

# Physiologic Assessment just for "Intermediate Angiographic Stenosis"?

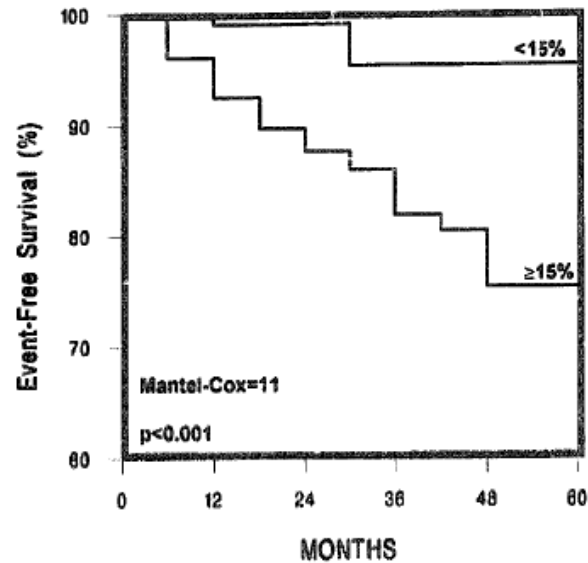
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Samsung Medical Center, Seoul, Republic of Korea

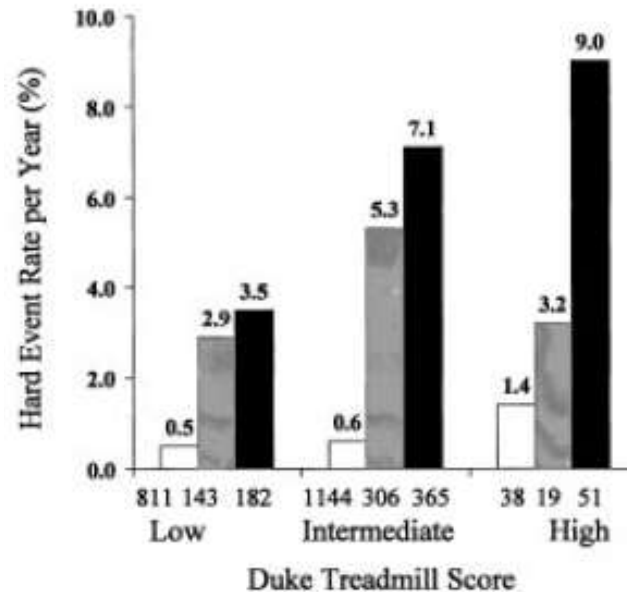


# Myocardial Ischemia is Important for Prognosis

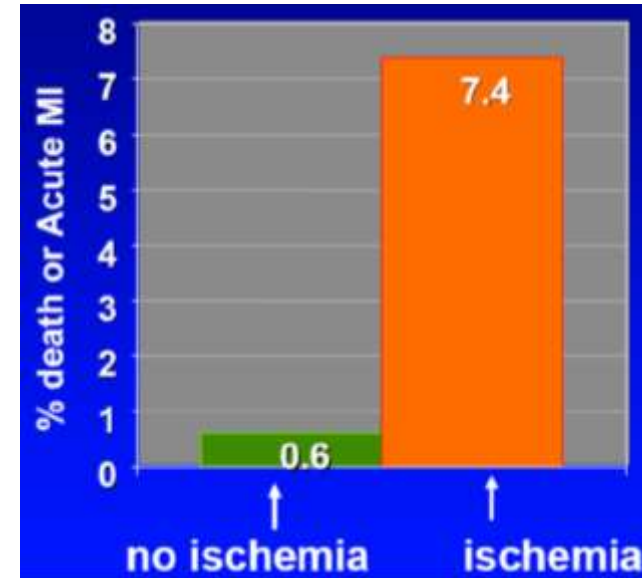
## SPECT



## Duke TMT Score

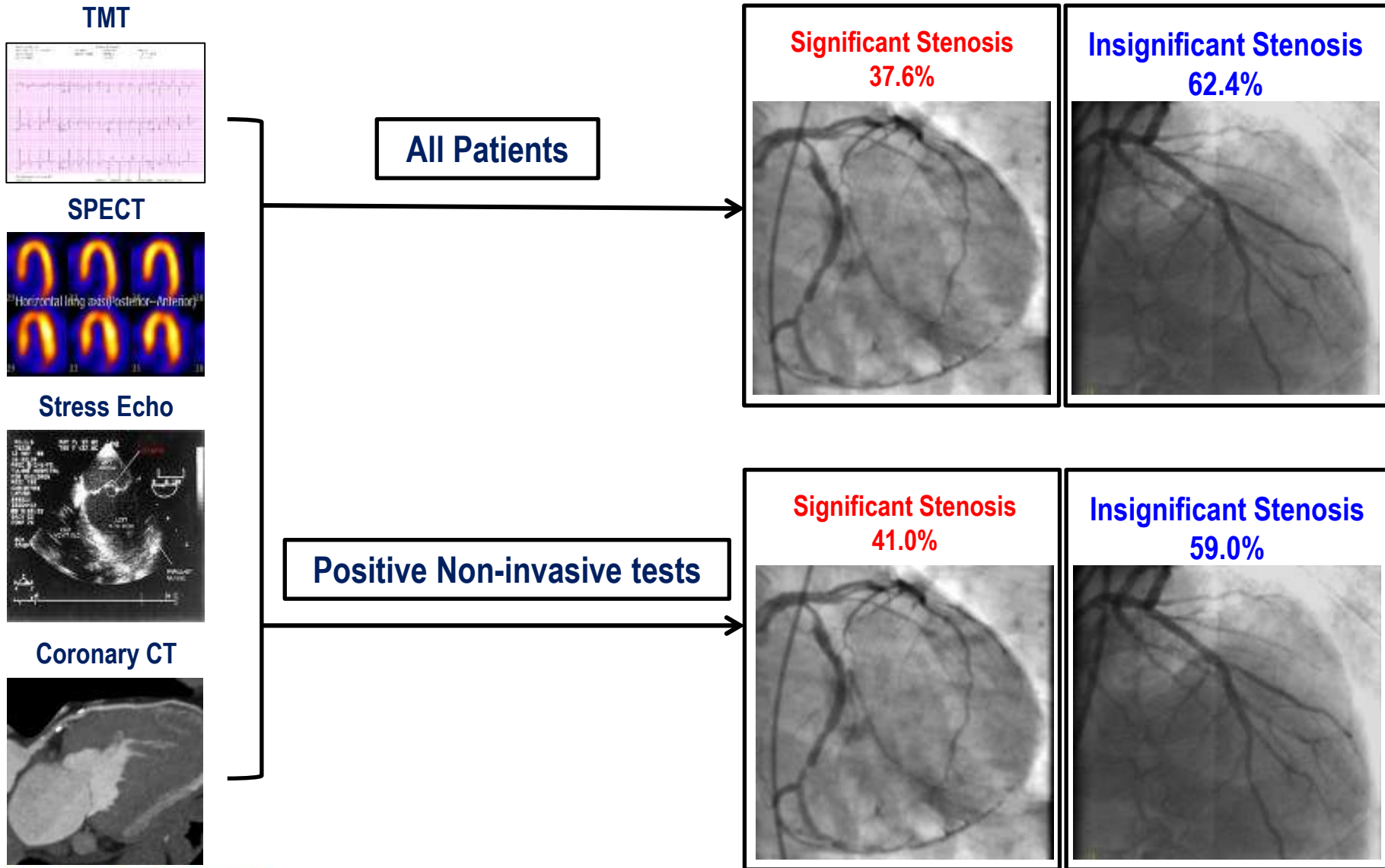


## Pooled Analysis (N=12,360)



We already know that Myocardial Ischemia,  
Is one of the most important prognostic Indicators,  
**Regardless of Patients Symptom or Presence of Obstructive CAD**

# Non-Invasive Tests for Ischemic Heart Disease



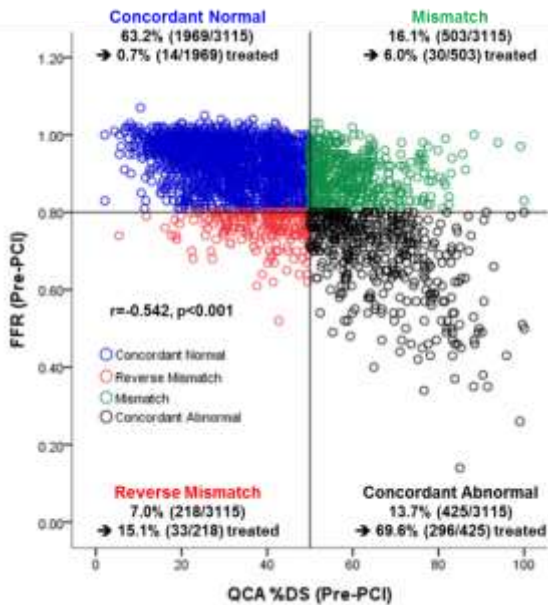
# FFR and QCA

## - Discordance Between Anatomy and Functional Significance -

Routine 3-Vessels FFR  
(Regardless of Stenosis Severity)

FFR as Clinical Indication  
(At least one Intermediate Stenosis)

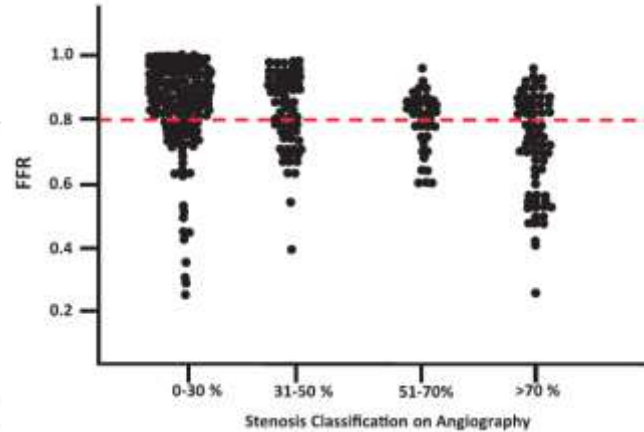
3V-FFR-FRIENDS Study



Among 3115 vessels  
Reverse Mismatch : 7.0%  
Mismatch : 16.1%

Total 23.1% Discordance

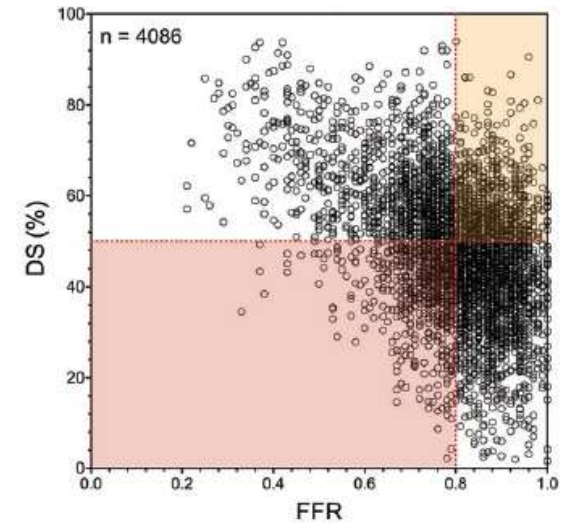
RIPCORD Trial



Among 569 vessels  
Reverse Mismatch : 13.1%  
Mismatch : 9.5%

Total 22.6% Discordance

Real-World Pooled Registry

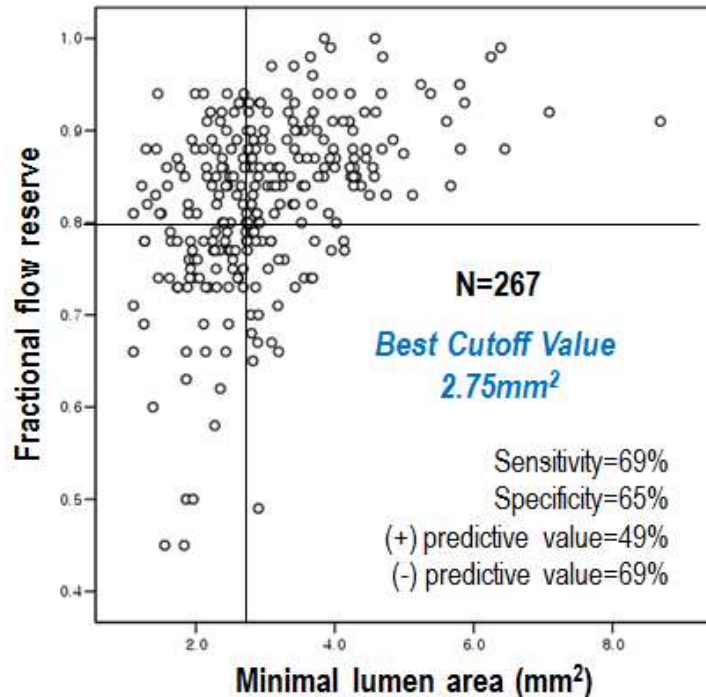


%DS > 50% to Predict  $FFR \leq 0.80$   
Sensitivity : 61.2%  
Specificity : 66.9%

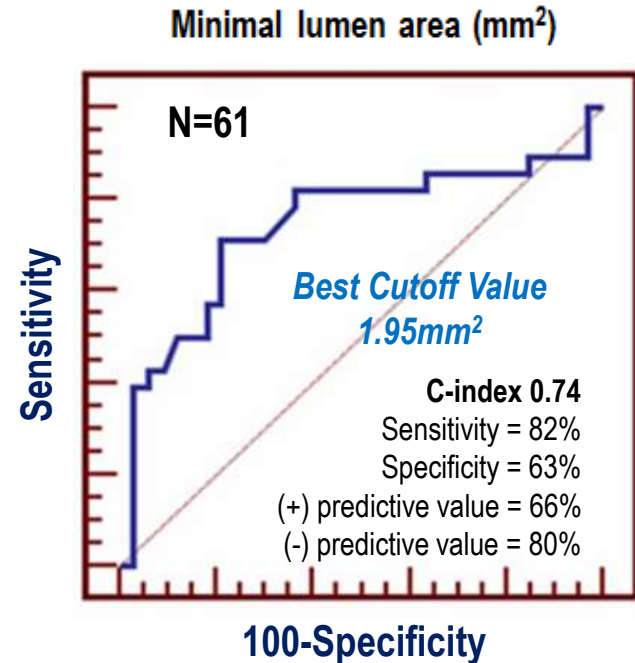
# FFR and Invasive Imaging

- Discordance Between Anatomy and Functional Significance -

IVUS



OCT

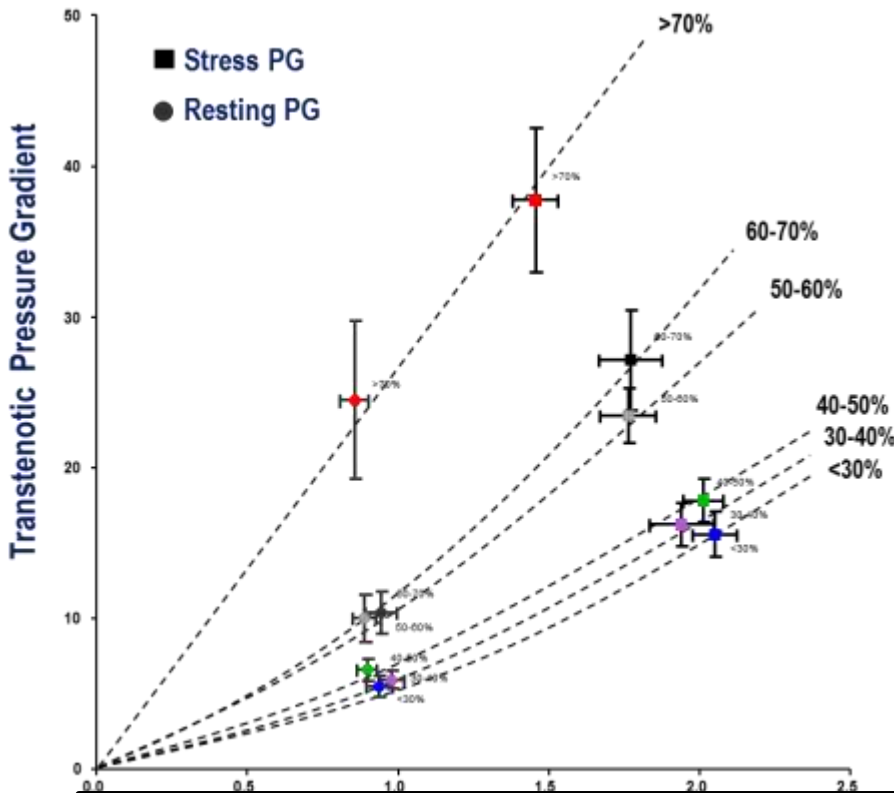


Discordance between stenosis severity and functional significance  
Is not a problem of “Accuracy in measuring stenosis severity”

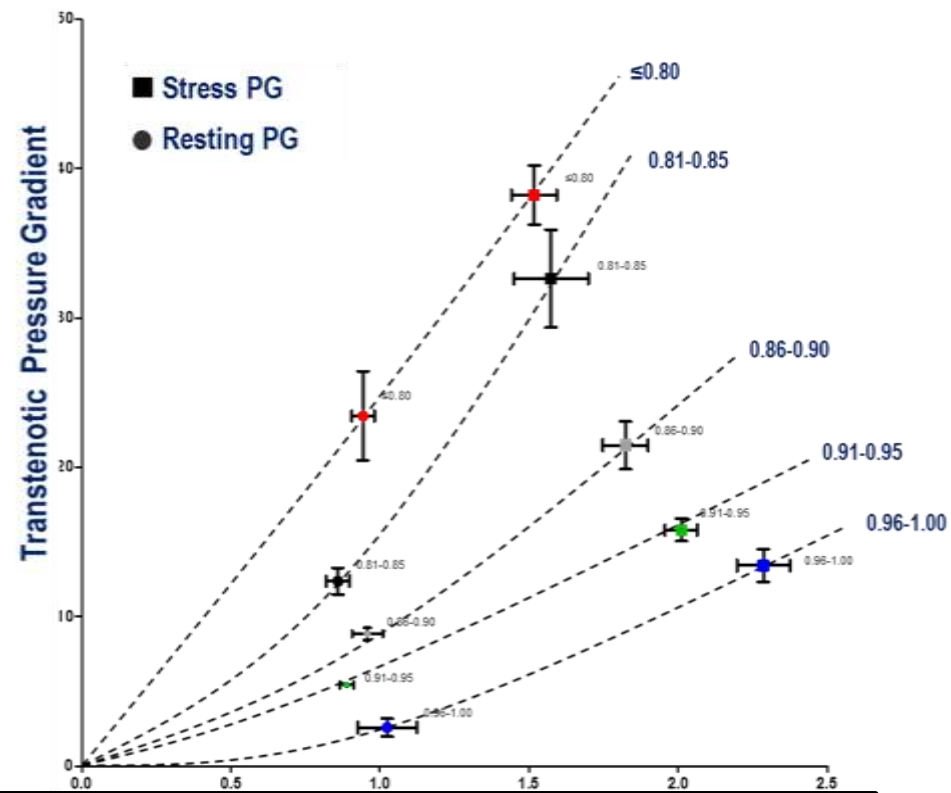
Functional significance cannot be predicted using stenosis severity.

# Physiologic Index is Better Marker of Stenosis Severity

## QCA Classification (%DS)



## iFR Classification



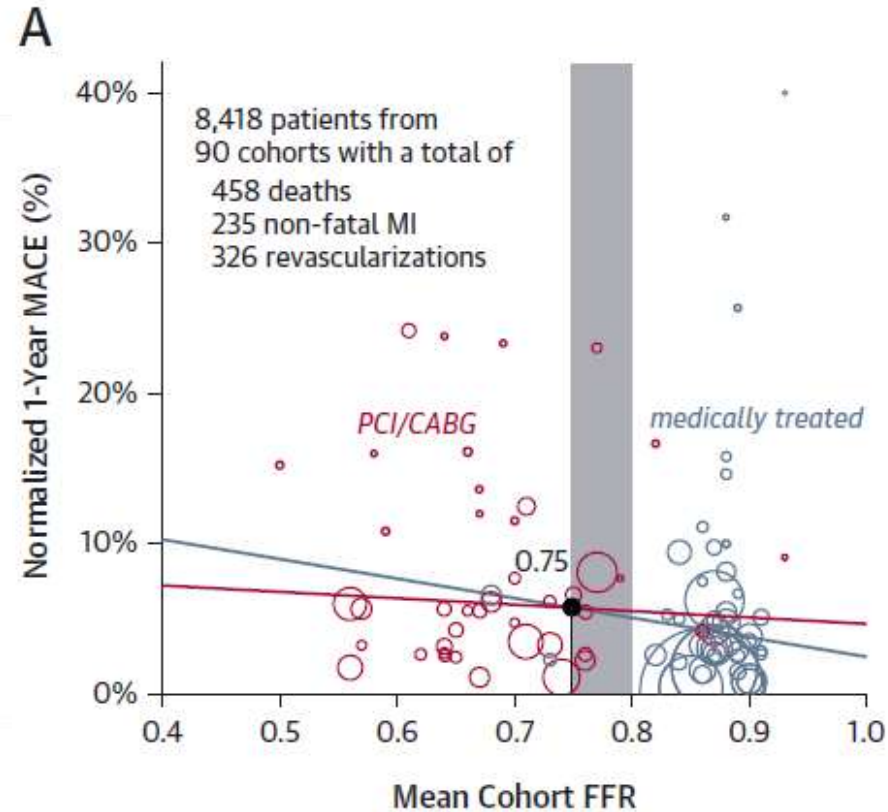
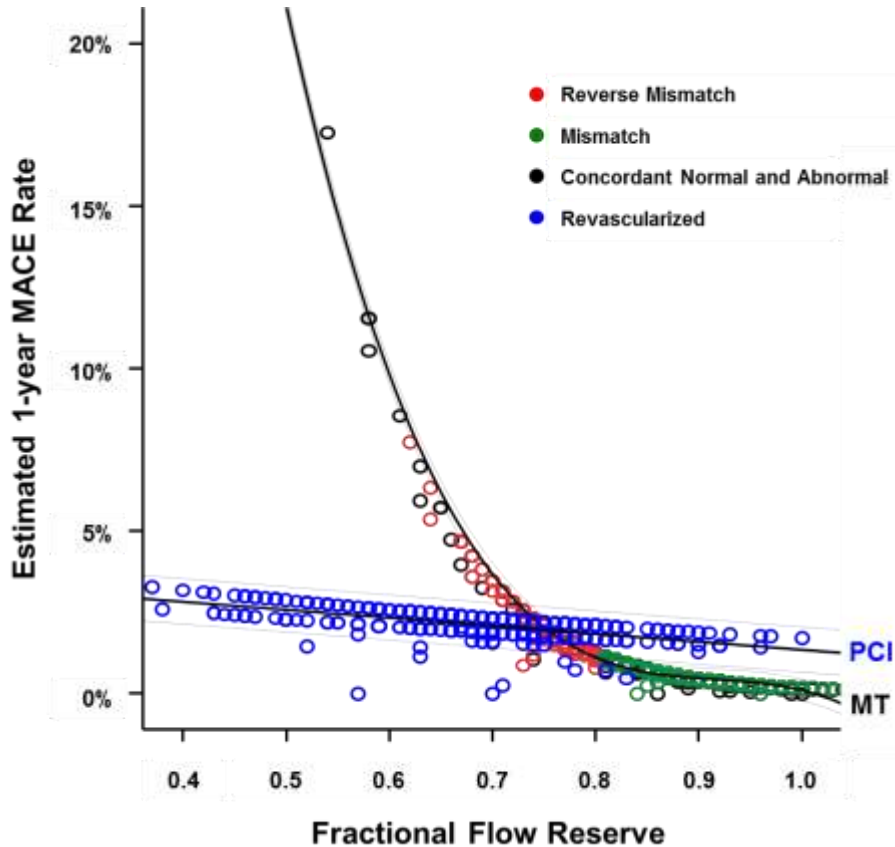
**Physiologic Index is a better marker of stenosis severity (anatomical and functional), than angiography itself.**

than by angiographic %DS.



# Cut-off Value of FFR

## - Validation using clinical outcome -



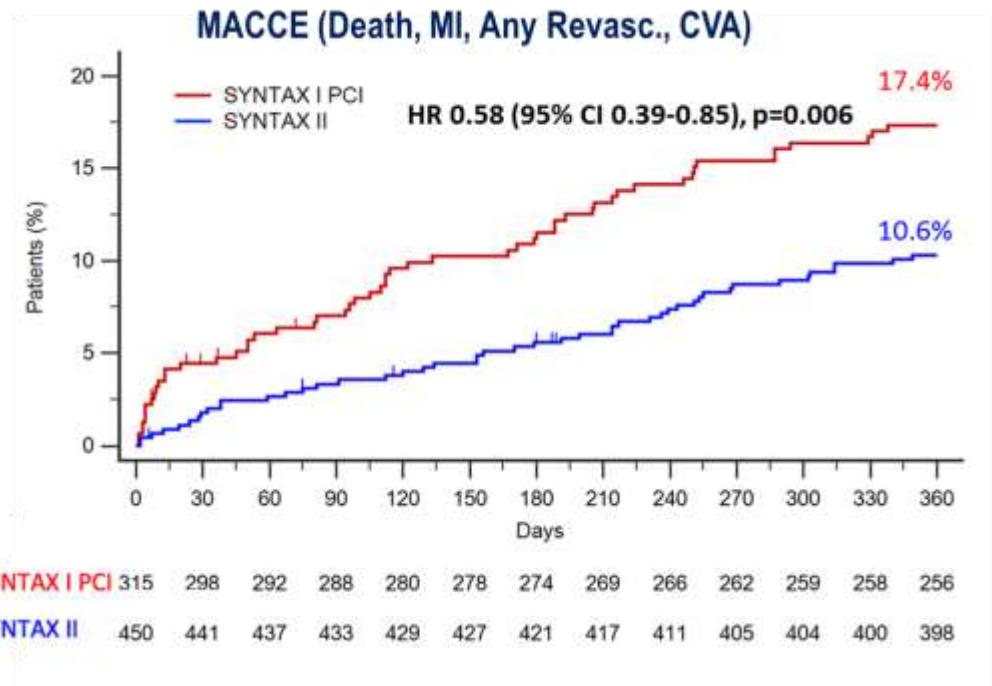
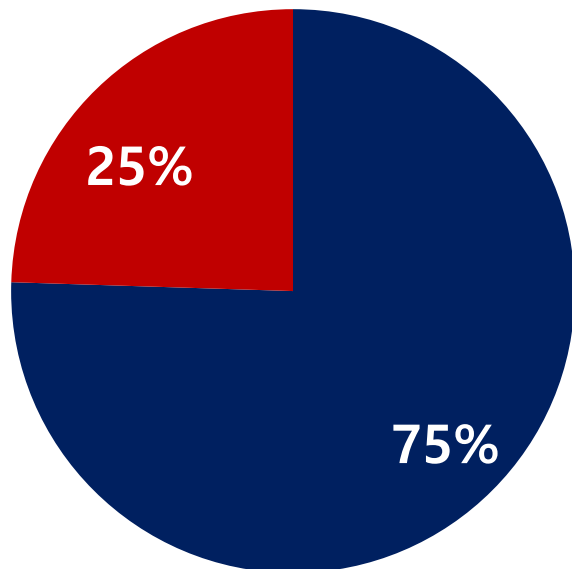
Lower the FFR value, Higher Benefit from PCI  
Higher the FFR value, Higher Benefit from Medical Treatment

# Physiology and Contemporary PCI Outcome - SYNTAX I vs. SYNTAX II PCI -

454 Patients with Complex Lesions and equipoise risk of 4-year mortality between PCI vs. CABG

## Physiology Guidance

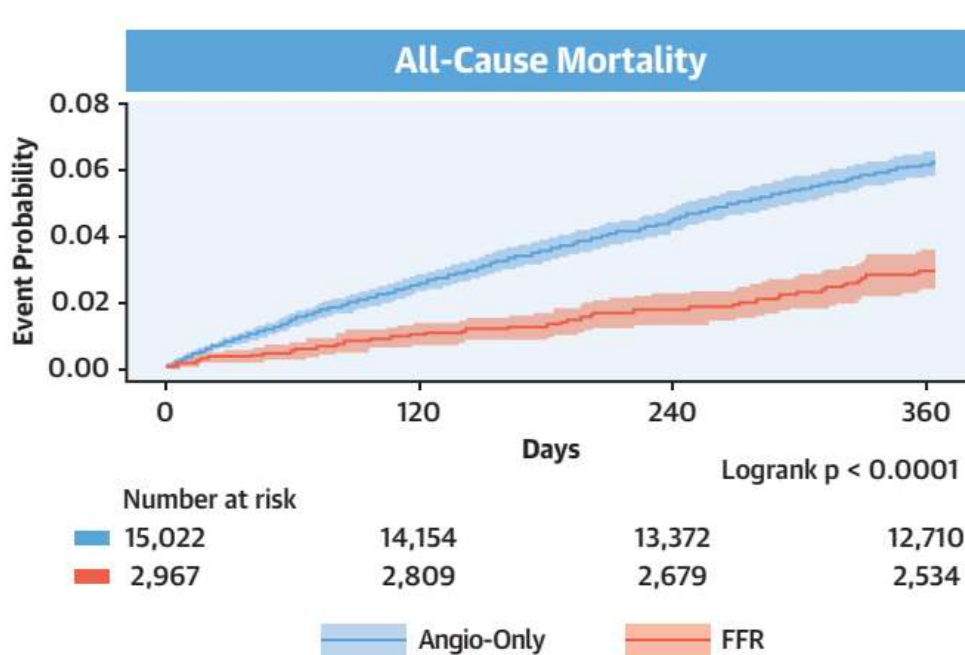
■ FFR/iFR Performed    ■ Not Performed



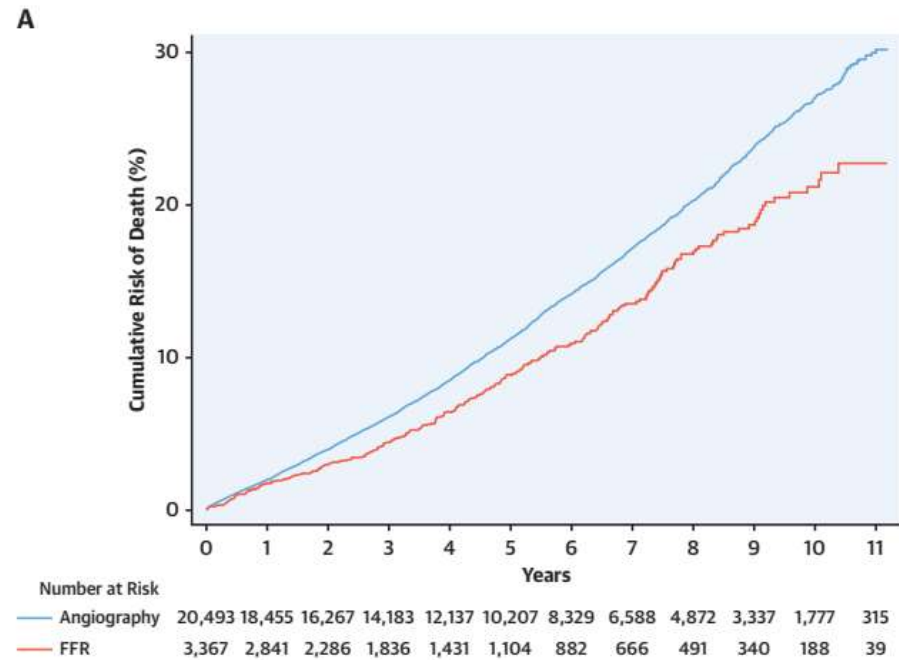


# Physiology and Contemporary PCI Outcome - Nationwide Cohort Studies -

## All-Cause Mortality FFR-Guided PCI versus Angiography-Only PCI

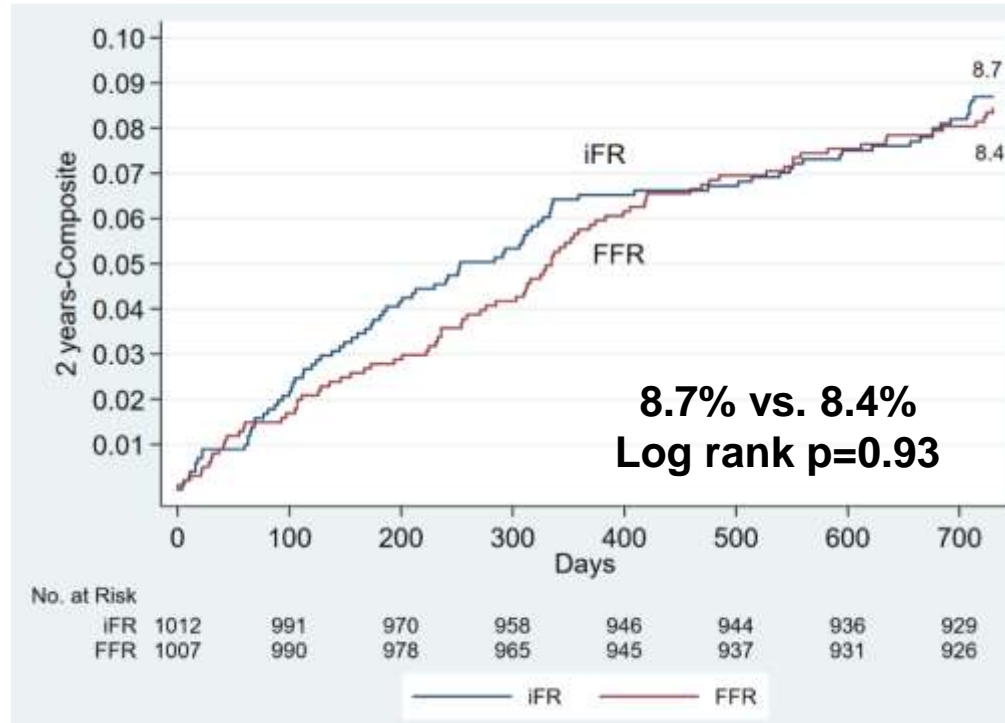
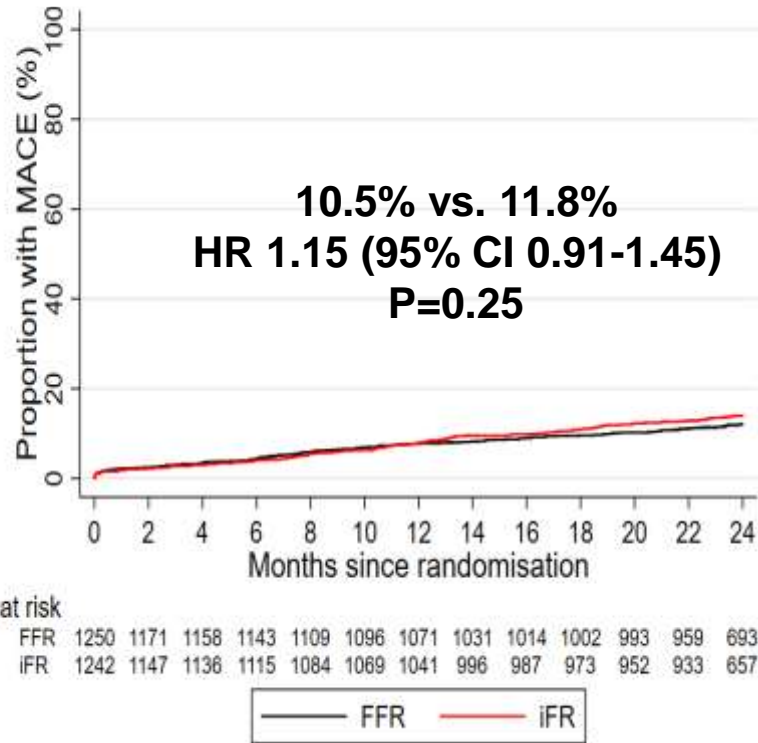


**Veterans Affairs registry 2009-2017**  
(Stable IHD N=17,989, 1 Year)



**SCAAR registry 2005-2016**  
(Stable IHD N=23,860, Median 4.7 Years)

# Non-Hyperemic Pressure Ratio (iFR) vs. FFR - 2 Year Clinical Outcome -



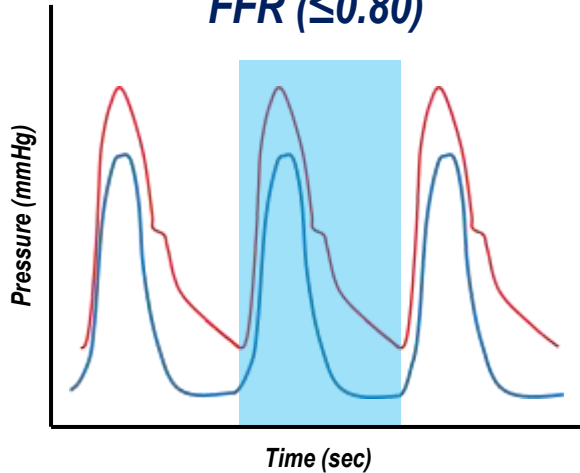
**DEFINE FLAIR**  
Defining the Impact of Non-Hyperemic Pressure Ratio (iFR) vs. Fractional Flow Reserve (FFR) in Percutaneous Coronary Intervention (PCI)



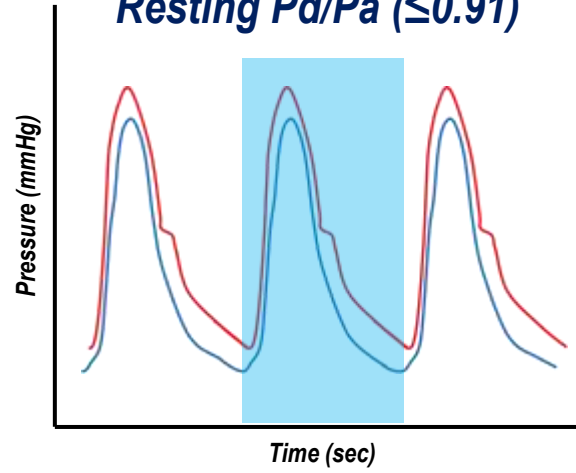
**2-Year Absolute difference in MACE was 1% between iFR vs. FFR  
With significantly lower rates of PCI in iFR group**

# Non-Hyperemic Pressure Ratios (NHPRs) Since iFR

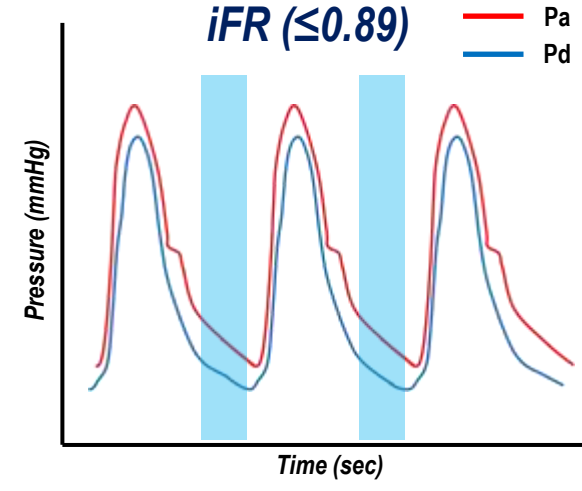
**FFR ( $\leq 0.80$ )**



**Resting Pd/Pa ( $\leq 0.91$ )**

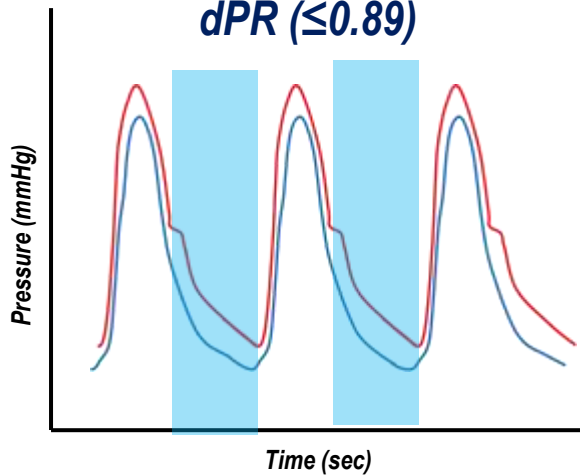


**iFR ( $\leq 0.89$ )**

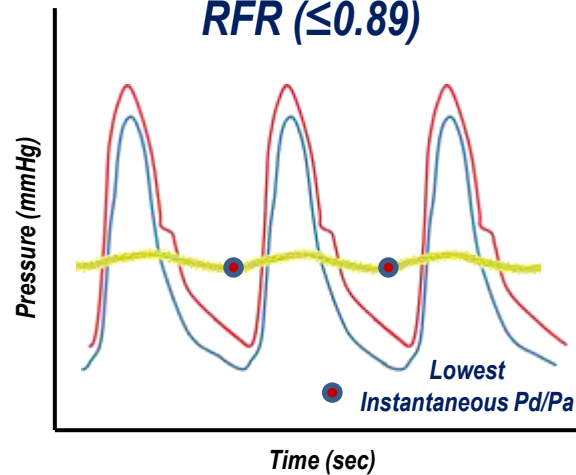


— Pa  
— Pd

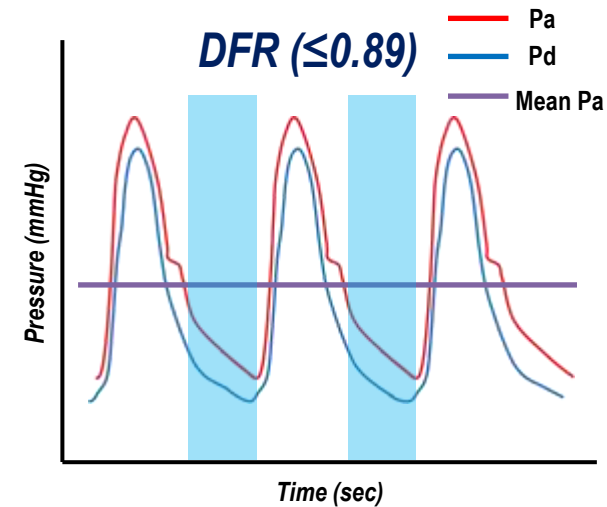
**dPR ( $\leq 0.89$ )**



**RFR ( $\leq 0.89$ )**



**DFR ( $\leq 0.89$ )**

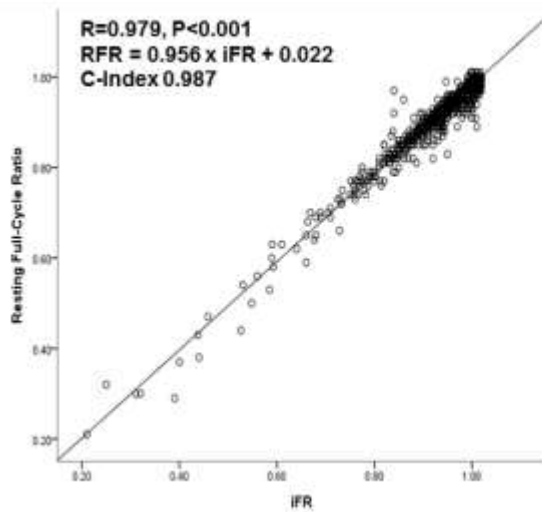


— Pa  
— Pd  
— Mean Pa

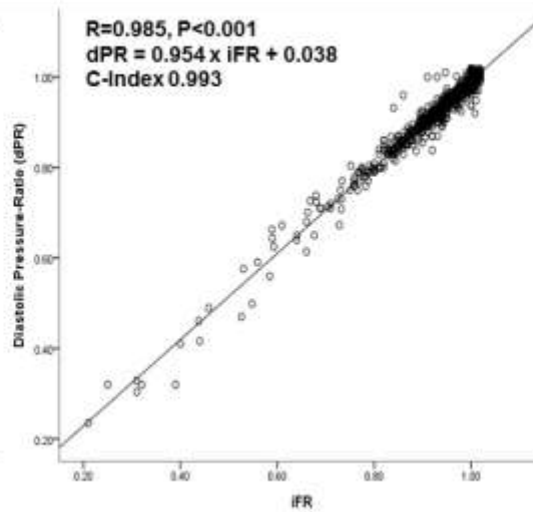
# All NHPRs share same correlation with iFR/FFR

## - 3V FFR FRIENDS registry -

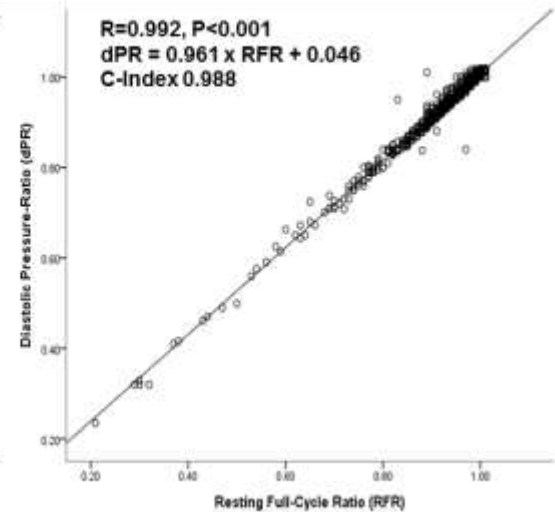
A. RFR - iFR



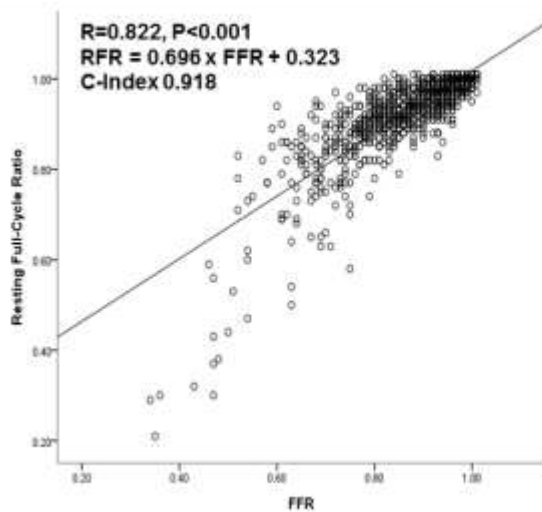
B. dPR - iFR



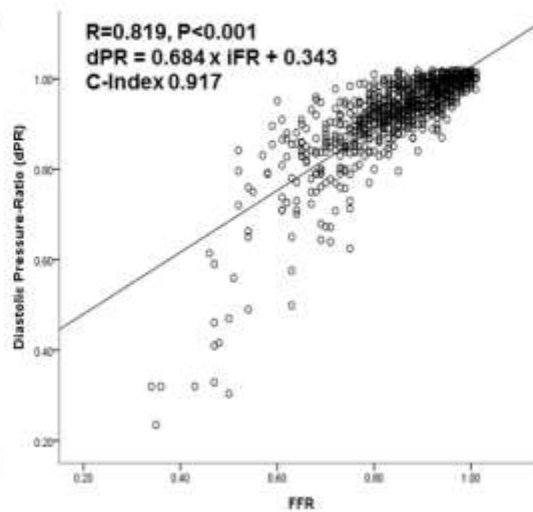
C. dPR - RFR



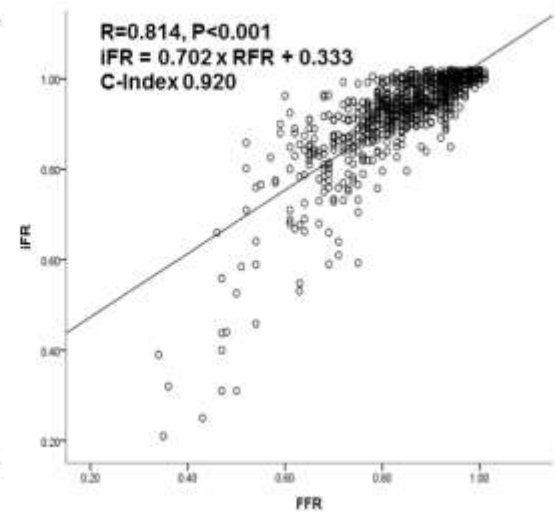
D. RFR - FFR



E. dPR - FFR



F. iFR - FFR

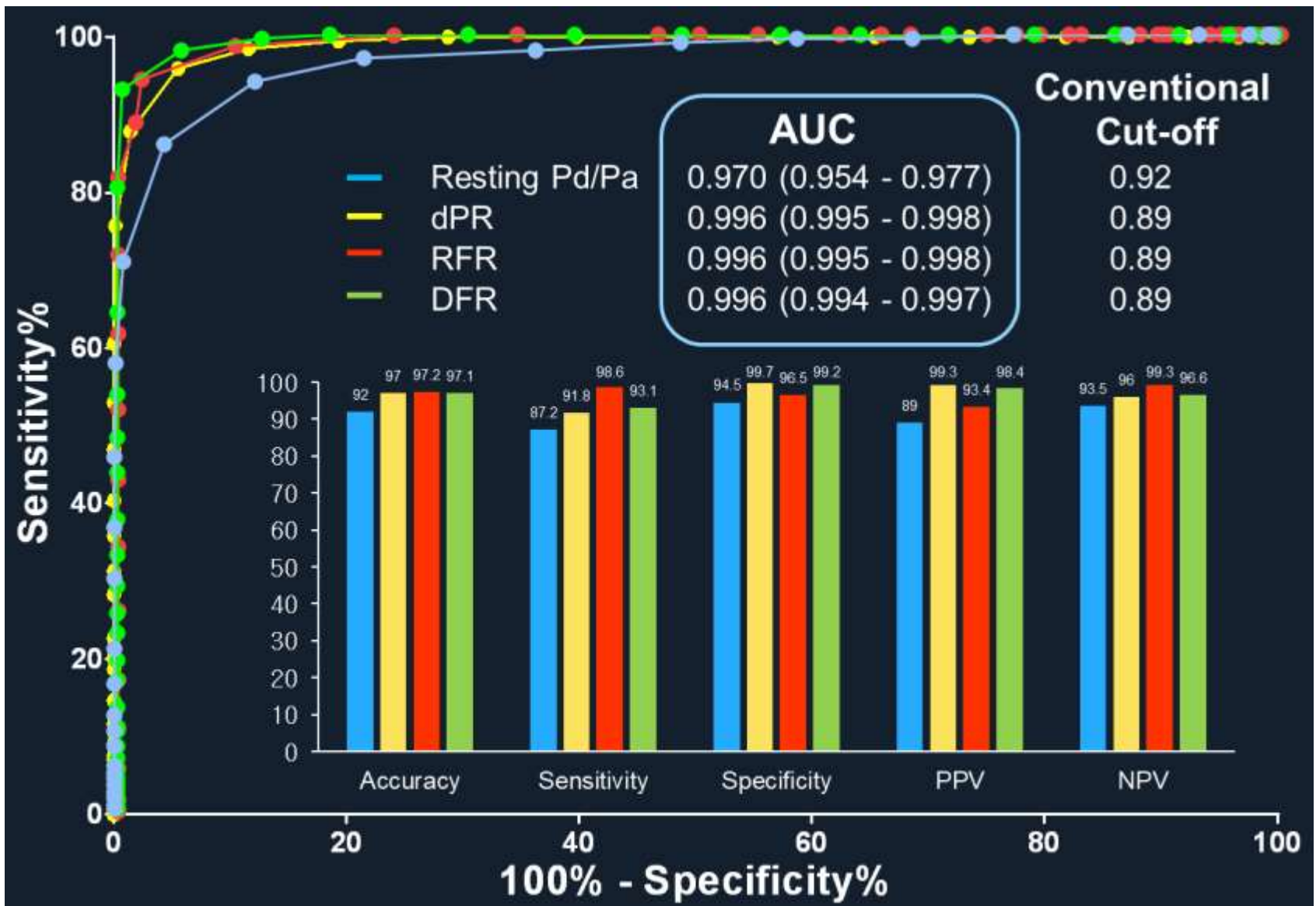


N=1,024 vessels (435 patients)

Lee JM, Koo BK, Circulation. 2019 Feb 12;139(7):889-900.

# All NHRs share same diagnostic accuracy for iFR $\leq 0.89$

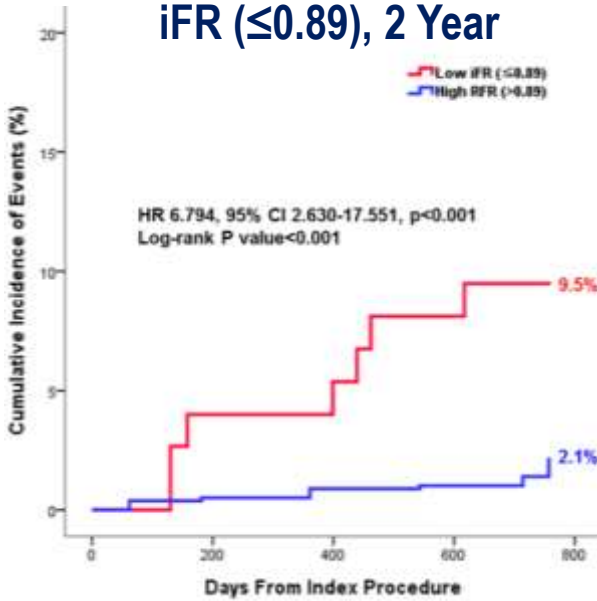
## - IRIS-FFR Registry -



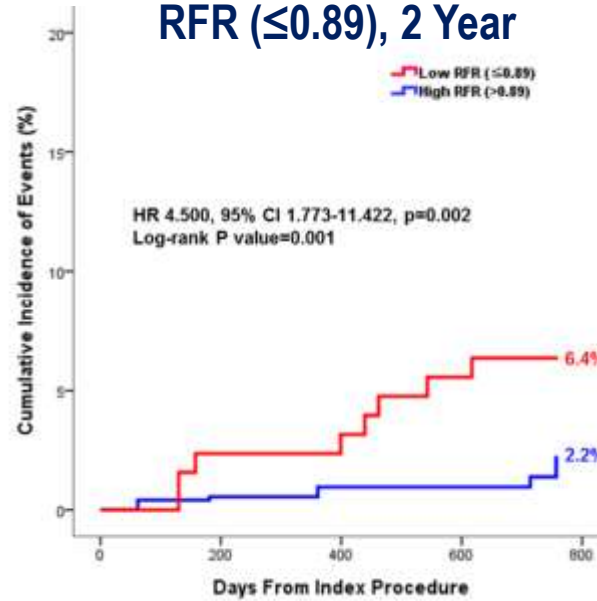


# All NHPRs share same cut-off value for prognosis of deferred lesions

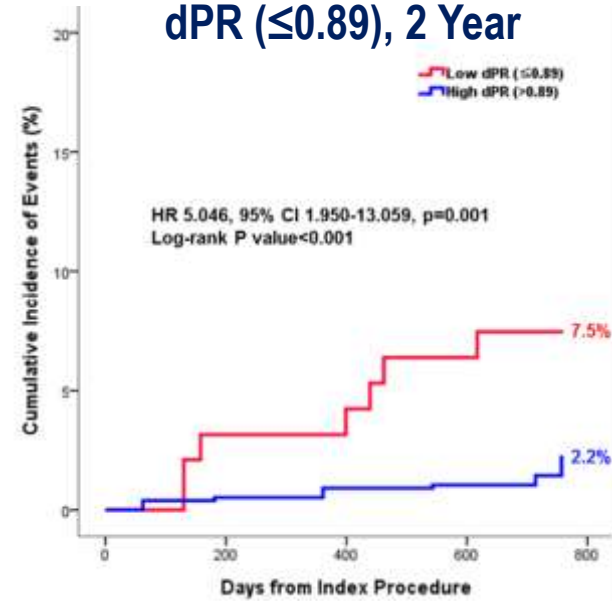
**iFR ( $\leq 0.89$ ), 2 Year**



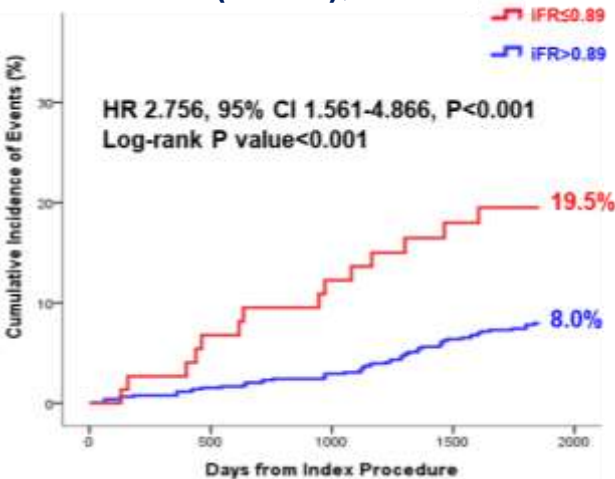
**RFR ( $\leq 0.89$ ), 2 Year**



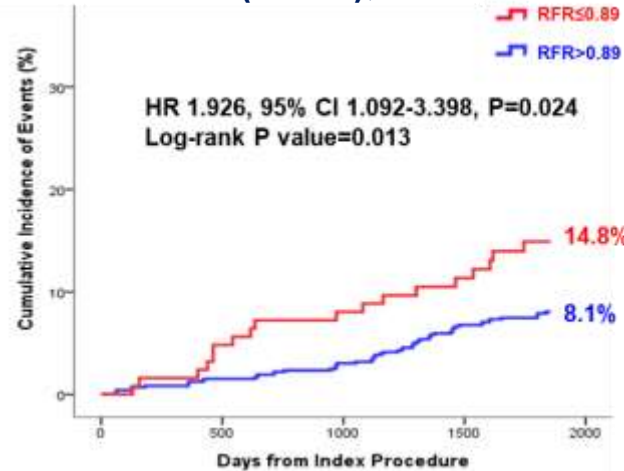
**dPR ( $\leq 0.89$ ), 2 Year**



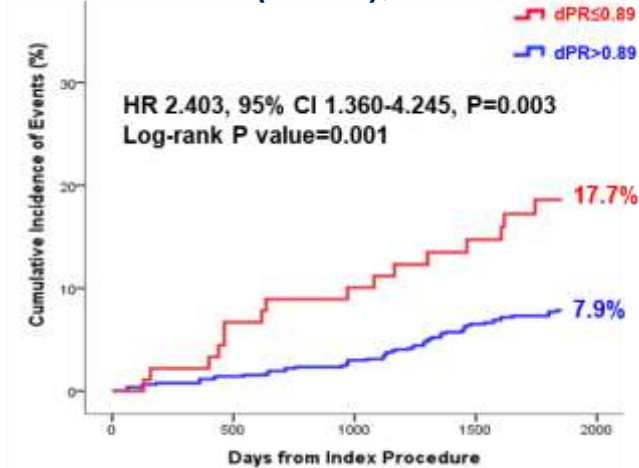
**iFR ( $\leq 0.89$ ), 5 Year**



**RFR ( $\leq 0.89$ ), 5 Year**



**dPR ( $\leq 0.89$ ), 5 Year**



N=864 deferred vessels

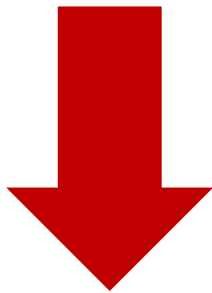


# Physiology-guided strategy

Benefit of **FFR/iFR-guided PCI strategy** for CAD has proved its benefit based on solid evidence

**FAME**

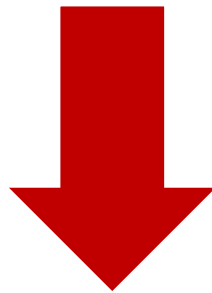
Death/MI  
At 2-Year



**35%**

**FAME**

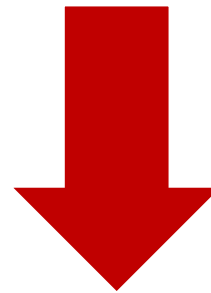
Cost  
At 1-Year



**\$ 2400**

**FAME 2**

Urgent RR  
In Stable CAD



**87%**

**DEFINE-FLAIR**  
**iFR-SWEDEHEART**  
**3V-FFR Registry**  
**IRIS-FFR Registry**

**FFR** ↔ **NHPRs**

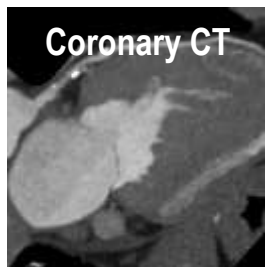
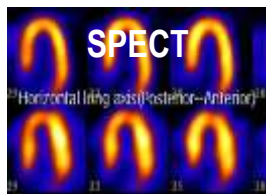
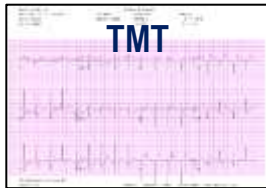
**Similar  
Outcome**

Pijls NH et al., J Am Coll Cardiol. 2010;56:177-184 / Van Nunen et al., Lancet 2015 Nov 7;386(10006):1853-60  
Fearon W. et al., Circulation 2010;122:2545-2550 / De Bruyne B, et al., N Engl J Med. 2014;371:1208-1217/  
N Engl J Med. 2017 May 11;376(19):1824-1834/ N Engl J Med. 2017 May 11;376(19):1813-1823.  
Lee JM et al. Circulation. 2019 Feb 12;139(7):889-900.

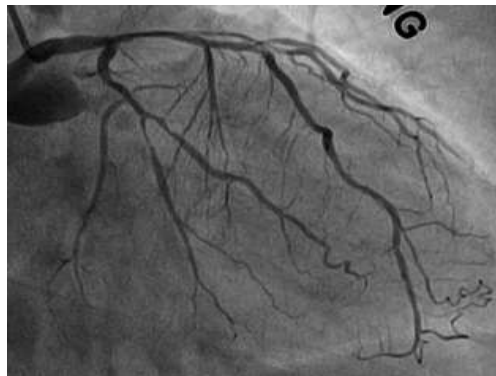
# Current Framework

Physician's clinical suspicion is changed based on angiographic stenosis

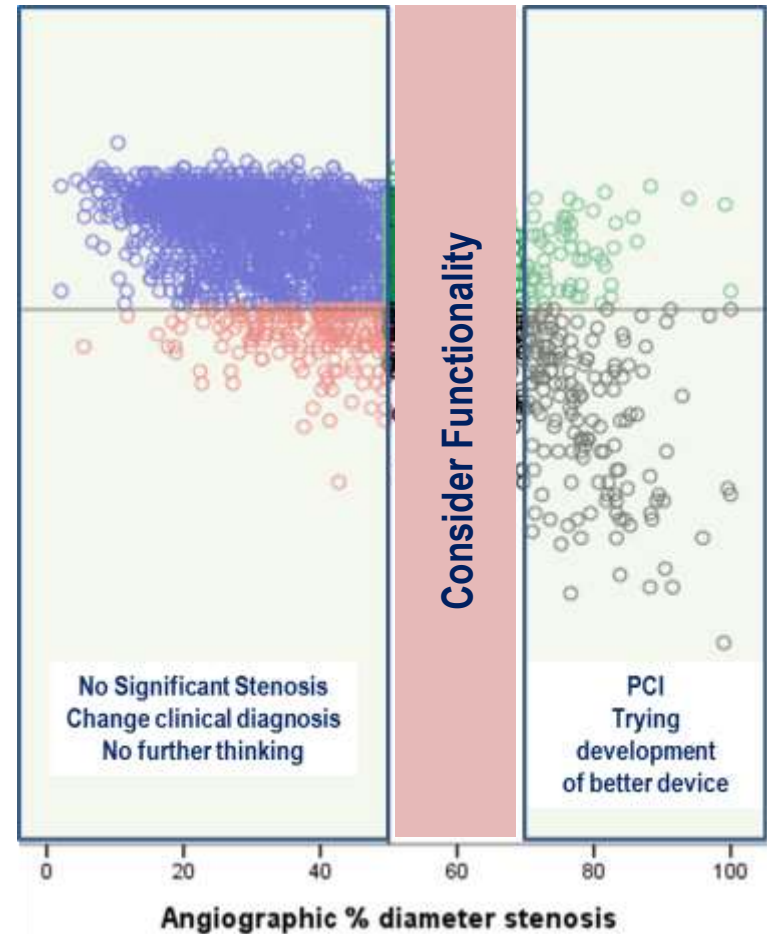
## Non-invasive Test



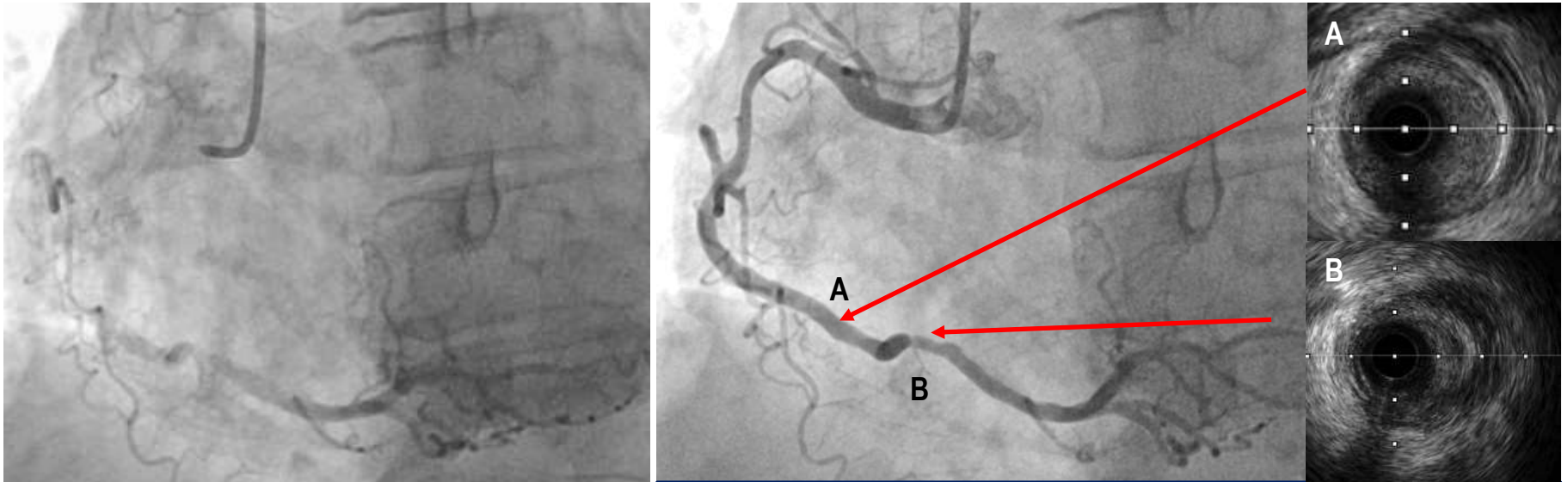
## CAG



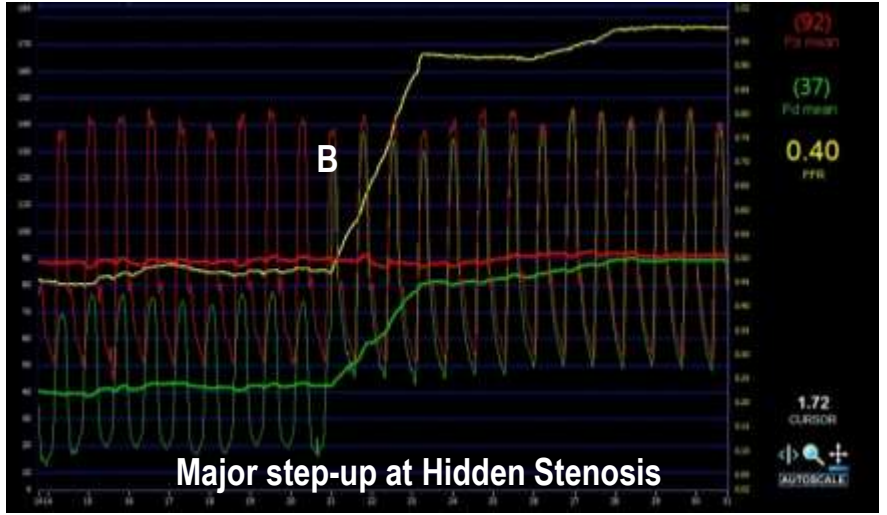
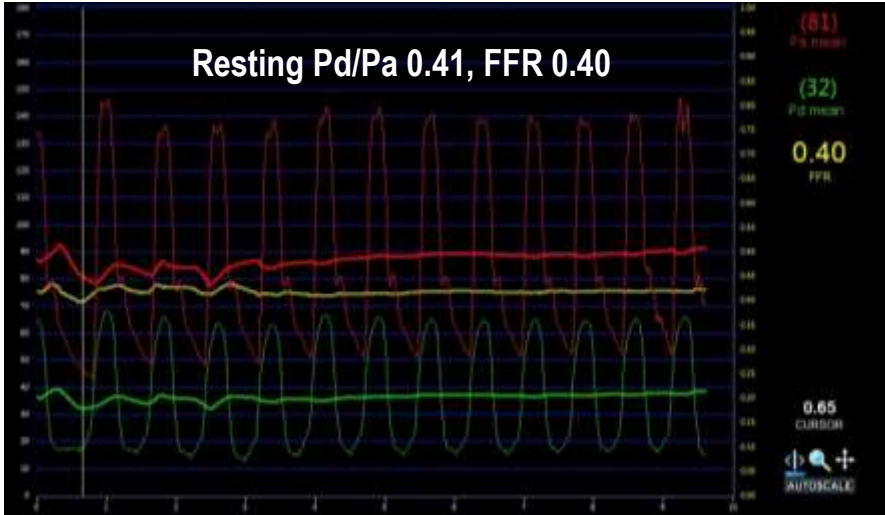
## All Decision Based on Anatomy



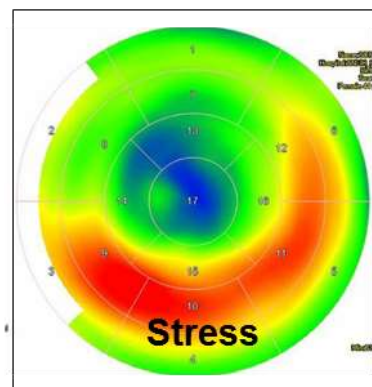
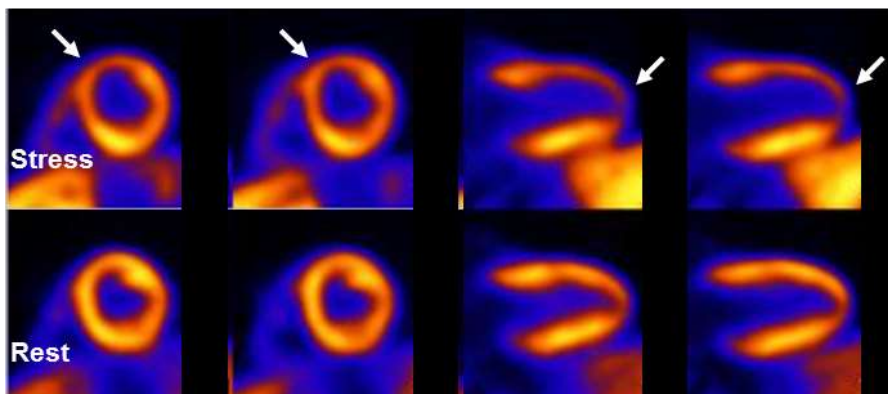
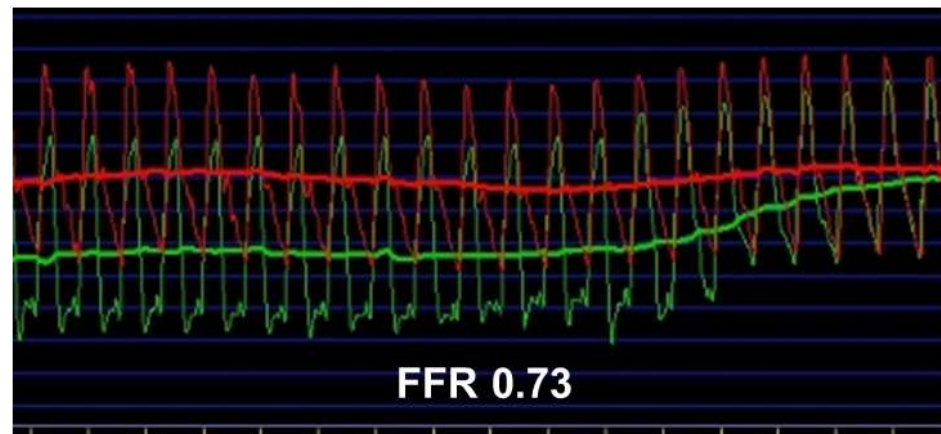
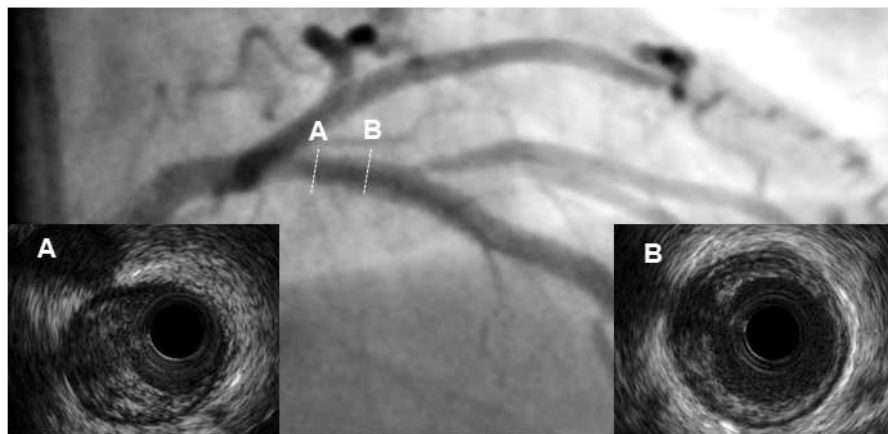
# Ischemic Heart Disease with Non-Obstructive CAD



Typical Chest Pain, Medically intractable (5 angina medications)



# Ischemic Heart Disease with Non-Obstructive CAD

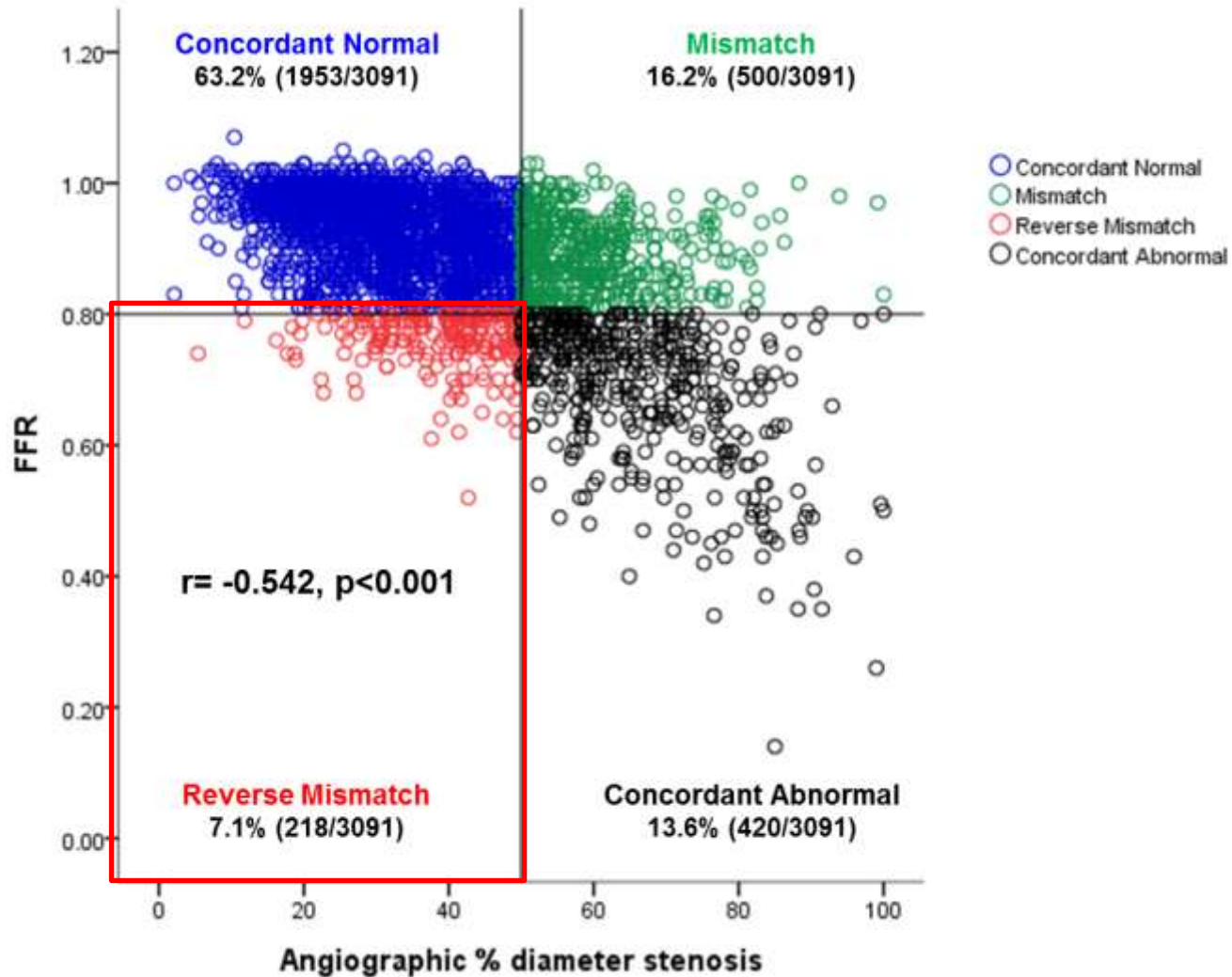


	Stress Flow (mL/g/min)	Rest Flow (mL/g/min)	CFR
LAD	1.69	1.03	1.64
LCX	2.21	1.05	2.09
RCA	2.27	1.08	2.11

**Hidden stenosis was the reason of myocardial ischemia.**

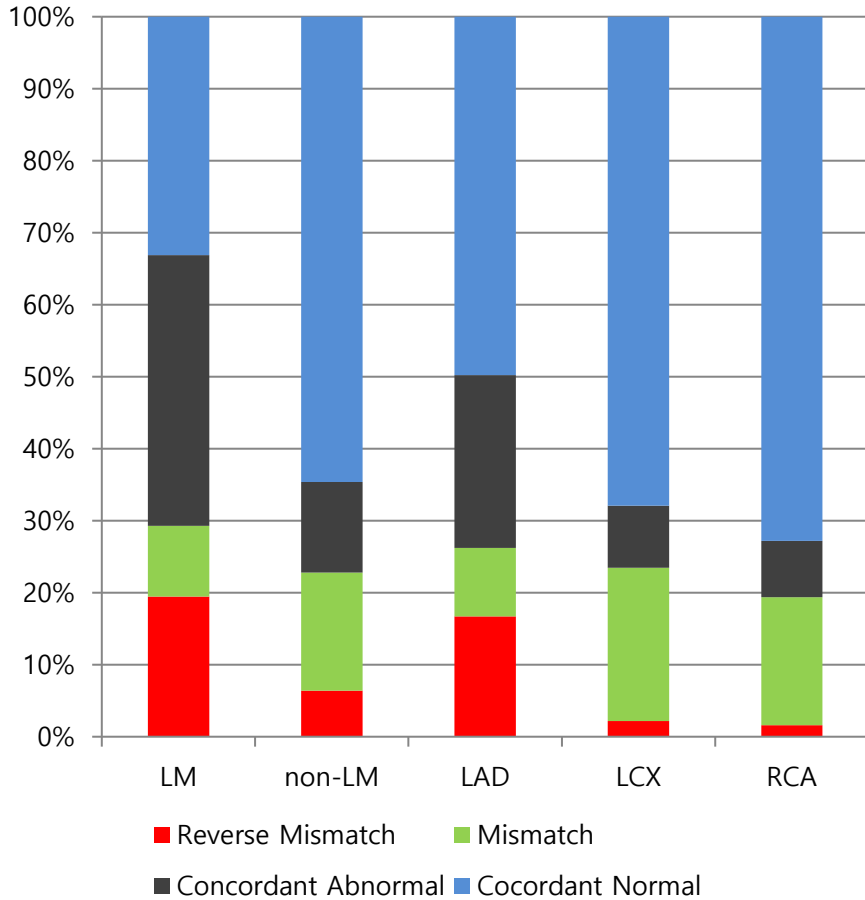


# FFR, only for intermediate stenosis ?

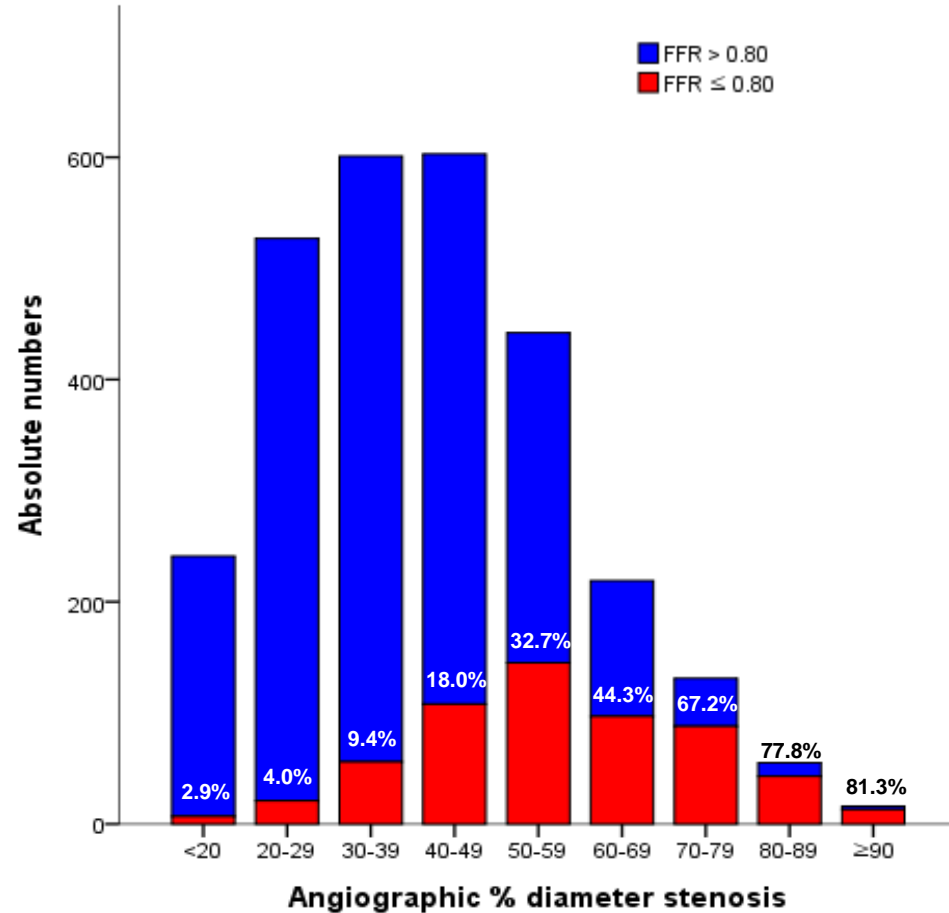


# Proportion of Lesions with Low FFR

**A**

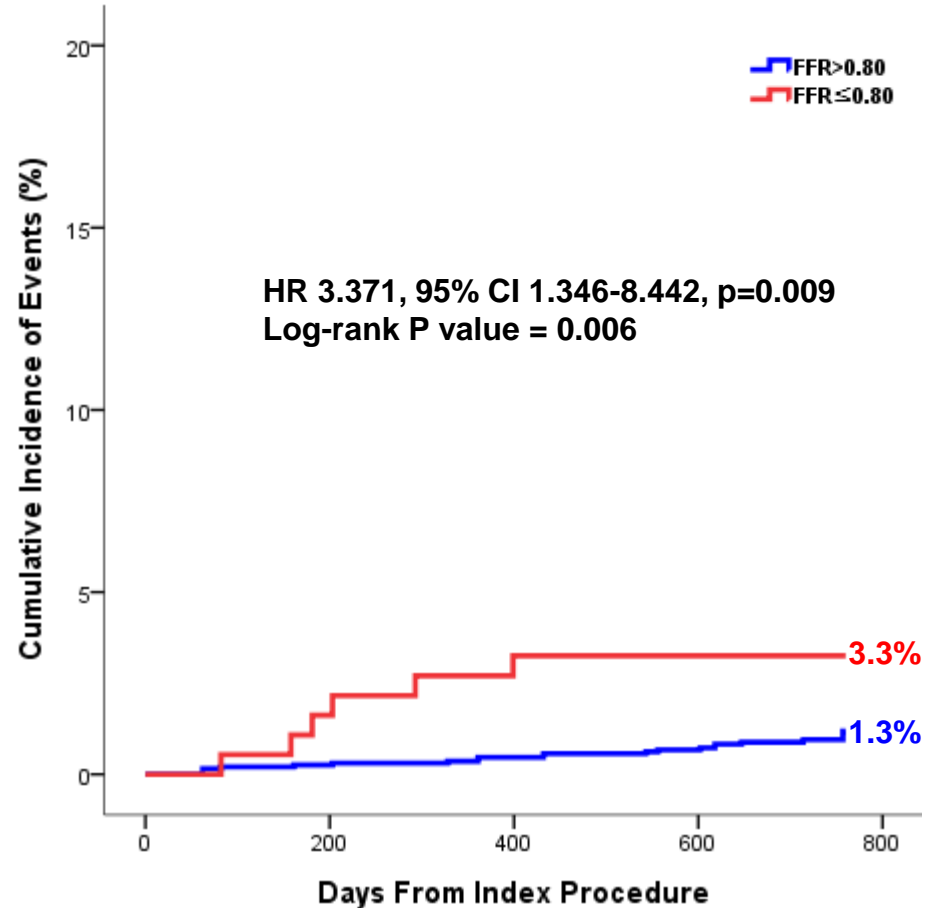
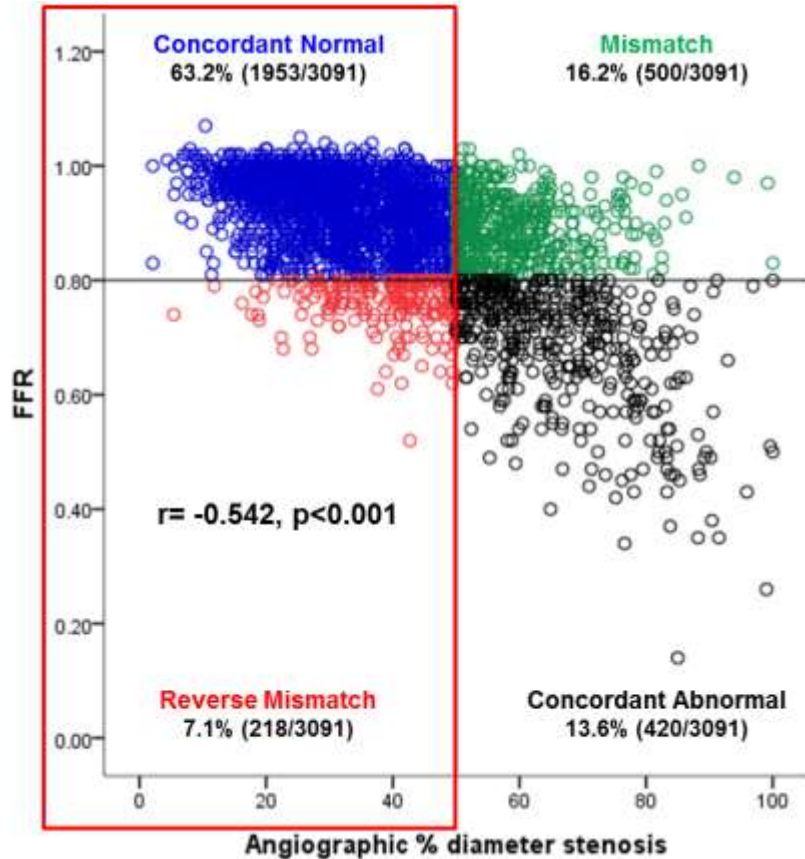


**B**





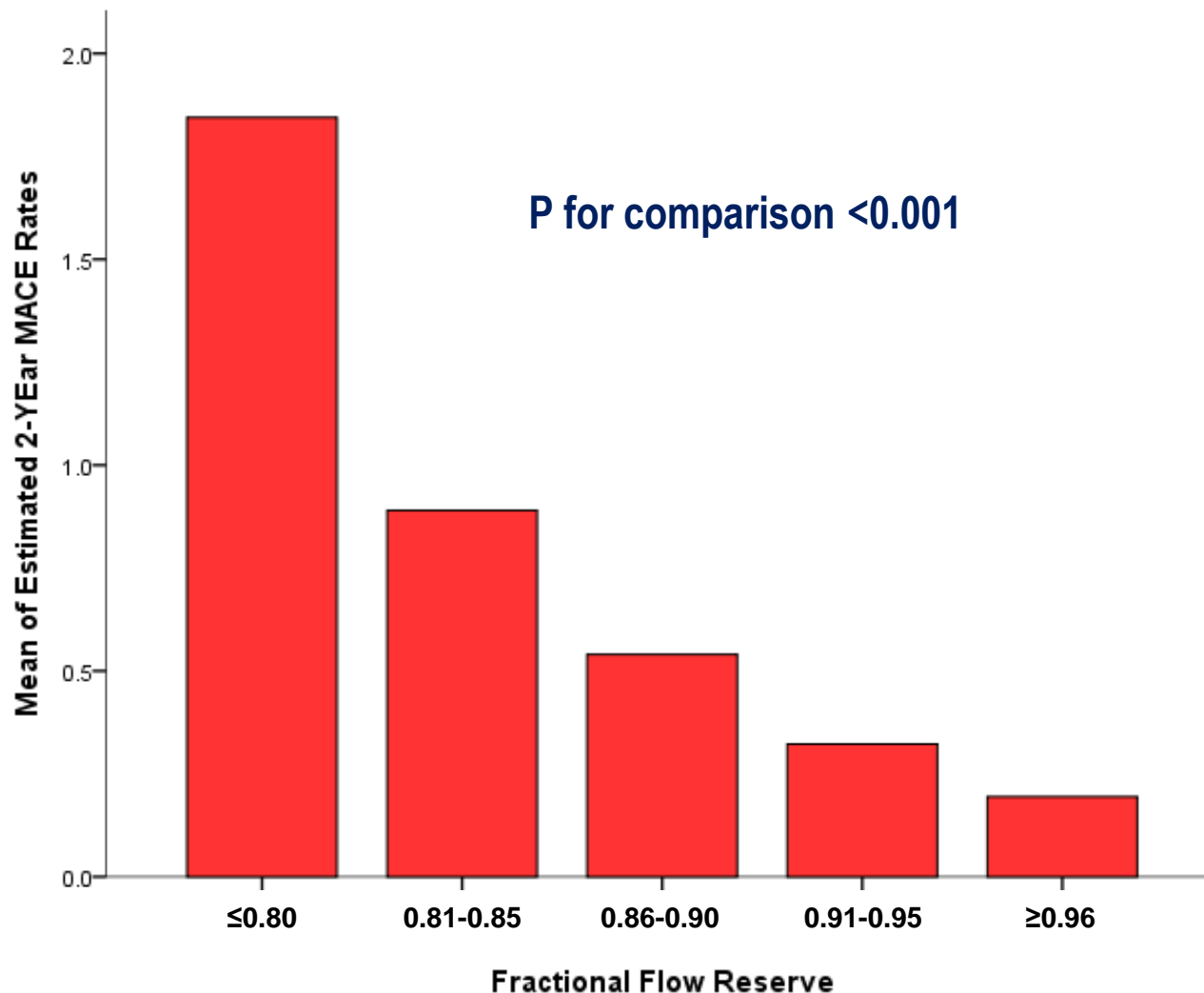
# Clinical Outcomes of Angiographically Insignificant Stenosis



No. at Risk

High FFR	1939	1931	1915	1911	1905
Low FFR	185	182	176	176	176

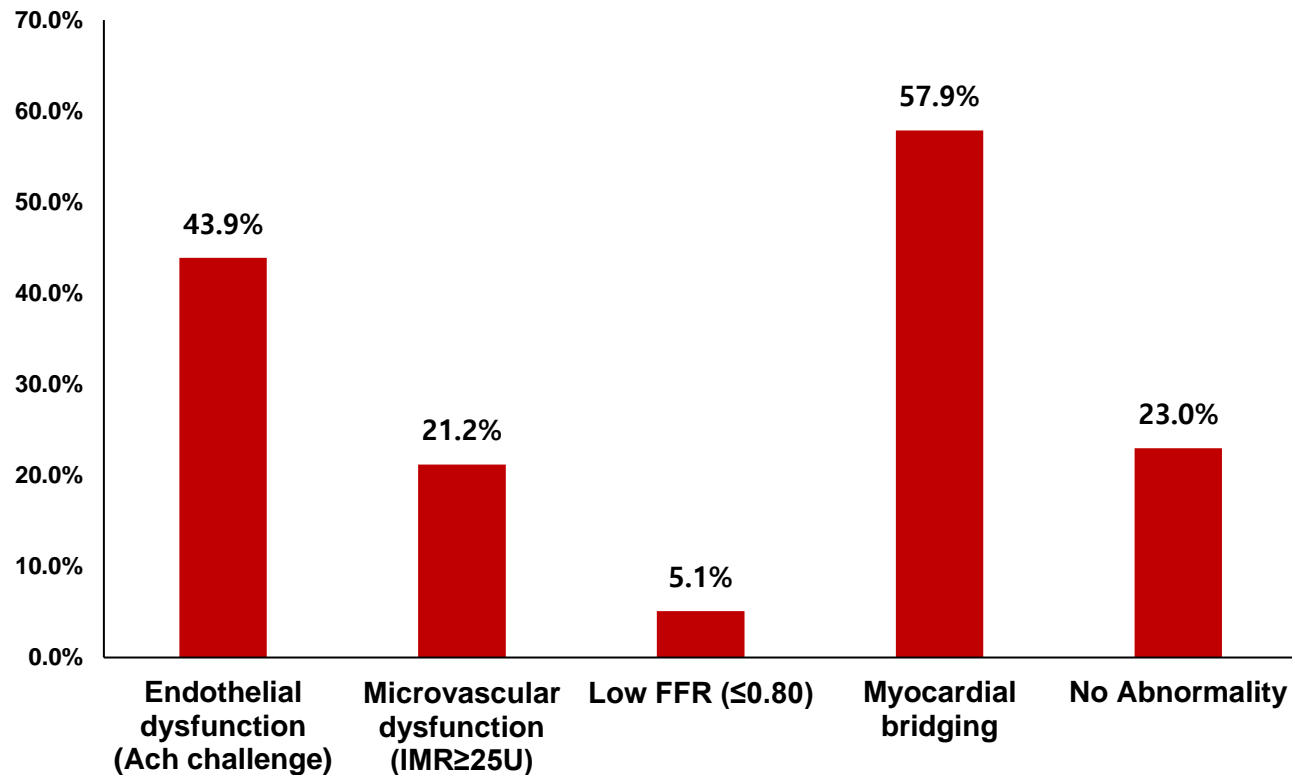
# Estimated MACE Rates according to FFR In Angiographically Insignificant Stenosis



# Evaluation of Microvascular Disease

## Why do we should look beyond epicardial coronary arteries?

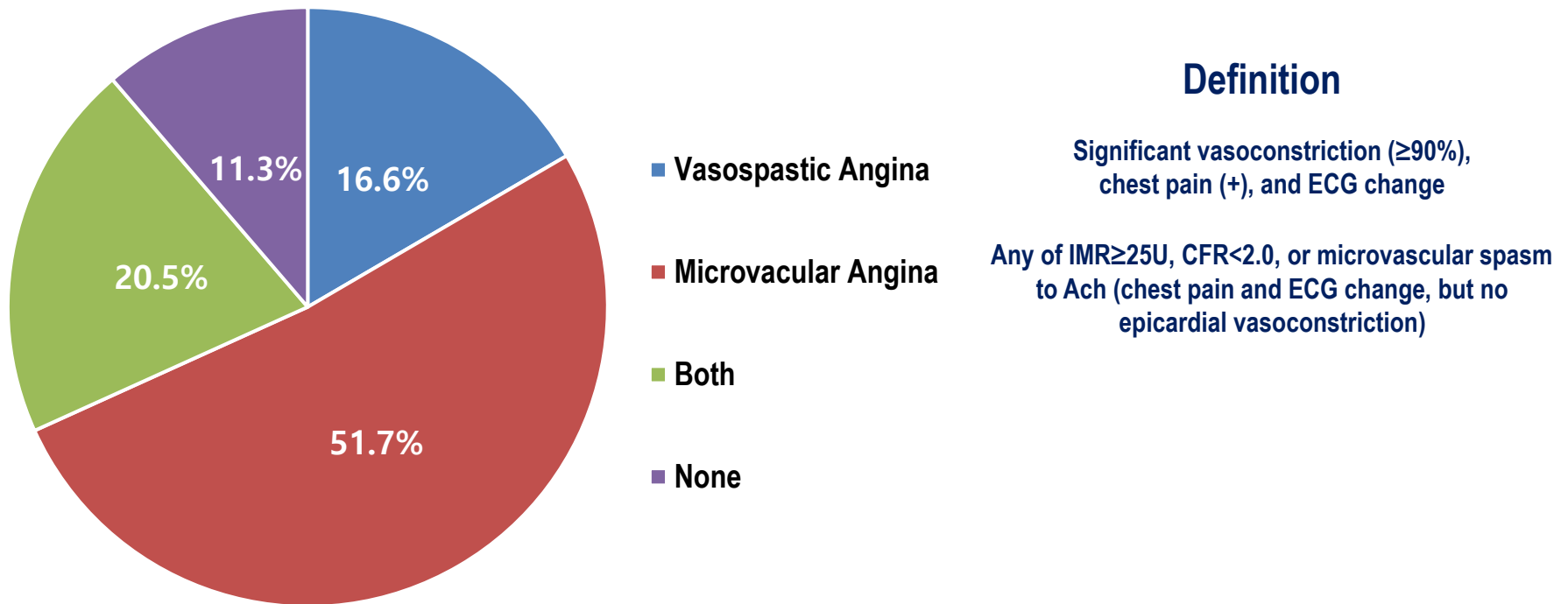
139 Stable Angina Patients (56% typical symptom) with <50% stenosis,  
Ach challenge test, FFR/CFR/IMR measurement, IVUS evaluation



# Why do we should look beyond epicardial coronary arteries?

## - Prevalence of non-epicardial coronary disease -

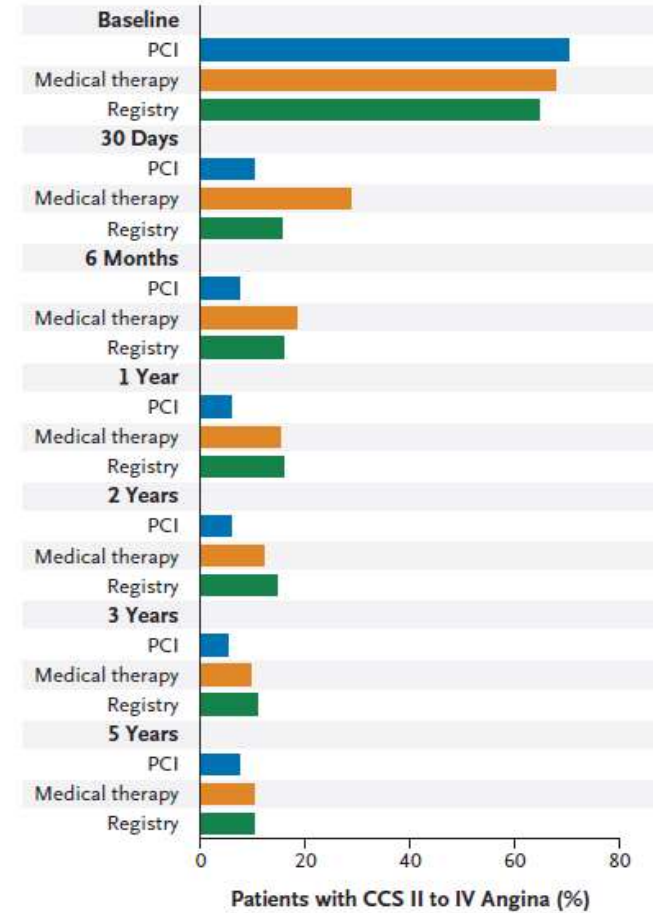
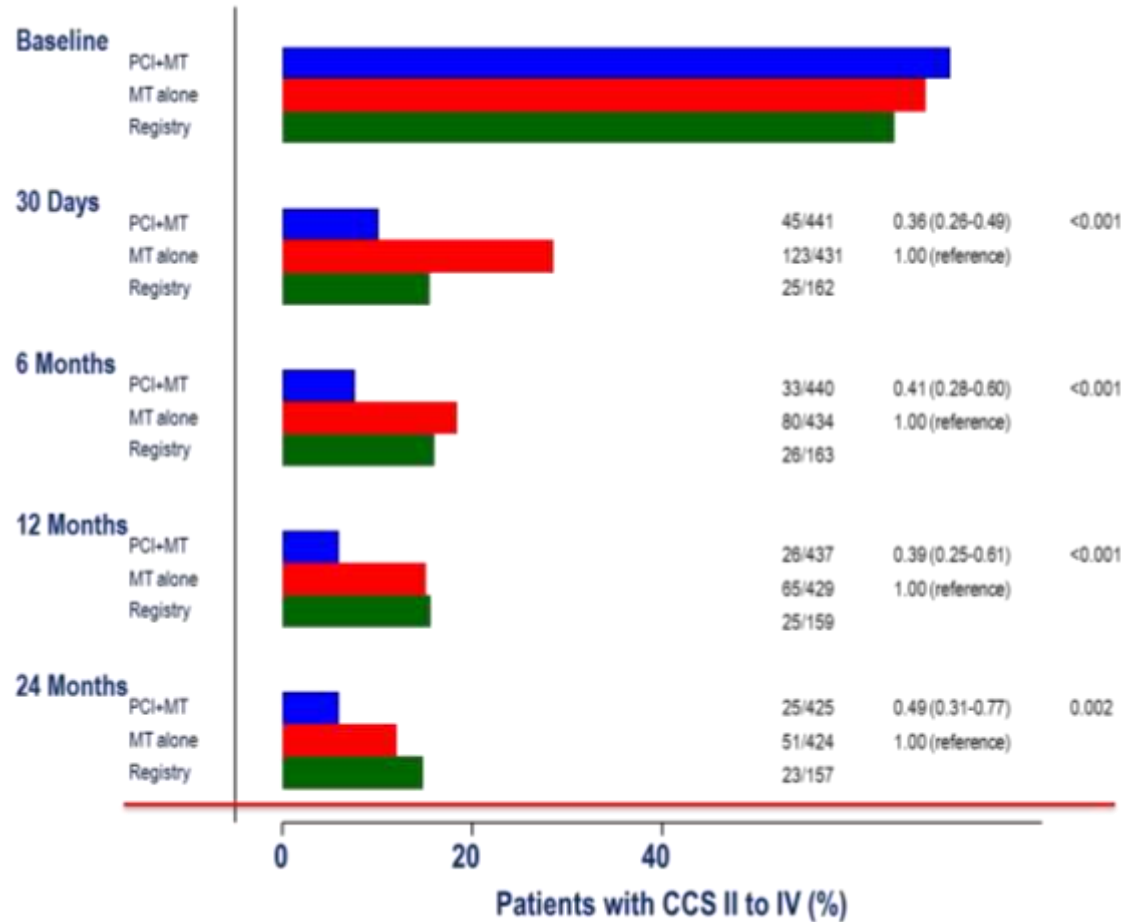
151 Stable Patients with  $<50\%$  stenosis and/or  $FFR > 0.80$ ,  
Ach challenge test and  $FFR/CFR/IMR$  measurement



**Substantial Proportion of Patients with No Obstructive Stenosis shows Abnormal Vasomotor / Microvascular Function**

# No significant epicardial coronary disease, No symptom?

## FAME 2: Registry Group (FFR>0.80)

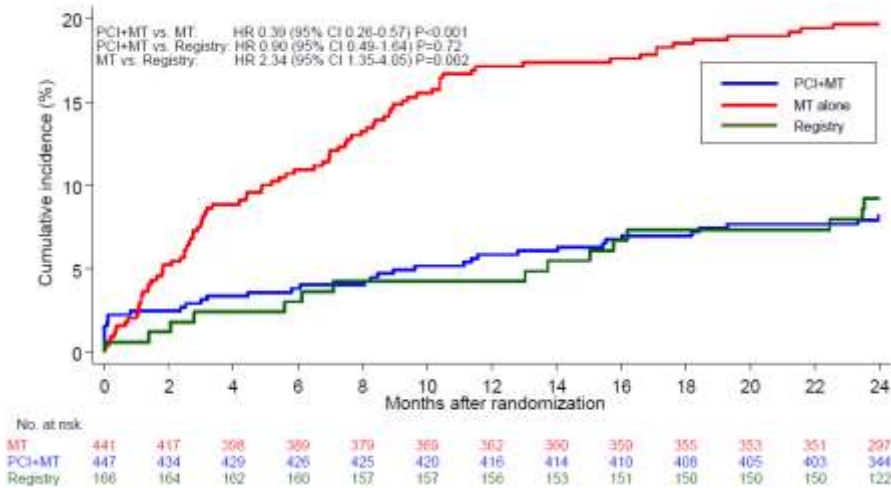


**Persistent Angina in Registry Group (FFR>0.80)**  
**14.6% (2Y), 10.9% (5Y)**

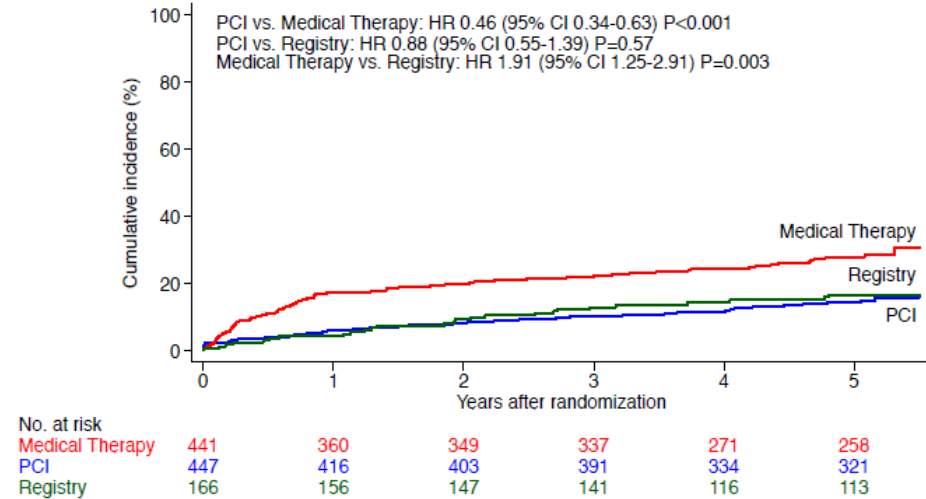
# No significant epicardial coronary disease, No event?

## FAME 2: Registry Group (FFR>0.80)

### Death, MI, Urgent Revasc at 2Y



### Death, MI, Urgent Revasc at 5Y



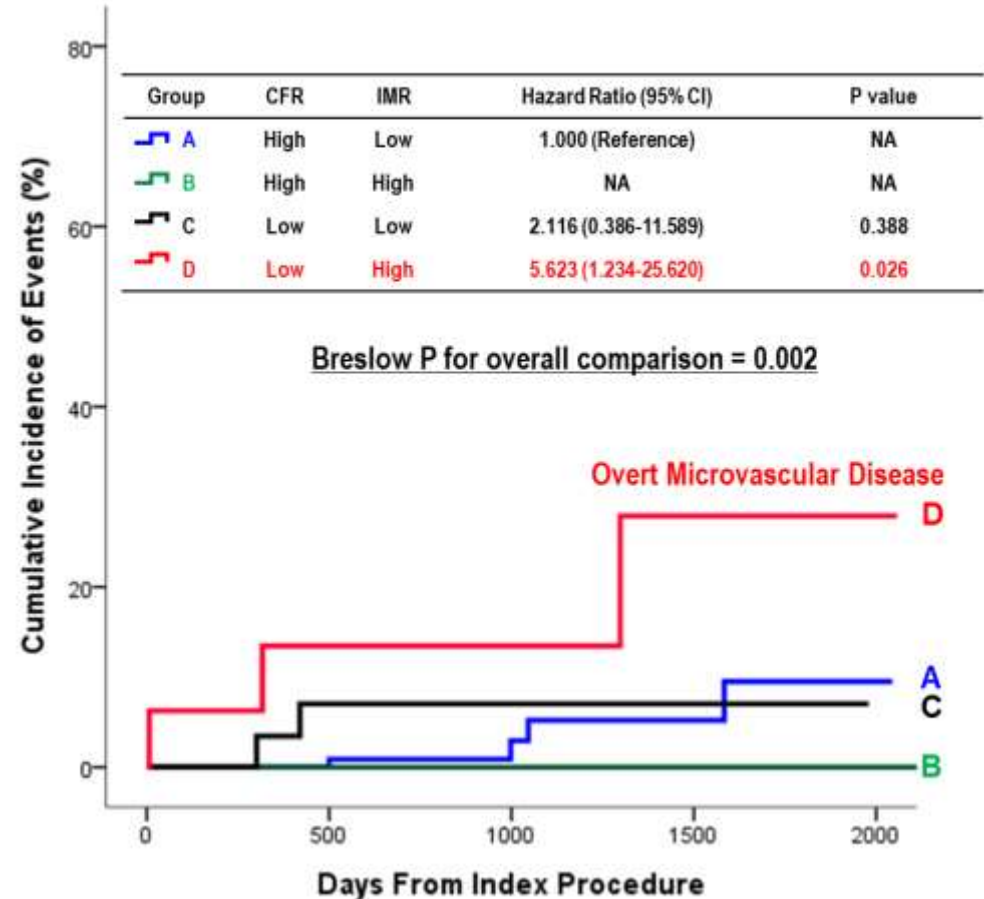
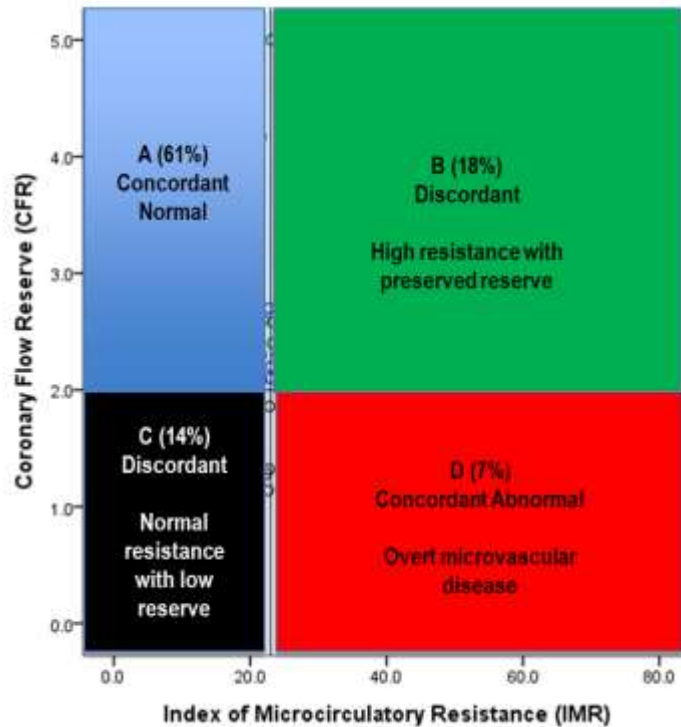
**Incidence of Primary Composite Endpoint in the Registry Group (FFR>0.80)**  
**9% (2Y), 15.7% (5Y)**



# Prognostic Impact of Microcirculatory Dysfunction

## - Defined by invasive physiologic indices -

230 Stable IHD Patients with FFR>0.80,  
Stratified by CFR ( $\leq 2.0$ ) and IMR( $\geq 23U$ ) measurement



POCO, Patient-oriented Composite Outcomes  
→ a Composite of any Death, any MI, and any Revascularization

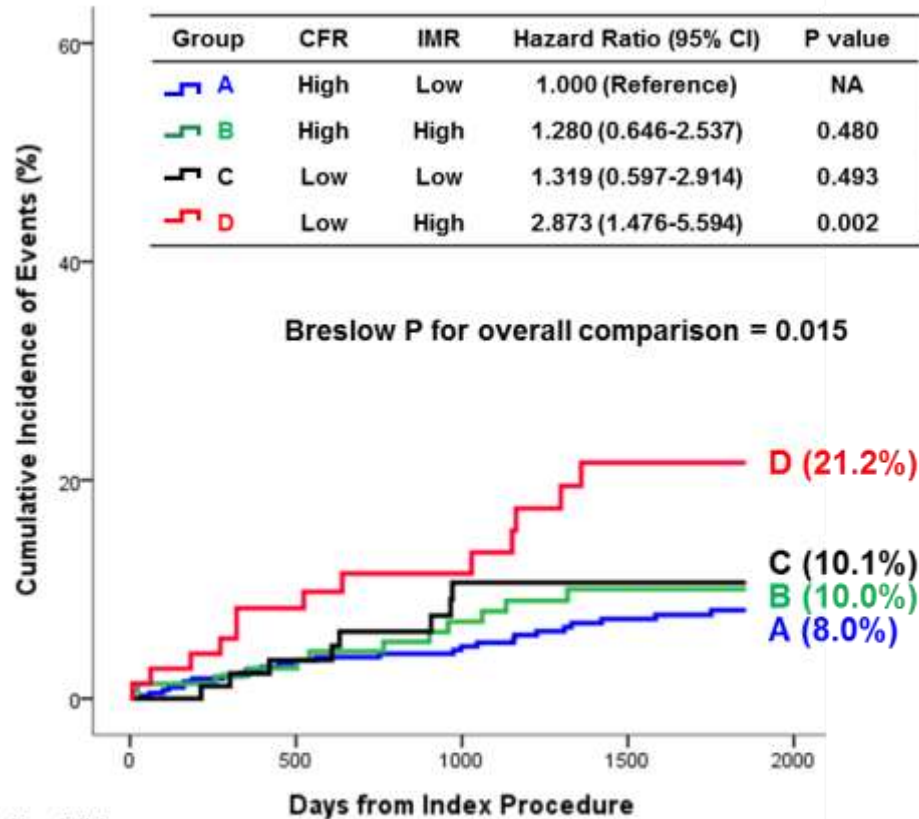
# Prognostic Impact of Microcirculatory Dysfunction

## - Long-term Prognosis (5 Years) -

### Patient-Oriented Composite Outcome

Group	CFR	IMR	Hazard Ratio (95% CI)	P value
A	High	Low	1.000 (Reference)	NA
B	High	High	1.280 (0.646-2.537)	0.480
C	Low	Low	1.319 (0.597-2.914)	0.493
D	Low	High	2.873 (1.476-5.594)	0.002

Breslow P for overall comparison = 0.015

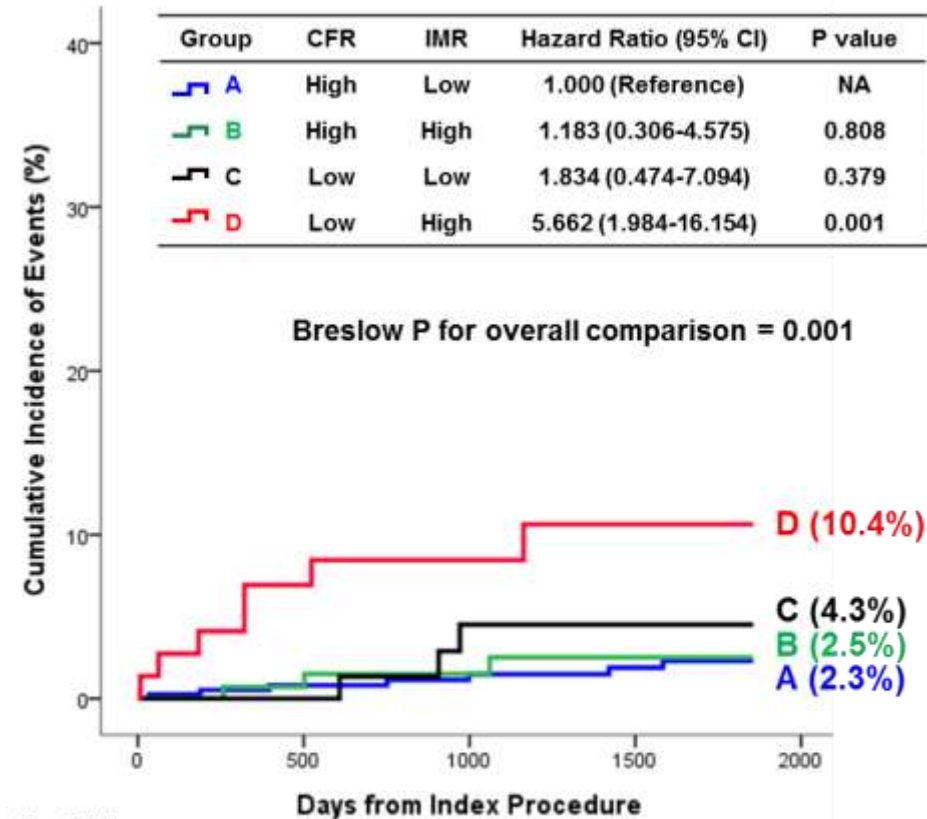


No. at Risk	0	500	1000	1500	2000
Group A	397	333	284	245	243
Group B	149	125	99	80	80
Group C	93	82	63	52	52
Group D	75	63	47	36	36

### Cardiac Death or Myocardial Infarction

Group	CFR	IMR	Hazard Ratio (95% CI)	P value
A	High	Low	1.000 (Reference)	NA
B	High	High	1.183 (0.306-4.575)	0.808
C	Low	Low	1.834 (0.474-7.094)	0.379
D	Low	High	5.662 (1.984-16.154)	0.001

Breslow P for overall comparison = 0.001



No. at Risk	0	500	1000	1500	2000
Group A	397	333	284	245	244
Group B	149	125	99	80	80
Group C	93	82	63	52	52
Group D	75	63	47	36	36

# Summary

## Functional Approach and Functional Angioplasty

All Decision Based on  
Anatomy Alone

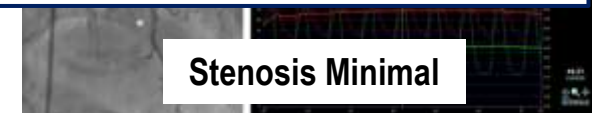
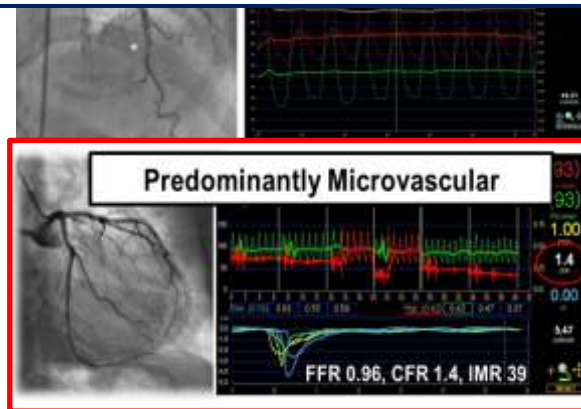
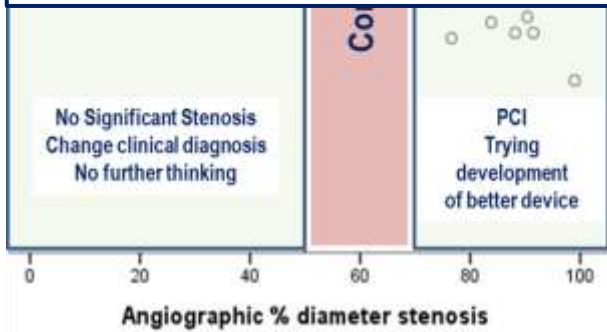
Functional Assessment  
Based on Clinical Judgement

Cause of Ischemia Based  
Decision

Revascularization

# We are clinician.

So, diagnosis and treatment should be driven by  
**clinical suspicion and judgement,**  
not by angiographic stenosis only.



### Meticulous Secondary Prevention

