IVUS vs FFR Debate: IVUS-Guided PCI

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Disclosure Statement of Financial Interest

Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Grant/Research Support	BostonScientific, Volcano
Consulting Fees/Honoraria	BostonScientific, Volcano, LightLab, Terumo
Major Stock Shareholder/Equity	Volcano
Royalty Income	
Ownership/Founder	
Intellectual Property Rights	
Other Financial Benefit	

Most of the concepts used in IVUS-guided intervention are no different from those used in angiography-guided intervention. However, unlike angiography±FFR - with the exception of the use of FFR to assess the severity of a lesion, IVUS is actually able to make precise measurements, assess lesion morphology, fine tune the final result, etc.

- Weigh potential problems (i.e. LM disease, significant proximal or distal disease)
- Assess lesion severity
- Assess unusual lesion morphology (i.e., aneurysms, calcium, thrombi, in-stent restenosis, etc.)
- Measure vessel size
- Measure lesion length
- Determine and fine-tune the final result of interventions
- Assess complications
- Assess thrombosis and restenosis

In BMS era, 10/12 studies supported IVUS-guided PCI

Study	Angio Better	IVUS Better	IVUS Also Cheaper
Choi et al (AHJ *2001;142:112-8)*		x	
CENIC (*JACC* 2002;39:54A)		X	
CRUISE (*Circulation 2000;102:523-30)*		X	
SIPS (*Circulation* 2000;102:2497-502 and AJC 2003;91:143-7)		X	X
AVID (*Circulation* 1999;100:I-234)		X	
Gaster et al (*Scan Cardiovasc J 2001;35:80-5 & Heart* 2003;89:1043-9)		X	x
RESIST (JACC 1998;32:320-8 & *Int J Cardiovasc Intervent* 2000;3:207-13)		X	
TULIP (*Circulation 2003;107:62-7)*		X	
BEST (*Circulation2003;107:545-551*)		X	
OPTICUS (Circulation. 2001;104:1343-9)	x		
PRESTO (Am Heart J. 2004;148:501-6)	x		
DIPOL (Am Heart J. 2007;154:669-75)		X	

Predictors of DES Thrombosis & Restenosis

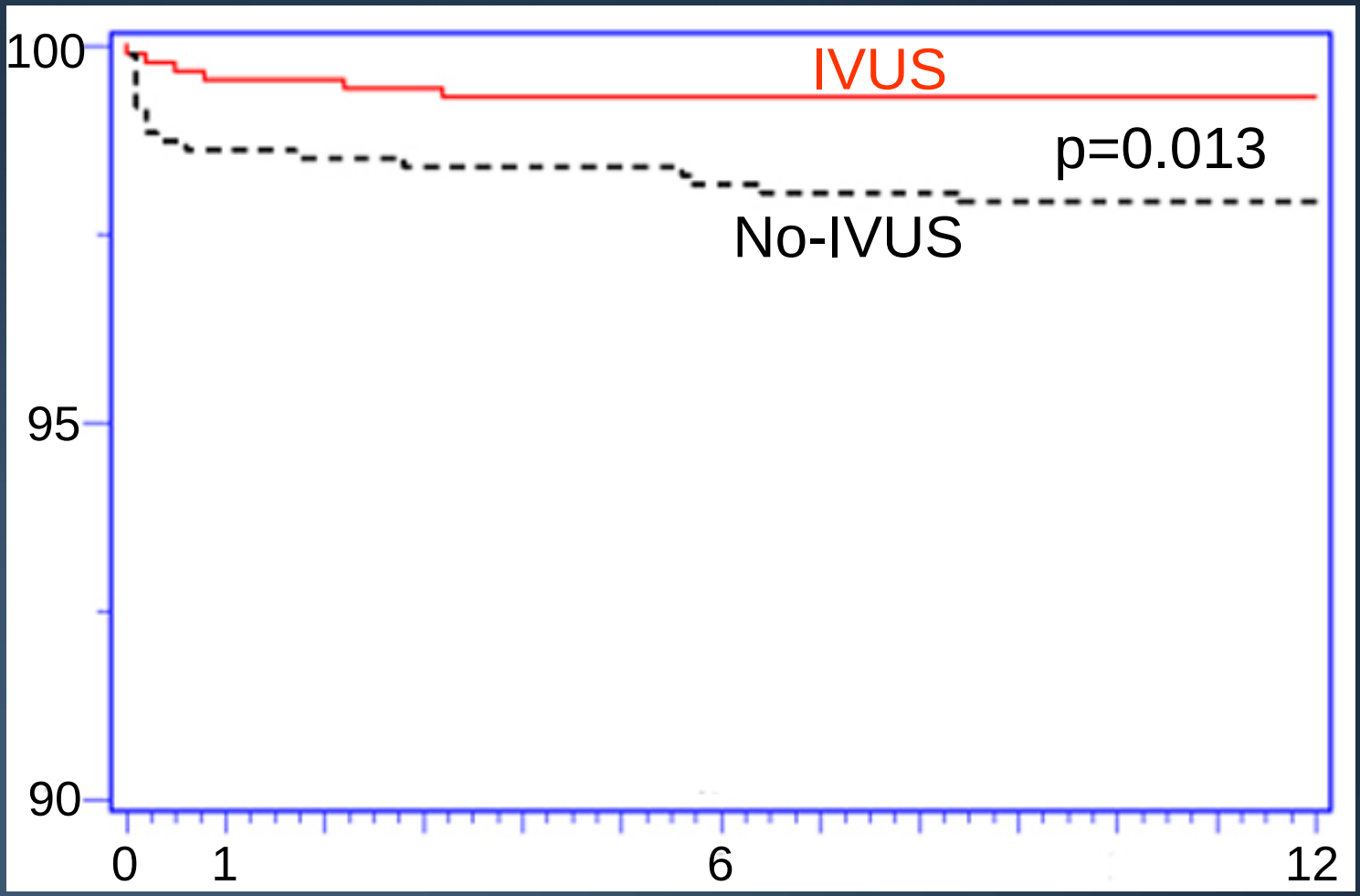
	DES Thrombosis	DES Restenosis
Underexpansion	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8)* •*Okabe et al., Am J Cardiol. 2007;100:615-20*	•*Sonoda et al. J Am Coll Cardiol 2004;43:1959-63* •*Hong et al. Eur Heart J 2006;27:1305-10* •*TAXUS IV, V, VI meta-analysis* •*Fujii et al. Circulation 2004;109:1085-1088*
Edge problems (geographic miss, secondary lesions, large plaque burden, etc)	•*Fujii et al. J Am Coll Cardiol 2005;45:995-8)* •*Okabe et al., Am J Cardiol. 2007;100:615-20*	•*Sakurai et al. Am J Cardiol 2005;96:1251-3* •*Liu et al, Am J Cardiol, in press* •*Costa et al, Am J Cardiol, 2008;101:1704-11*

1296 IVUS-guided, DES-treated lesions in 884 pts vs 1312 propensity-score-matched, angio-guided, DES-treated lesions in 884 pts

	IVUS-guided	Angio-guided	p
30 day			
MACE	2.8%	5.2%	0.01
Stent thrombosis	0.5%	1.4%	0.045
TLR	0.7%	1.7%	0.045
1 year			
MACE	14.5%	16.2%	0.3
Definite stent thrombosis	0.7%	2.0%	0.014
Probably stent thrombosis	4.0%	5.8%	0.08
TLR	5.1%	7.2%	0.06
Late definite stent thrombosis	0.2%	0.7%	0.3

(Roy et al. Eur Heart J 2008;29:1851-7)

Stent-thrombosis Free Survival (%)



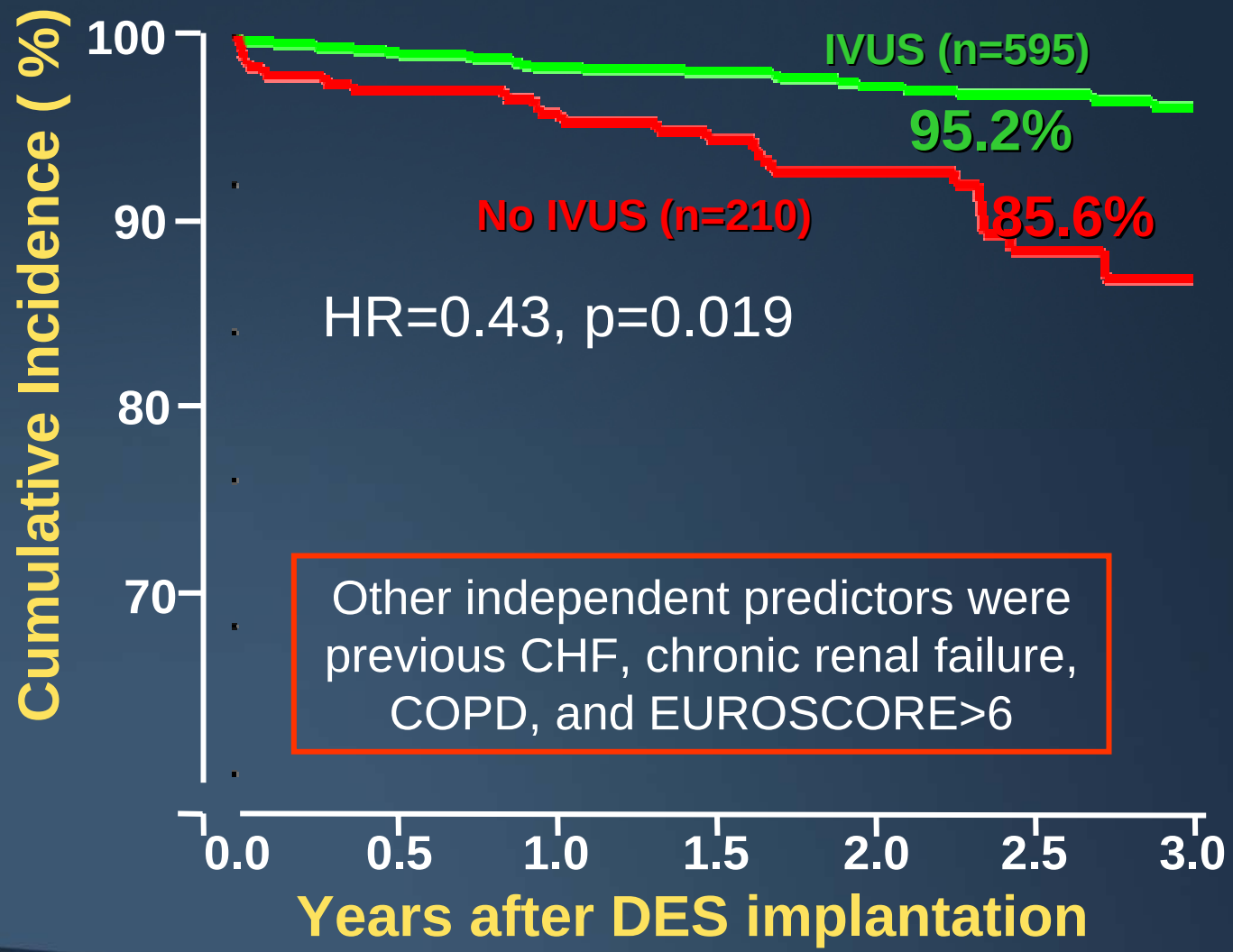
(Roy et al. Eur Heart J 2008;29:1851-7)

Independent predictors of mortality in 805 patients with LMCA disease treated with DES

	HR	95% CI	P
Previous CHF	2.66	1.03-6.85	0.043
Chronic Renal Failure	4.87	2.10-11.26	<0.001
COPD	2.93	1.00-8.53	0.049
Euroscore $\geq$ 6	3.24	1.48-7.09	0.003
IVUS guidance	0.43	0.21-0.87	0.019

(SJ Park et al. TCT 2007)

All-Cause Mortality After LMCA DES Implantation: Impact of IVUS Guidance



(SJ Park et al. TCT 2007)

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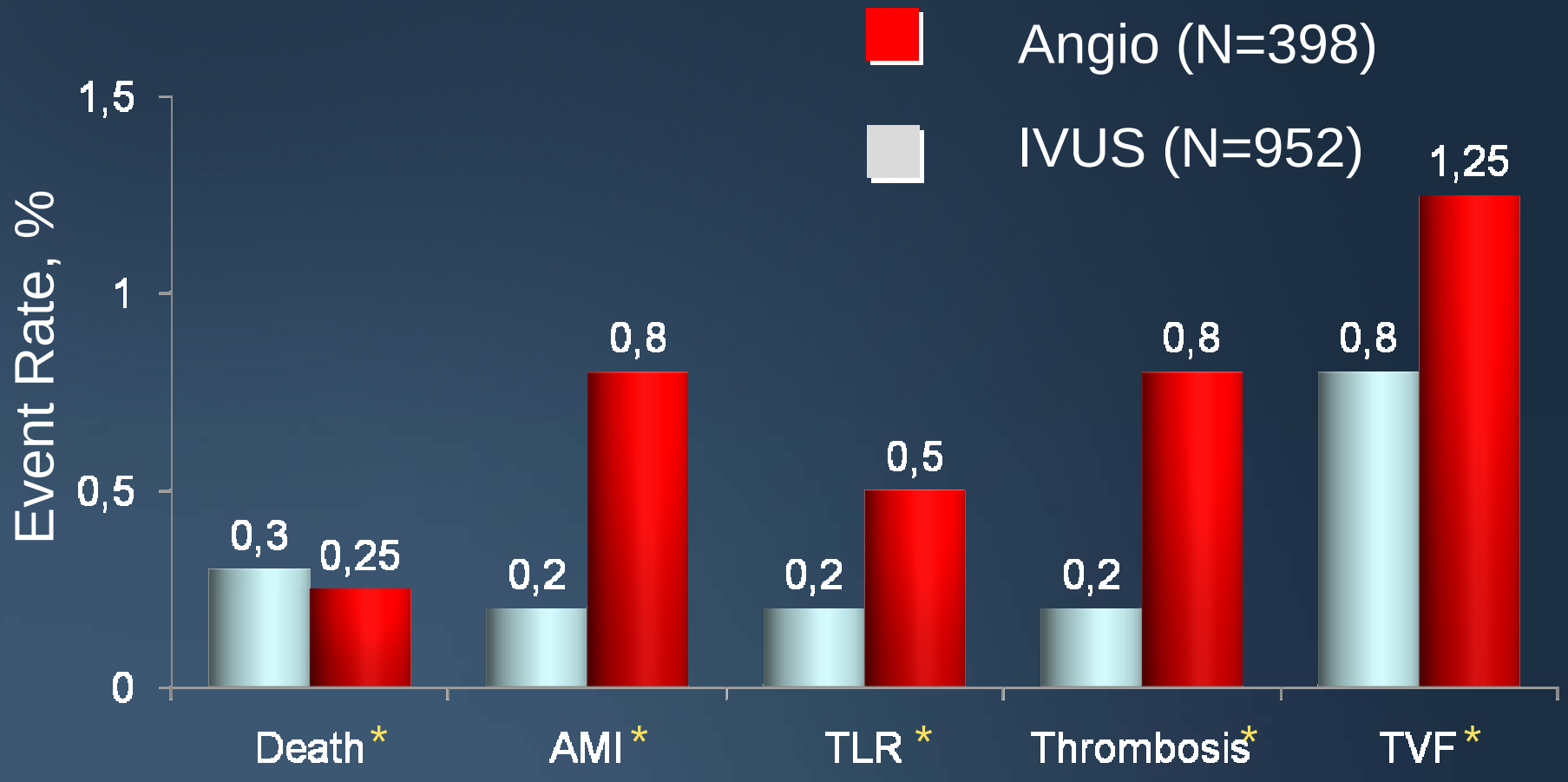
1350 pts receiving at least 1 DES (952 IVUS-guided vs 398 angio-guided) with ≥6 month follow-up

	IVUS-guided	Angio-guided	p
Age	63.4±0.36 yrs	63.5±0.42 yrs	
Diabetes	27%	35%	0.007
ACS	26%	27%	NS
Multivessel disease	54%	45%	0.001
LAD	46%	15%	<0.001
Stents/lesion	1.01	1.04	NS
%DES	93%	81%	<0.01
Stent diameter (mm)	3.0±0.4	2.9±0.5	<0.001
Stent length (mm)	24.0±7.4	22.9±7.8	<0.0001
Post-dilation	14%		

(Costantini et al. TCT 2008)

1 Month Outcome



* p=NS for all comparisons

(Costantini et al. TCT 2008)

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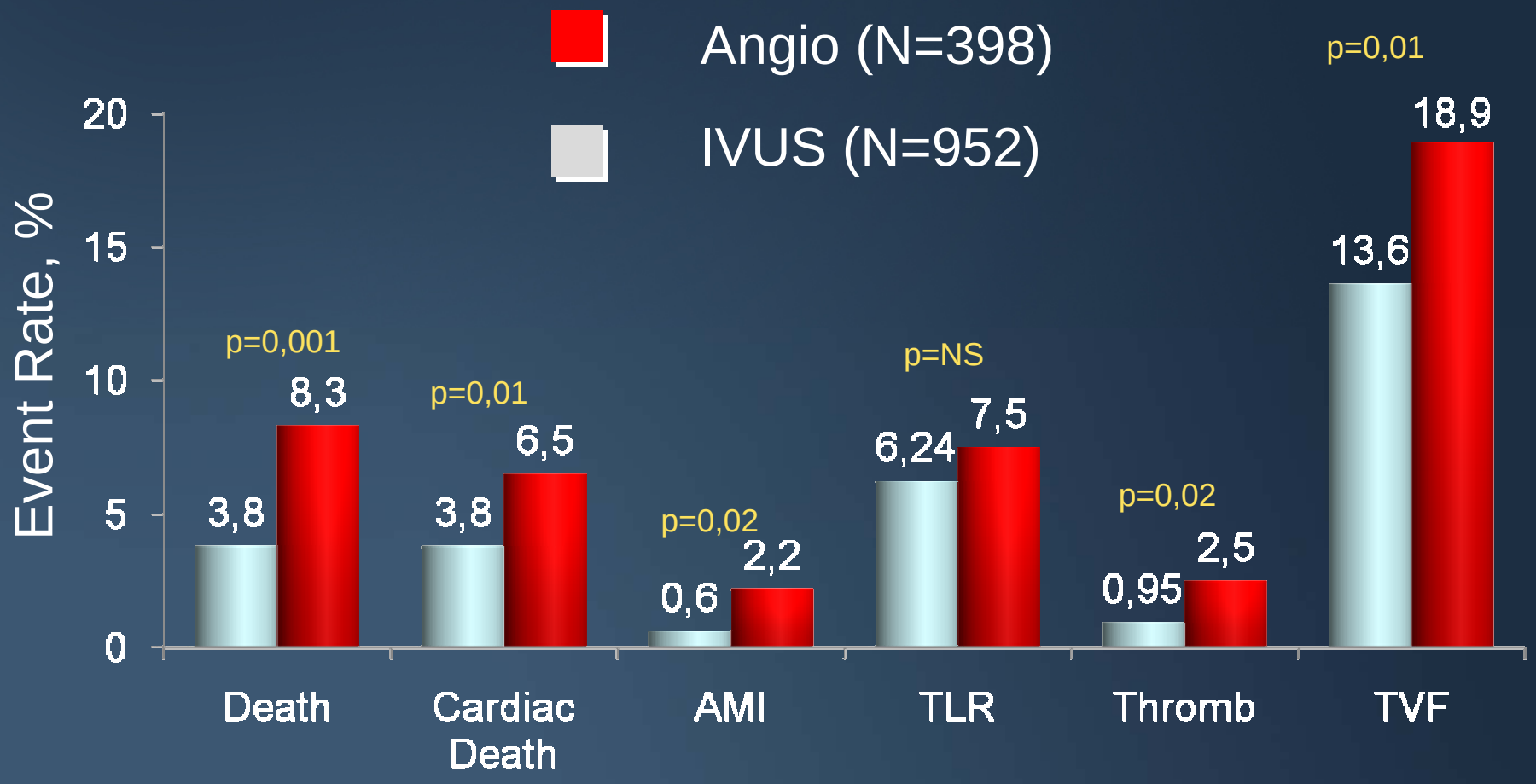
Long Term Outcome

Mean Follow Up Time: 31,9± 15,3 Months



(Costantini et al. TCT 2008)

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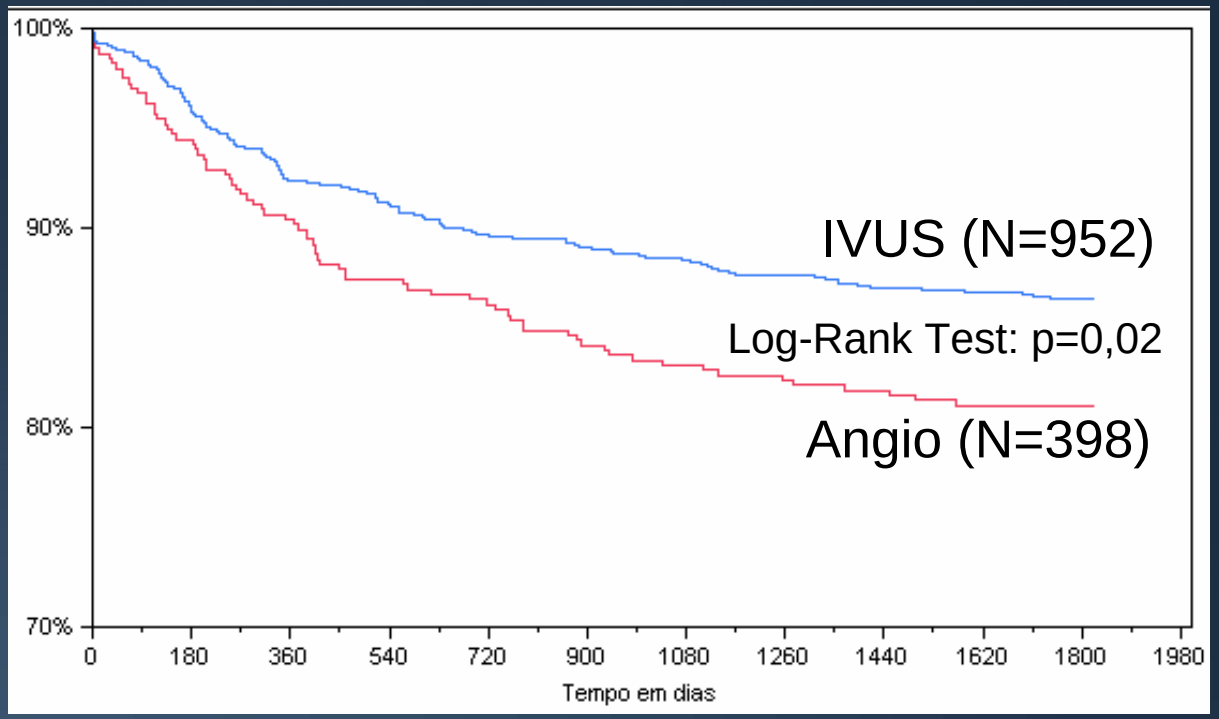
TVF Survival



	Lower CL	Upper CL	P Value
Age	-0,38	-0,09	0,001
Diabetes	-0,25	0,03	0,1
MVD	-0,29	-0,11	<0,0001
Non IVUS Guidance	-0,03	0,25	0,1

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(Costantini et al. TCT 2008)

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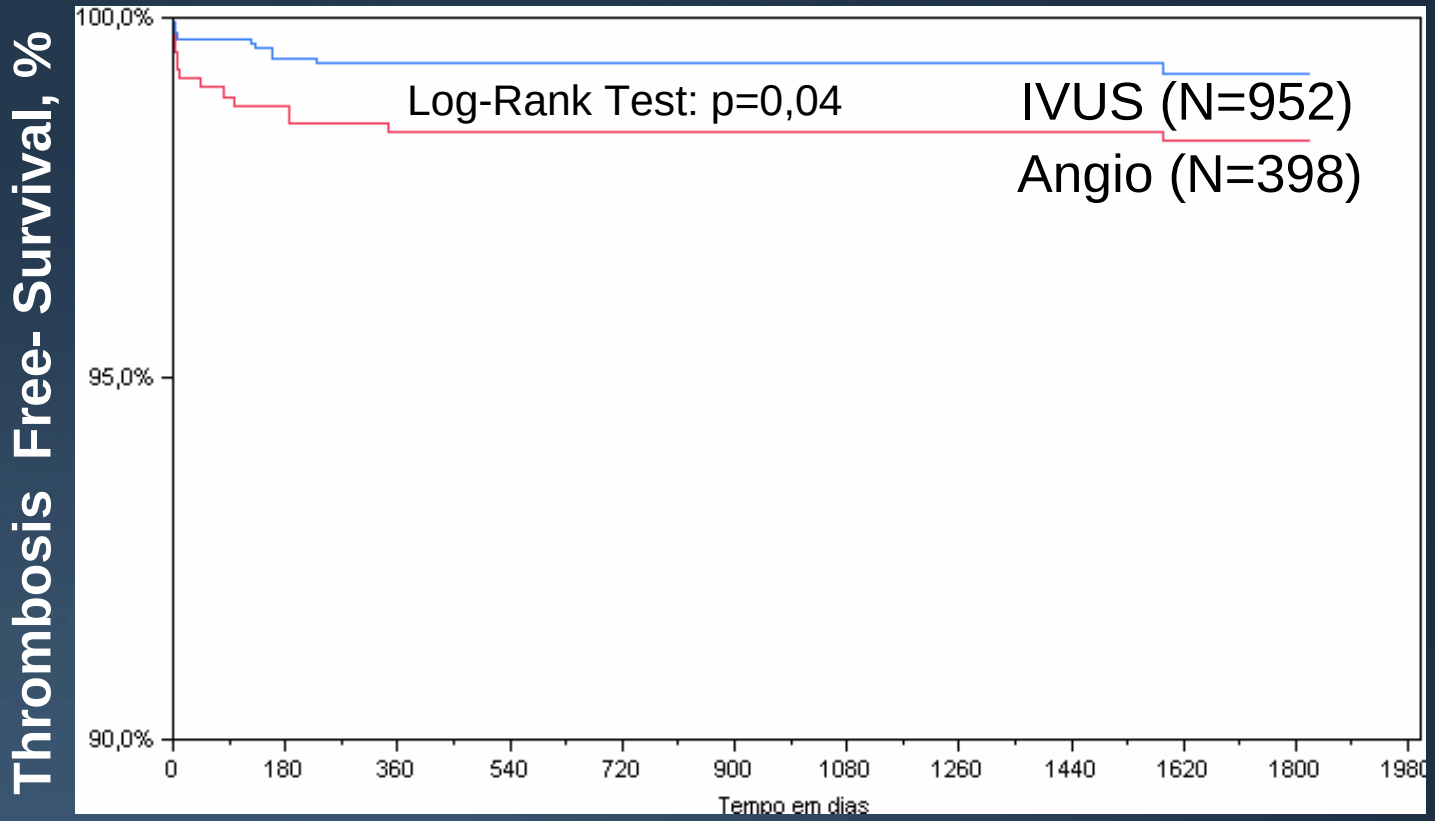
Thrombosis Free Survival



	Lower CL	Upper CL	P Value
MVD	-0,77	0,17	0,2
Bifurcation	0,95	0,02	0,06
Non IVUS Guidance	0,13	1,06	0,01

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(Costantini et al. TCT 2008)

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What about FFR-guidance?

- I searched Index Medicus for FFR+PCI, FFR+Stent, and FFR+DES and found only 2 published articles specifically discussing the use of FFR to guide optimal performance and optimizing the endpoint of an intervention.
- The rest deal primarily with deferred intervention.

Coronary pressure measurement after stenting predicts adverse events at follow-up: a multicenter registry

- In 750 patients, poststenting FFR was calculated and related to major adverse events at 6 months ($p<0.001$).
  - In 36% of the patients, FFR normalized (>0.95), and event rate was 4.9%
  - In 32% of the patients, poststent FFR was between 0.90 and 0.95, and event rate was 6.2%.
  - In 32% of patients, poststent FFR was <0.90, and event rate was 20.3%.
  - In 6% of the patients, FFR was <0.80, and event rate was 29.5%.

(Pijls et al. Circulation 2002;105:2950-4)

FFR compared with IVUS guidance for optimizing stent deployment.

- 84 stable patients with isolated coronary lesions underwent coronary stent deployment starting at 10atm and increased by 2atm until the FFR was ≥0.94 or 16atm was achieved.
  - Over a range of IVUS criteria, the highest sensitivity, specificity, and predictive accuracy of FFR were 80%, 30%, and 42%, respectively.
  - ROC analysis defined an optimal FFR cut point of ≥0.96; at this threshold, the sensitivity, specificity, and predictive accuracy of FFR were 75%, 58%, and 62%, respectively.
  - Therefore, FFR<0.96, measured after stent deployment, predicted a suboptimal result based on validated IVUS criteria (sensitivity of 75%); however, an FFR ≥0.96 did not reliably predict an optimal stent result (poor specificity).

(Fearon et al. Circulation 2001;104:1917-22)

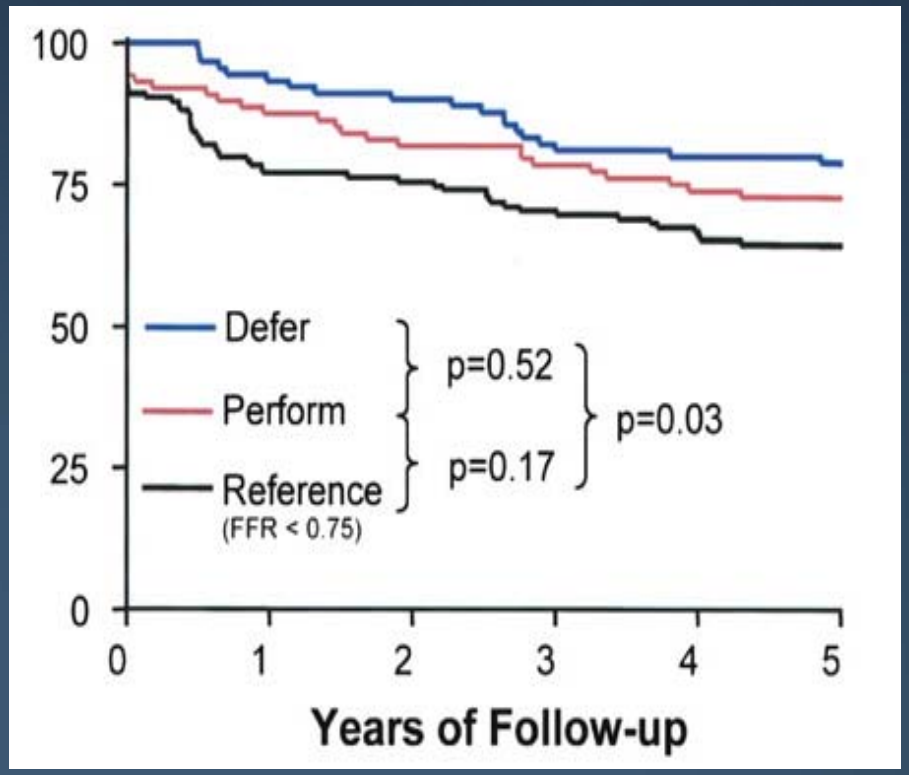
Thirty-month outcome after FFR-guided versus conventional multivessel percutaneous coronary intervention.

- FFR-PCI and conventional PCI were compared in 137 patients (312 vessels) with MVD
  - In the FFR-PCI group (n=57), FFR of all vessels was performed, and PCI of stenoses with a FFR <0.75 was performed in 48 pts (53 vessels).
  - 80 pts (184 vessels) in the conventional PCI group underwent PCI.
  - The average number of vessels per patient that underwent PCI and the cost of procedure were significantly greater in the conventional PCI group than in the FFR-PCI group.
  - The 30-month Kaplan-Meier event-free survival estimate was significantly higher in the FFR-PCI group than in the conventional PCI group (89% vs 59%, p <0.01).
  - Therefore, FFR-PCI significantly reduces the number of vessels undergoing PCI, the event rate, and the cost of the procedure.

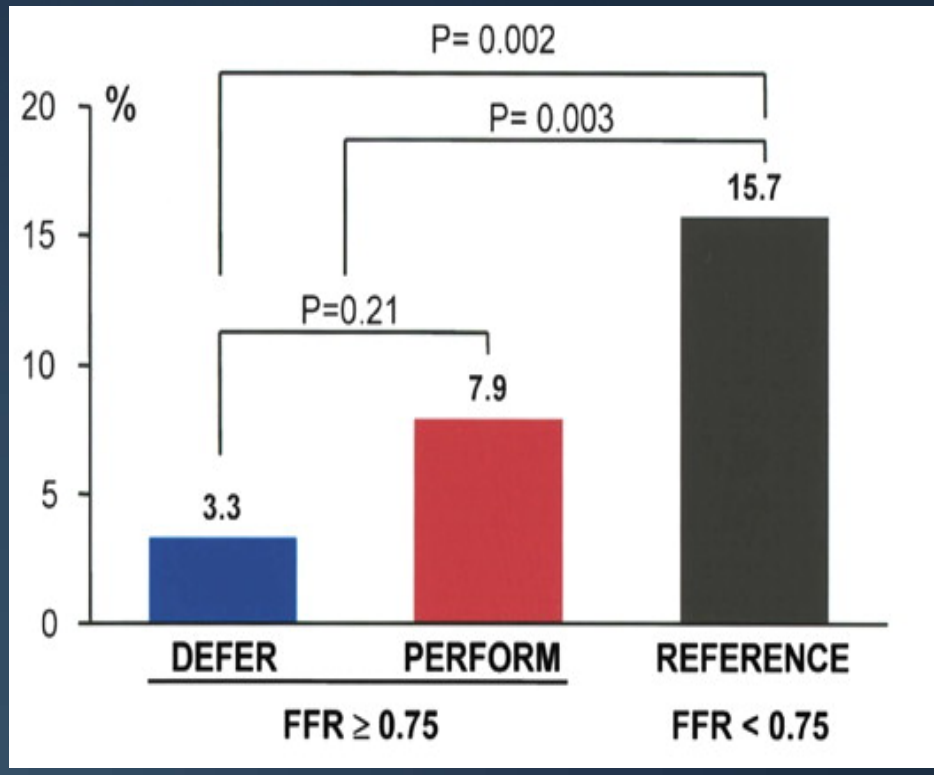
(Leesar et al. Am J Cardiol 2005;96:877-84)

DEFER 5 Year Results

Event Free Survival



Cardiac Death and MI



Pijls et al. J Am Coll Cardiol 2007;49:2105-11

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FAME: FRACTIONAL FLOW RESERVE *versus* ANGIOGRAPHY FOR GUIDING PCI IN PATIENTS WITH MULTIVESSEL CORONARY ARTERY DISEASE

Late Breaking Trial at
TCT, October 14 th , 2008

Nico H.J.Pijls, MD, PhD
Catharina Hospital, Eindhoven
The Netherlands,
on behalf of the ***FAME investigators***

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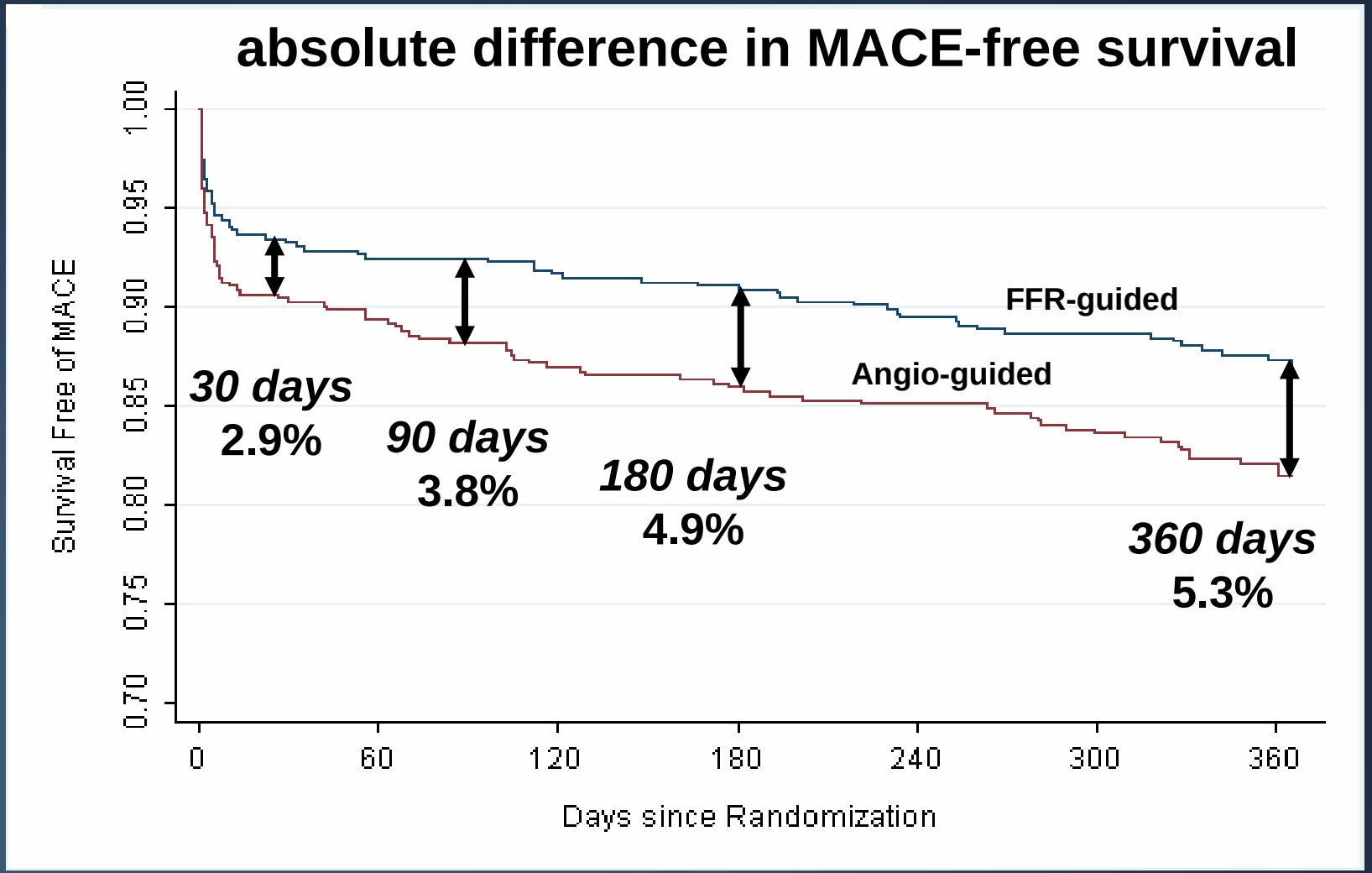
FAME study: Event-free Survival



FAME study: Adverse Events at 1 year

	ANGIO-group N=496	FFR-group N=509	P-value
Events at 1 year, No (%)			
Death, MI, CABG, or repeat-PCI	**91 (18.4)**	**67 (13.2)**	**0.02**
Death	**15 (3.0)**	**9 (1.8)**	0.19
Death or myocardial infarction	**55 (11.1)**	**37 (7.3)**	0.04
CABG or repeat PCI	**47 (9.5)**	**33 (6.5)**	0.08
Total # of MACE	**113**	**76**	0.02
Myocardial infarction			
All myocardial infarctions	**43 (8.7)**	**29 (5.7)**	0.07
Small periprocedural CK-MB 3-5xNL	**16**	**12**	
Other infarctions (“late or large”)	**27**	**17**	

FAME study: Procedural Results

	ANGIO-group N=496	FFR-group N=509	P-value
# indicated lesions per patient	**2.7 ± 0.9**	**2.8 ± 1.0**	0.34
FFR results			
Lesions succesfully measured, No (%)	**-**	**1329 (98%)**	**-**
Lesions with FFR ≤ 0.80, No (%)	**-**	**874 (63%)**	**-**
Lesions with FFR > 0.80, No (%)	**-**	**513 (37%)**	**-**
Stents per patient	**2.7 ± 1.2**	**1.9 ± 1.3**	<0.001
Lesions succesfully stented (%)	**92%**	**94%**	**-**
DES, total, No	**1359**	**980**	**-**

What does greyscale IVUS do well?

- Pre-intervention lesion assessment
  - Lesion severity
  - Vessel size and lesion length
  - Overall plaque burden
  - Unusual lesion morphology (i.e., plaque rupture, aneurysms)
  - Calcium
  - Overall plaque burden
- Guidance of PCI procedures
  - Stent size and length
- Post-intervention lesion assessment
  - Final lumen dimensions
  - Residual disease
  - Complications
  - Predicting restenosis and subacute stent thrombosis
- Follow-up
  - Mechanisms and causes of restenosis
  - Endpoints in restenosis trials

What does greyscale IVUS do poorly?

- Pre-intervention lesion assessment
  - 3-D orientation and spatial relationships
  - Plaque composition (except calcium)
  - Vulnerable plaque
  - High risk PCI lesions
  - Thrombus
- Post-intervention lesion assessment
  - Subtle dissections, stent malapposition, plaque prolapse, etc.
  - Thrombus
- Follow-up
  - Subtle malapposition
  - Small amounts of intimal hyperplasia
  - Predicting late events (especially very late stent thrombosis)

What does FFR do well?

- Pre-intervention lesion assessment
  - Lesion significance

In other words, avoiding unnecessary interventions. . .

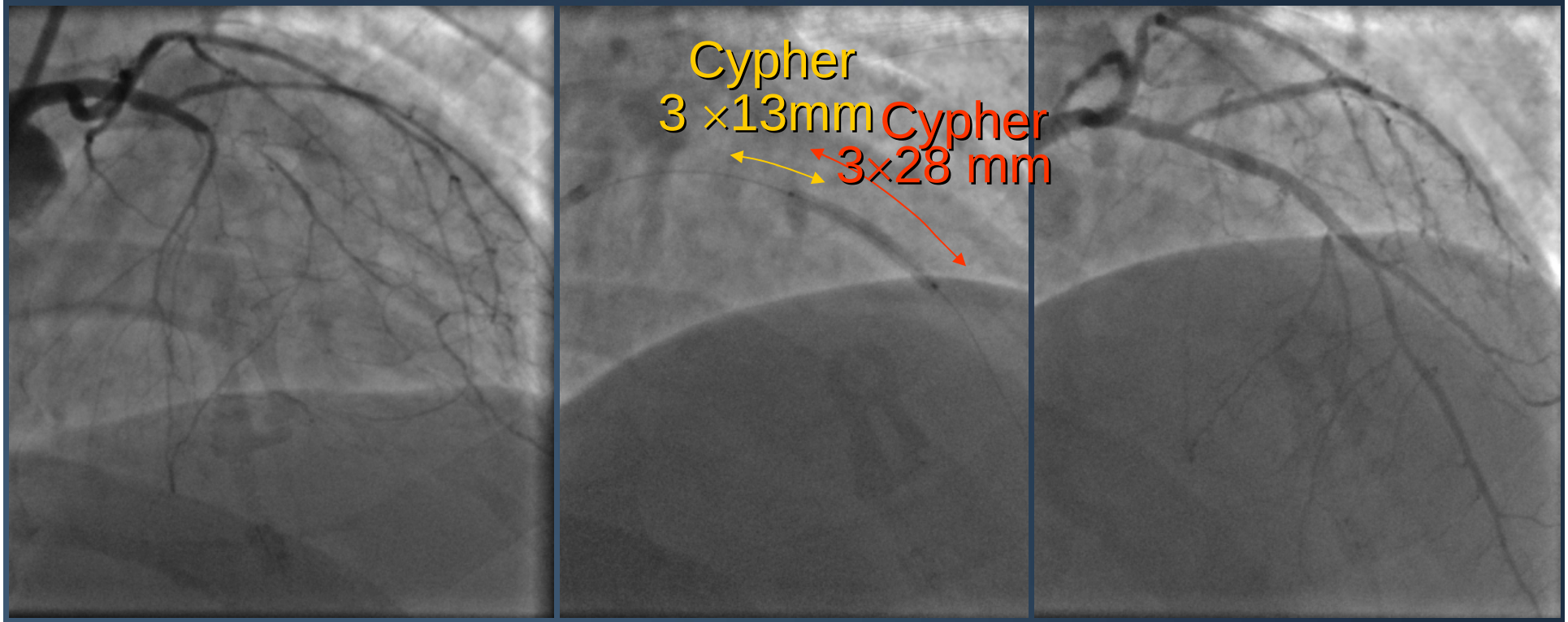
What does FFR IVUS do poorly?

Everything else!

38 year old male with

- Hypertension, hyperlipidemia, smoking, and obesity
- Previous inferior MI treated with primary PCI and BMS (obtuse marginal) with subsequent treatment of BMS restenosis
- Recurrent chest pain

PCI to LAD with 2 Cypher Stents



18 months later

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Stent Thrombosis

Stent Fracture