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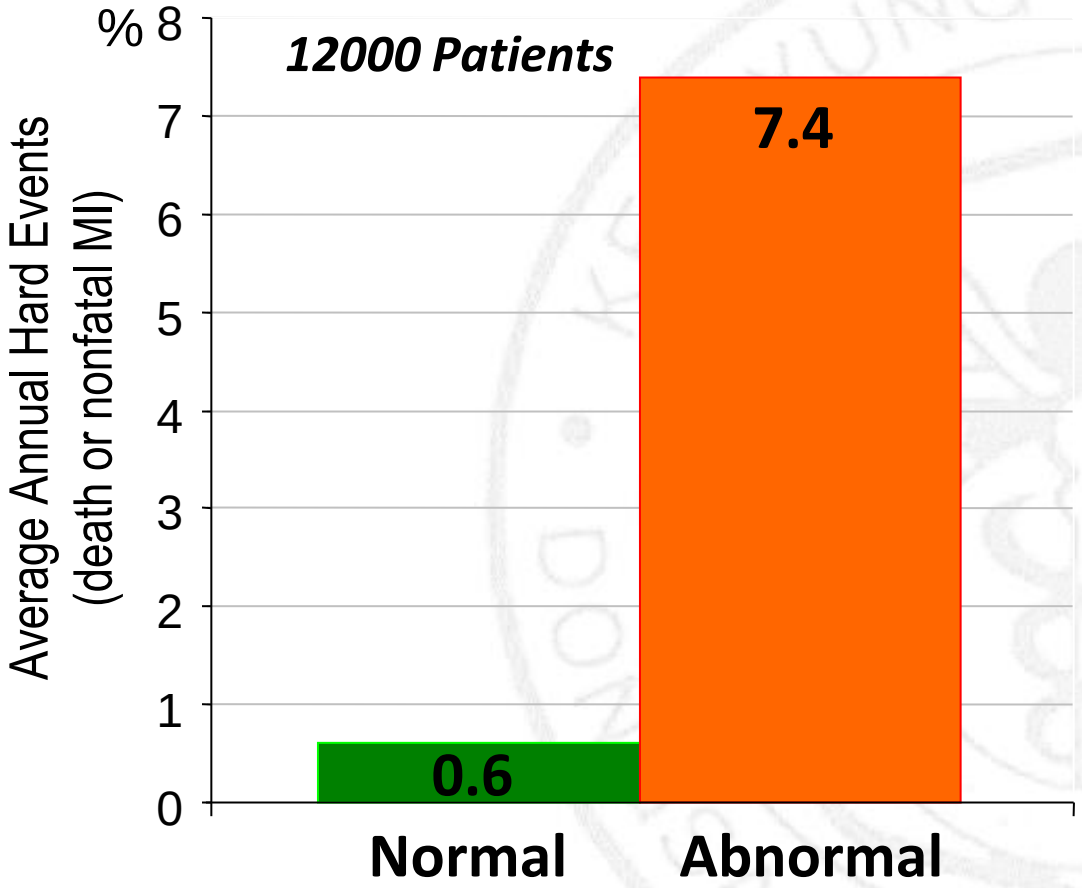
FFR Guided PCI:

Future Perspective

Keimyung University Dongsan Medical Center
NAM, Chang-Wook MD PhD FACC

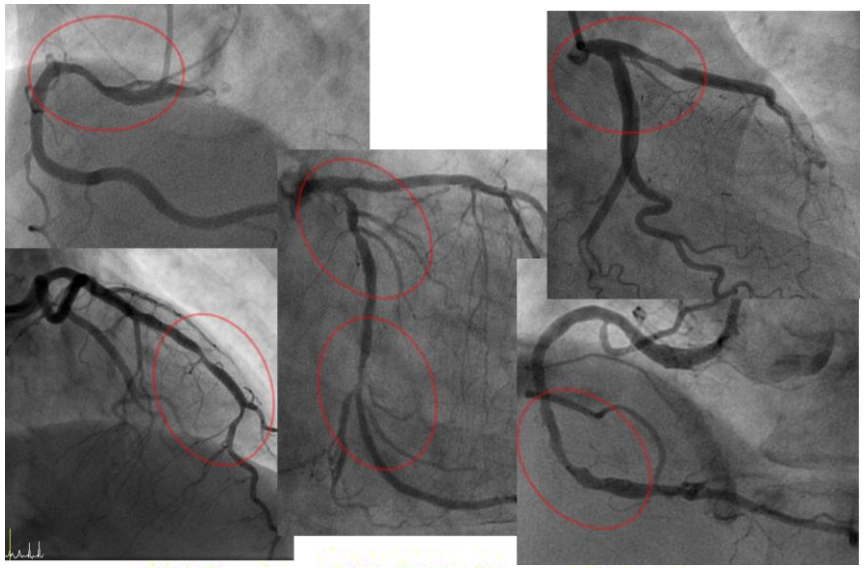
Prognosis of Reversible Ischemia

^{99m}Tc-Sestamibi Perfusion Imaging



Iskander S, Iskandrian A E JACC 1998; 32(1):57

How to Evaluate…



1st Validation of FFR

Experimental Basis of Determining Maximum Coronary, Myocardial, and Collateral Blood Flow by Pressure Measurements for Assessing Functional Stenosis Severity Before and After Percutaneous Transluminal Coronary Angioplasty

Nico H.J. Pijls, MD, Jacques A.M. van Son, MD, Richard L. Kirkeeide, PhD, Bernard De Bruyne, MD, and K. Lance Gould, MD

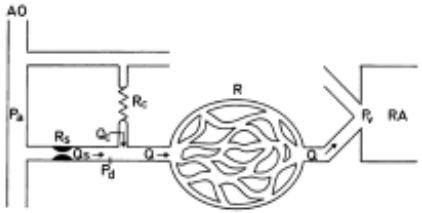


FIGURE 1. *Schematic model representing the coronary circulation. AO, aorta; P_a, arterial pressure; P_d, distal coronary pressure; P_v, venous pressure; Q, blood flow through the myocardial vascular bed; Q_c, collateral blood flow; Q_s, blood flow through the supplying epicardial coronary artery; R, resistance of the myocardial vascular bed; R_c, resistance of the collateral circulation; R_s, resistance of the stenosis in the supplying epicardial coronary artery; RA, right atrium.*

$$FFR_{cor} = \frac{Q_s}{Q_s^N} = \frac{P_d - P_w}{P_a - P_w}$$

$$= 1 - \frac{\Delta P}{P_a - P_w}$$

$$FFR_{myo} = \frac{Q}{Q^N} = \frac{P_d - P_v}{P_a - P_v}$$

$$= 1 - \frac{\Delta P}{P_a - P_v}$$

Keimyung University, Korea

Pijls NH, et al. Circ 1993;86:1354-1367

1st Animal Validation of FFR

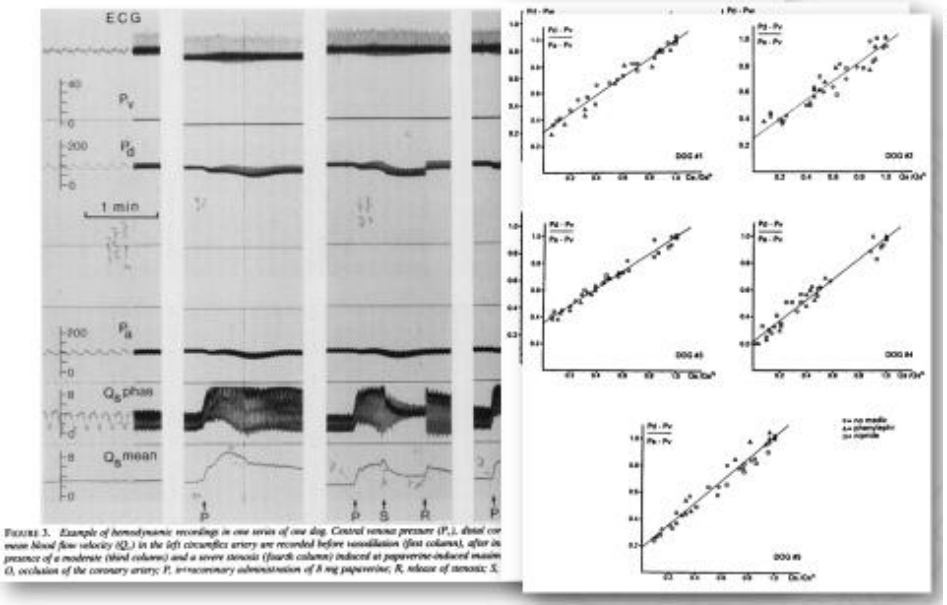


FIGURE 3. *Example of hemodynamic recordings in one series of one dog. Central venous pressure (P,), distal coronary pressure (Pd), mean blood flow velocity (Qs) in the left circumflex artery are recorded before vasodilation (first column), after induction of a moderate (third column) and a severe stenosis (fourth column) induced at papaverine-induced maximum hyperemia, after full occlusion of the coronary artery; P, i.v.=coronary administration of 8 mg papaverine; R, release of stenosis; S,*

Keimyung University, Korea

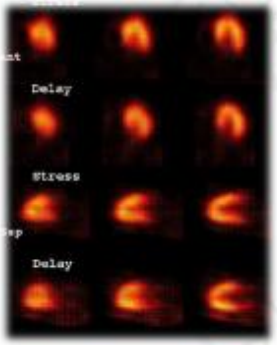
Pijls NH, et al. Circ 1993;86:1354-1367

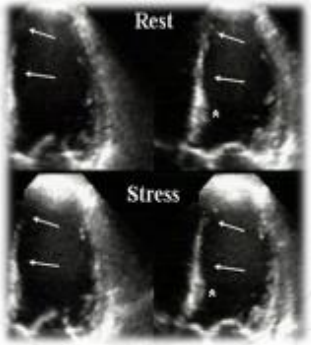
1st Human Validation of FFR 0.75

MEASUREMENT OF FRACTIONAL FLOW RESERVE TO ASSESS THE FUNCTIONAL SEVERITY OF CORONARY-ARTERY STENOSES

NICO H.J. PIJLS, M.D., PH.D., BERNARD DE BRUYNE, M.D., KATHINKA PEELS, M.D., PEPIJN H. VAN DER VOORT, M.D., HANS J.R.M. BONNIER, M.D., PH.D., JOZEF BARTUNEK, M.D., AND JACQUES J. KOOLEN, M.D., PH.D.

45 patients, single moderate coronary stenosis in proximal epicardial artery





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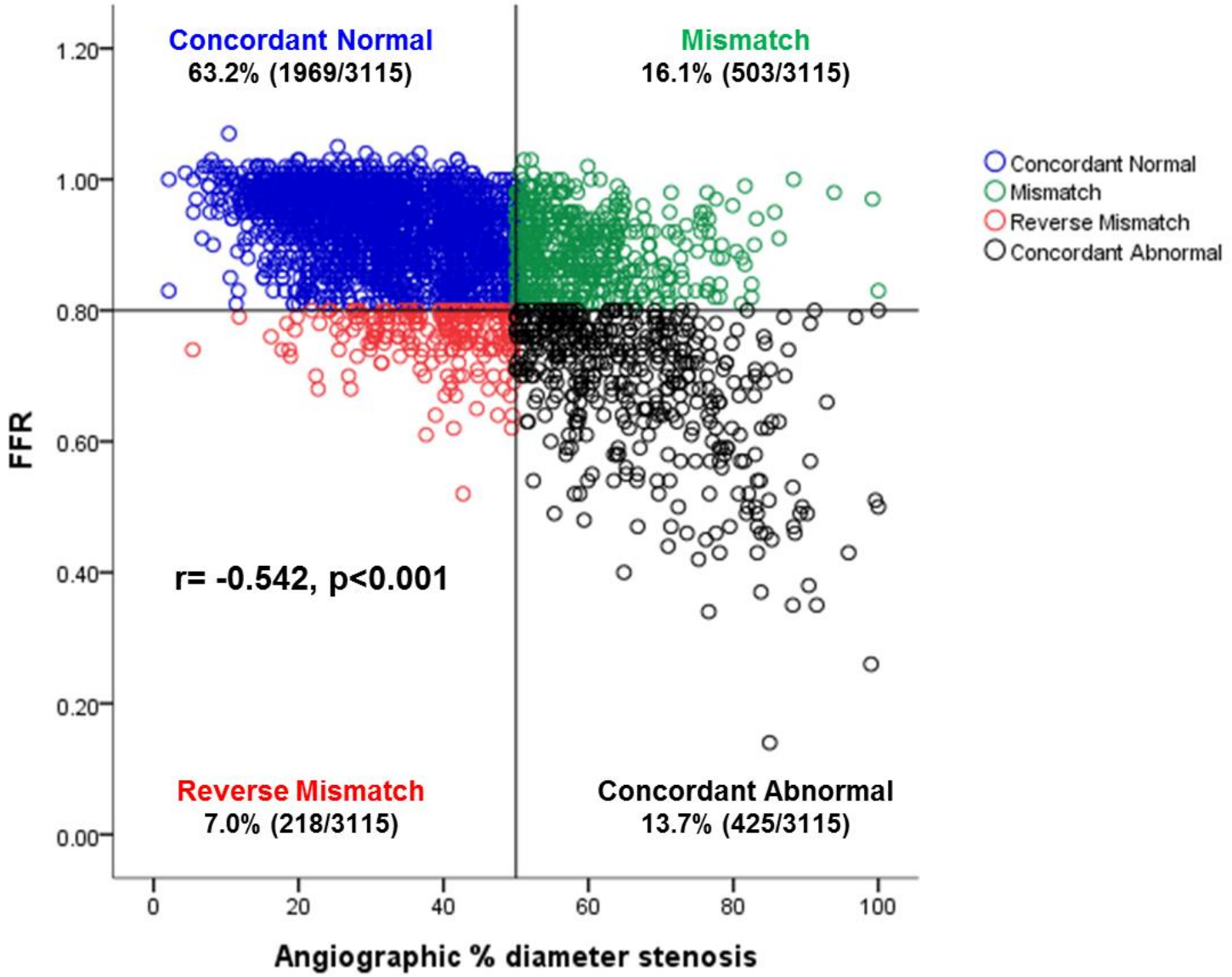
Pijls NH, et al. NEJM 1996;334:1703

Coronary artery disease in Daily cath



Anatomic Evaluation is Not Enough

FFR vs IVUS

11 centers or investigators with prospectively collected IVUS and FFR database

973 patients, 1032 lesions with IVUS and FFR

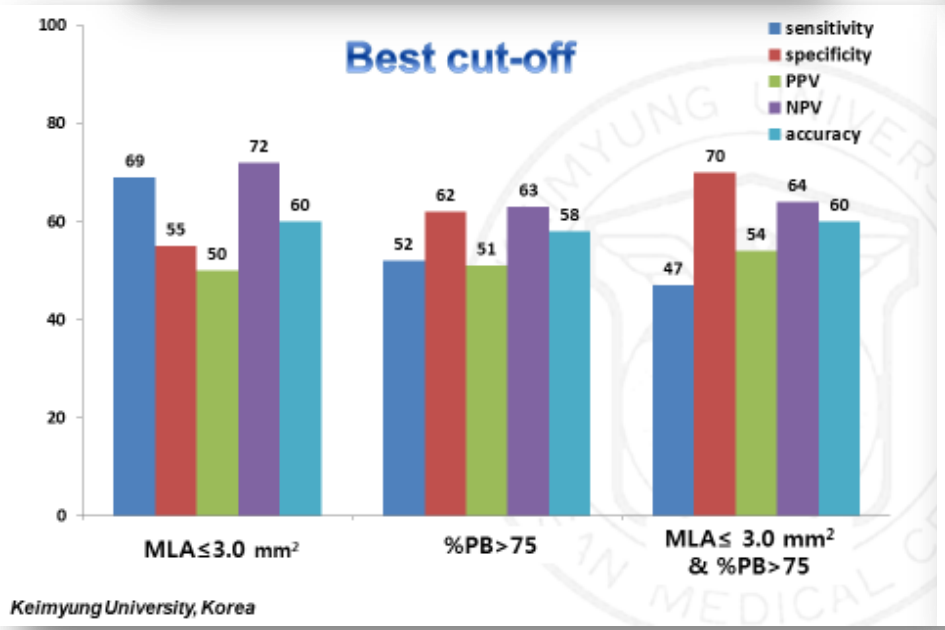
- Intermediate stenosis
- De novo coronary lesion
- Non-left main major coronary arteries
- Vessel size ≥2.5 mm & <4.5mm
- Lesion length <40mm

886 patients, 945 lesions

Excluded cases

- 24 patients, with incomplete clinical information
- 1 patient, <18 years old
- 14 patients, LVEF <35%
- 25 patients, incomplete angiographic data

822 patients, 881 lesions



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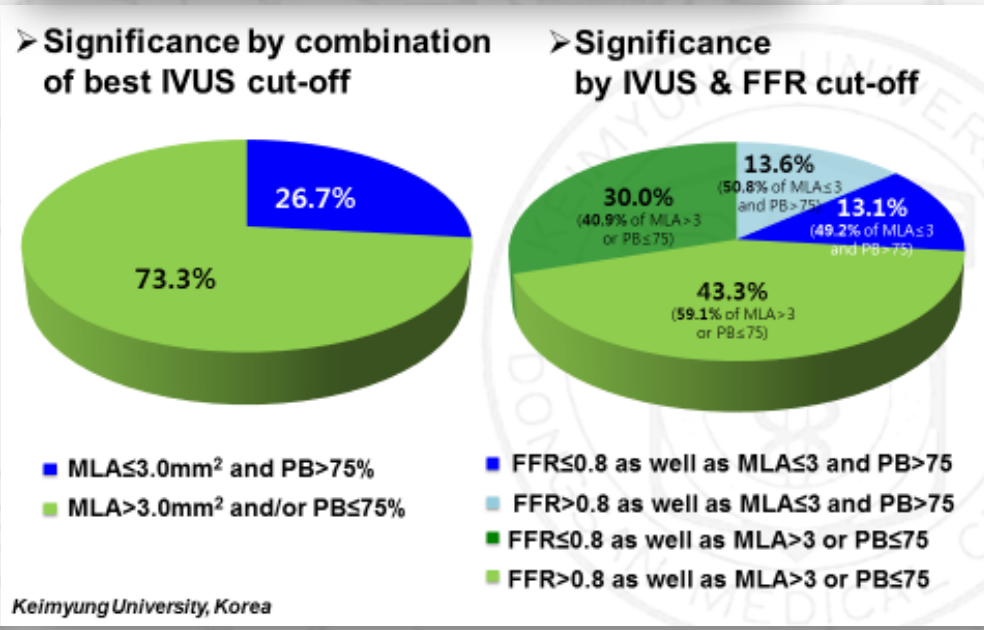
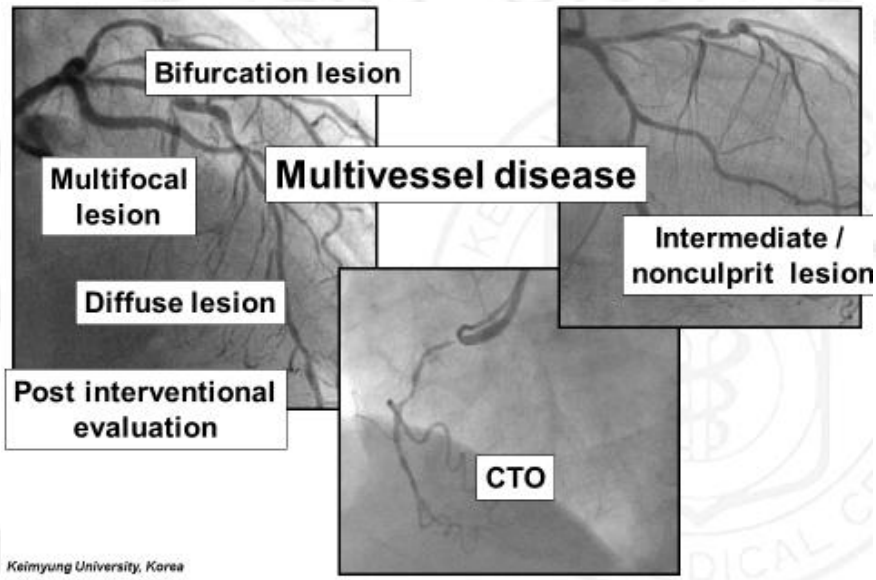


Keimyung University, Korea

Cho YK, Nam CW, et al. EuroIntervention. 2015;11:163-70

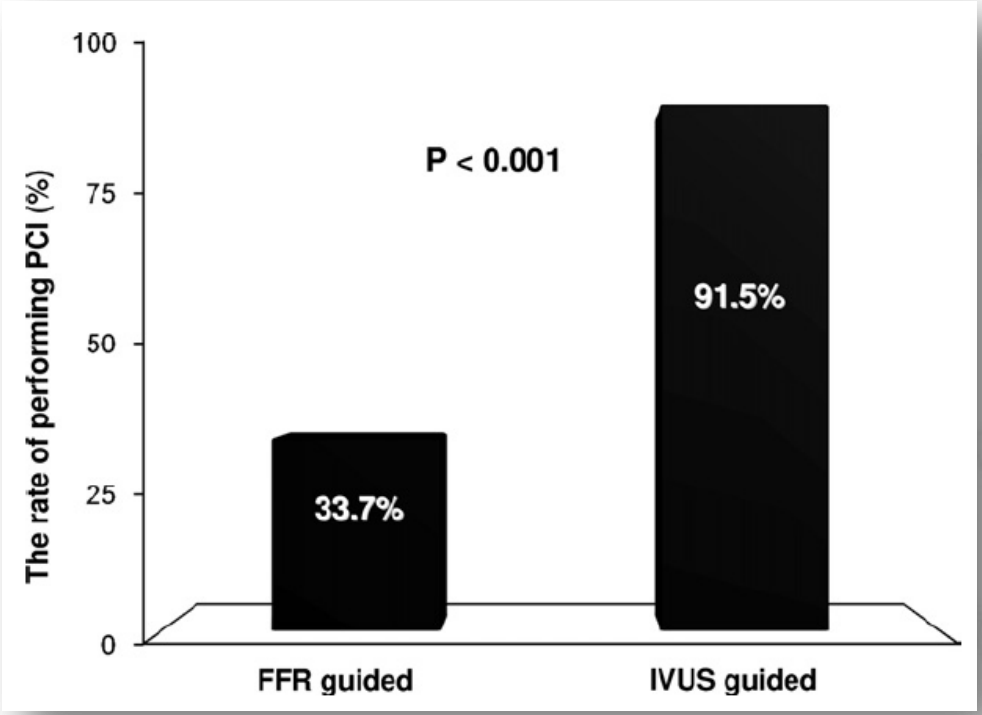
Where can we use physiology?

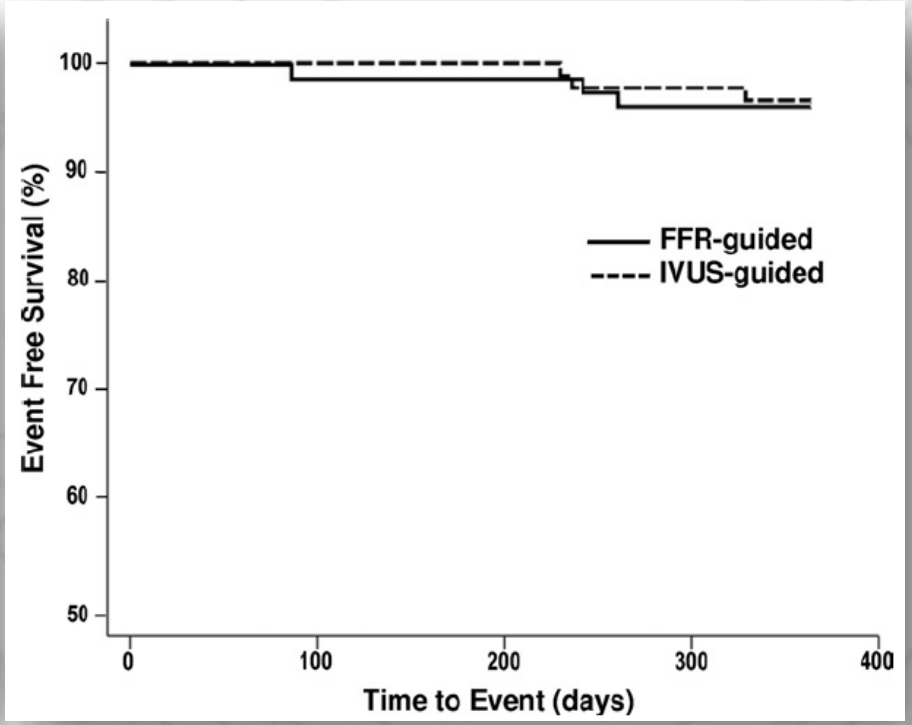
- Intermediate or ambiguous lesion
- Multi-vessel CAD
- Multi-focal (Tandem) lesion
- Diffuse long lesion
- Left main coronary lesion
- Bifurcation lesion
- Instent restenosis lesion
- Post-interventional evaluation
- Acute coronary syndrome
- Chronic total occlusion



Functional vs. Anatomy-guided PCI

167 consecutive patients, with intermediate coronary lesions evaluated by FFR or IVUS (FFR-guided, 83 lesions vs. IVUS-guided, 94 lesions)

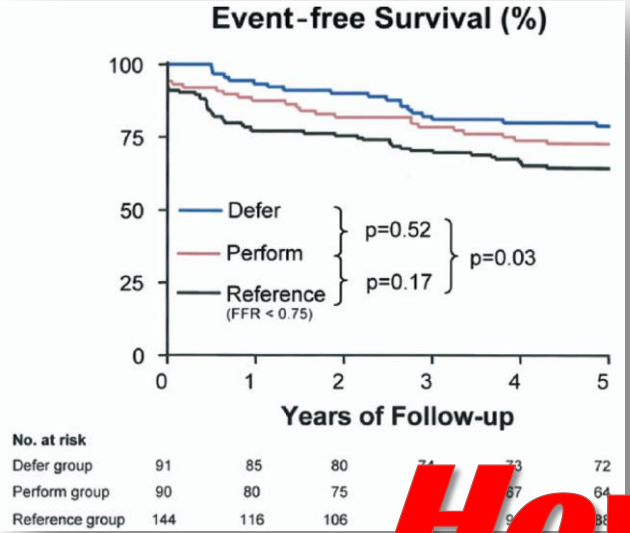




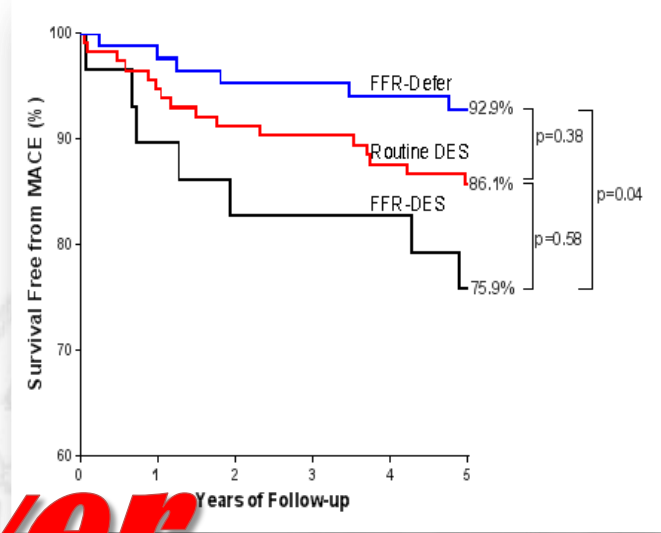
Nam CW et al. JACC Intv 2010;3:812

Fate of nonobstructive CAD

DEFER 5 years

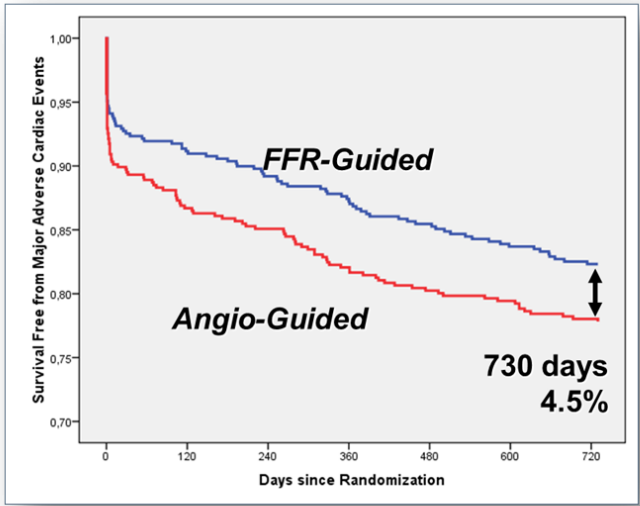


DEFER DES 5 years

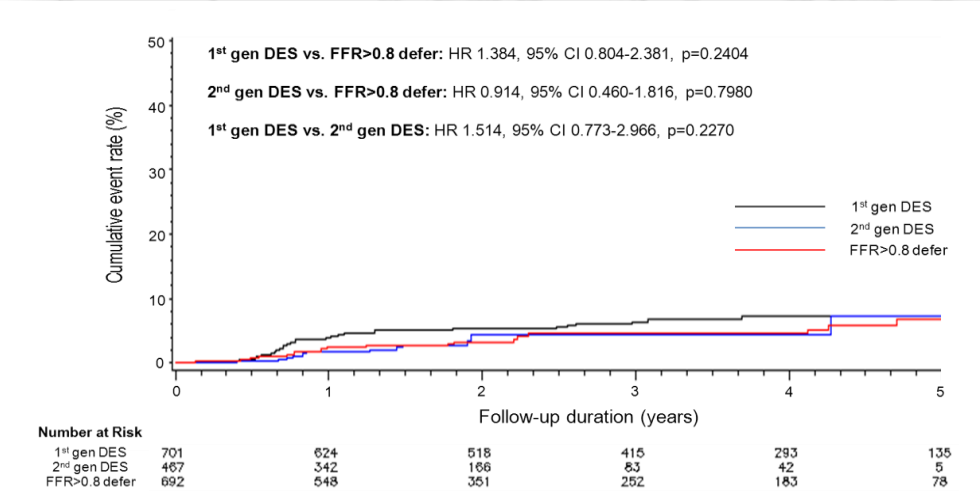


However…

FAME 1



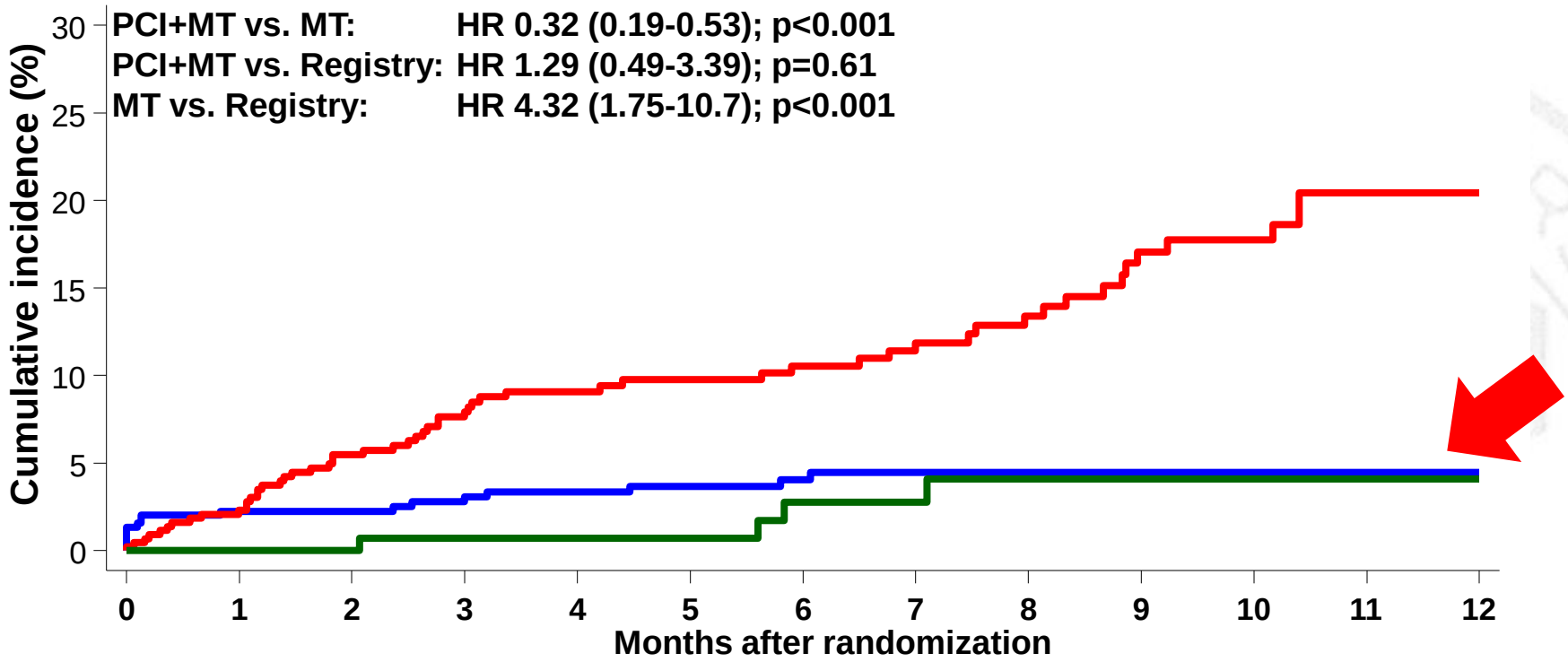
Korean Registry



JACC 2007;49:2105; Revision in Circ intv; JACC 2010;56:177-84; J Invasive Cardiol. 2015 Sep;27:410

FAME 2

Efficacy & Safety issue for FFR-guided PCI (FFR≤0.80)

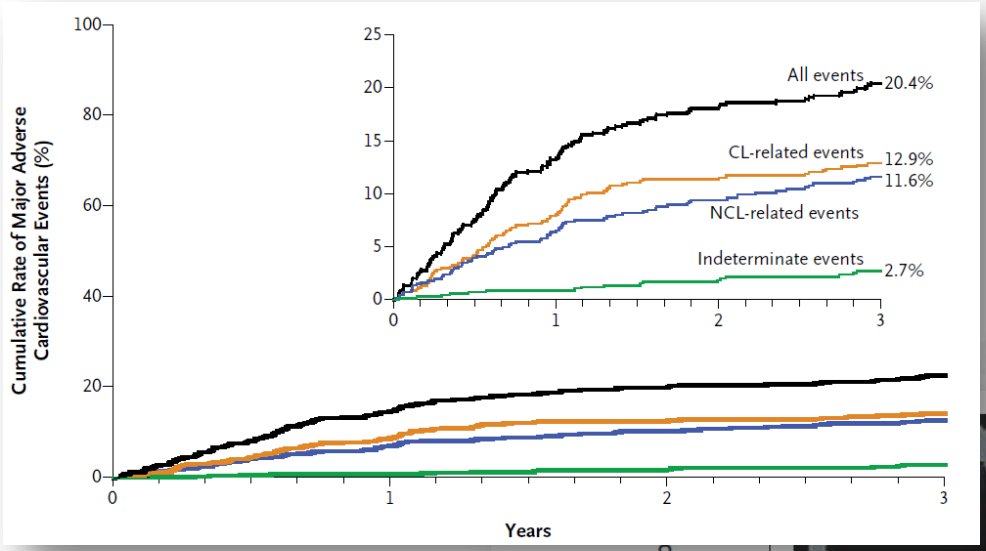


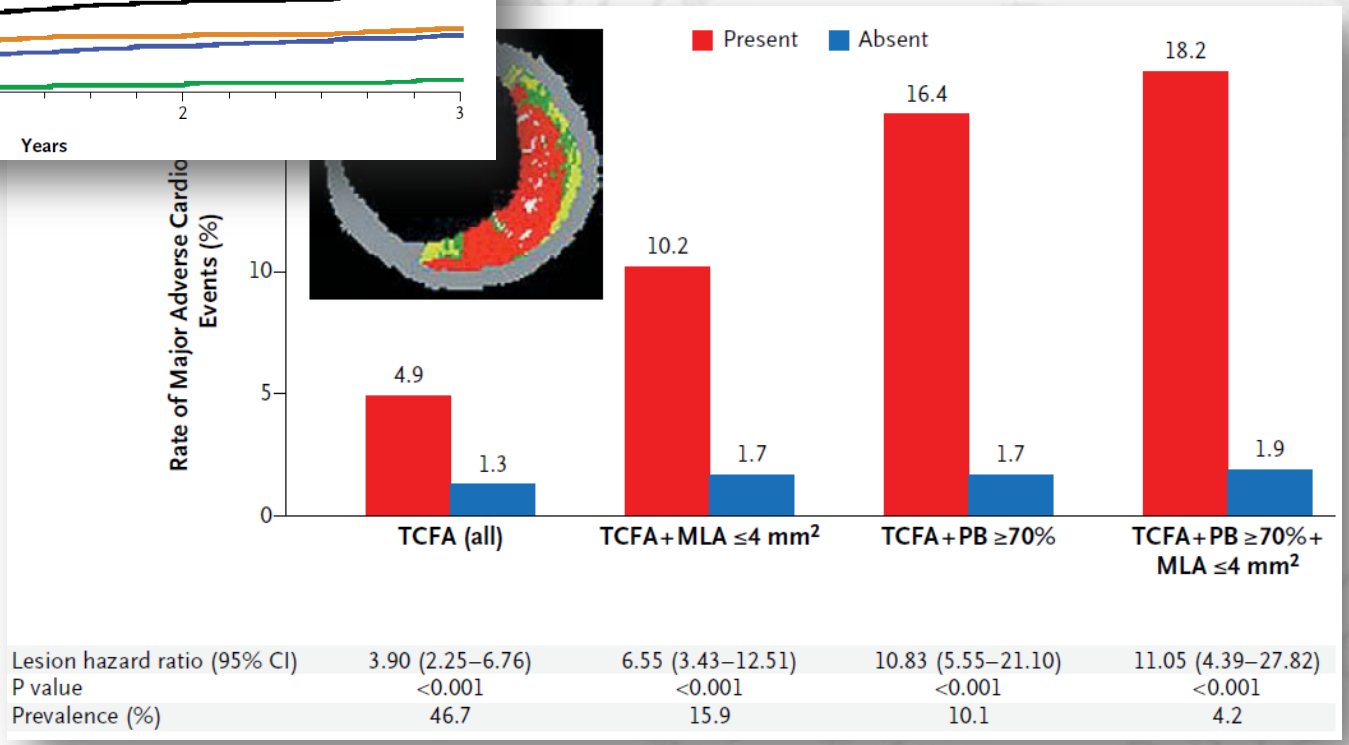
No. at risk

MT	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI+MT	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

De Bruyne, et al. New Engl J Med 2012;367:991-1001

Nonculprit lesion related events: Vulnerability

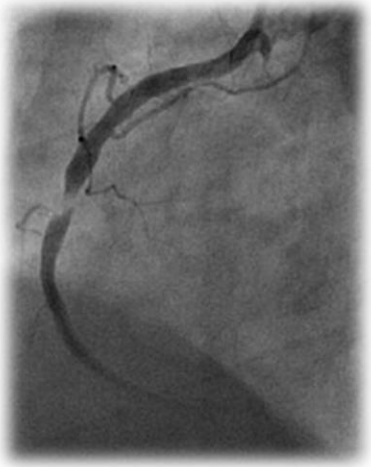




Lesion hazard ratio (95% CI)	3.90 (2.25–6.76)	6.55 (3.43–12.51)	10.83 (5.55–21.10)	11.05 (4.39–27.82)
P value	<0.001	<0.001	<0.001	<0.001
Prevalence (%)	46.7	15.9	10.1	4.2

PROSEPCT, NEJM 2011;364:226

Question…



What we have to tell…

Large vulnerable plaque ≠ **Coronary flow disturbance**

≠ ≠

Clinical outcomes

3-year Outcomes after FFR-guided Defer

Among 1294 patients and 1628 lesions in Korean FFR registry, 665 patients with 781 deferred coronary lesions, categorized 4 groups according to FFR; group 1: >0.95, group 2: 0.86–0.95, group 3: 0.81–0.85, and group 4: ≤0.80, MACE defined as the composites of all death, MI, and TVR

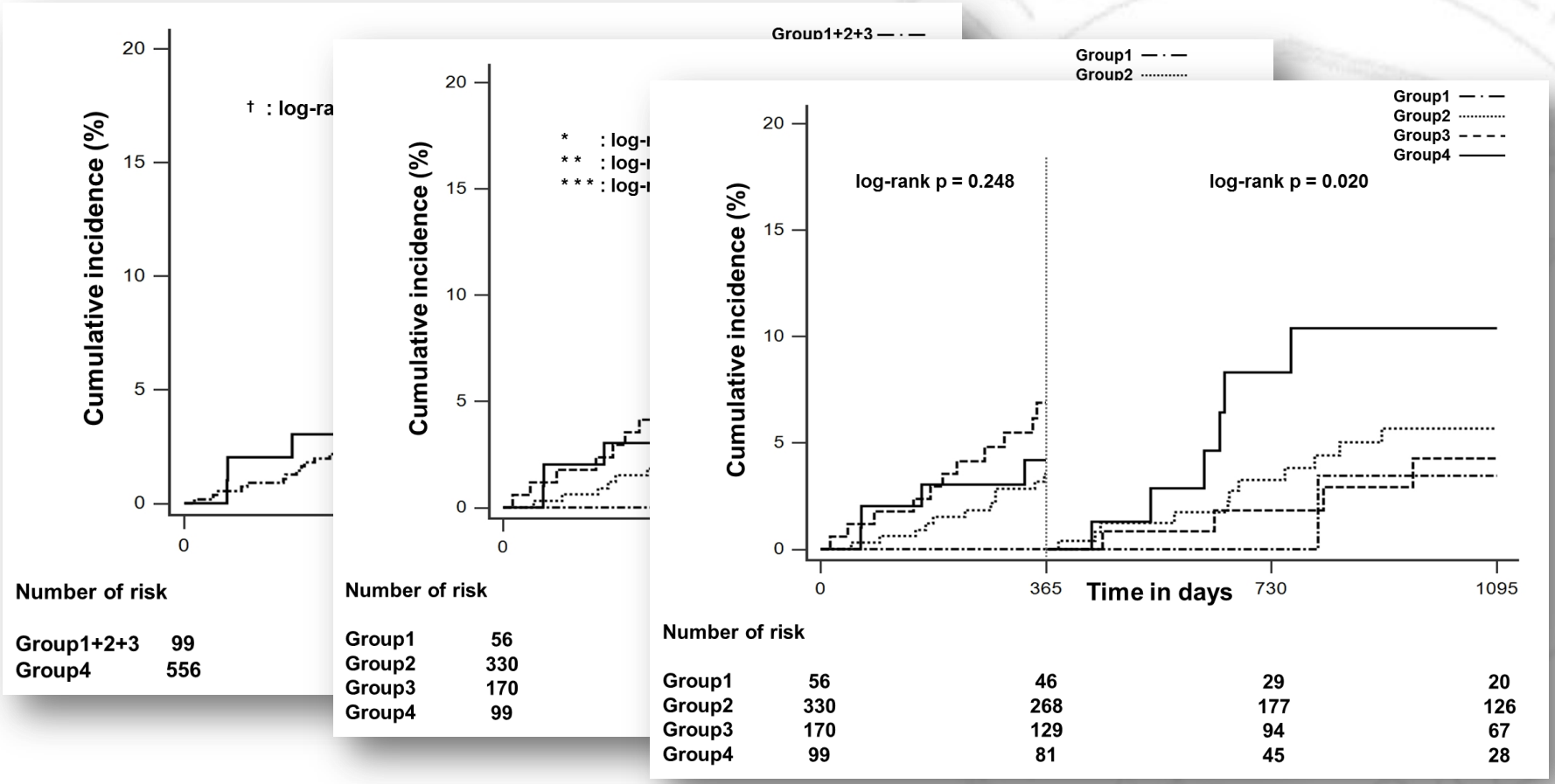
Near normal → *More plaque*

Characteristic	Group 1 (n=89)	Group 2 (n=398)	Group 3 (n=189)	Group 4 (n=105)	P
Target vessel					**<0.001**
LAD	**17 (19.1)**	**200 (50.3)**	**130 (68.8)**	**82 (78.1)**	
Non-LAD	**72 (80.9)**	**198 (49.7)**	**59 (31.2)**	**23 (21.9)**	
QCA					
Reference diameter, mm	**3.18 ± 0.68**	**3.02 ± 0.55**	**2.86 ± 0.43**	**2.75 ± 0.52**	**<0.001**
MLD, mm	**1.77 ± 0.60**	**1.58 ± 0.46**	**1.36 ± 0.43**	**1.27 ± 0.36**	**<0.001**
% DS	**44.62 ± 12.61**	**47.5 ± 12.83**	**52.41 ± 14.22**	**53.60 ± 12.52**	**<0.001**
Lesion length, mm	**14.94 ± 8.80**	**17.09 ± 8.51**	**21.63 ± 11.67**	**25.61 ± 15.01**	**<0.001**
FFR	**0.98 ± 0.01**	**0.90 ± 0.03**	**0.83 ± 0.01**	**0.75 ± 0.06**	**<0.001**

Unpublished data from Korean FFR registry

3-year Outcomes after FFR-guided Defer

Among 1294 patients and 1628 lesions in Korean FFR registry, 665 patients with 781 deferred coronary lesions, categorized 4 groups according to FFR; group 1: >0.95, group 2: 0.86–0.95, group 3: 0.81–0.85, and group 4: ≤ 0.80, MACE defined as the composites of all death, MI, and TVR



Unpublished data from Korean FFR registry

3-year Outcomes after FFR-guided Defer

	All participants					
	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
Age	1.03	1.00–1.06	0.041	1.02	0.99–1.05	0.240
Male	1.22	0.69–2.15	0.498			
Diabetes mellitus	1.95	1.14–3.34	0.016	1.59	0.90–2.78	0.109
Dyslipidemia	1.23	0.72–2.11	0.447			
Smoking	1.67	0.94–2.97	0.081			
Previous MI	2.35	1.11–4.99	.0	1.09	0.44–2.66	0.856
Previous PCI	2.13	1.22–3.7	0.8	1.7	.9 3.4	09
ACS	2.04	1.16–3.60	0.014	1.86	0.99–3.49	0.055
LVEF	0.96	0.93–0.99	0.008	0.99	0.96–1.02	0.335
Multi-VD	2.31	1.28–4.15	0.005	1.36	0.73–2.55	0.334
LAD	0.51	0.30–0.88	0.015	0.56	0.31–1.01	0.052
Reference diameter	1.03	0.62–1.71	0.923			
% DS	1.03	1.00–1.05	0.020	1.01	0.98–1.03	0.587
Lesion length>20 mm	1.59	0.92–2.75	0.096			
Previous PCI-MLD	0.57	0.31–1.03	0.064			
FFR	0.95	0.92–0.98	0.001	**0.95**	**0.92–0.99**	**0.005**

However…

Unpublished data from Korean FFR registry

5-year Outcomes after FFR-guided Defer, Verified by IVUS

Total number	493 patients / 607 lesions
Age ,years	61.11±10.39
Male	432 (71.2%)
Diabetes mellitus	155 (25.5%)
Smoking	276 (45.5%)
Dyslipidemia	296 (48.8%)
HTN	365 (60.1%)
Clinical presentation	
SA	453 (74.6%)
ACS	154 (25.4%)
Multi-VD	254 (41.8%)
LVEF, %	63.35±8.21
Medication	
Aspirin	478 (78.7%)
Clopidogrel	334 (55.0%)
Statin	505 (83.2%)
Beta-blocker	201 (33.1%)
ACE inhibitor	200 (32.9%)
Target vessel	
LAD	265 (43.7%)
Non-LAD	342 (56.3%)

Total number	493 patients / 607 lesions
QCA	
Reference diameter, mm	3.09±0.66
MLD, mm	1.80±0.68
% DS	42.47±14.23
Lesion length, mm	15.81±7.39
IVUS	
MLA, mm^2	4.58±2.26
Vessel area at MLA site, mm^2	12.62±4.81
Plaque burden, %	64.36±11.58
FFR	0.90±0.06

Keimyung University, Korea

Slides from Dr Cho YK
Unpublished data from Korean FFR/IVUS registry

5-year Outcomes after FFR-guided Defer, Verified by IVUS

Grouping of FFR, MLA, and %PB

	FFR	MLA	%PB
Group 1	0.95 ~ 1.00	5.0mm^2 ~	~ 58%
Group 2	0.90 ~ 0.95	4.0mm^2 ~ 5.0mm^2	58% ~ 66%
Group 3	0.85 ~ 0.90	3.0mm^2 ~ 4.0mm^2	66% ~ 73%
Group 4	0.80 ~ 0.85	~ 3.0mm^2	73%~

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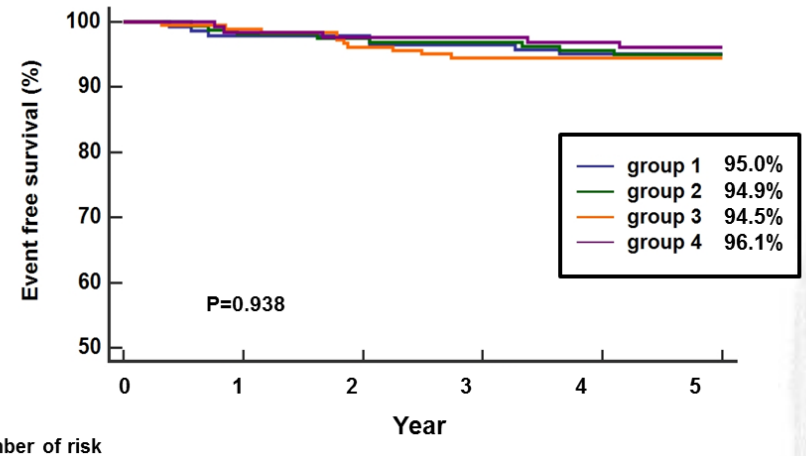
Unpublished data from Korean FFR/IVUS registry

5-year Outcomes after FFR-guided Defer, Verified by IVUS

MACE according to FFR quartile

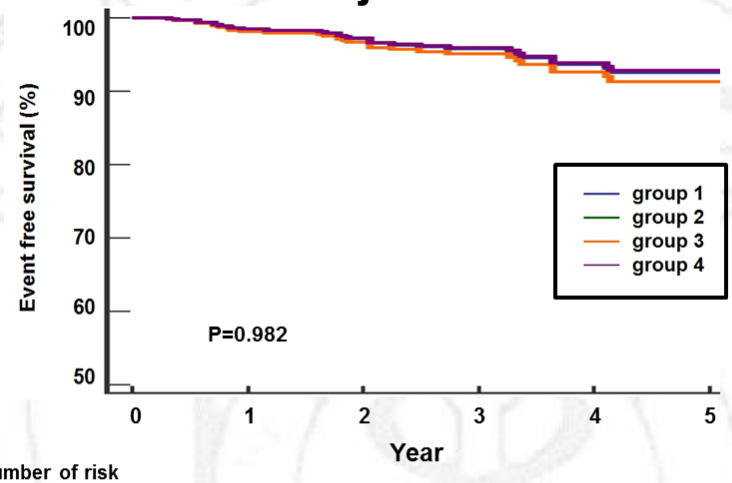
Unadjusted



Number of risk						
Group1	141	138	138	136	134	134
Group2	158	155	154	153	151	150
Group3	181	179	174	171	171	171
Group4	127	125	124	124	123	122

	HR	95% CI	p
Group1	1.00	-	-
Group2	0.90	0.33-2.49	0.838
Group3	0.96	0.36-2.52	0.929
Group4	0.75	0.24-2.37	0.626

Adjusted



Number of risk						
Group1	141	138	138	136	134	134
Group2	158	155	154	153	151	150
Group3	181	179	174	171	171	171
Group4	127	125	124	124	123	122

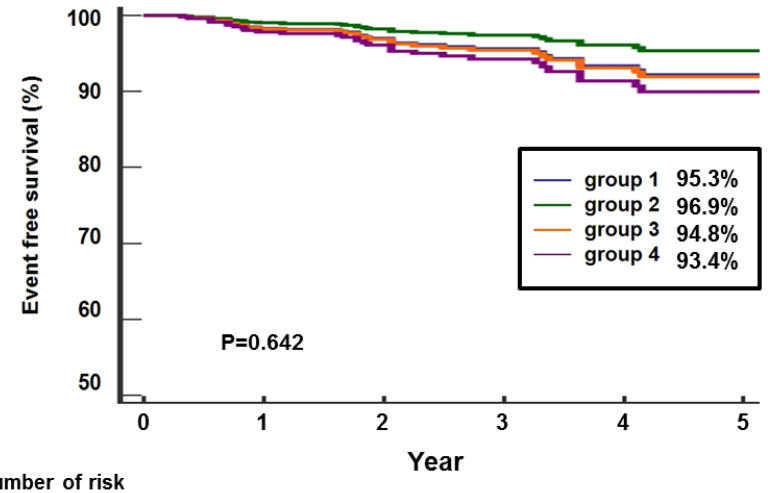
	HR	95% CI	p
Group1	1.00	-	-
Group2	0.96	0.33-2.77	0.943
Group3	1.17	0.39-3.54	0.782
Group4	0.96	0.26-3.55	0.954

Slides from Dr Cho YK
Unpublished data from Korean FFR/IVUS registry

5-year Outcomes after FFR-guided Defer, Verified by IVUS

MACE according to MLA & %PB quartile

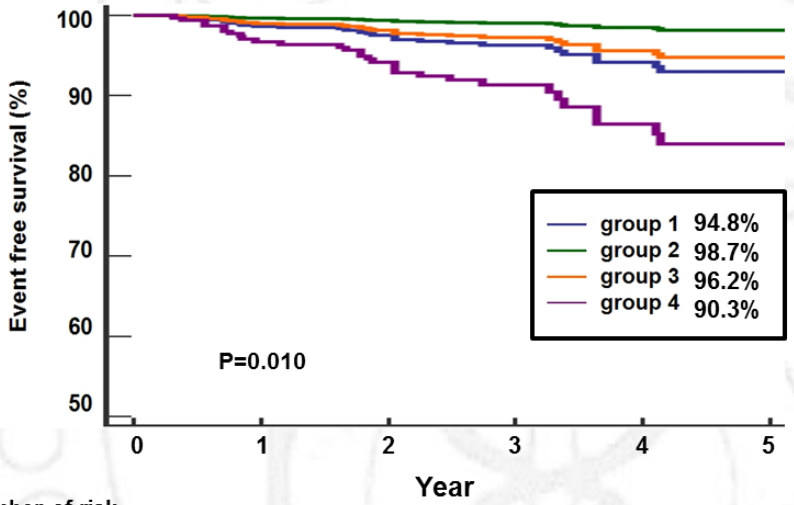
MLA, Adjusted



Number of risk						
Group1	169	167	164	162	161	161
Group2	127	125	125	125	124	123
Group3	174	172	171	168	166	165
Group4	137	133	130	129	128	128

	HR	95% CI	p
Group1	1.00	-	-
Group2	0.62	0.19-2.07	0.440
Group3	1.13	0.43-2.98	0.810
Group4	1.48	0.55-3.98	0.440

%PB, Adjusted



Number of risk						
Group1	155	151	148	147	147	147
Group2	151	151	150	149	149	149
Group3	157	156	156	153	151	151
Group4	144	139	136	135	132	130

	HR	95% CI	p
Group1	1.00	-	-
Group2	0.26	0.05-1.21	0.087
Group3	0.74	0.25-2.17	0.586
Group4	2.41	0.96-6.06	0.063

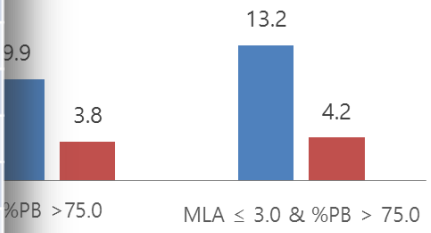
Slides from Dr Cho YK
Unpublished data from Korean FFR/IVUS registry

5-year Outcomes after FFR-guided Defer, Verified by IVUS

MACE Predictors

	Univariate			Multivariate		
	HR	95% CI	P-value	HR	95% CI	P-value
Age	1.019	0.983-1.055	0.313			
Male vs Female	0.716	0.341-1.505	0.378			
Diabetes mellitus	**4.246**	**2.059-8.757**	**<0.0001**	**3.949**	**1.909-8.168**	**<0.0001**
Smoking	1.025	0.500-2.102	0.945			
Dyslipidemia	0.498	0.233-1.064	0.072			
HTN	0.957	0.461-1.988	0.907			
SA vs ACS	0.694	0.317-1.519	0.361			
Multi-VD	1.007	0.489-2.075	0.984			
LVEF	0.975	0.936-1.015	0.218			
LAD vs NonLAD	0.767	0.368-1.599	0.479			
MLA	0.976	0.826-1.153	0.777			
Vessel area at MLA site	1.041	0.971-1.116	0.258			
Plaque burden	1.021	0.987-1.057	0.234			
FFR	1.012	0.947-1.083	0.720			
MLA 3.0 **mm² ≤**	1.500	0.687-3.275	0.309			
%PB ≥75%	**2.904**	**1.379-6.112**	**0.005**	1.979	0.669-5.855	0.217
MLA 3.0 mm² ≤ & %PB ≥75%	**3.257**	**1.397-7.593**	**0.006**	1.575	0.458-5.415	0.471

Best cut-off to FFR



	%PB		MLA & %PB	
	% <	75 ≥	3.0mm² ≥ & 75% <	others
	1	19	7	23
	11	496	53	554
	0.008		0.011	

Slides from Dr Cho YK
Unpublished data from Korean FFR/IVUS registry

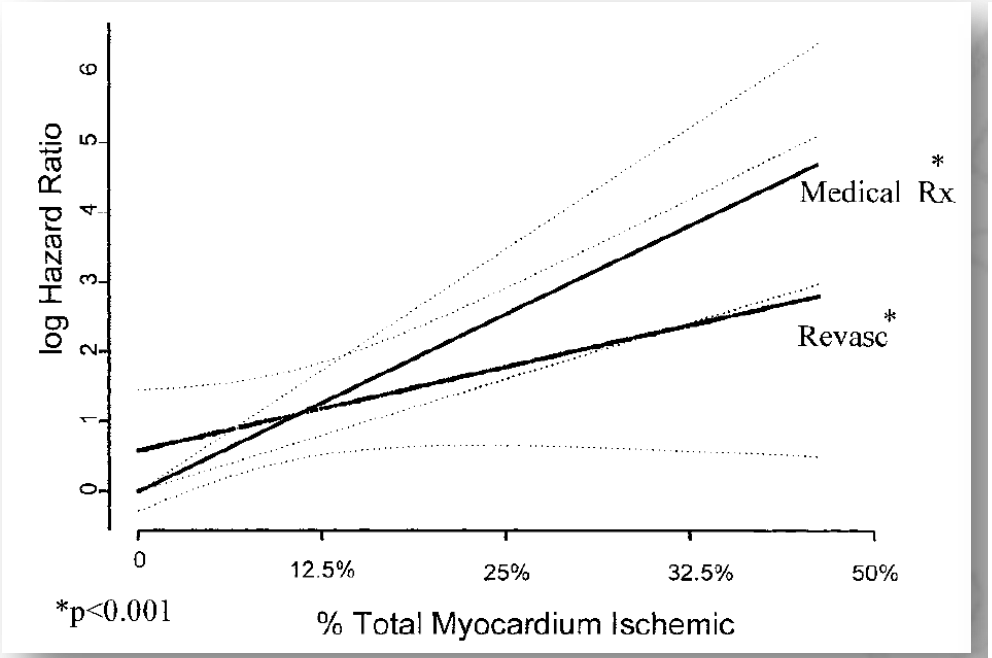
What we have to tell: Usual suspect…

- **Large plaque burden**
- **Vulnerable plaque characteristics**
- **Significant coronary flow disturbance**
- **Underlying clinical risk factors in Nonobs. CAD**

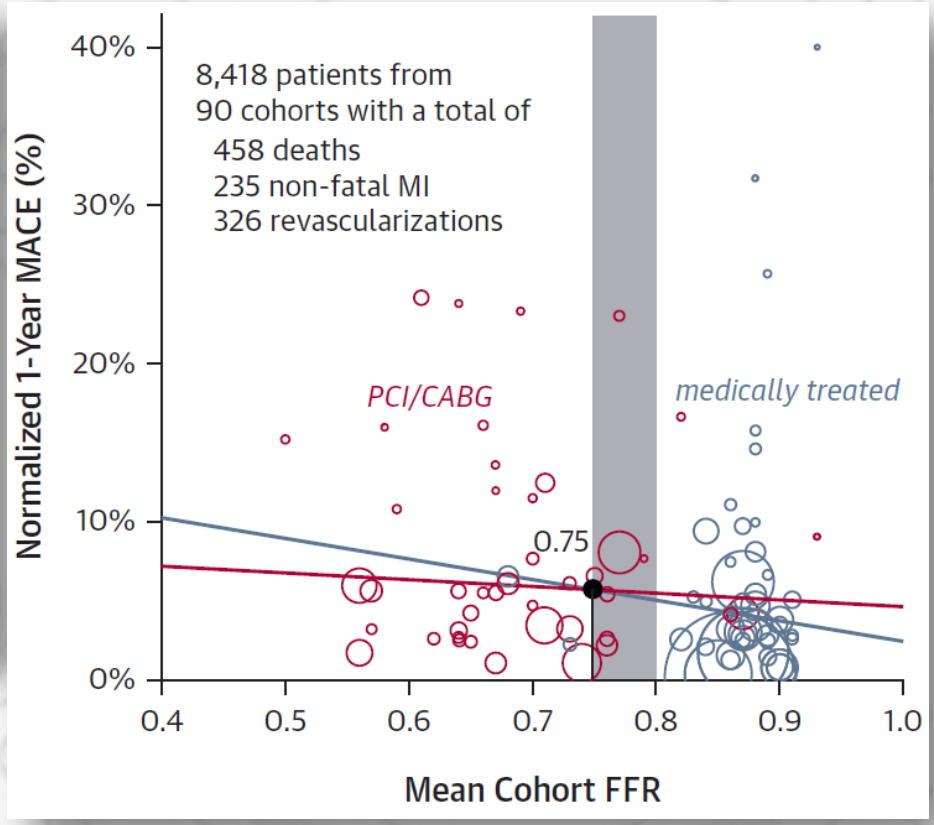
Then, What we have to do…

FFR & Burden of ischemia

Burden of Ischemia



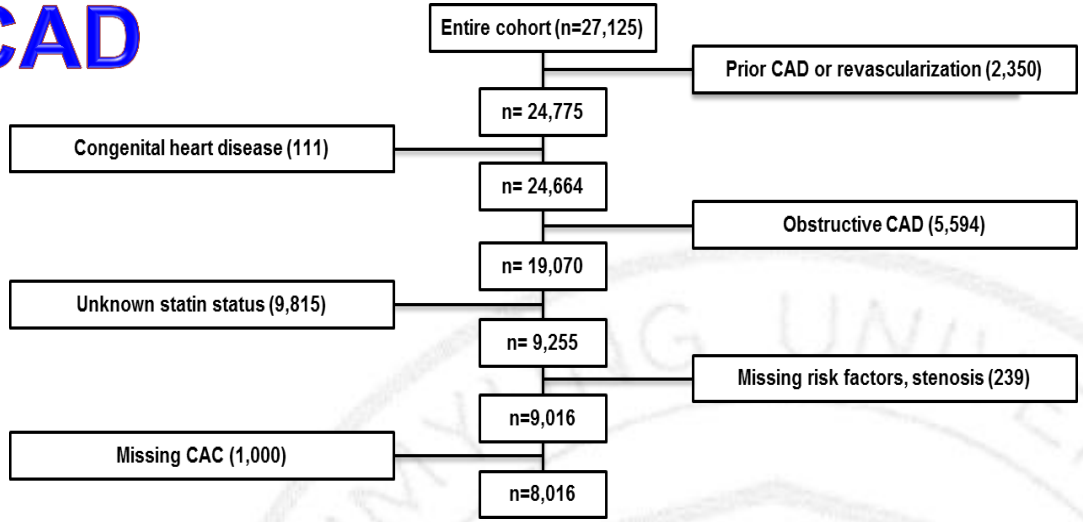
FFR



Circ 2003;107:2900
JACC 2014;64:1641

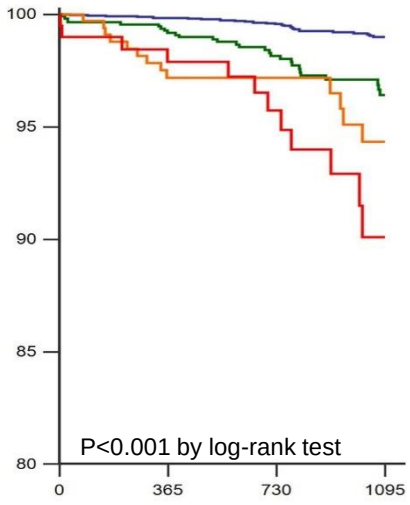
Nonobstructive CAD

From CONFIRM registry

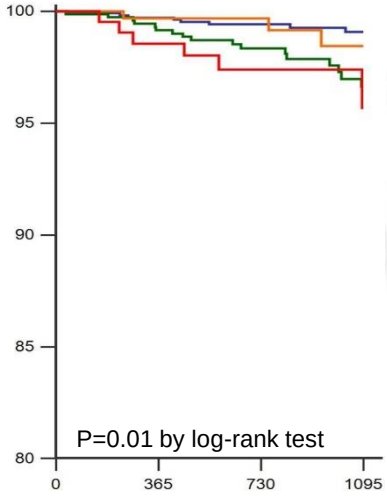


SIS Quartiles

Even-free survival without statin

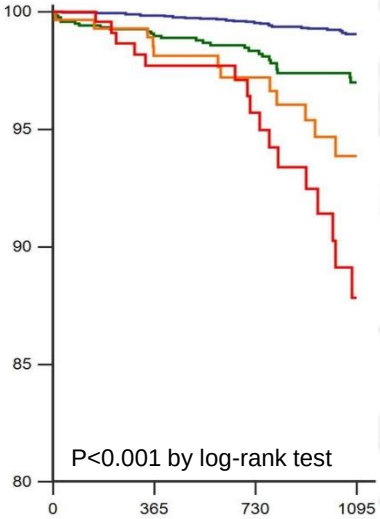


Even-free survival with statin

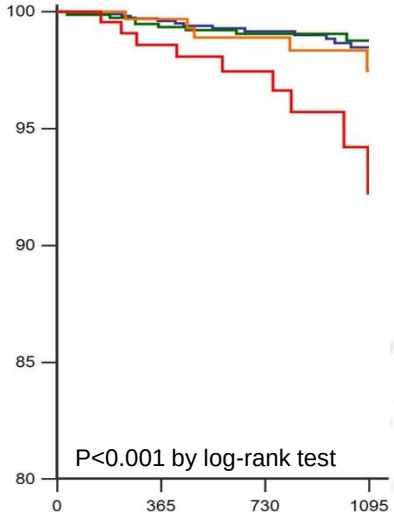


Calcium score Quartiles

Even-free survival without statin



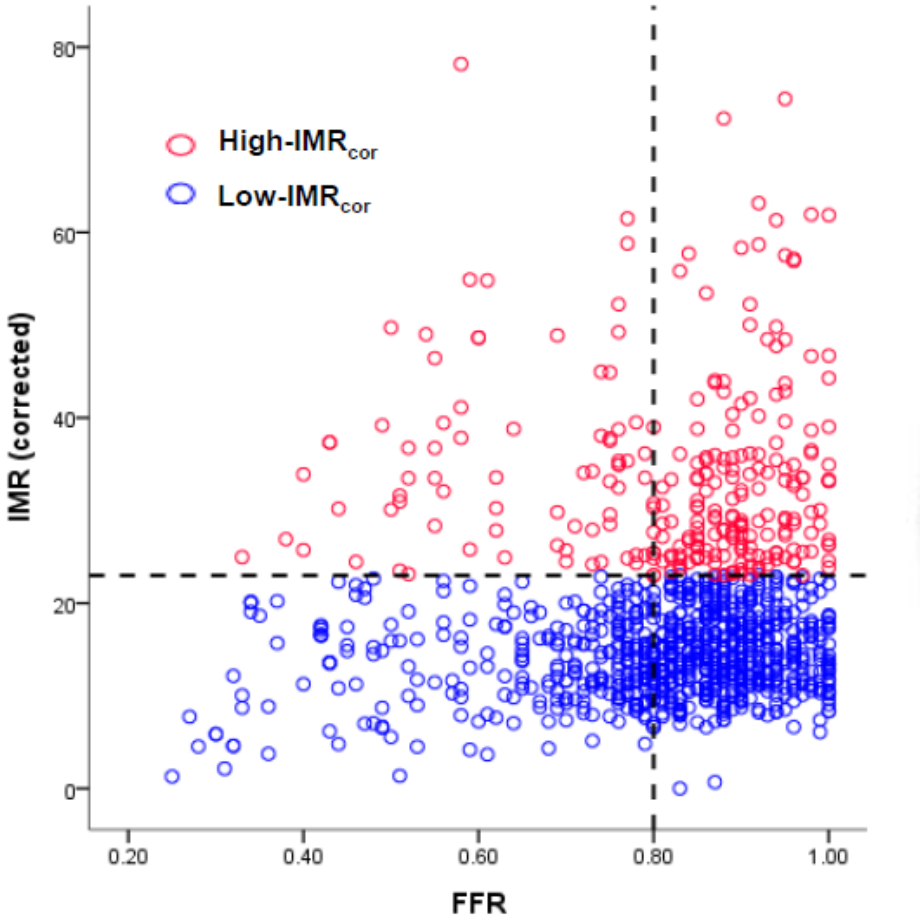
Even-free survival with statin

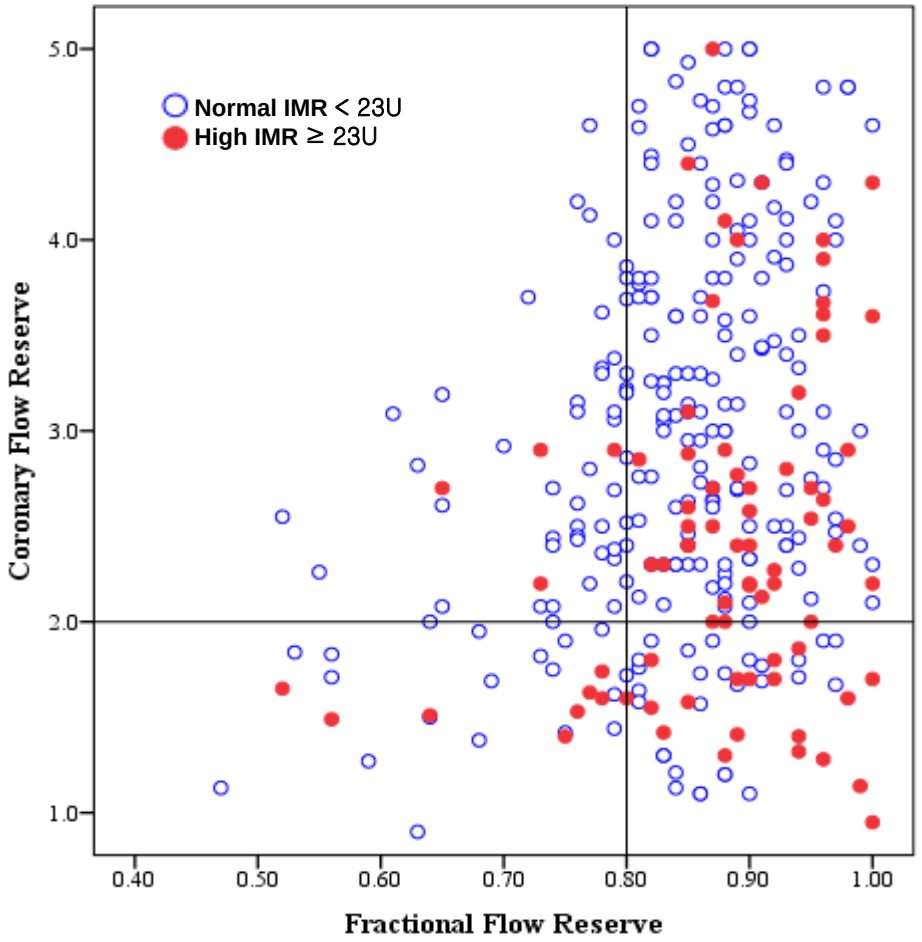


Cho YK, et al. 2014 AHA, KSC

From “macro-” to “micro-circulation”

Classification of Patients According to the FFR, CFR, and IMR

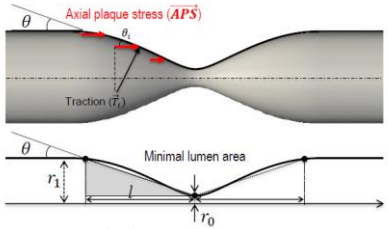




Keimyung University, Korea

In press in Circ CV intv
Revision in JACC

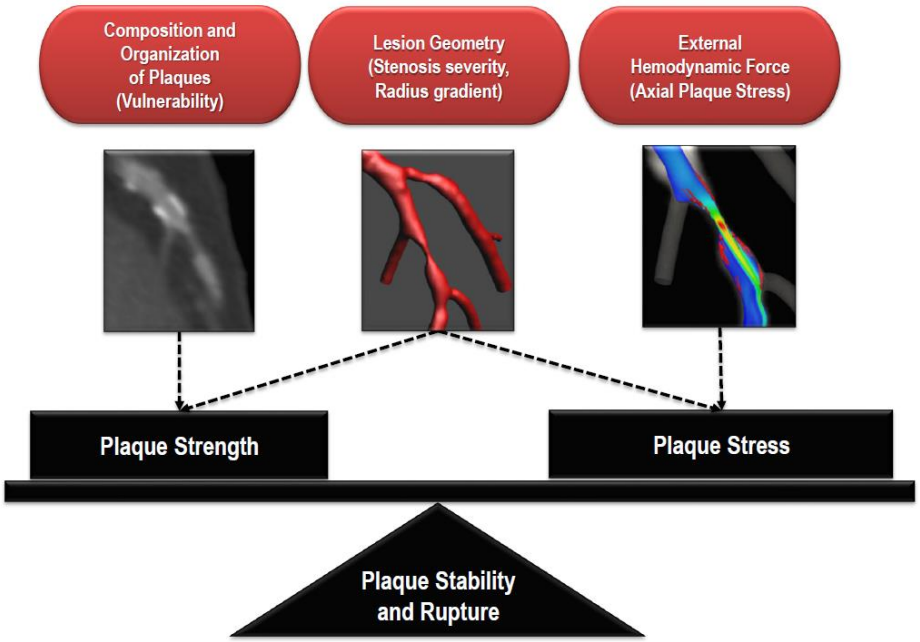
If we can predict…

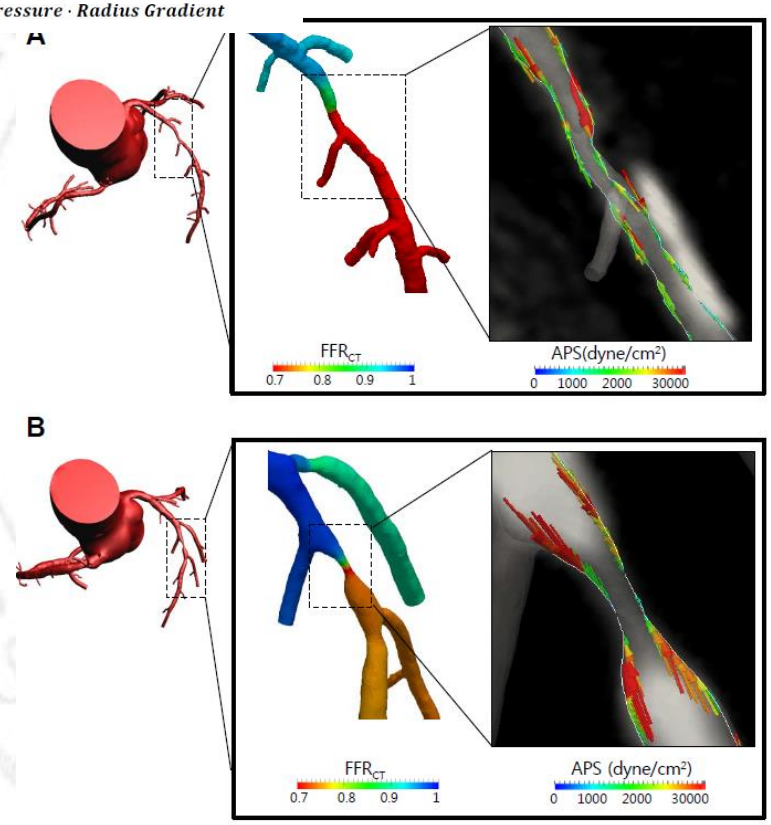


$$\overrightarrow{\mathbf{APS}}_{\mathbf{upstream}} = \sum \vec{T}_i sin\theta_i \approx Pressure \frac{r_1 - r_0}{\sqrt{l^2 + (r_1 - r_0)^2}}$$

$$= Pressure \frac{\frac{r_1 - r_0}{l}}{\sqrt{1 + (\frac{r_1 - r_0}{l})^2}} \approx Pressure \frac{r_1 - r_0}{l}$$

$$= \boldsymbol{Pressure \cdot Radius\ Gradient}$$





Keimyung University, Korea

JACC Cardiovasc Imaging. 2015;8:1156

BVS in nonobstructive CAD

The ***PREVENT***ive Implantation of Bioresorbable Vascular Scaffold on Stenosis With Functionally Insignificant Vulnerable Plaque

PREVENT Trial

Any Epicardial Coronary Stenosis (DS>50% by visual estimation)
with *FFR >0.80* and with *Two* of the following

1. MLA ≤4.0mm^2
2. Plaque Burden$_{MLA}$ >70%
3. Lipid-Rich Plaque on NIRS ($_{max}$LCBI$_{4mm}$>315)
4. TCFA defined by OCT or VH-IVUS

R

BVS+OMT	OMT
N=800	N=800

Primary endpoint *at 2 years*:
CV death, MI, Hospitalization d/t unstable angina

OCT sub-study/ NIRS sub-study, (300 patients in each arm at 2 years)

What we have to do: Usual suspect…

- **Optimal medical therapy**
- **Understanding of CAD: not only macro, but micro**
- **Upcoming novel technology to predict event**
- **Upcoming new devices to prevent event**

What we have to do and tell about Nonobstructive CAD

- **"Plaque means future event, no plaque no event" is true. However, non-flow limiting plaque is still indication for optimal medical therapy with life style modification, not for revascularization, to prevent future event.**
- **Coronary event can not be explained by a single simple dogma. Therefore, more comprehensive understanding for coronary atherosclerosis and its natural course is warranted.**
- **Developing novel technology may change the future direction of diagnosis and treatment…**

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FFR Guided PCI:

Future Perspective

Keimyung University Dongsan Medical Center
NAM, Chang-Wook MD PhD FACC