



Physiologic Lesion Assessment is Necessary in Multi-Vessel PCI

- *Insights from FAME* -

TCT Asia, April 22, 2009

No conflicts to declare

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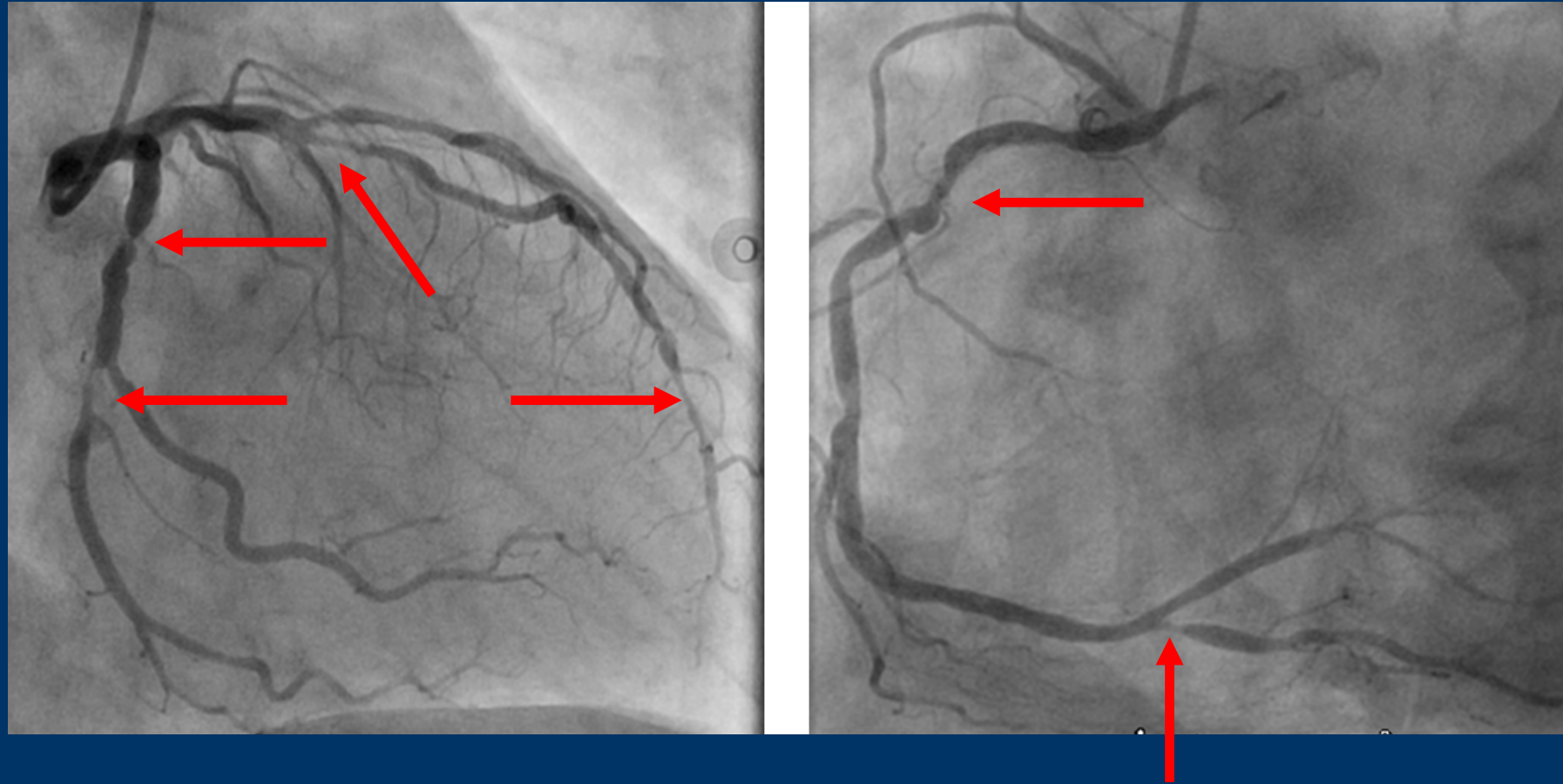
FAME



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

NEJM 2009; 360:215-224

Stent all *or* measure FFR first?



FAME study: BACKGROUND (1)



- Stenting of non-ischemic stenoses has no benefit compared to medical treatment only
- Stenting of ischemia-related stenoses improves symptoms and outcome
- In multivessel coronary disease (MVD), identifying which stenoses cause ischemia is difficult:

Non-invasive tests are often unreliable in MVD and coronary angiography often results in both under- or overestimation of functional stenosis severity

FAME study: BACKGROUND (2)



- Fractional Flow Reserve (FFR), is the most accurate and selective index to indicate whether a particular stenosis is responsible for inducible ischemia
- FFR can be easily determined in the cath lab just prior to stenting

FAME study: HYPOTHESIS



**FFR – guided PCI
in multivessel disease
is superior to
current angiography – guided PCI**

FAME study: DESIGN



Randomized multicenter study in 1005 patients undergoing DES-stenting for multivessel disease in 20 US and European centers

- independent core-lab
- independent data analysis
- blinded adverse event committee

Multivessel disease:

Stenoses of > 50% in at least 2 of the 3 major coronary arteries

FAME study: Study Population



The FAME study was designed to *reflect daily practice* in performing PCI in patients *with multivessel disease*

Inclusion criteria:

- **ALL** patients with multivessel disease
- At least 2 stenoses $\geq 50\%$ in 2 or 3 major epicardial coronary arteries, amenable for stenting

Exclusion criteria:

- Left main disease or previous bypass surgery
- Acute STEMI
- Extremely tortuous or calcified coronary arteries

Note: patients with previous PCI were *not* excluded

FLOW CHART



**Patient with stenoses $\geq 50\%$
in at least 2 of the 3 major
epicardial vessels**

**Indicate all stenoses $\geq 50\%$
considered for stenting**

Randomization

Angiography-guided PCI

FFR-guided PCI

**Stent all indicated
stenoses**

**Measure FFR in all
indicated stenoses**

**Stent only those
stenoses with $FFR \leq 0.80$**

1-year follow-up

FAME study: PRIMARY ENDPOINT



***Composite of death, myocardial infarction,
or repeat revascularization (“MACE”)
at 1 year***

FAME study: SECONDARY ENDPOINTS



- Individual components of MACE at 1 year
- Functional class
- Use of anti-anginal drugs
- Health-related quality of life (EuroQOL-5D)

- Procedure time
- Amount of contrast agent used during procedure
- Cost of the procedure

FAME study: TREATMENT



- PCI according to local routine
- Only drug-eluting stents (DES)
- FFR measured by Pressure Wire
(*Certus wire, RADI Medical Systems*)
- Hyperemia induced by i.v. adenosine 140 µg/kg/min
in femoral vein
- EKG, CK, CK-MB, etc during hospital stay
- Follow-up at 1 month, 6 months, 1 year
- Plavix (clopidogrel) in all patients for 1 year

FAME study: Baseline Characteristics (1)



	ANGIO-group N=496	FFR-group N=509	P- value
Age, mean±SD	64±10	65±10	0.47
Male, %	73	75	0.30
Diabetes, %	25	24	0.65
Hypertension, %	66	61	0.10
Current smoker, %	32	27	0.12
Hyperlipidemia, %	74	72	0.62
Previous MI, %	36	37	0.84
Unstable angina, %	36	29	0.11
Previous PCI, %	26	29	0.34
LVEF, mean±SD	57±12	57±11	0.92
LVEF < 50%, %	27	29	0.47

FAME study: **Baseline Characteristics (1)**



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FAME study: **Baseline Characteristics (2)**



	ANGIO-group N=496	FFR-group N=509	P- value
<i>Indicated lesions/patient (n=)</i>	2.7±0.9	2.8±1.0	0.34

FAME study: **Baseline Characteristics (2)**



	ANGIO-group N=496	FFR-group N=509	P-value
<i>Indicated lesions/patient (n=)</i>	2.7±0.9	2.8±1.0	0.34
50-70% narrowing, No (%)	550 (41)	624 (44)	-
70-90% narrowing, No (%)	553 (41)	530 (37)	-
90-99% narrowing, No (%)	207 (15)	202(14)	-
Total occlusion, No (%)	40 (3)	58 (4)	-
Pts. with ≥1 total occlusion (%)	7.5	10.6	0.08
Prox. LAD involved, No (%)	186 (38)	210 (41)	0.39
Lesions in prox.or mid segment, No (%)	960 (71)	1032 (73)	0.42

FAME study: Procedural results (1)



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

FAME study: Procedural results (2)



	ANGIO-group N=496	FFR-group N=509	P- value
Procedure time (min)	70 ± 44	71 ± 43	0.51
Contrast agent used (ml)	302 ± 127	272 ± 133	<0.001
Procedural materials (US \$)	6007	5332	<0.001
Length of hospital stay (days)	3.7 ± 3.5	3.4 ± 3.3	0.05

FAME study: Adverse events at 1 year



	ANGIO-group N=496	FFR-group N=509	P- value
<i>Events at 1 year, No (%)</i>			
Death, MI, CABG, repeat-PCI	91 (18.3)	67 (13.2)	0.02

FAME study: Adverse events at 1 year



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Death	15 (3.0)	9 (1.8)	0.19

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Death or myocardial infarction	55 (11.1)	37 (7.3)	0.04

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CABG or repeat PCI	47 (9.5)	33 (6.5)	0.08

FAME study: Adverse events at 1 year



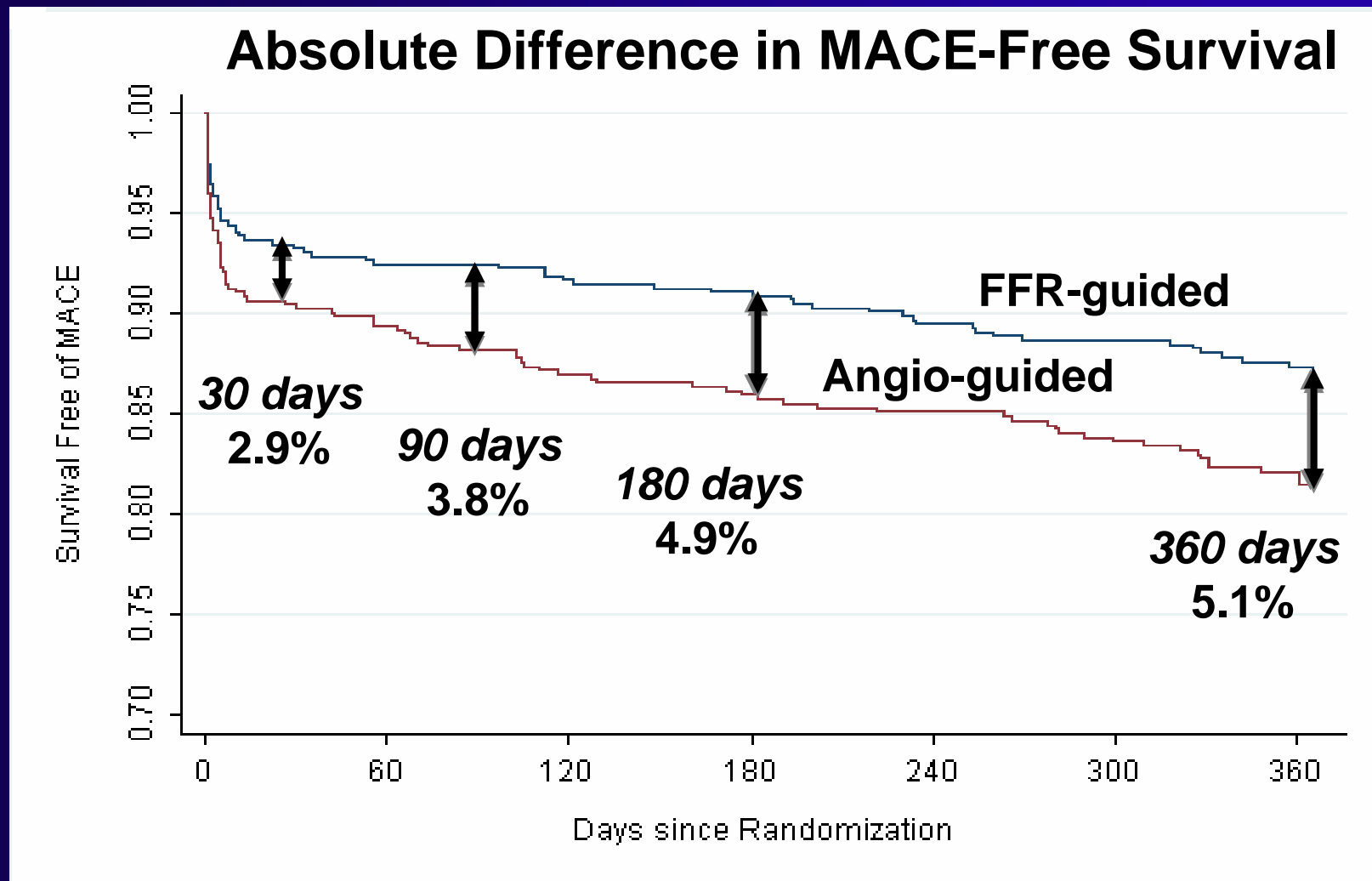
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Death or myocardial infarction	55 (11.1)	37 (7.3)	0.04
CABG or repeat PCI	47 (9.5)	33 (6.5)	0.08
Total no. of MACE	113	76	0.02

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, repeat-PCI	91 (18.3)	67 (13.2)	0.02
MI, specified			
All myocardial infarctions	43 (8.7)	29 (5.7)	0.07
Small periprocedural (CKMB 3-5 x ULN)	16 (3.2)	12 (2.4)	
Other infarctions (late, large)	27 (5.5)	17 (3.3)	

FAME study: *Event-free Survival*

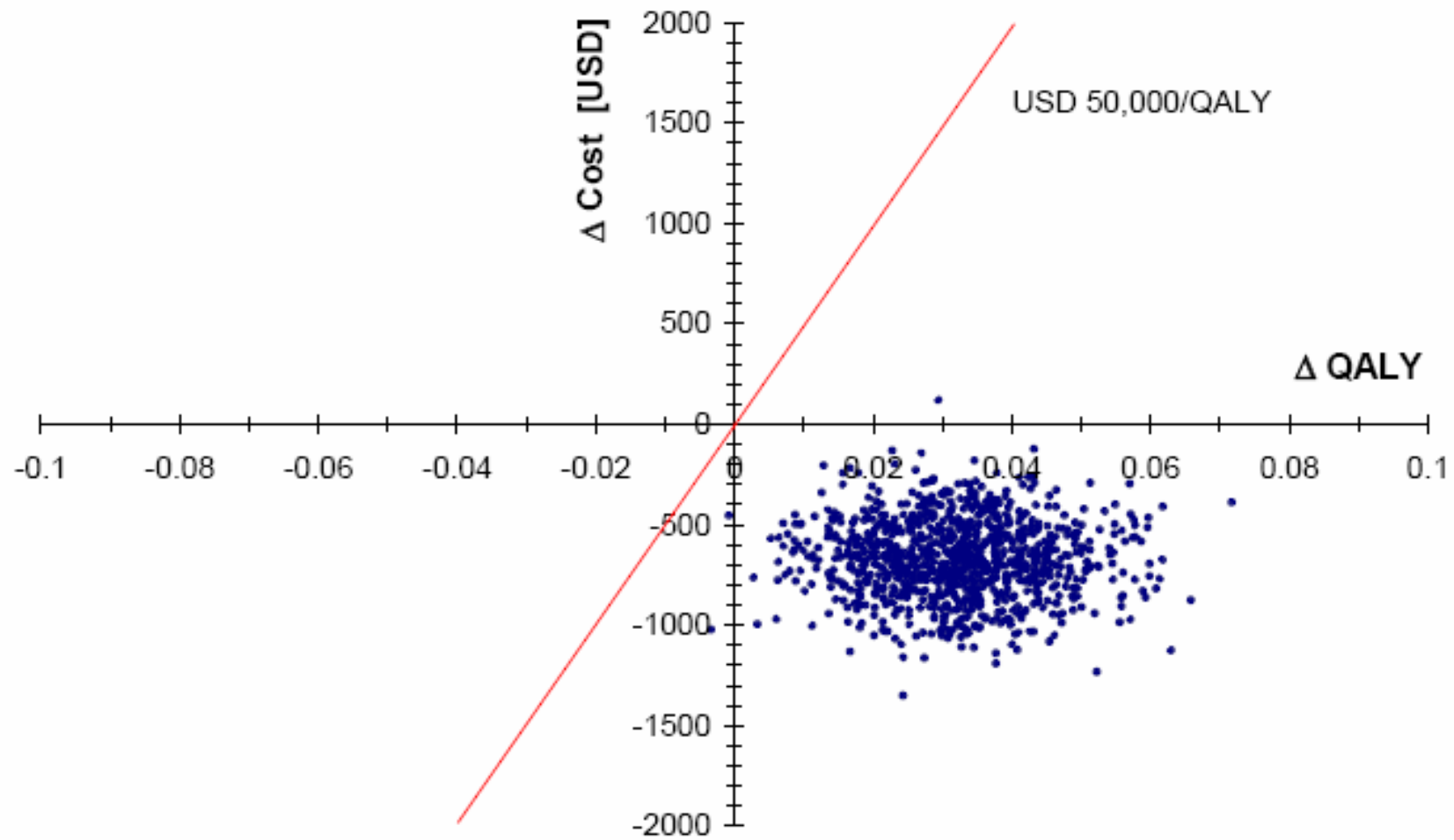


FAME study: Functional class at 1 year



	ANGIO-group N=496	FFR-group N=509	P- value
Patients without event and free from angina	326 (68)	360 (73)	0.07
Pts. free from angina, No. (%)	374 (78)	399 (81)	0.20
Anti-anginal meds, No.	1.2 ± 0.7	1.2 ± 0.8	0.48
EQ-5D visual analogue scale	74 ± 16	75 ± 16	0.65

Cost-Effectiveness Plane FFR vs. Angio



What about prognosis of deferred lesions?



1329 lesions measured by FFR

What about prognosis of deferred lesions?



1329 lesions measured by FFR



513 (37%) lesions $FFR > 0.80$



874 (63%) lesions $FFR \leq 0.80$

What about prognosis of deferred lesions?



1329 lesions measured by FFR



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7 out of 513 (1.4%) were stented

What about prognosis of deferred lesions?



1329 lesions measured by FFR



513 (37%) lesions FFR > 0.80



7 out of 513 (1.4%) were stented

6 had FFR \leq 0.80

1 protocol violation (FFR 0.86)

What about prognosis of deferred lesions?



1329 lesions measured by FFR



513 (37%) lesions FFR > 0.80



7 out of 513 (1.4%) were stented

0 out of 513 were related to AMI: 0%

- A very low event rate for deferred lesions in the FFR-guided arm at 1 year
- Deferring PCI of lesions with FFR > 0.80 in MVD patients is safe

FAME study: CRITICS IN EDITORIAL BY ELLIS



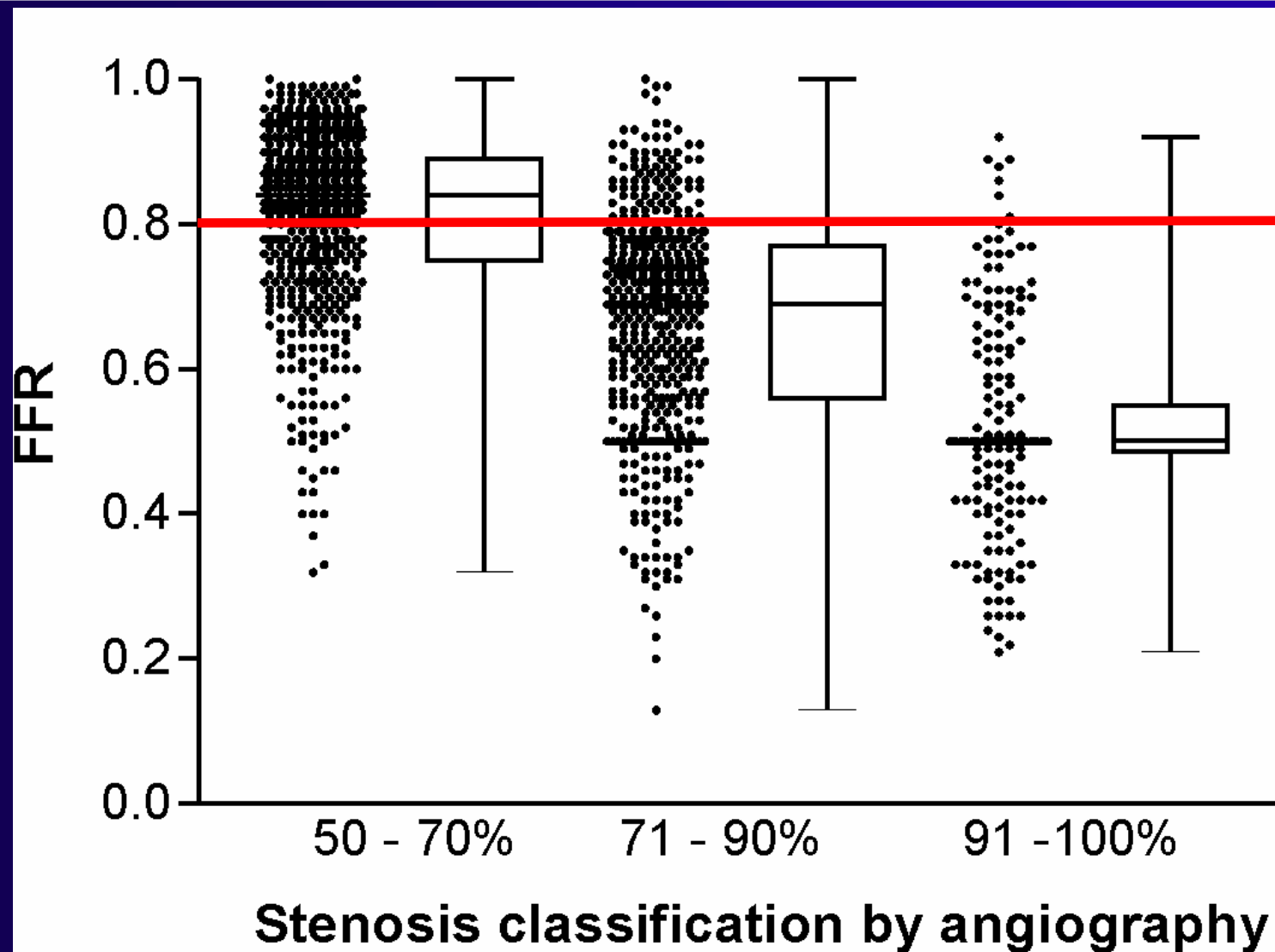
- use of thienopyridines? → ***ALL patients 1 year***
- high percentage of small peri-procedural infarctions?
→ ***Not at All : 3.2 % and 2.4 % respectively***
- favourable clinical characteristics ?
→ ***Not correct: FAME included previous MI, ACS, poor LV, previous PCI (30% each!), 30% diabetes, 40% prox LAD, 10% CTO***
- FFR measurement in 50-70 % lesions would be sufficient?



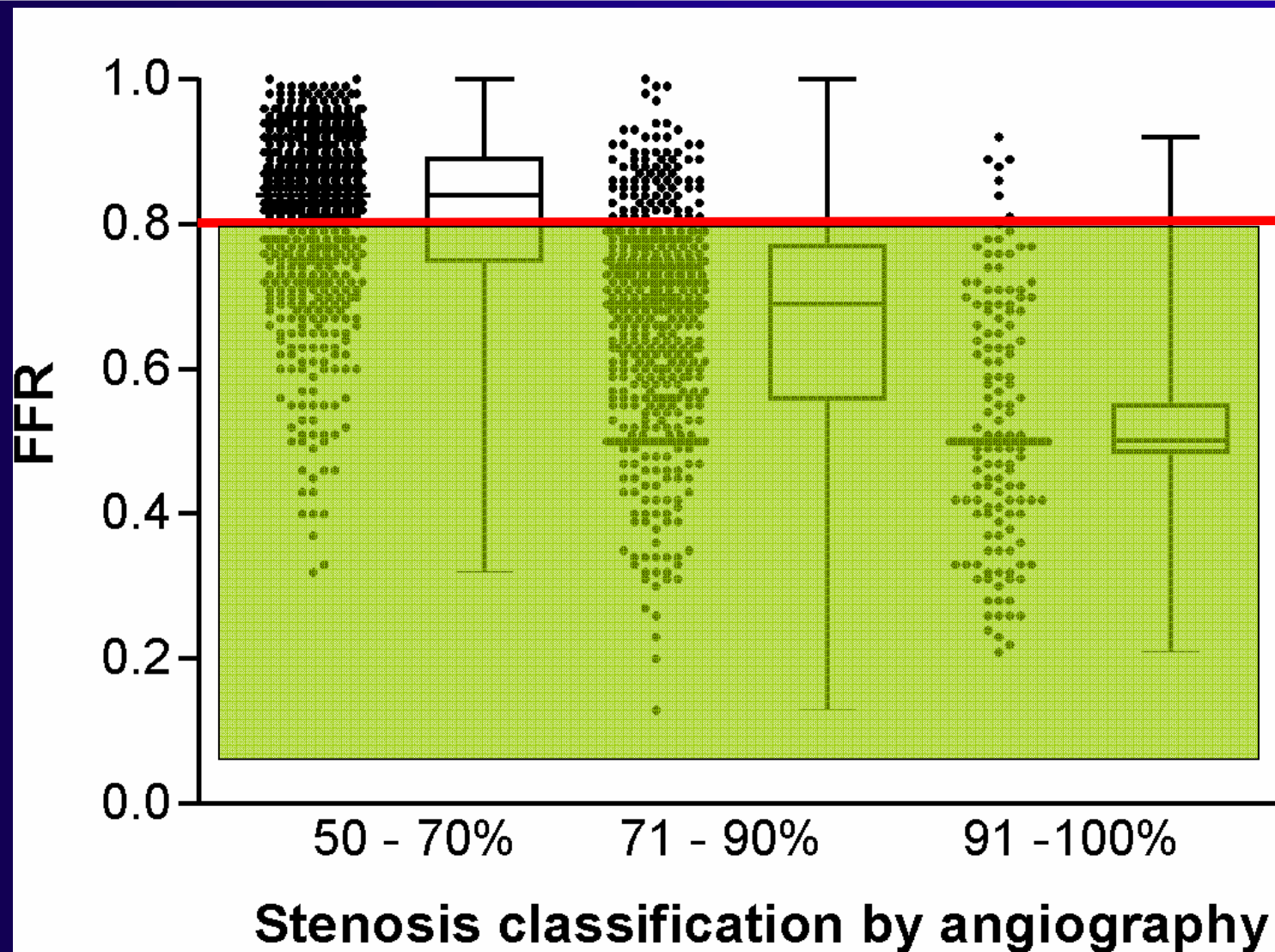
“I do not stent lesions of 50-70%”

1329 lesions in FFR-arm

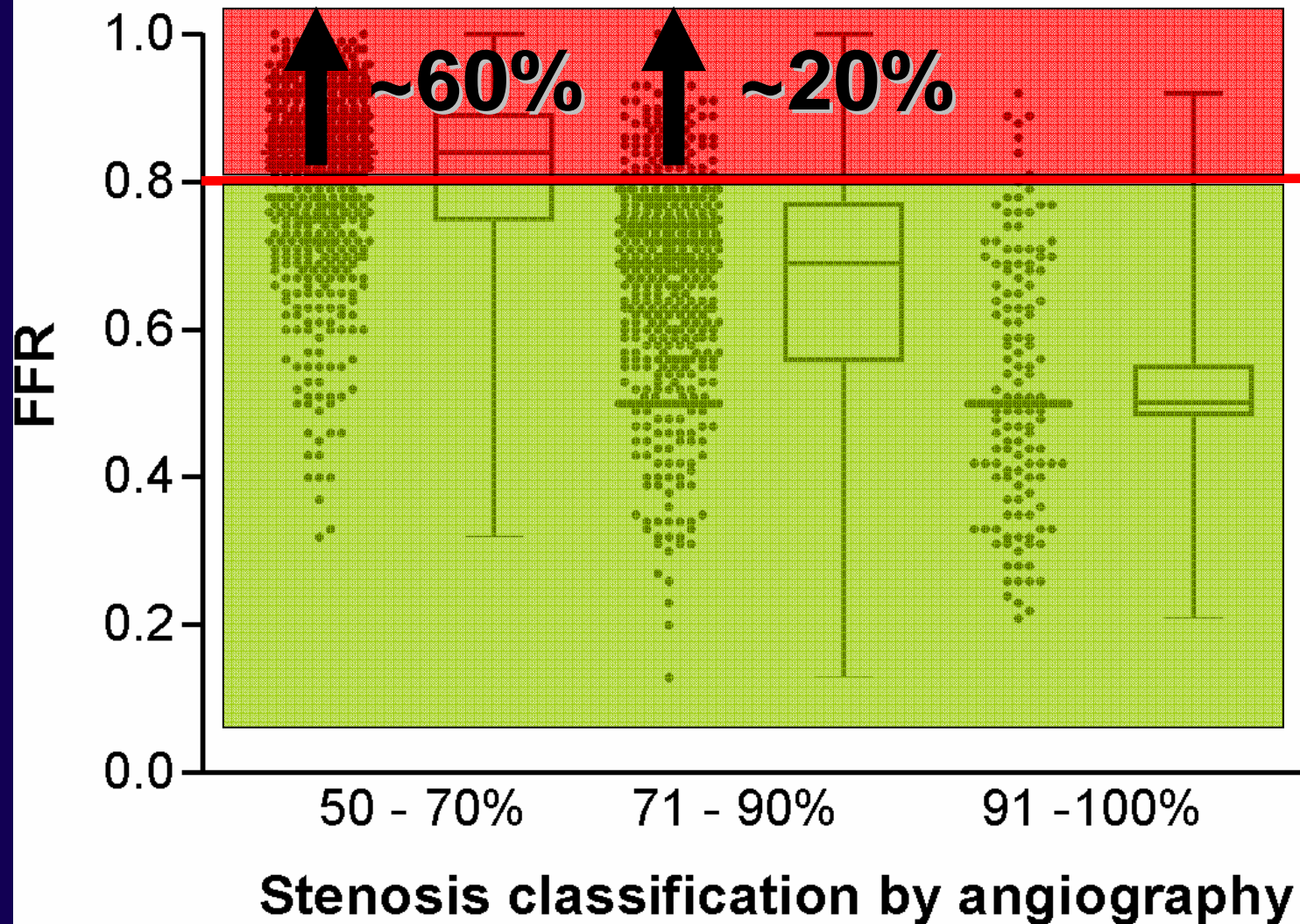
Ischemic threshold 0.80



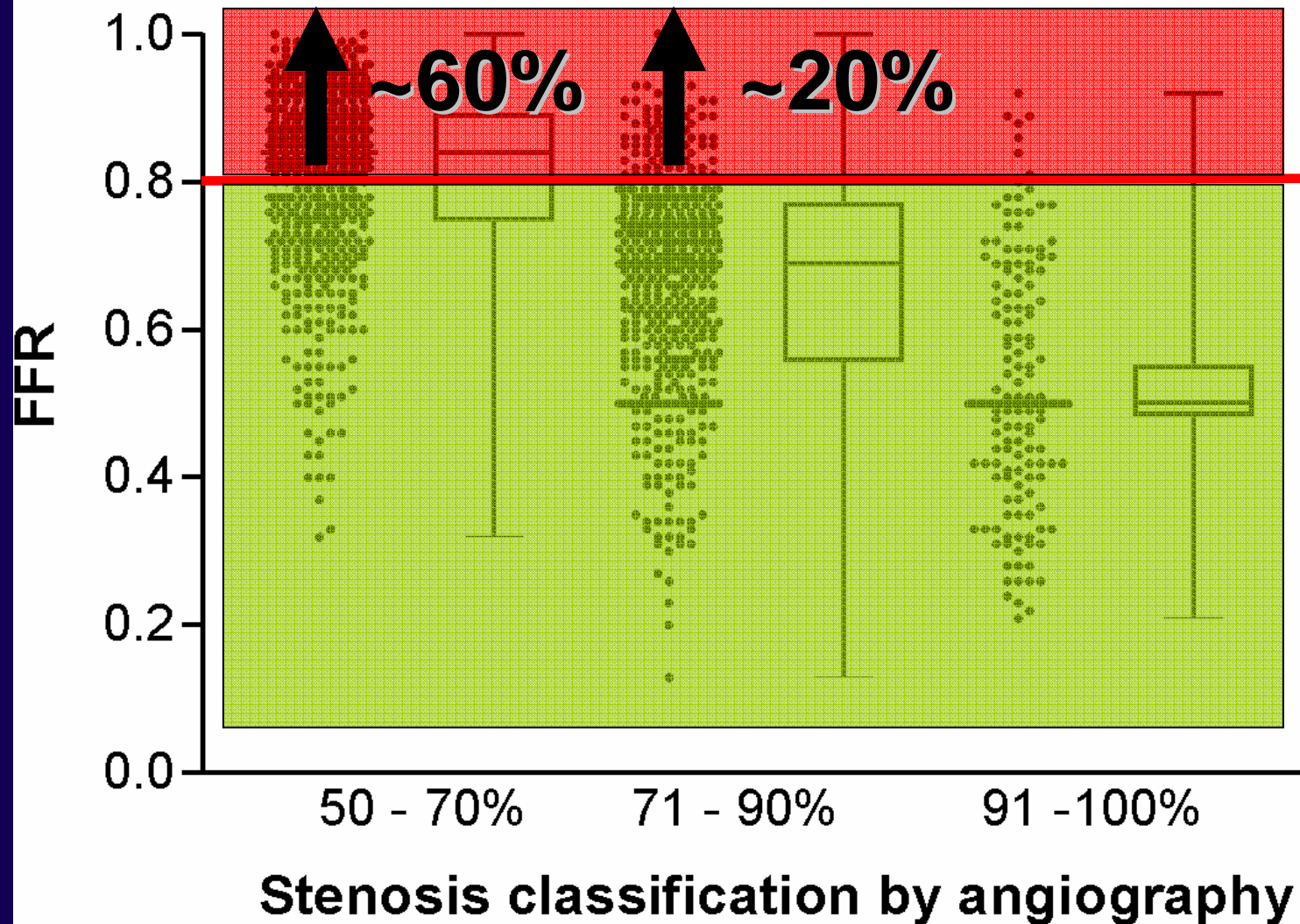
Lesions significant by angio and by FFR



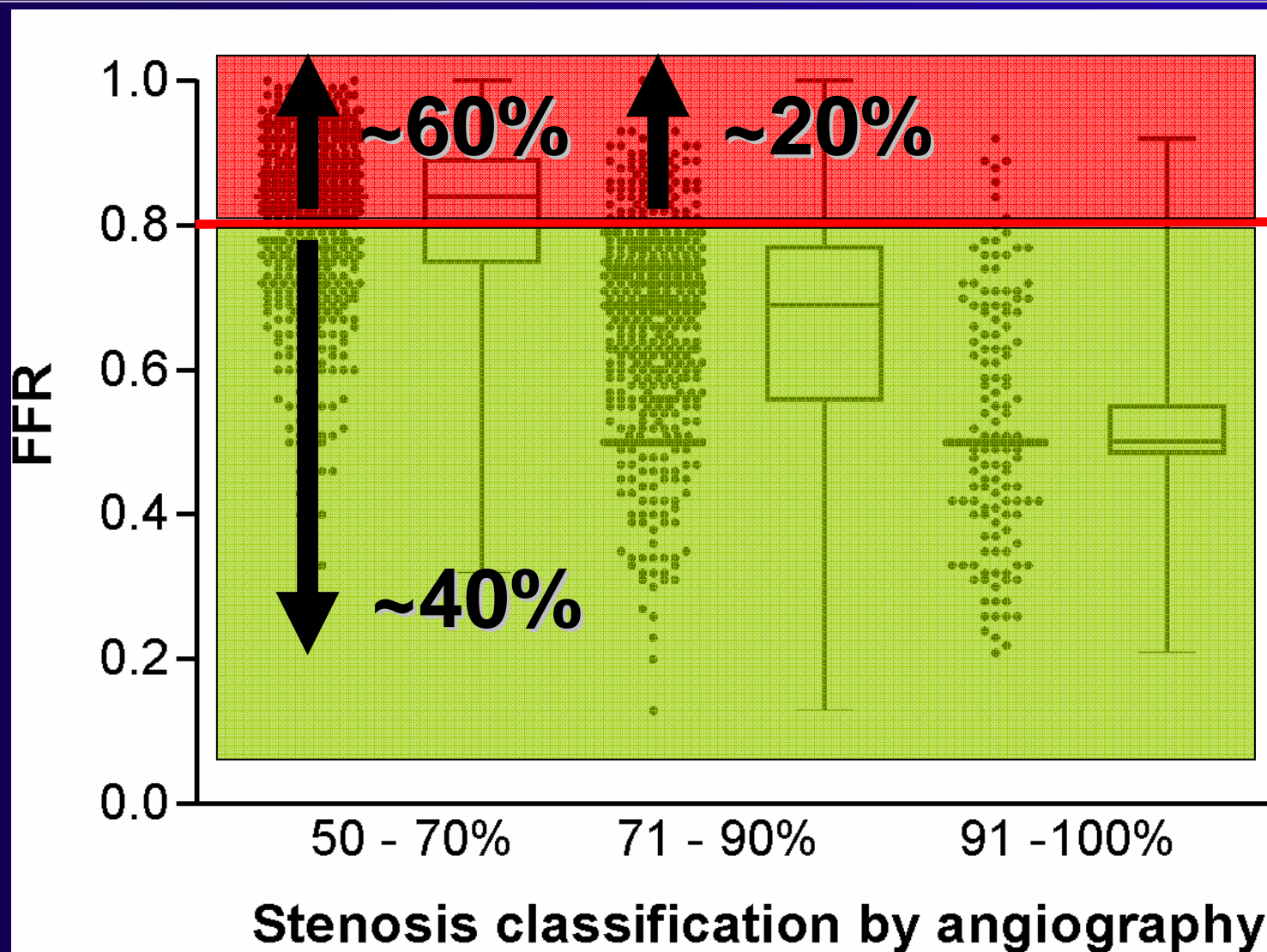
Lesions non-significant by FFR



Should we than take 70% as cut-off?



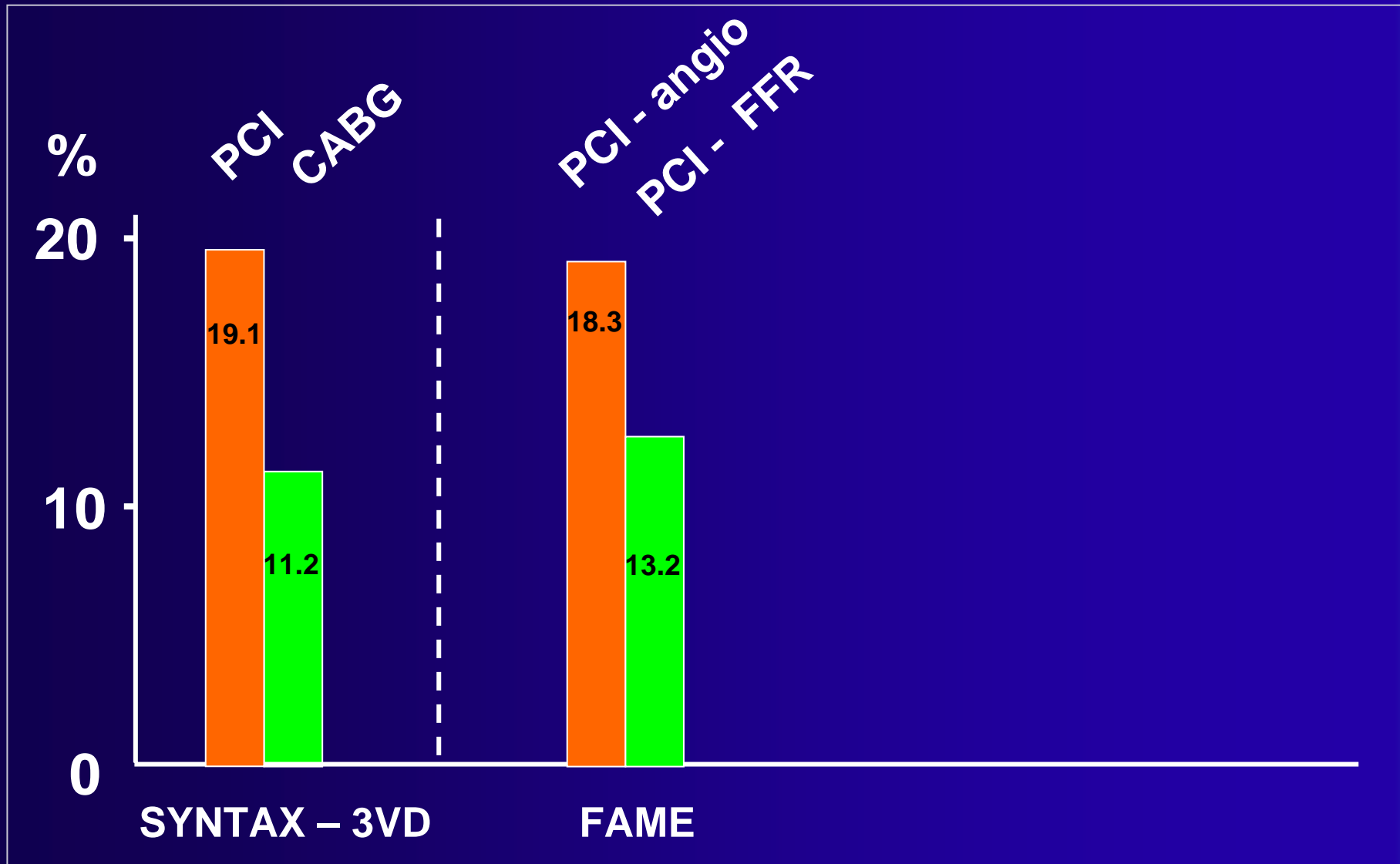
40% of 50-70% category is functionally significant !!





How does FAME fit with other recently performed RCT's to (DES) stenting in Multivessel Disease?

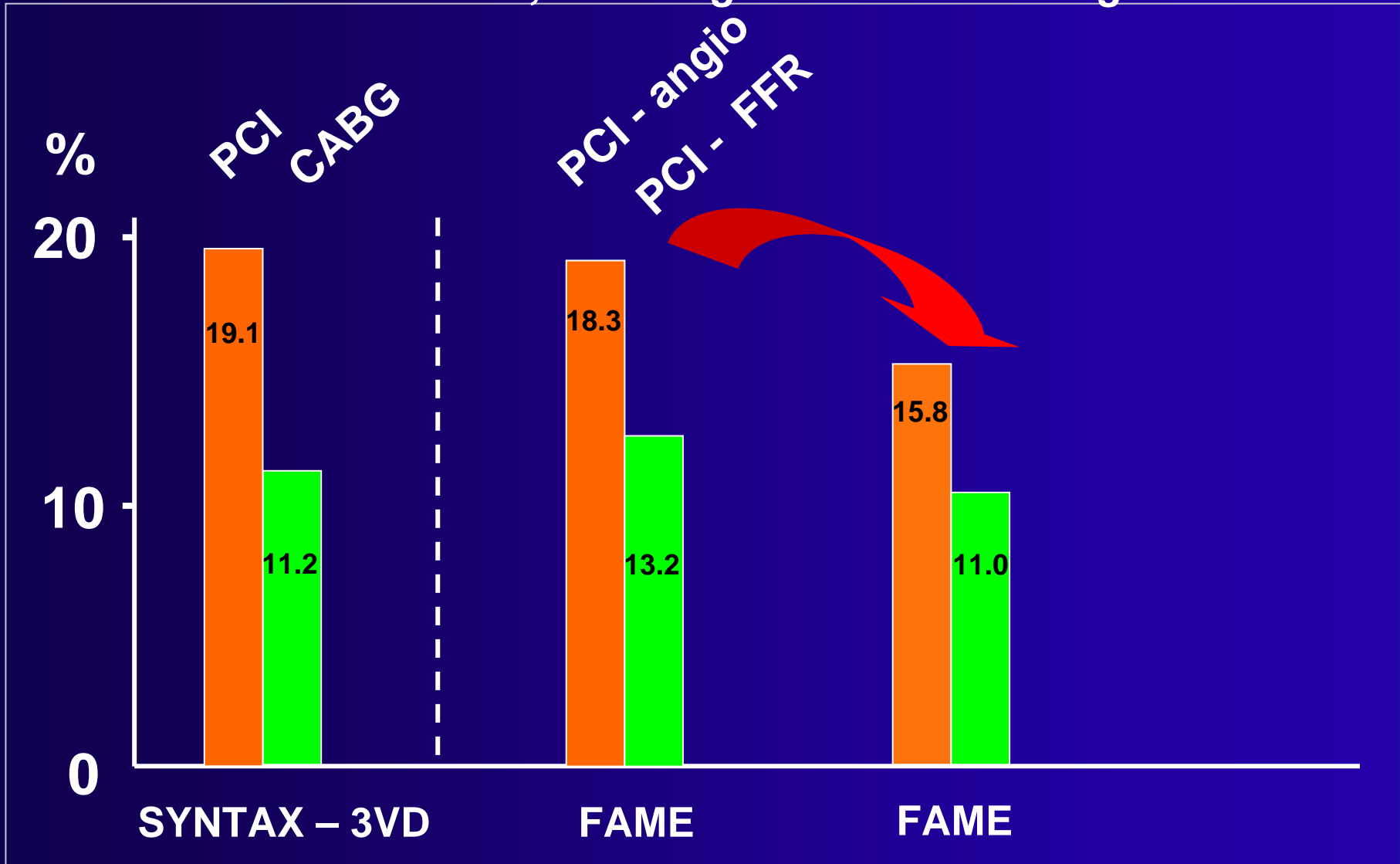
MACE in SYNTAX – 3VD and FAME



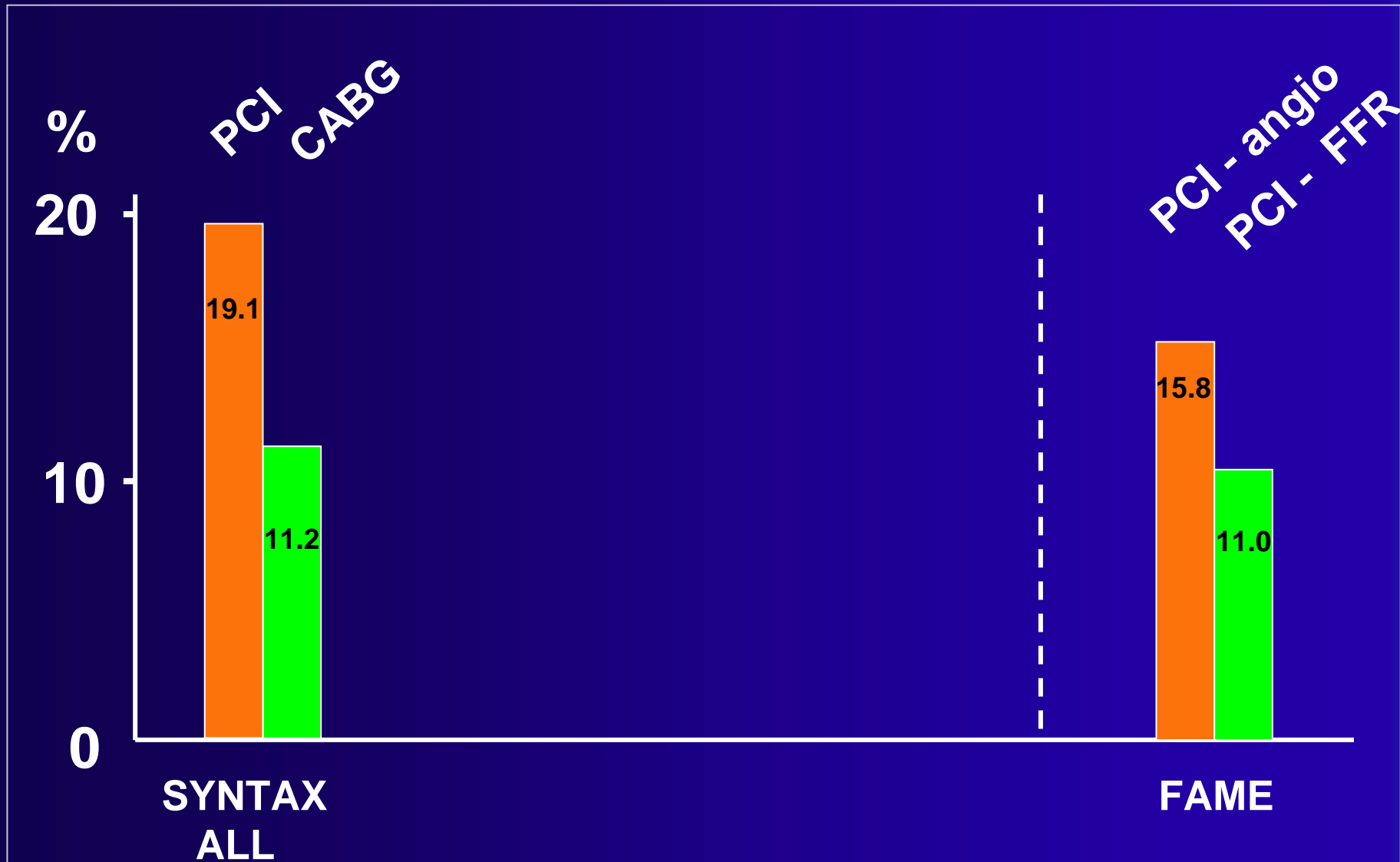
MACE in SYNTAX – 3VD and FAME



similar definition of MACCE, including CVA and excluding CKMB 3-5 x N



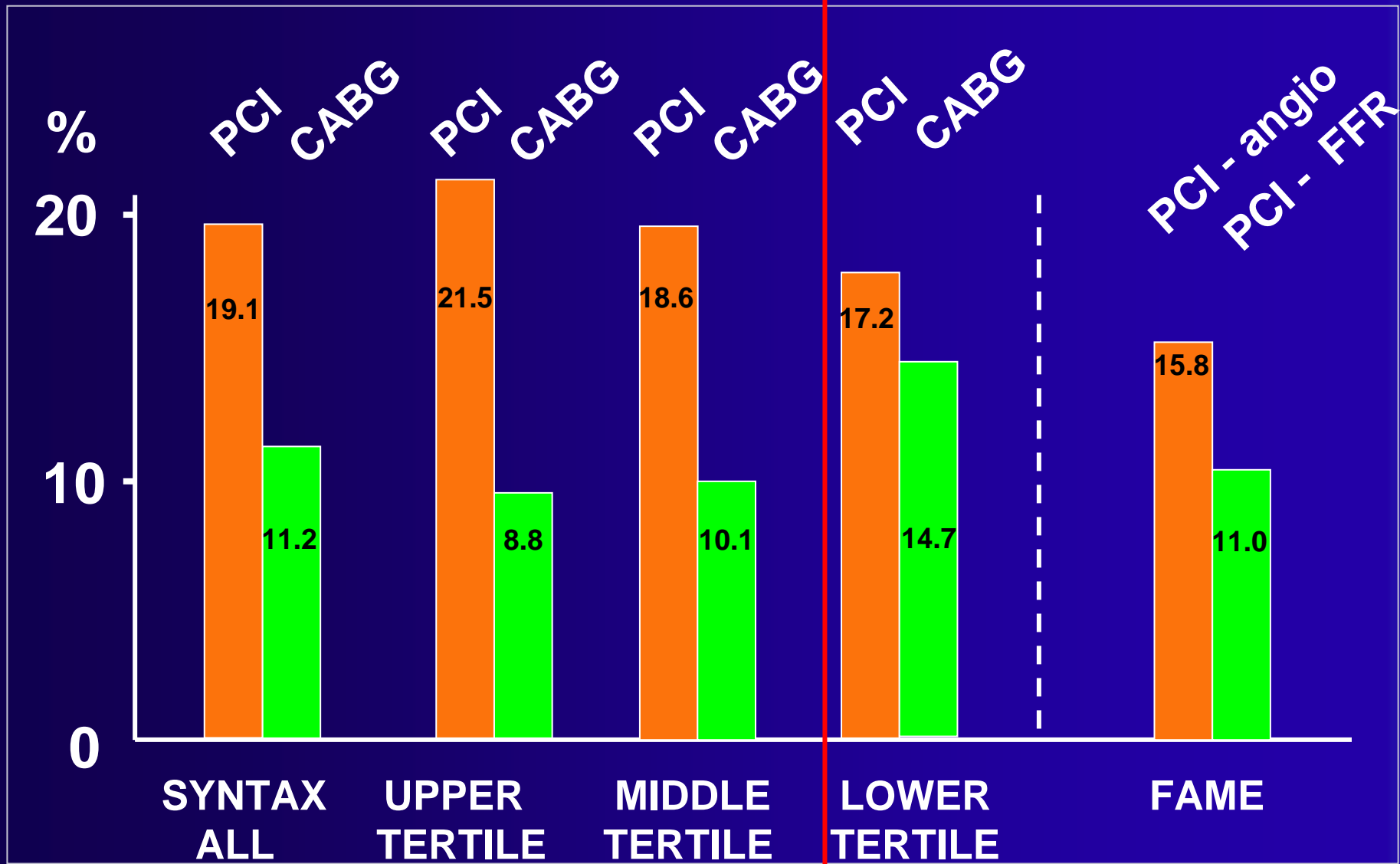
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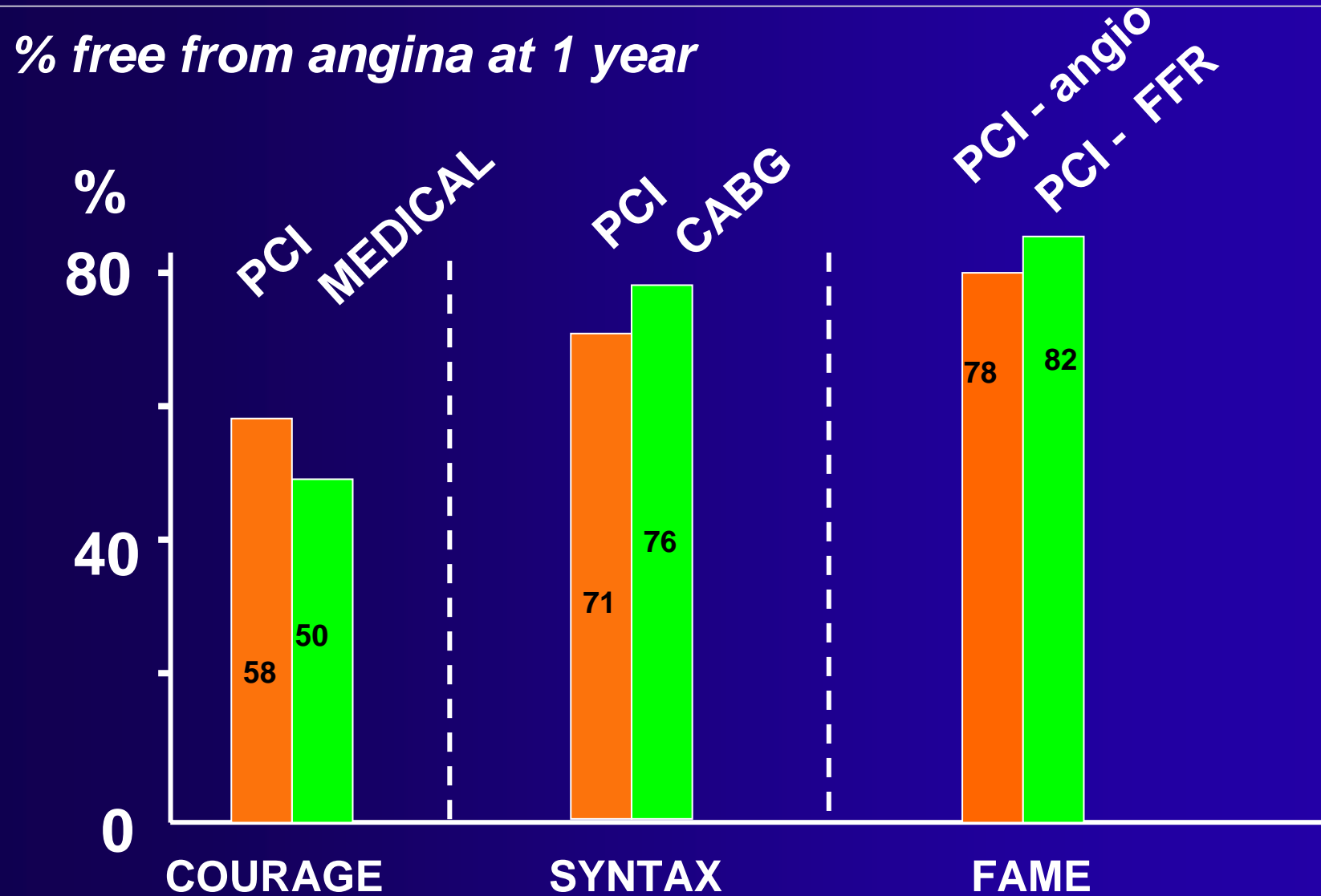
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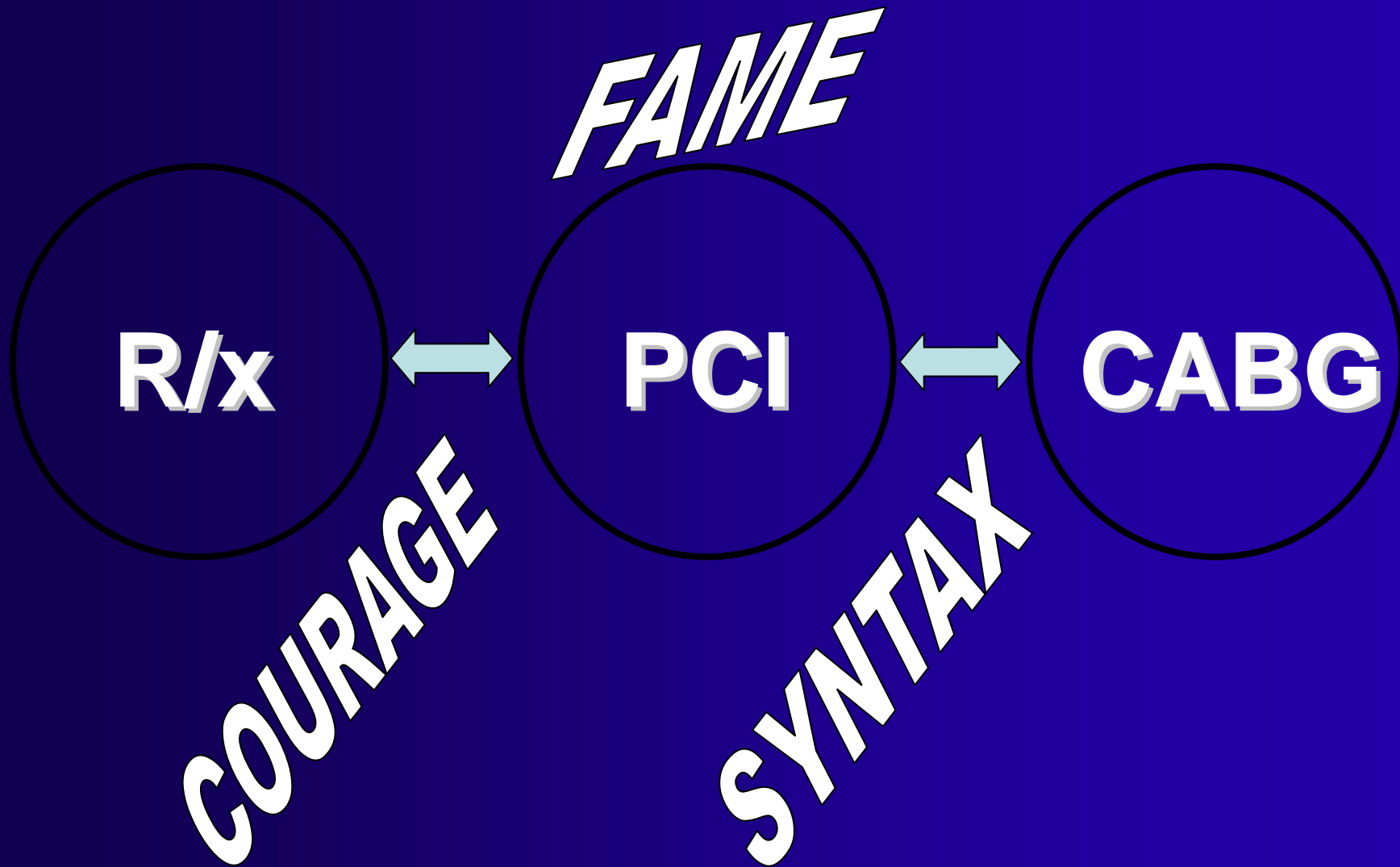
Stratified per SYNTAX score tertile



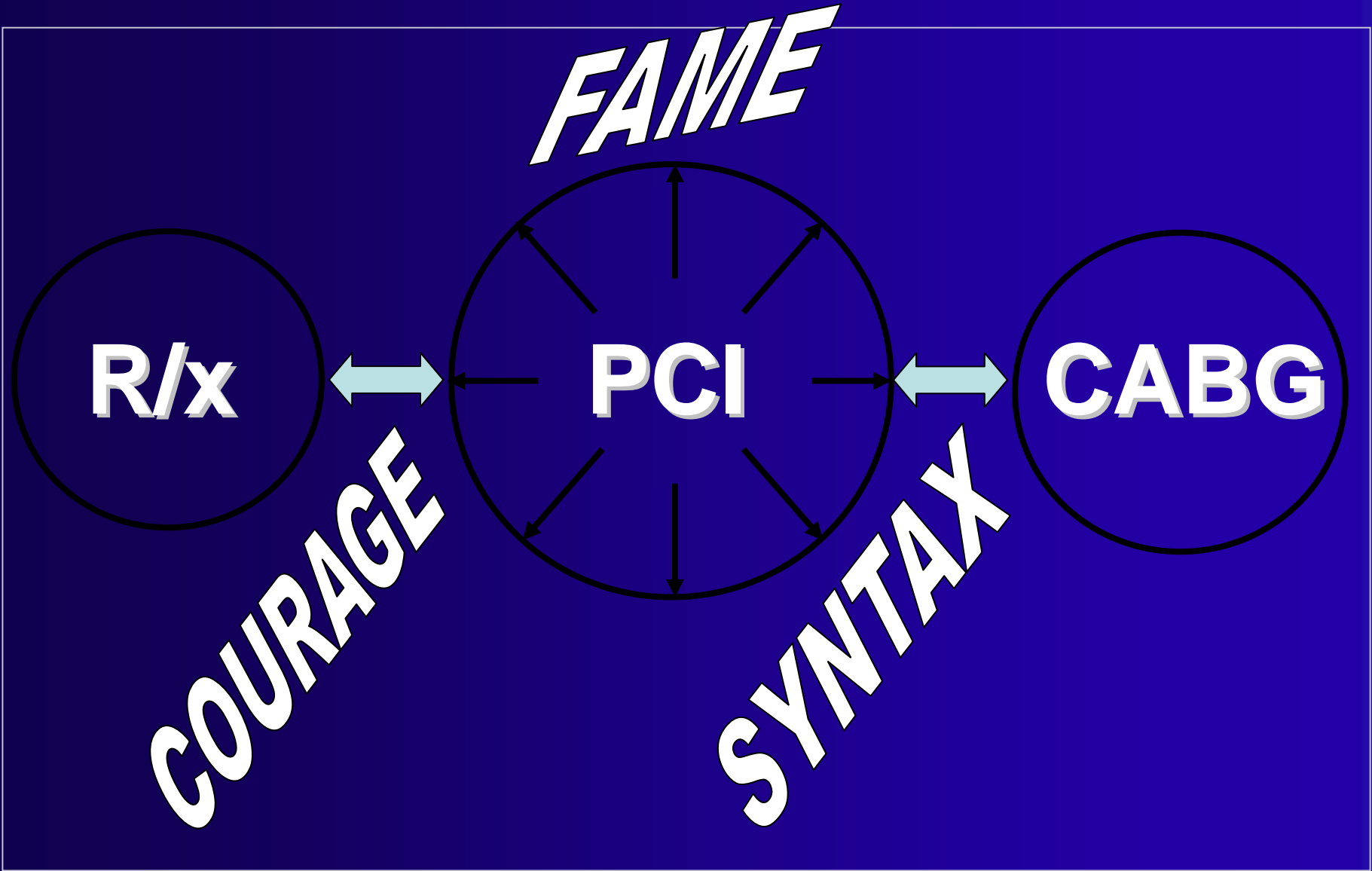
FUNCTIONAL CLASS in COURAGE, SYNTAX – 3VD and FAME



TREATMENT OPTIONS FOR MVD



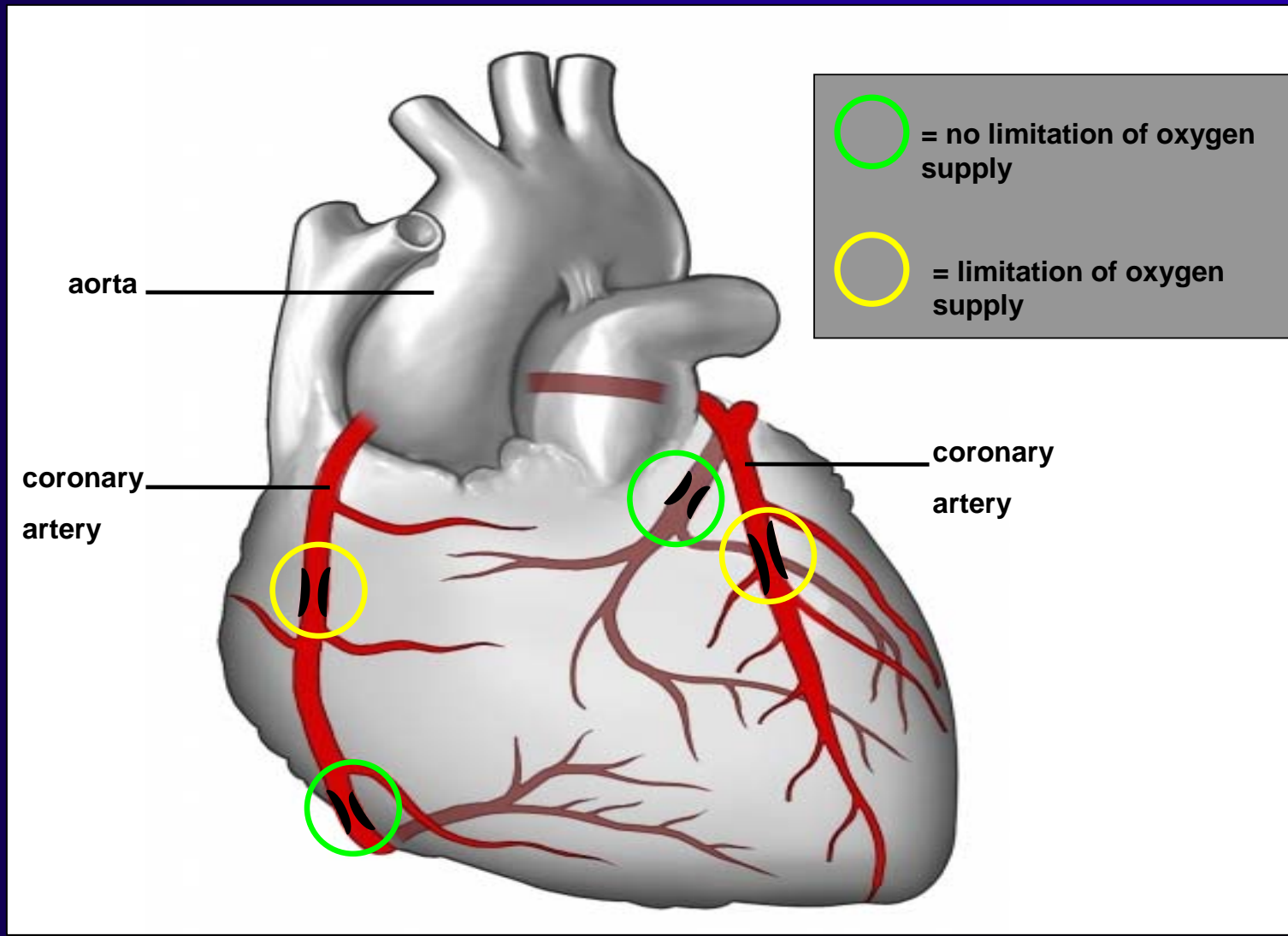
TREATMENT OPTIONS FOR MVD

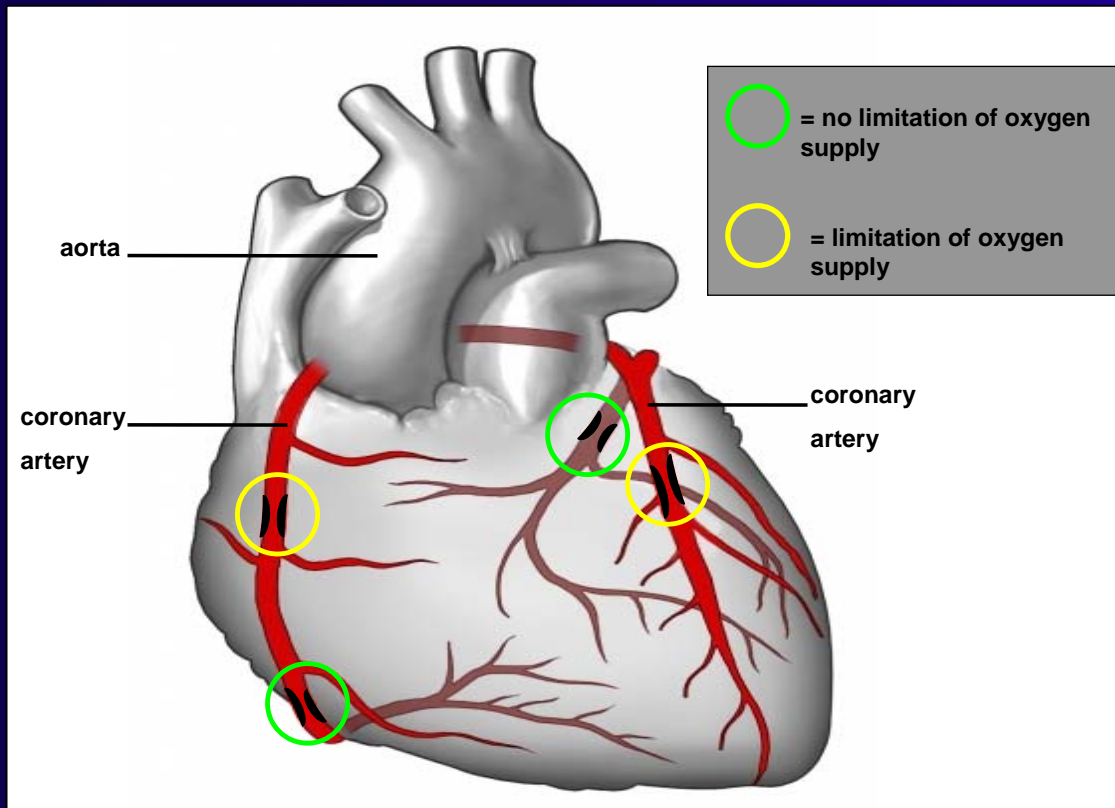




Why is outcome of FFR guided procedures so good?

Intrinsic risk of death and myocardial infarction?





Ischemic lesion → *intrinsic risk 5 % per year*
Non-ischemic lesion → *intrinsic risk 1 % per year*
Stented stenosis → *intrinsic risk 3 % per year*

“stent ‘m all” → **intrinsic risk 12% → 12%**
“stent only the ischemic ones” → **intrinsic risk 12 → 8 %**
both strategies eliminate ischemia → **similar functional class**

FAME study: CONCLUSIONS (1)



Routine measurement of FFR during PCI with DES in patients with multivessel disease, when compared to current angiography guided strategy

- Reduces the rate of the composite endpoint of death, myocardial infarction, re-PCI and CABG at 1 year by ~ 30%***
- Reduces mortality and myocardial infarction at 1 year by ~ 35 %***

FAME study: CONCLUSIONS (2)



Routine measurement of FFR during PCI with DES in patients with multivessel disease, when compared to current angiography guided strategy

- ***Is cost-saving and does not prolong the procedure***
- ***Reduces the number of stents used***
- ***Decreases the amount of contrast agent used***
- ***Results in a similar, if not better, functional status***

FAME study: CONCLUSIONS (3)



Routine measurement of FFR during DES-stenting in patients with multivessel disease is superior to current angiography guided treatment

It improves outcome of PCI significantly

It supports the evolving paradigm of

***“Functionally Complete Revascularization”,
i.e. stenting of ischemic lesions and
medical treatment of non-ischemic ones***

What about ref diameter, vessel size?



Reference diameter:

- **FAME 2.5mm**
- **Pivotal DES trials 2.6-2.8mm**

selection bias

single vessel disease

excluding lesions <2.5mm

less extensive disease

→ **Most studies on PCI in MVD: no QCA**
(MASII, ARTS, SYNTAX)