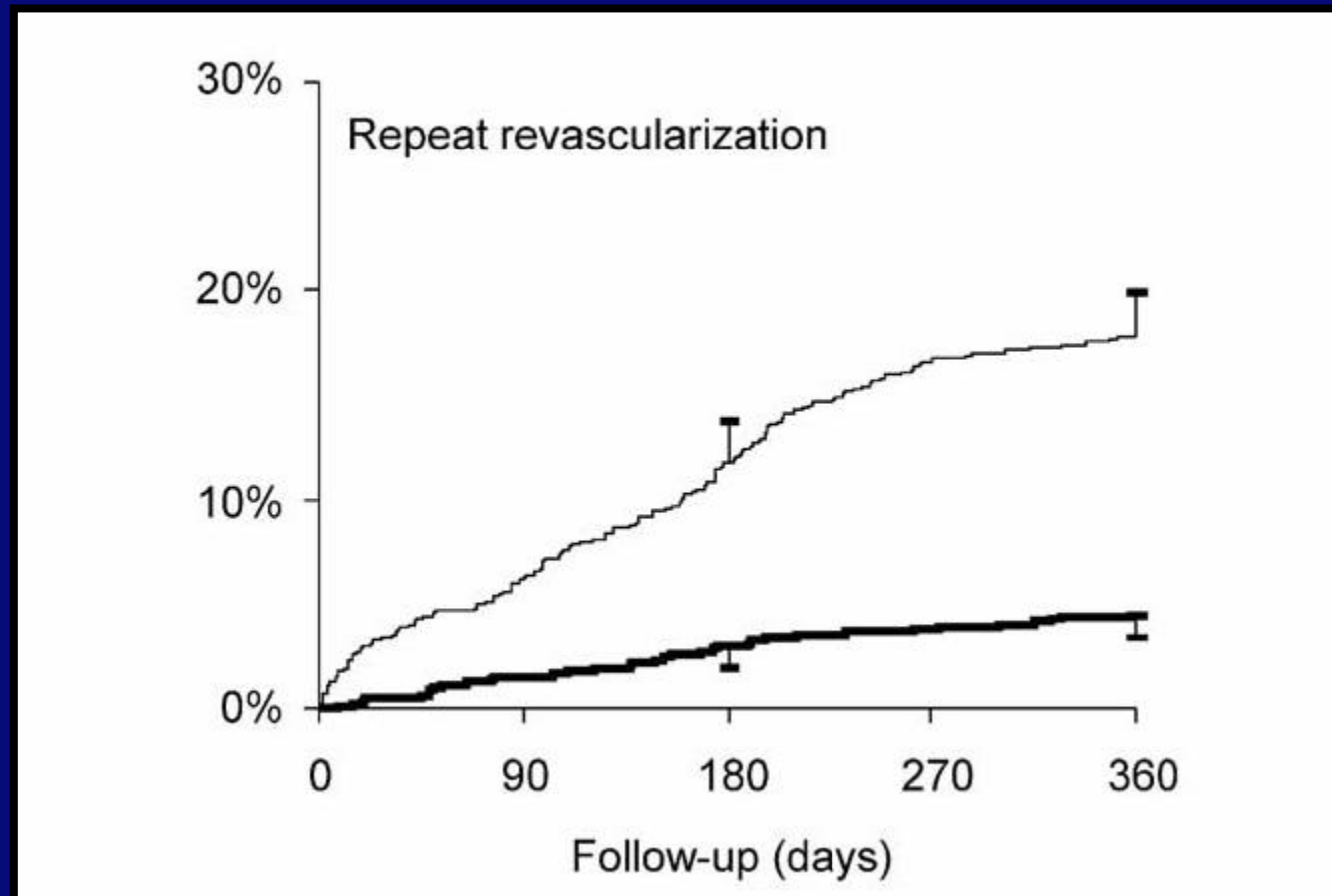


## Three Great Myths of Cardiac Surgery

- **Myth # 1: “Cardiologists do not obtain informed consent from patients prior to multivessel PCI.”**
  - No surgical consultation obtained
  - Risk of restenosis not disclosed
- **How many cardiac surgeons do you know who inform patients that their saphenous vein graft only have about a 50% chance of patency within 5 years?**
- **How many cardiac surgeons do you know who inform patients that their underlying native vessel disease will accelerate due to SVG bypass, making their overall coronary diseased burden much worse when the SVG occludes?**



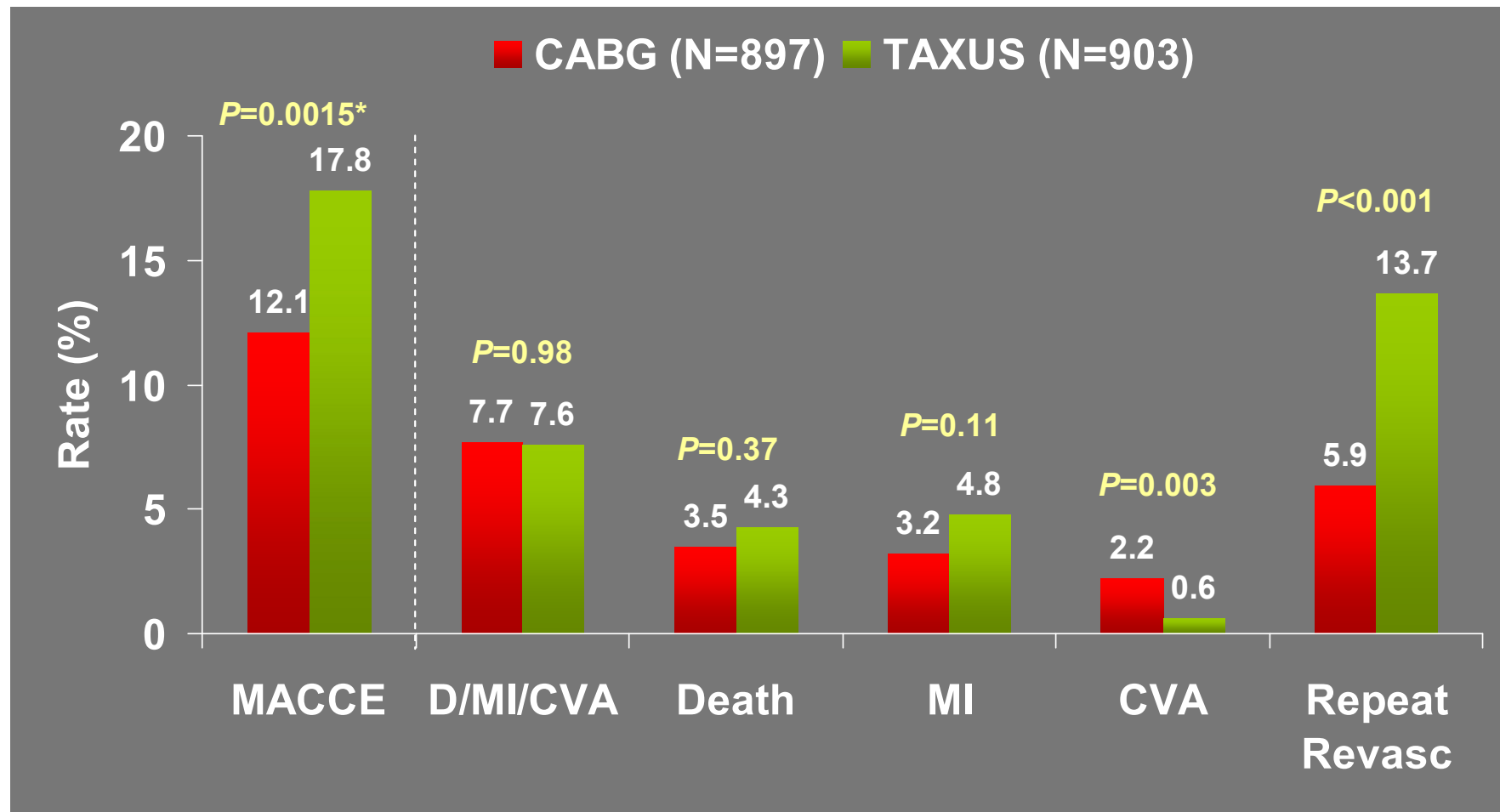
# One-year Rates of Repeat Revascularization in 4 CABG vs. Stent Assisted PCI Trials



Mercado et al, *J thoracic Cardiovasc Surg*, 2005

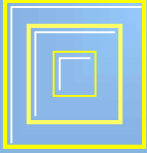
# SYNTAX

## One Year Clinical Outcomes



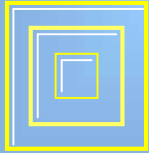
Serruys, Mohr ESC 2008

\*Primary Endpoint



## Three Great Myths of Cardiac Surgery

- **Myth # 2: Target vessel revascularization rates are much higher following PCI compared to CABG**

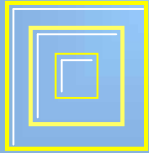


# **Is CABG more durable than PCI?**

## **Interpreting Clinical Trial Results:**

- **Several years post CABG, both the native vessel and SVG often progress to a total occlusion or diffuse disease resulting in limited options for PCI.**
- **Given the high threshold for repeat bypass surgery (particularly in the presence of a patent LIMA graft), many post CABG patients are not offered repeat revascularization; not because they wouldn't benefit from re-intervention, but because the risks are prohibitive and the likelihood of success is low.**
- **Thus, much of the relative increase in repeat revascularization following PCI observed in clinical trials is because the post PCI patient, in contradistinction to the post CABG patient, remains a good candidate for further revascularization.**

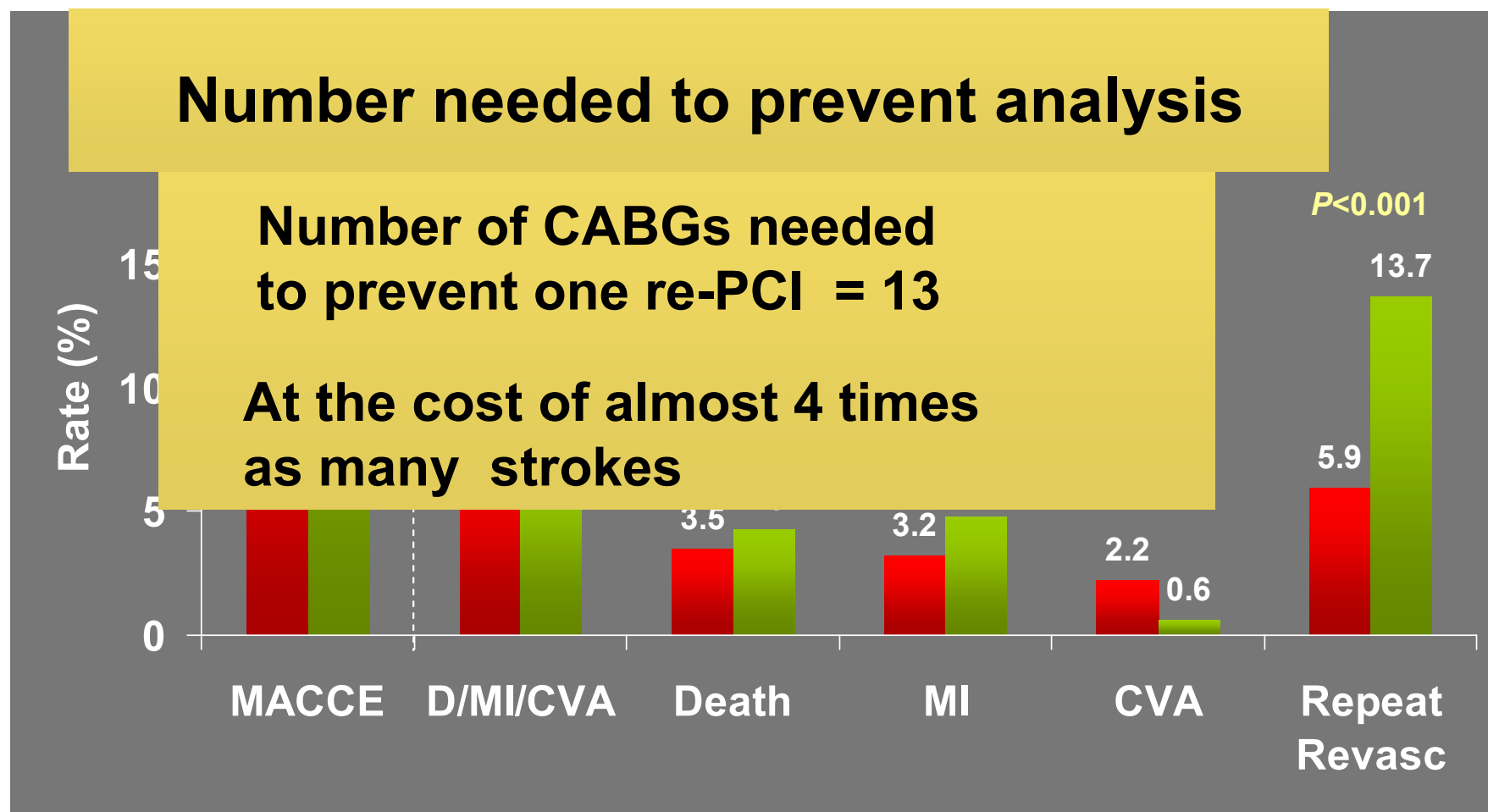




## **The TVR Trade-off: Good data – Bad interpretation**

- **The clinician's perspective**
  - **Most of my patients tell me they would rather go through 3, 4 or even 5 PCI procedures rather than go through one bypass surgery**
- **Yet some are using left main trial data to say exactly the opposite**

# One Year Clinical Outcomes



Serruys, Mohr ESC 2008

\*Primary Endpoint

# Two Year Outcome in LM Subgroup

CABG TAXUS<sup>®</sup> Express<sup>®</sup> Stent

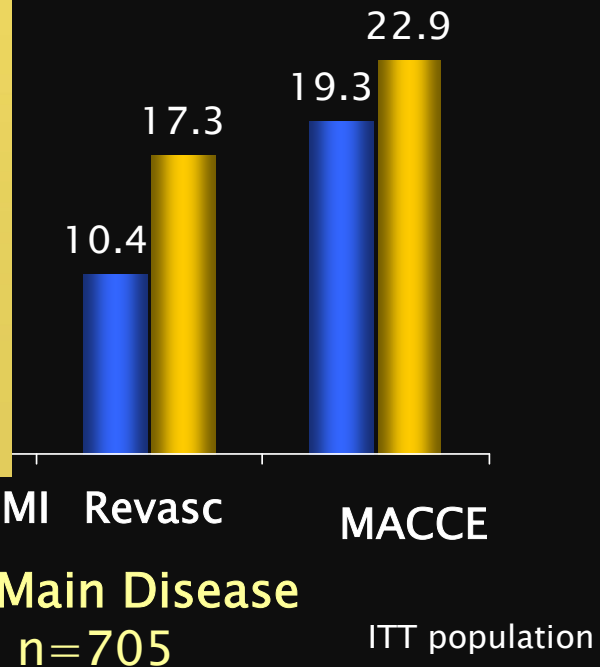
## Number Needed to Prevent

Number of CABGs needed to prevent one re-PCI = 15

This means 14 of every 15 CABGs were unnecessary!

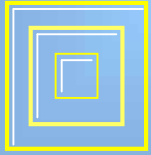
40

$P=0.01$   $P=0.27$



Presented at ESC September 2009 by A. Pieter Kappetein MD PhD

The safety and effectiveness of the TAXUS<sup>®</sup> Stent Systems have not been established in the following patient populations: lesions located in the unprotected left main coronary artery, or patients with multi-vessel disease.



# What's missing from the PCI vs CABG trial data discussion?

- **Why does the debate seem to always focus on mortality and repeat revascularization?**
- **Shouldn't we include morbidity endpoints?**

# PREVENT 4

JAMA 2005

**Table 6.** Safety Events

Type of Event	No. (%) of Patients	
	CABG + Edifoligide (n = 1508)	CABG + Placebo (n = 1506)
Atrial fibrillation	379 (25.1)	402 (26.7)
Perioperative MI in CABG surgery	145 (9.6)	149 (9.9)
Renal failure	49 (3.2)	50 (3.3)
Bleeding requiring reoperation	40 (2.7)	36 (2.4)
Pneumonia	33 (2.2)	37 (2.5)
Stroke	28 (1.9)	18 (1.2)
Adult respiratory distress syndrome	10 (0.7)	16 (1.1)
Mediastinitis	9 (0.6)	12 (0.8)
Pulmonary embolism	12 (0.8)	5 (0.3)

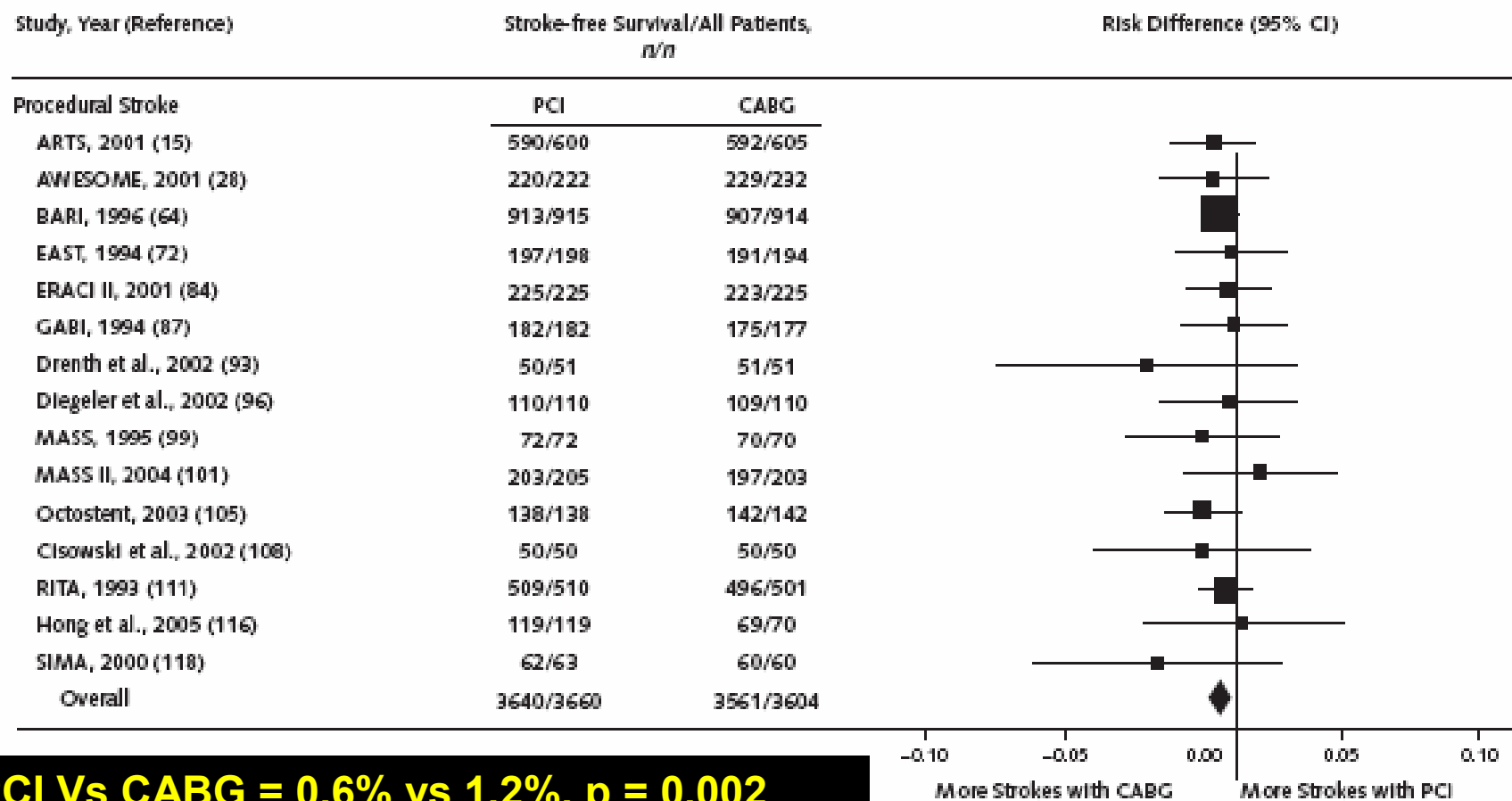
Abbreviations: CABG, coronary artery bypass graft; MI, myocardial infarction.

# Systematic Review: The Comparative Effectiveness of Percutaneous Coronary Interventions and Coronary Artery Bypass Graft Surgery

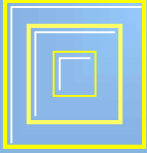
Dena M. Bravata, MD, MS; Allison L. Glenger, BA; Kathryn M. McDonald, MM; Vandana Sundaram, MPH; Marco V. Perez, MD; Robin Varghese, MD, MS; John R. Kapoor, MD, PhD; Reza Ardehali, MD, PhD; Douglas K. Owens, MD, MS; and Mark A. Hlatky, MD

## Risk of Procedural Stroke

20 November 2007 | *Annals of Internal Medicine* | Volume 147 • Number 10



**PCI Vs CABG = 0.6% vs 1.2%, p = 0.002**



## Three Great Myths of Cardiac Surgery

- **Myth # 3: Given differences in morbidity, bypass surgery can even be compared to PCI.**
  - If my PCI patient has a pseudo aneurysm requiring surgical repair of the femoral artery, it is considered a major complication that I have to defend at M&M and QA committee. The untoward event is a small surgical incision in the groin.
  - All CABG patients have a major surgical incision in the chest. Therefore 100% of all CABG patients, by this definition, suffer a major complication as a result of their care plan.

## The war of attrition:

Don't fall for the argument that, given enough years, PCI mortality will be significantly higher than CABG mortality in SYNTAX

*“Beware of the p Value”*

*STATISTICAL SIGNIFICANCE IS NOT ALWAYS  
CLINICAL SIGNIFICANCE*

*“A “p” value does not a substitute for a brain”*



January 24, 2008

## Bypasses Outshine Stents in Study

Patients Fared Better  
By Choosing Surgery  
For Multiple Blockages

By **KEITH J. WINSTEIN**

*January 24, 2008*

Patients with multiple clogged arteries are better off getting bypass surgery than stents, a study found.



Original Article

# Drug-Eluting Stents vs. Coronary-Artery Bypass Grafting in Multivessel Coronary Disease

Edward L. Hannan, et al N Engl J Med, Volume 358(4):331-341 Jan 24, 2008

**Mortality (after adjustment) 7.3% for DES Vs. 6.0% for CABG**

**This 1.3% absolute difference (p=0.03) yields a NNT of 77**

**If we need to do 77 bypasses to save one life, I believe the mortality benefit is clinically meaningless!**

**This point was completely missed by the lay press and many physicians**



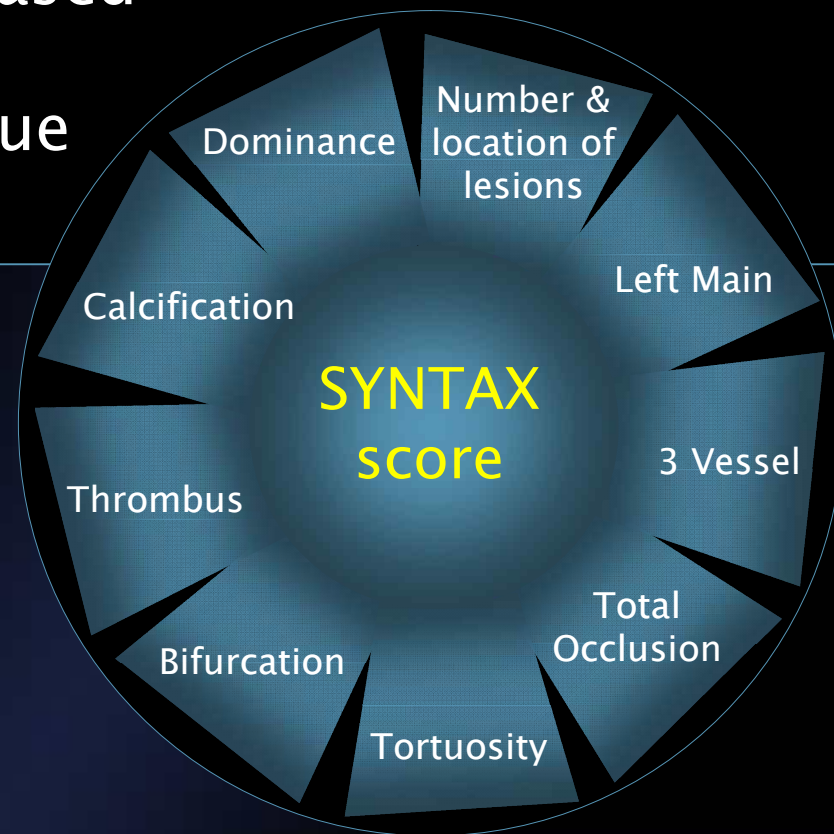
The NEW ENGLAND  
JOURNAL of MEDICINE

# SYNTAX Score



- A prospective angiographic tool to grade the complexity of coronary artery disease
- Goal: Obtain evidence-based guidelines for selecting revascularization technique (surgery or PCI)

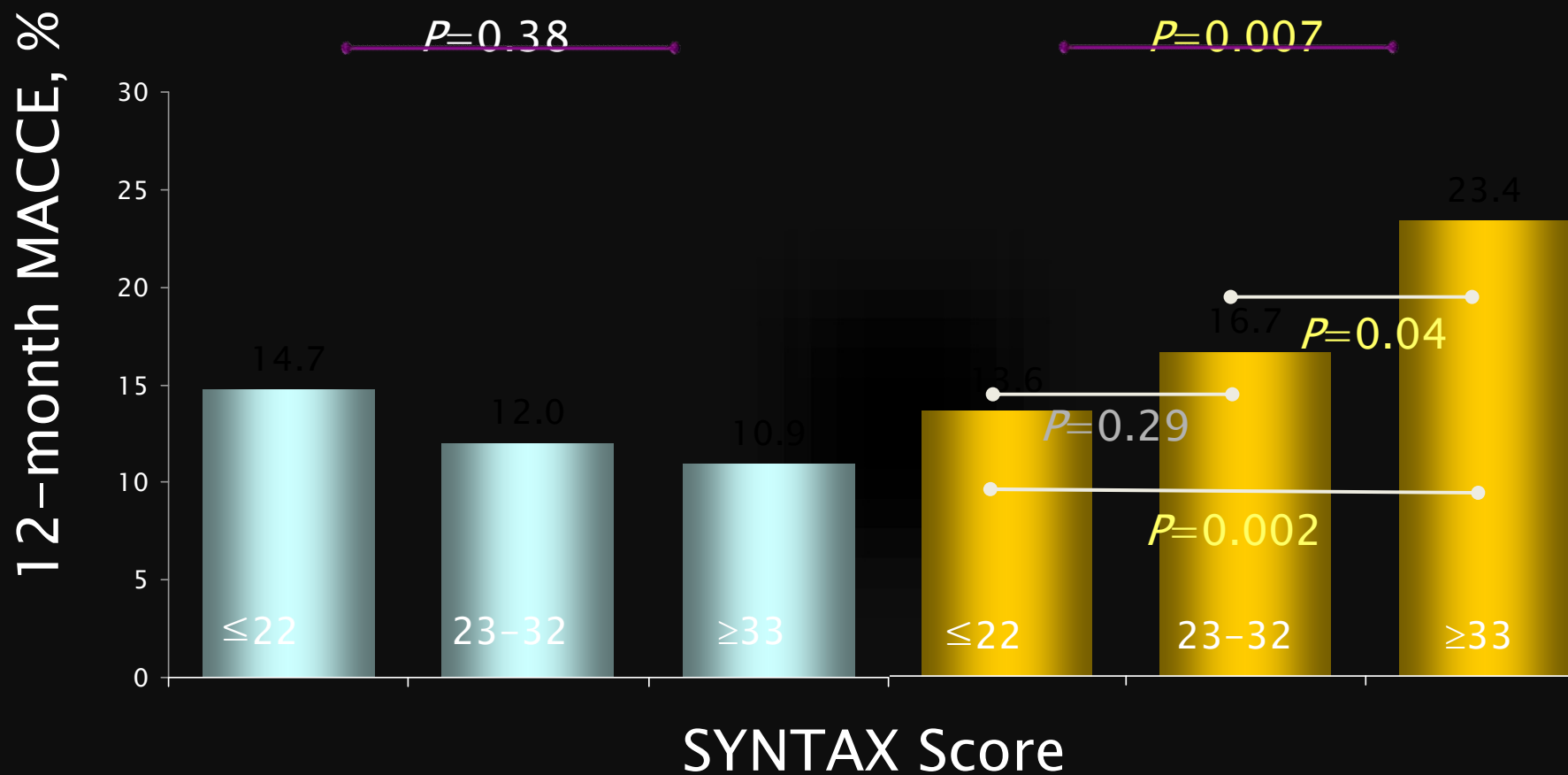
The SYNTAX Score will be retroactively weighted based on MACCE at 1 and 5 years to optimize its prognostic value



# MACCE to 12-Months vs SYNTAX Score™

■ CABG (N=897)

■ TAXUS® Express® Stent (N=903)



RCT ITT pts; site-reported data

Presented by Dr. Serruys; TCT 2008

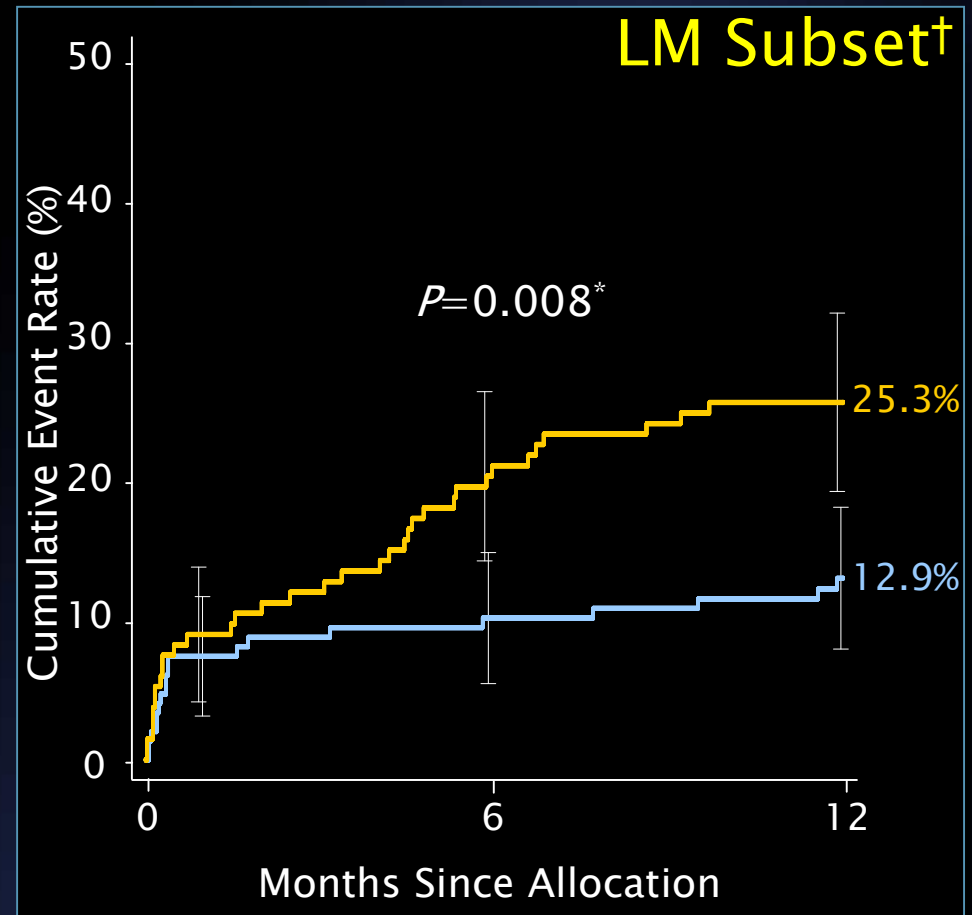
The safety and effectiveness of the TAXUS® Express® Stent System have not been established in the following patient populations: lesions located in the unprotected left main coronary artery or patients with multi-vessel disease.

# MACCE to 12 Months by SYNTAX Score Tertile *High Scores (33+)*



	CABG	PCI	<i>P</i> -value*
Death	4.1%	9.7%	0.06
CVA	3.4%	0.8%	0.22
MI	6.0%	7.6%	0.65
Death, CVA or MI	10.8%	14.1%	0.40
Revasc.	4.9%	17.8%	0.001

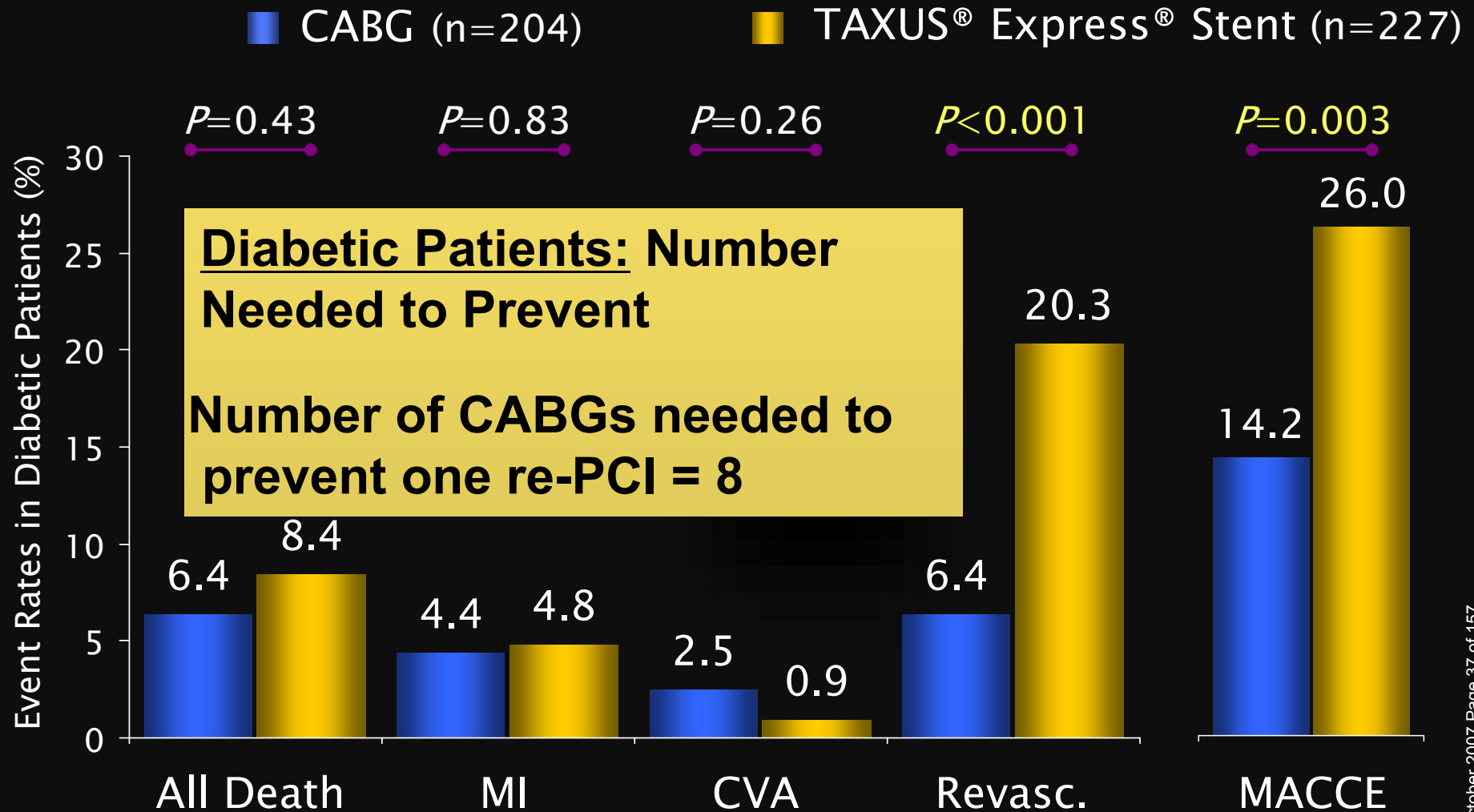
■ CABG (N=150)  
■ TAXUS (N=135)



KM Event rate  $\pm$  1.5 SE, \*chi square or Fisher exact test

<sup>†</sup>Patients with isolated LM or LM +1, +2 or +3 vessel disease  
Site-reported Data; ITT population

# Higher 12-Month MACCE in Diabetics\* Driven by Revascularization



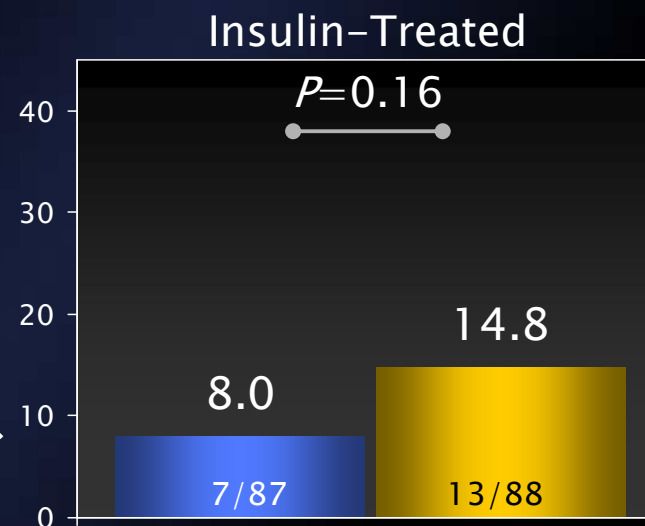
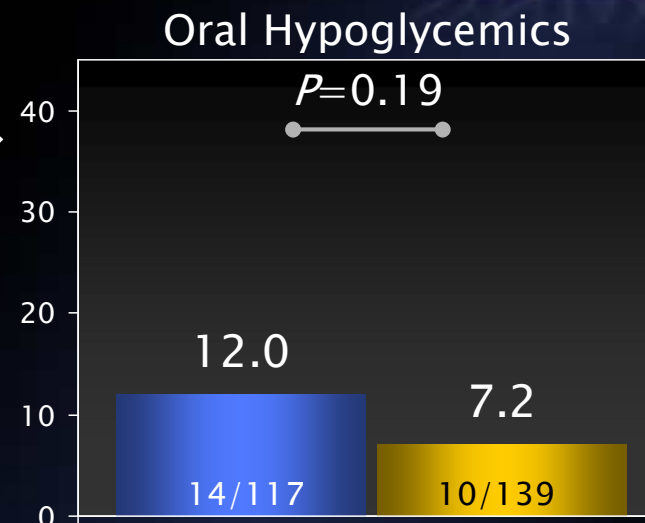
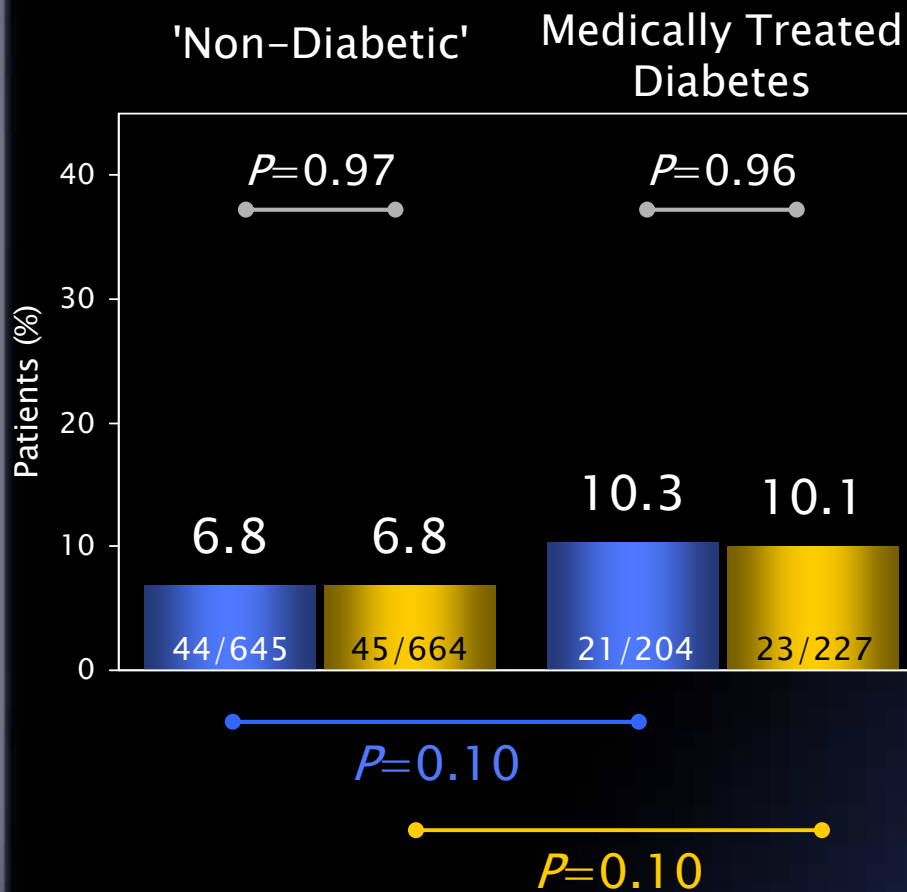
\*Medically treated diabetes  
Presented by Dr. Dawkins; TCT 2008  
The TAXUS Express Stent System has not been specifically indicated for patients with diabetes.

# Death/CVA/MI at 12 Months

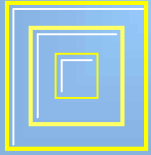
## Diabetic Subgroups



■ CABG    ■ TAXUS\*



\*The safety and effectiveness of the TAXUS® Express® Stent have not been established in the following patient populations: patients with vessel thrombus at the lesion site; patients with coronary artery lesions longer than 28 mm or requiring more than one TAXUS stent; lesions located in the unprotected left main coronary artery, or lesions located at a bifurcation/trifurcation; patients with moderate or severe calcification in the lesion or a chronic total occlusion; or patients with multi-vessel disease or patients with diabetes



## **Current Evidence Justifies Left Main and 3 vessel PCI**

**----- with qualifications**

- **Is the syntax score high?**
- **Is it a simple ostial or mid-shaft lesion?**
- **Can we achieve complete revascularization?**
  - Is revascularization of an occluded RCA important?
- **Is the left main heavily calcified?**
- **Is the left main small, and/or tortuous?**
- **Is the patient an insulin dependent diabetic?**
- **Do co-morbid considerations make the patient a poor candidate for CABG?**

Filter: Filter 5

**60 yo male  
with angina**





Filter: Filter 8

**Three  
bifurcations**



Derived

**Syntax  
Score is 34**

**Patient  
“demands”  
stents**



**Two weeks post robotic surgery**

**LIMA take-down by robot; small incision at  
4<sup>th</sup> intercostal for anastomosis**

**Working in yard on POD #2**

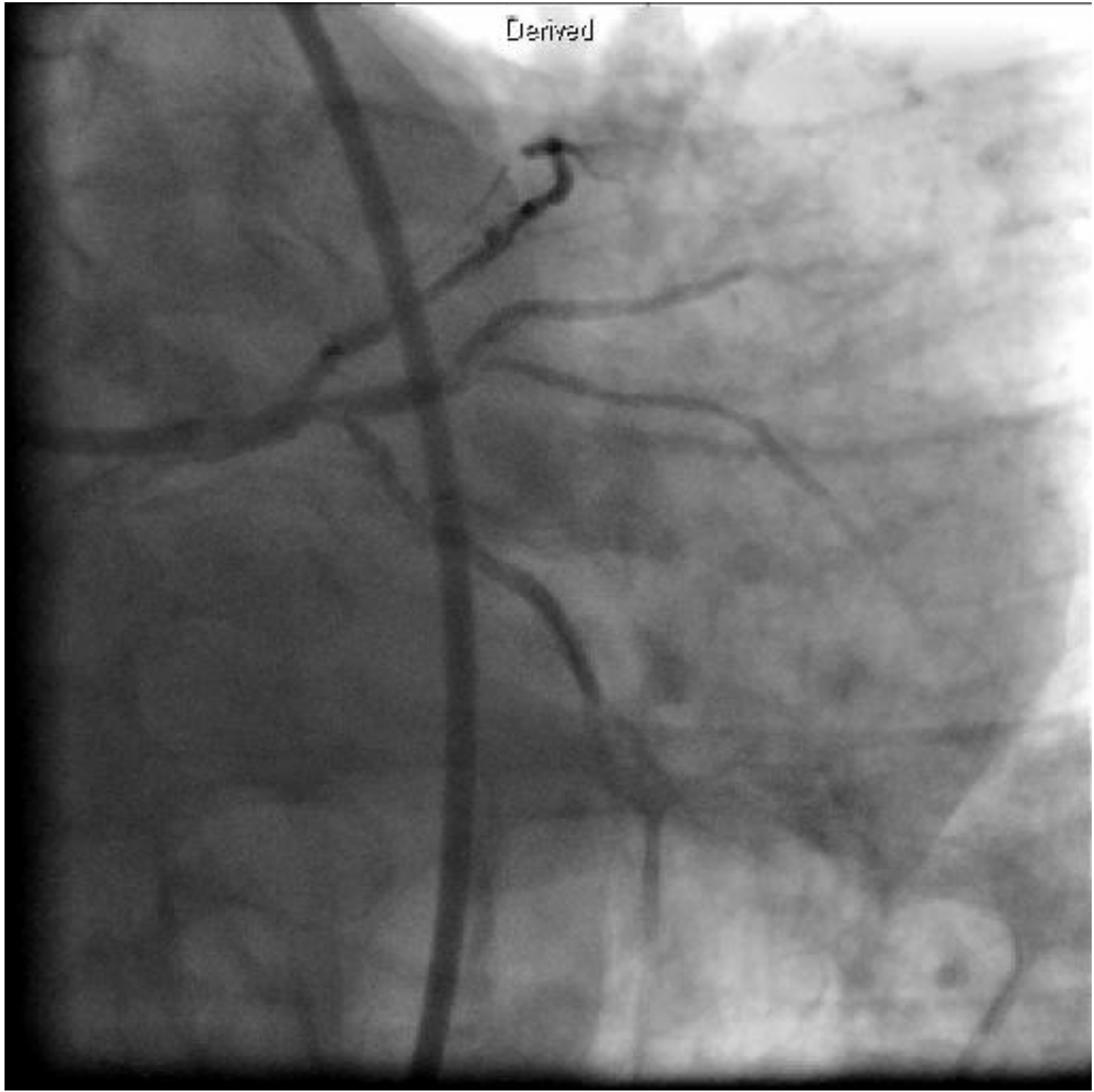
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**Two weeks  
post robotic  
surgery**

**Now his  
Syntax  
Score is 23**

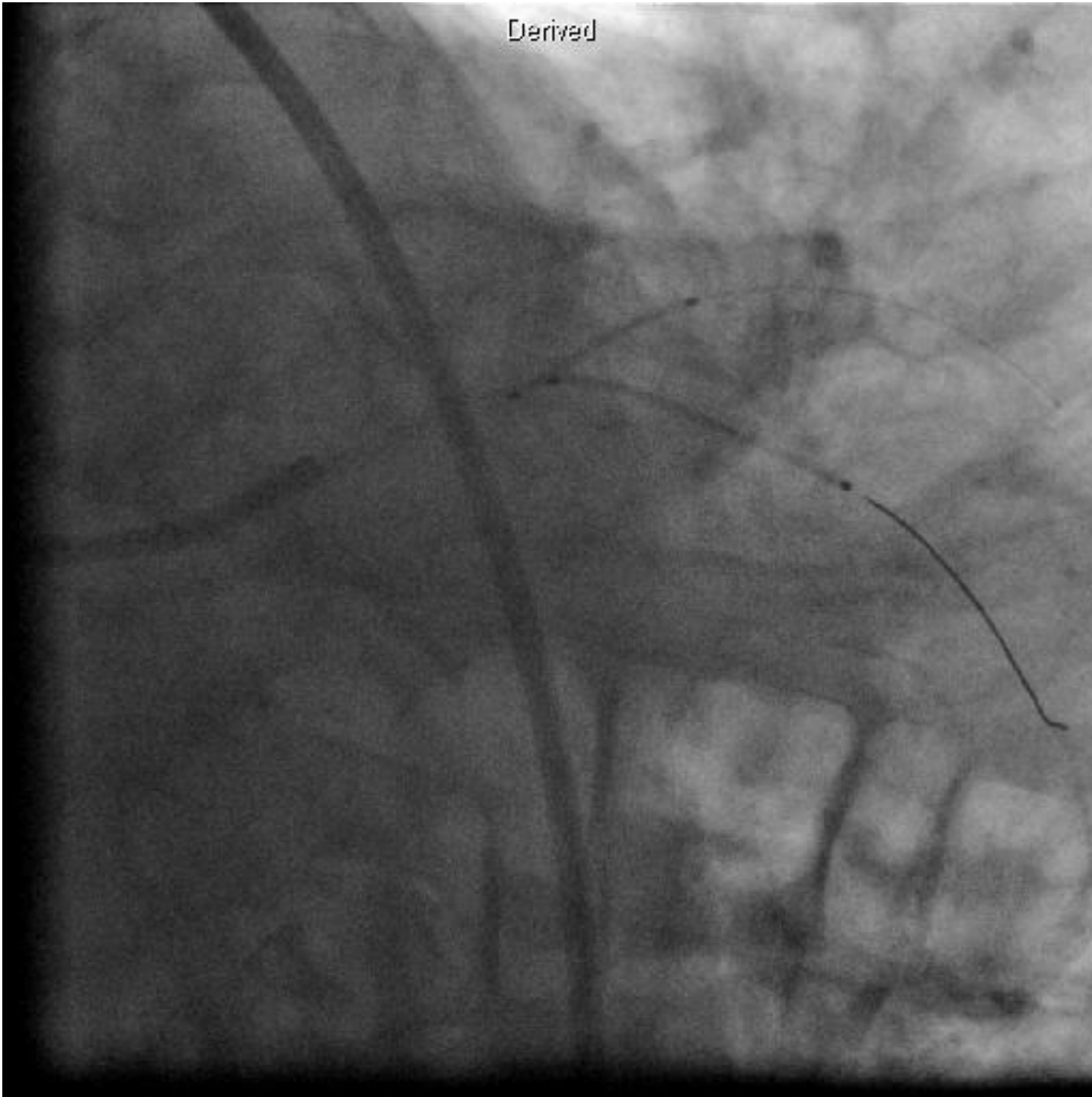


Derived



Derived

## **Bifurcation DES**



Derived





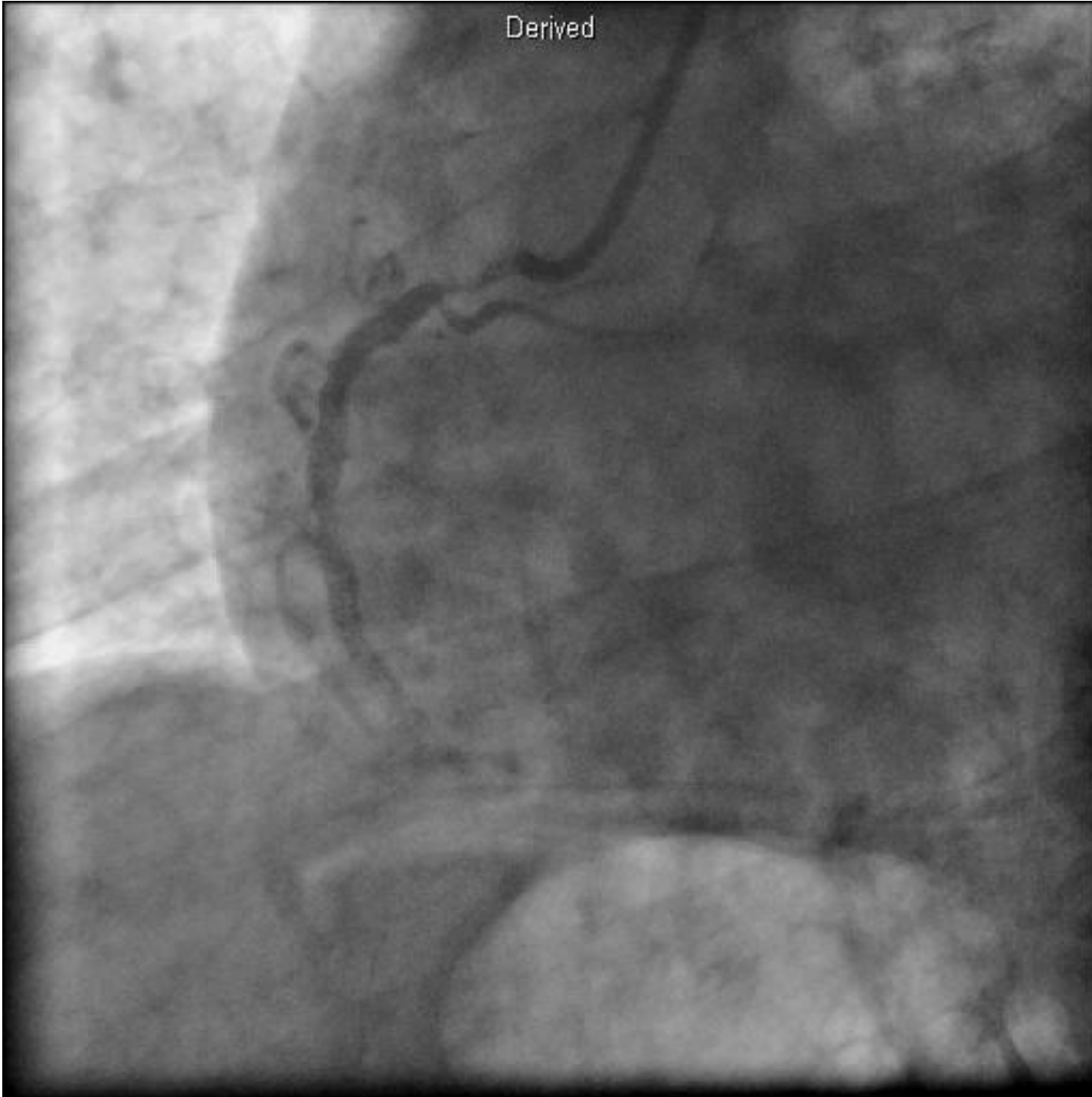
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**Left Main  
DES with  
ostial  
circumflex  
kissing  
balloon**

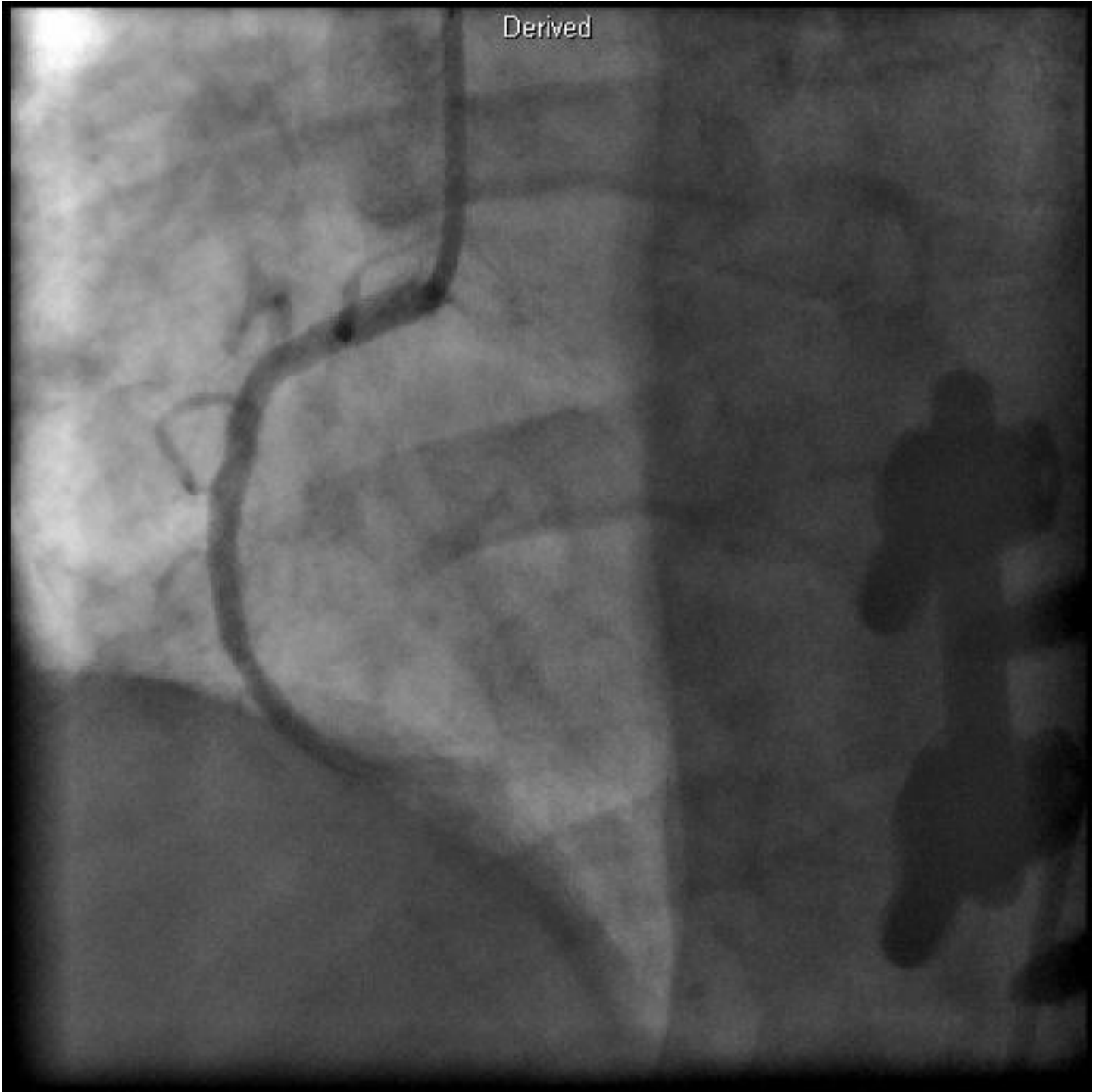
Derived



Derived



Derived



**RCA  
stenting**

Bypass the ~~Bypass~~ Venous Bypass!

