The Basics of Coronary Physiology Measurement: FFR, iFR and other NHPRs

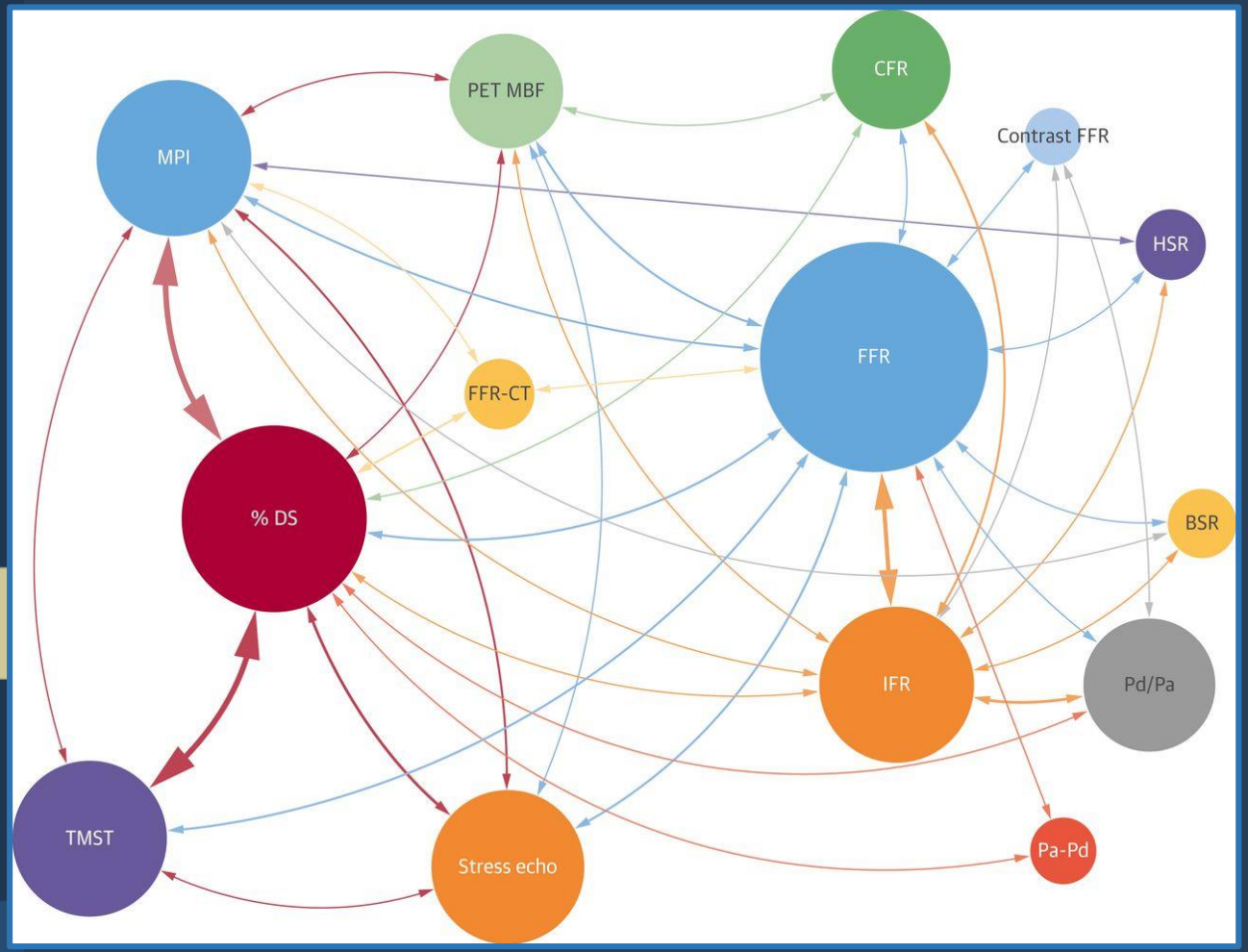
Jung-Min Ahn, MD

Departement of Cardiology, Asan Medical Center, Seoul, Korea

Disclosure

- I, Jung-Min Ahn, have NO conflict of interest related to this presentation.

Many Indices



- Non-Invasive Functional Study
  - Treadmill test
  - Stress echocardiography
  - Myocardial perfusion imaging
    - SPECT
    - MRI, CT
- Fractional Flow Reserve (FFR)
- Non-Hyperemic Pressure Ratio (NHPR)
  - iFR
  - Resting Pd/Pa
  - dPR
  - RFR

Morton J. Kern et al. JACC 2017;70(17):2124-7

How To Detect Objective Ischemia

- During ***Stress***, Decreased Coronary Blood Flow To Induce

Myocardial Perfusion Imaging		Myocardial Perfusion Abnormality
Stress Echo		Contractile Abnormality
Treadmill Test		Electrical Abnormality

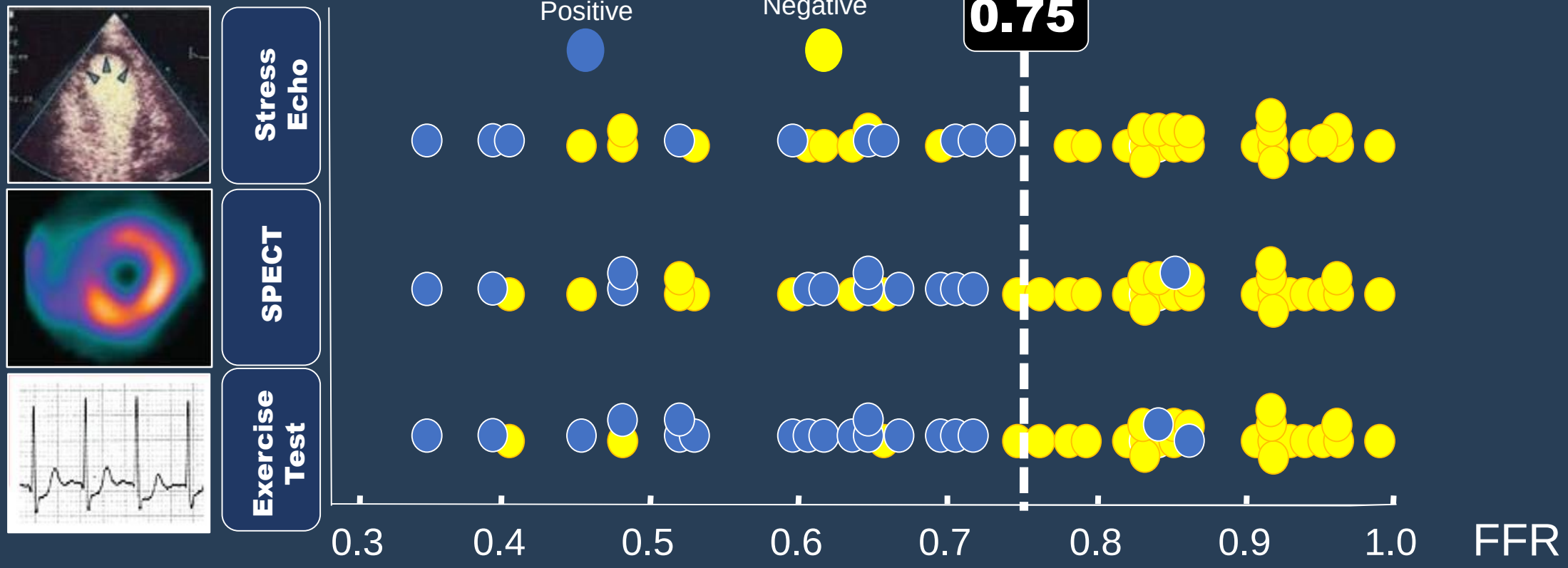
Direct Evidence of Ischemia

Ischemia Test in Cath Lab ?

N H Pijls et al. N Engl J Med 1996;334:1703-8,

FFR as A Non-Invasive Functional Study In Cath Lab

Comparison with 3 Non-Invasive Functional Studies



- N = 45 patients
- Sensitivity 88%, Specificity 100%, PPV 100%, NPV 88%

Current Cut-off Value of FFR: 0.80

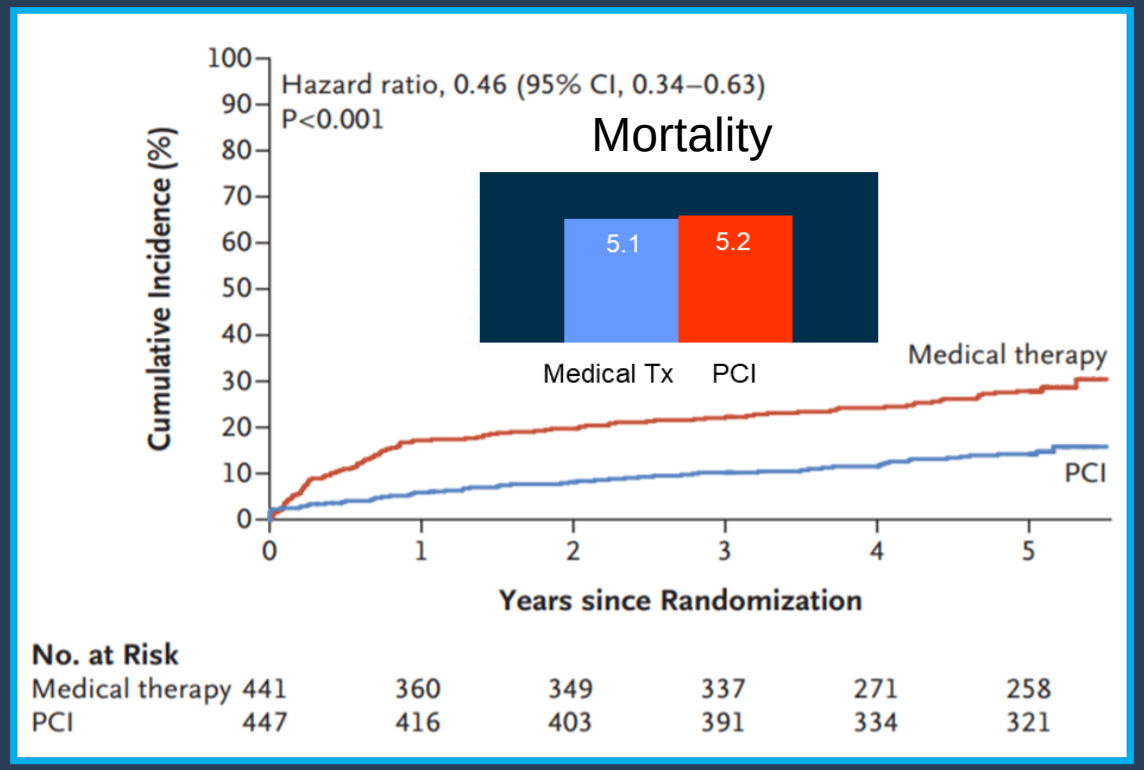
0 ⟷ 0.75 ⟷ 0.80 ⟷ 1.0

Significant	grey zone	Non-significant

Author	Number	Stress Test	BCV	Accuracy
Pijls et al.	60	X-ECG	0.74	97
DeBruyne et al.	60	X-ECG/SPECT	0.72	85
Pijls et al.	45	X-ECG/SPECT/pacing/DSE	0.75	93
Bartunek et al.	37	DSE	0.68	90
Abe et al.	46	SPECT	0.75	91
Chamuleau et al.	127	SPECT	0.74	77
Caymaz et al.	40	SPECT	0.76	95
Jimenez-Navarro et al.	21	DSE	0.75	90
Usui et al.	167	SPECT	0.75	79
Yanagisawa et al.	167	SPECT	0.75	76
Meuwissen et al.	151	SPECT	0.74	85
DeBruyne et al.	57	MIBI-SPECT post-MI	0.78	85
Samady et al.	48	MIBI-SPECT post-MI	0.78	85
Ahn JM et al.(2011)	151	SPECT	0.77	89

FFR ≤ 0.80: Stenting Justified

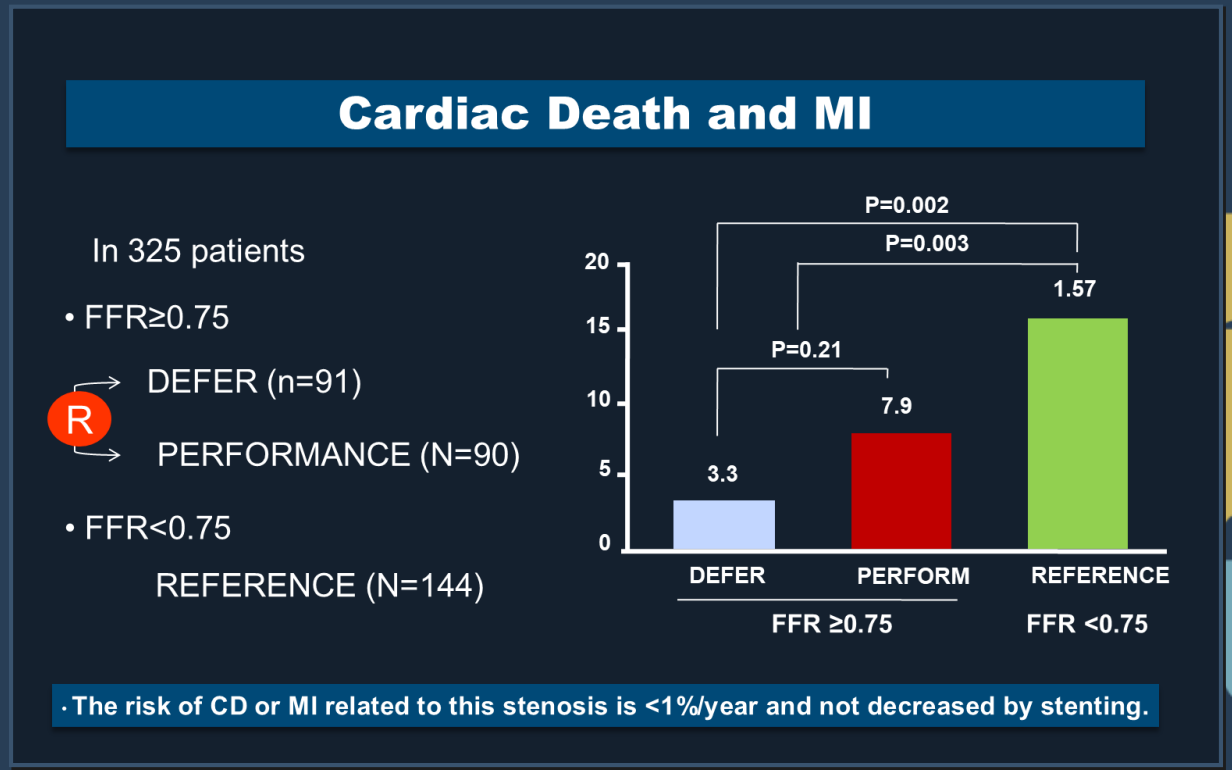
FAME 2



De Bruyne, et al. New Engl J Med 2014;371:1208-17.

FFR > 0.80: Defer

DEFER

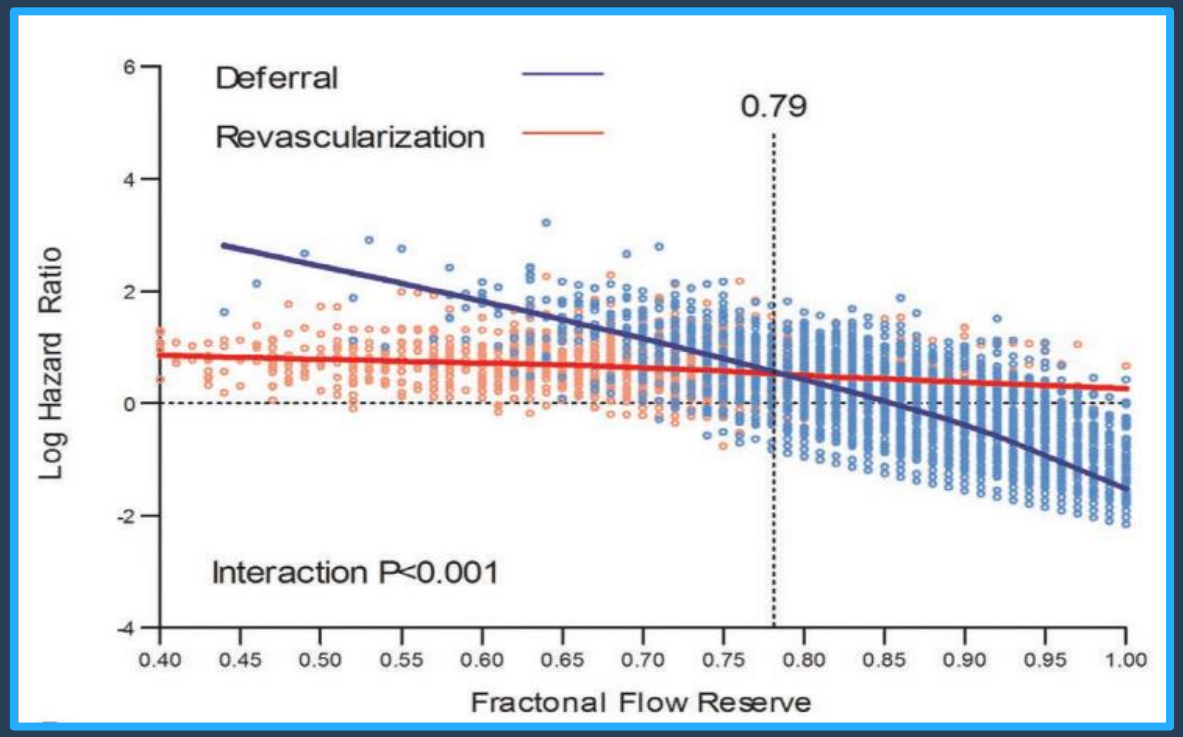


J Am Coll Cardiol 2007;49:2105–11.

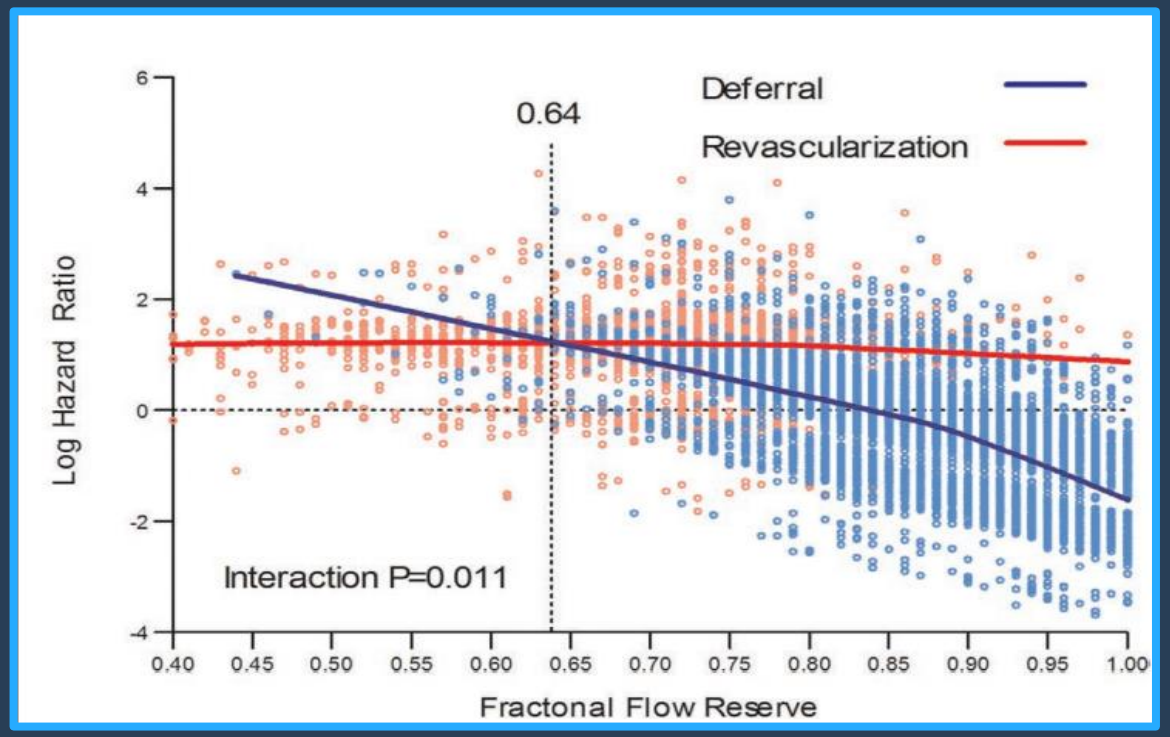
Outcome Derived Revascularization Threshold

FFR: Clinical Index To Decide Revascularization

Cardiac Death, MI, and TVR



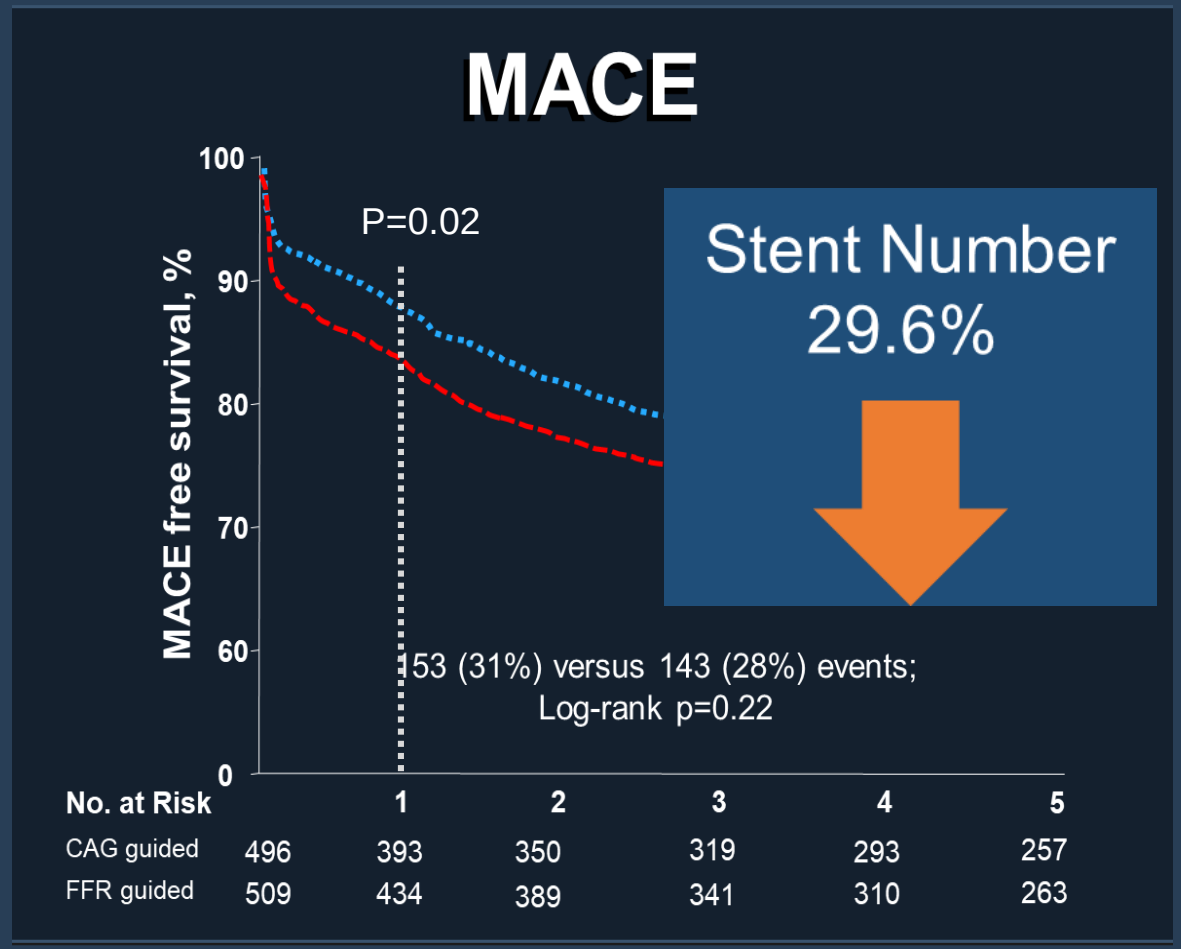
Cardiac Death, and MI



Ahn JM, Park SJ et al. Circulation 2017 Jun 6;135(23):2241-2251

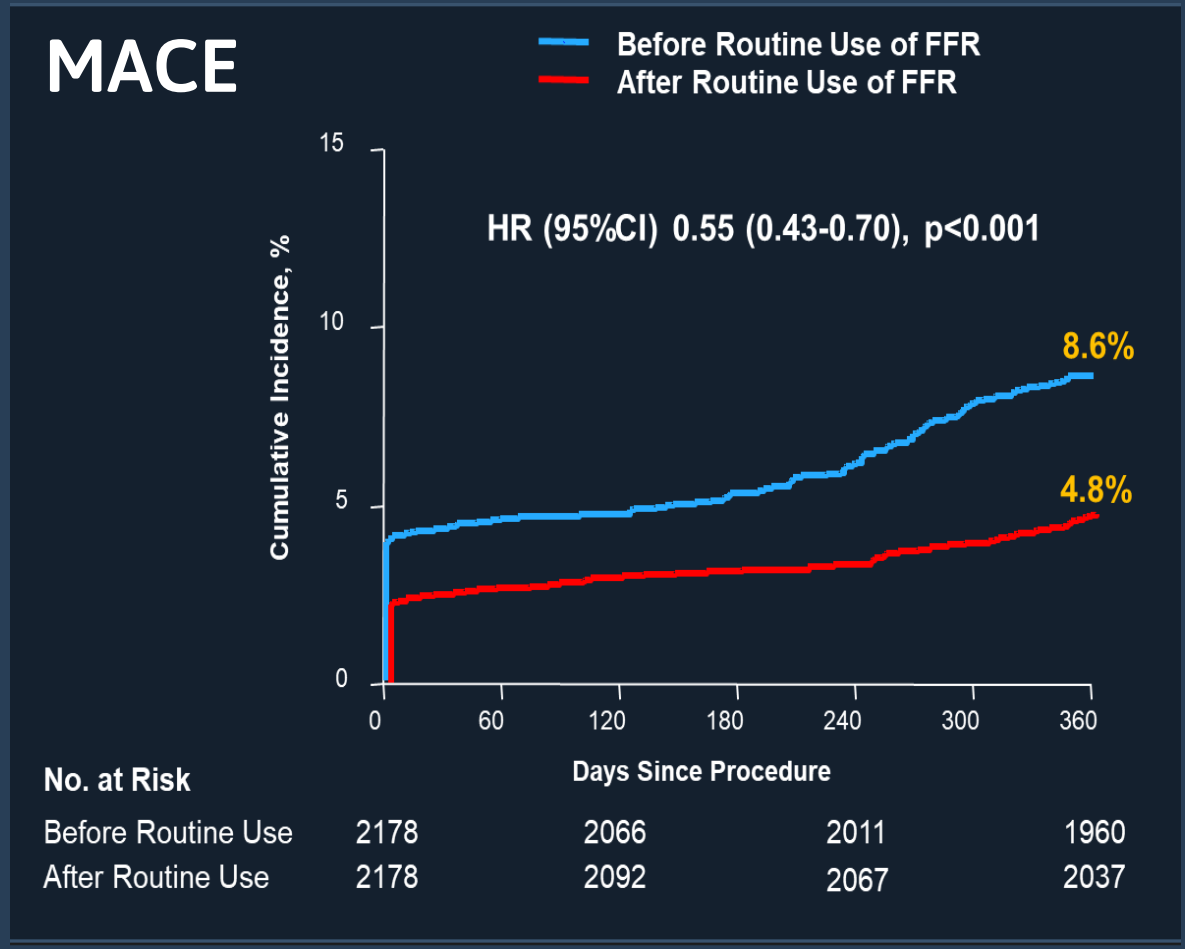
FFR Guided PCI

FAME I



van Nunen LX, Zimmermann FM et al. LANCET 2015;386(10006):1853-60

Asan PCI Registry

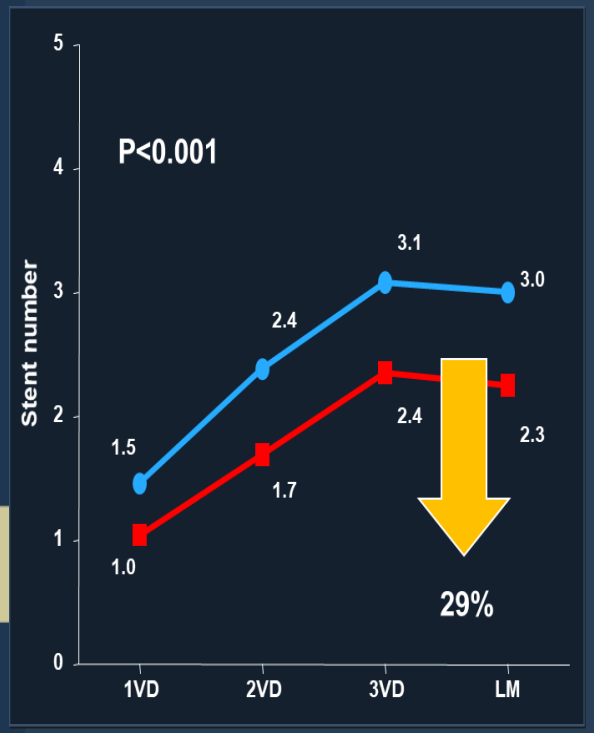


Park SJ, Ahn JM et al. Eur Heart J. 2013 Nov;34(43):3353-61

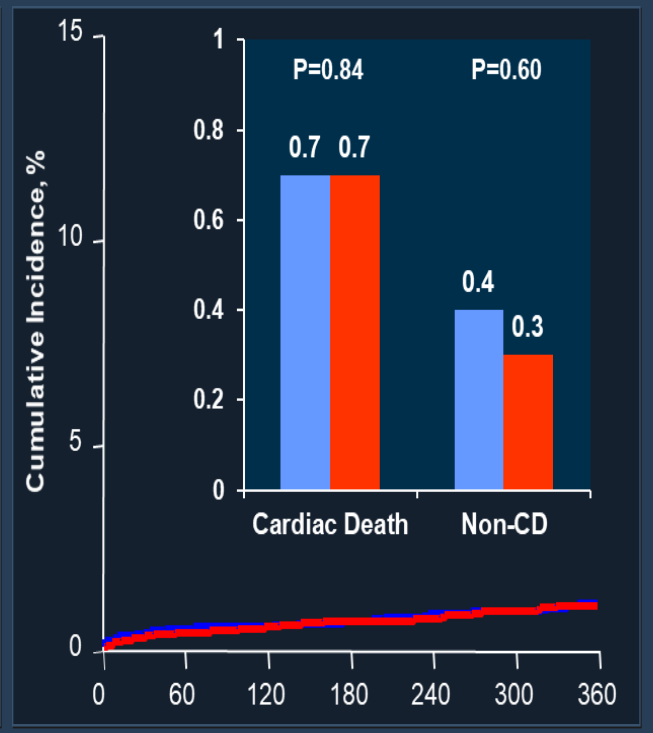
Asan PCI Registry

Before Routine Use
After Routine Use

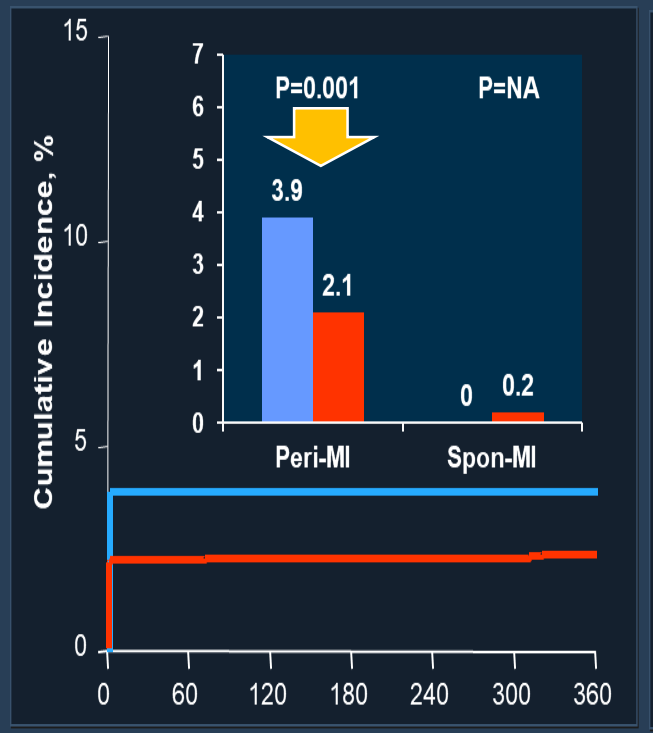
Stent Number



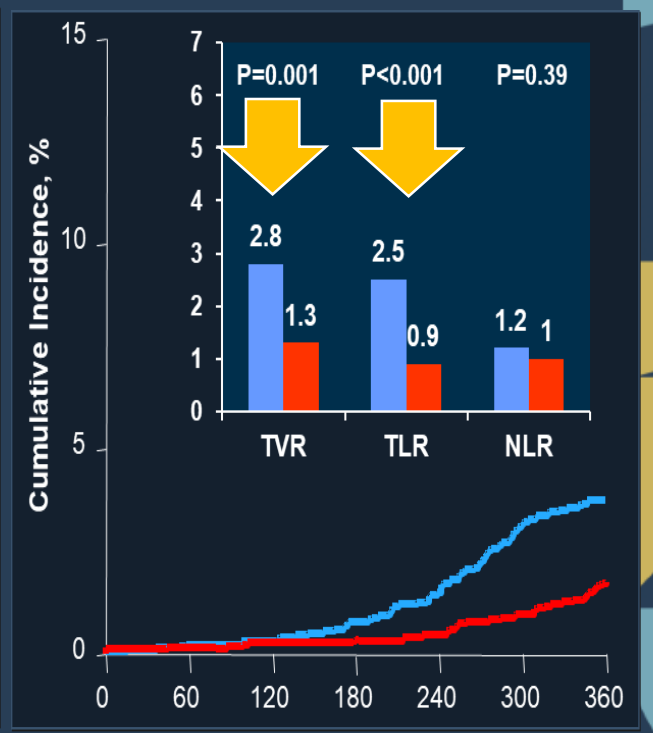
Death



Myocardial Infarction



Repeat Revascularization



- The benefit of FFR guided PCI is primarily due to
  1) The reduced number of stents per patient
  2) The subsequent decreased risk of peri-procedural MI and repeat revascularization
  3) Favorable outcome with less stenting

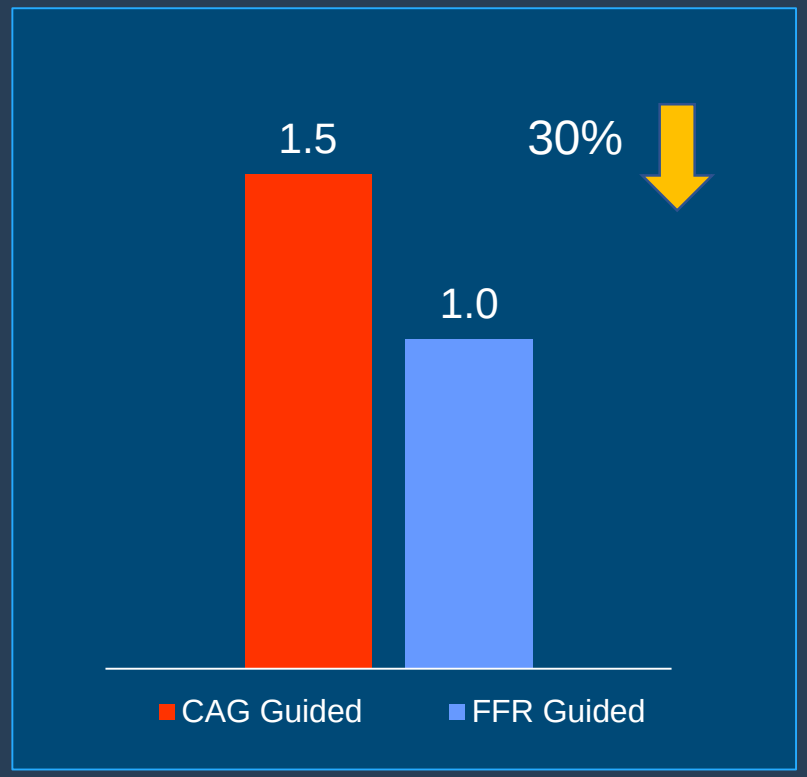
Park SJ, Ahn JM et al. Eur Heart J. 2013 Nov;34(43):3353-61

Treatment Strategy

Reduced Stent Number and Increased Medical Treatment

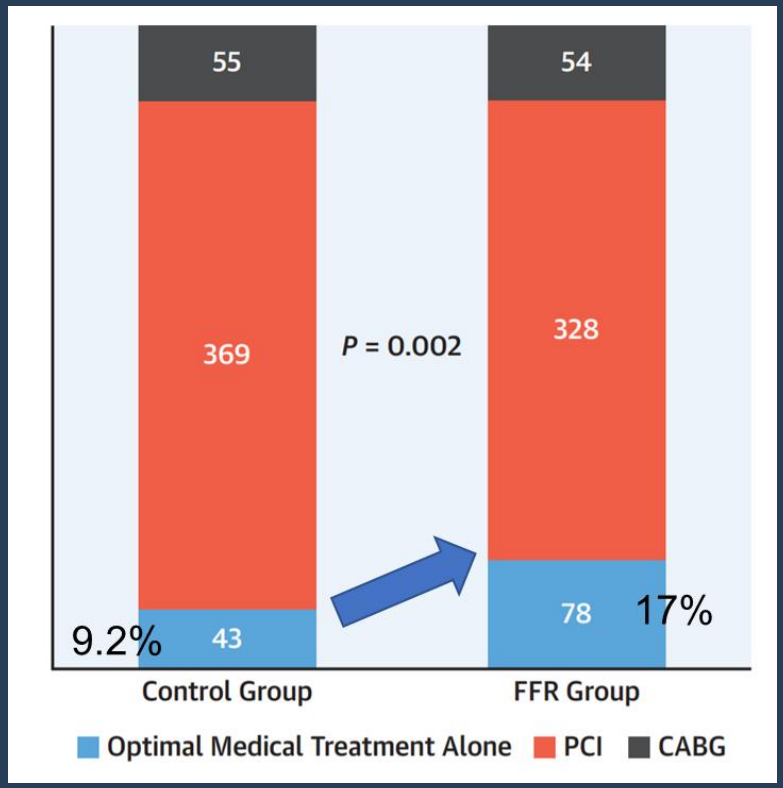
FLOWER-MI

Number of stents per patient



N Engl J Med 2021;385:297-308

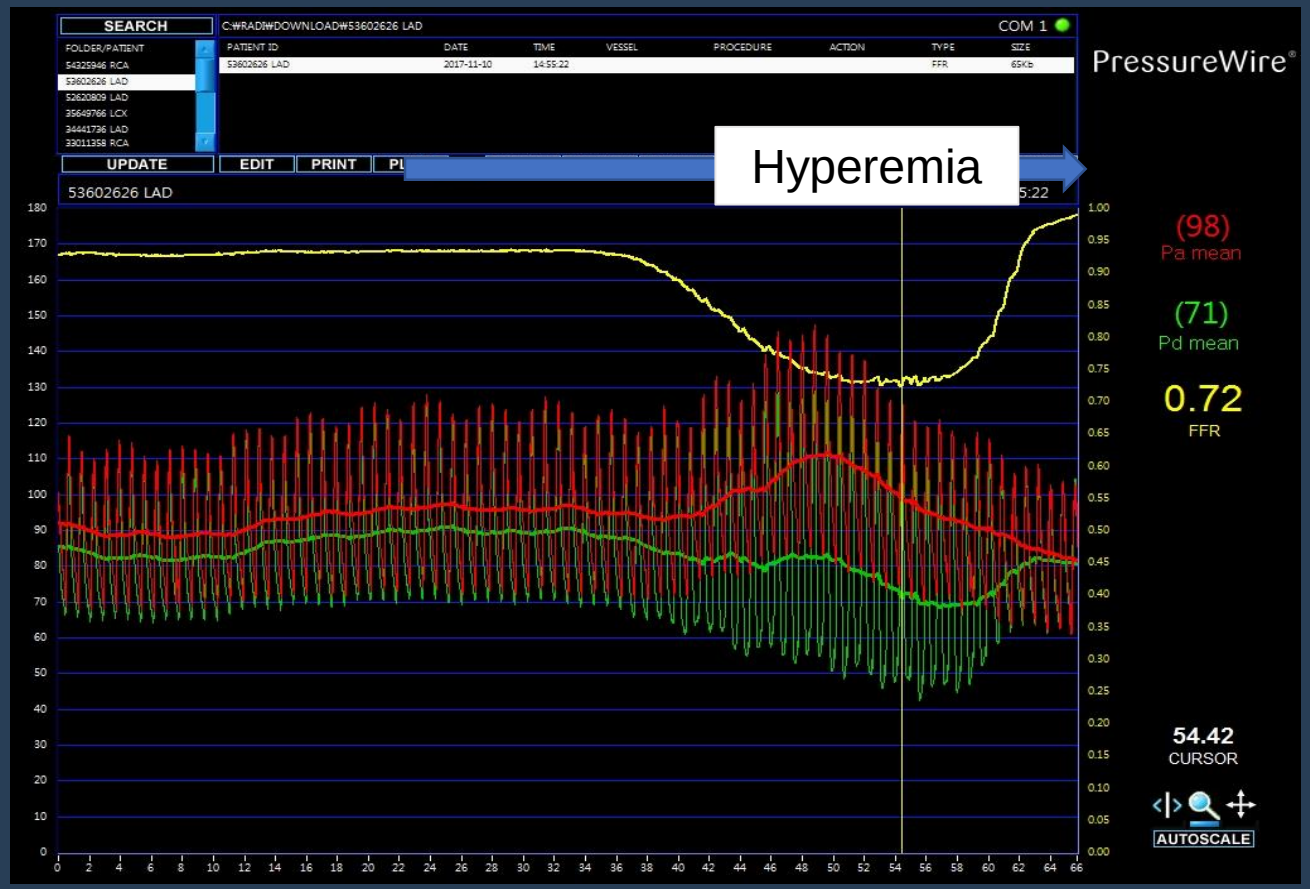
FUTURE Trial



J Am Coll Cardiol 2021;78:1875–1885

FFR Requires Hyperemia

(Adenosine, ATP, Nicorandil etc.)



- Contraindicated or disliked by patients
- Adds costs and time
- Adds inconvenience and risk

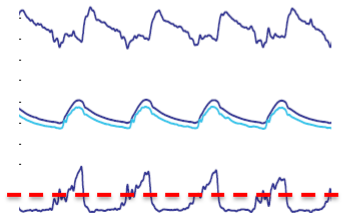
Since TCT 2011,

iFR, Instantaneous wave-free ratio

Hypothesis 1

Resistance measured at rest durir
free period is similar to mean resi
hyperaemia.

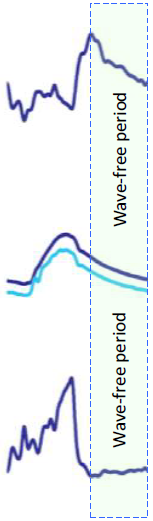
Hyperaemic mean resistance



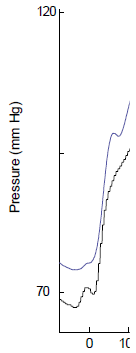
ADVISE study

Hypothesis 2

The Pd/Pa ratio ***(iFR)*** during the ***re***
period was similar to ***FFR***.



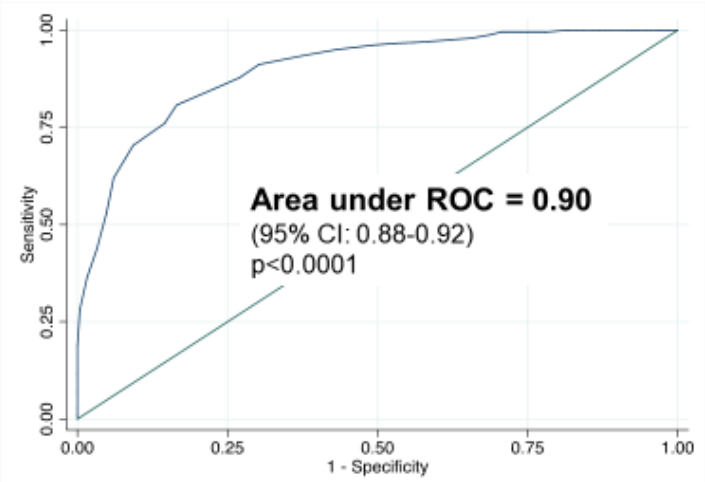
ADVISE study



Diagnostic accuracy of iFR

Compared with FFR, 0.80

- Best iFR cut-off:
  ≤0.89
- Properly classified by iFR:
  82.46%
- Specificity:
  87.78%
- Sensitivity:
  72.98%
- Positive predictive value:
  77.02%
- Negative predictive value:
  85.27%



tct 25

CARDIOVASCULAR RESEARCH FOUNDATION

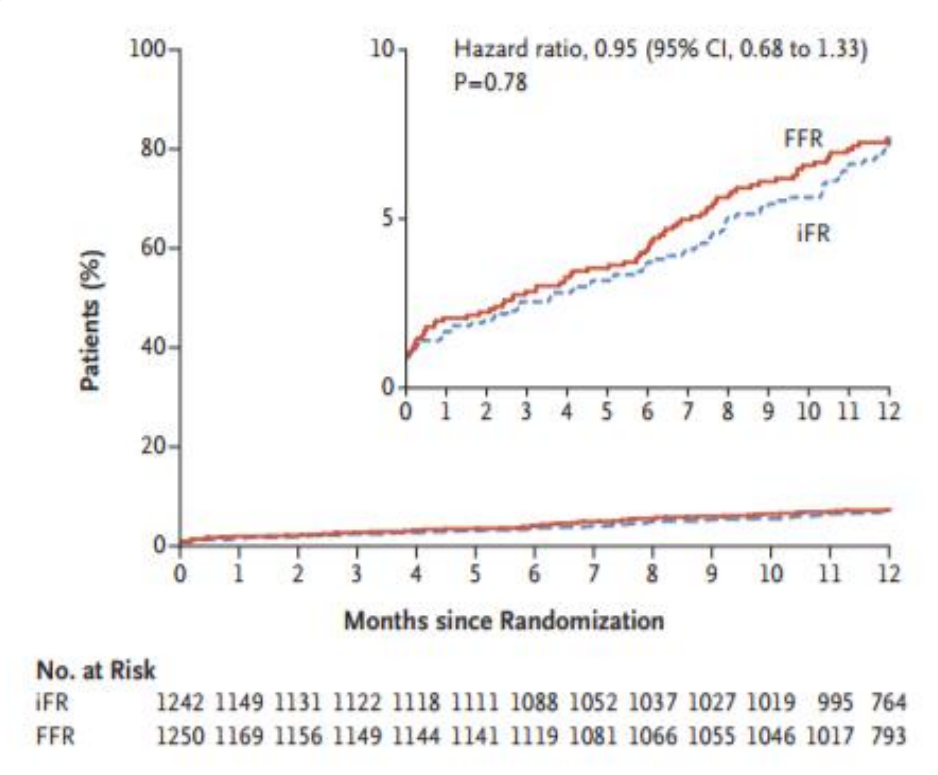
Justin Davies and Javier Escaned , ADVICE I and II study presentation

TCTAP 2022

ACC 2017,

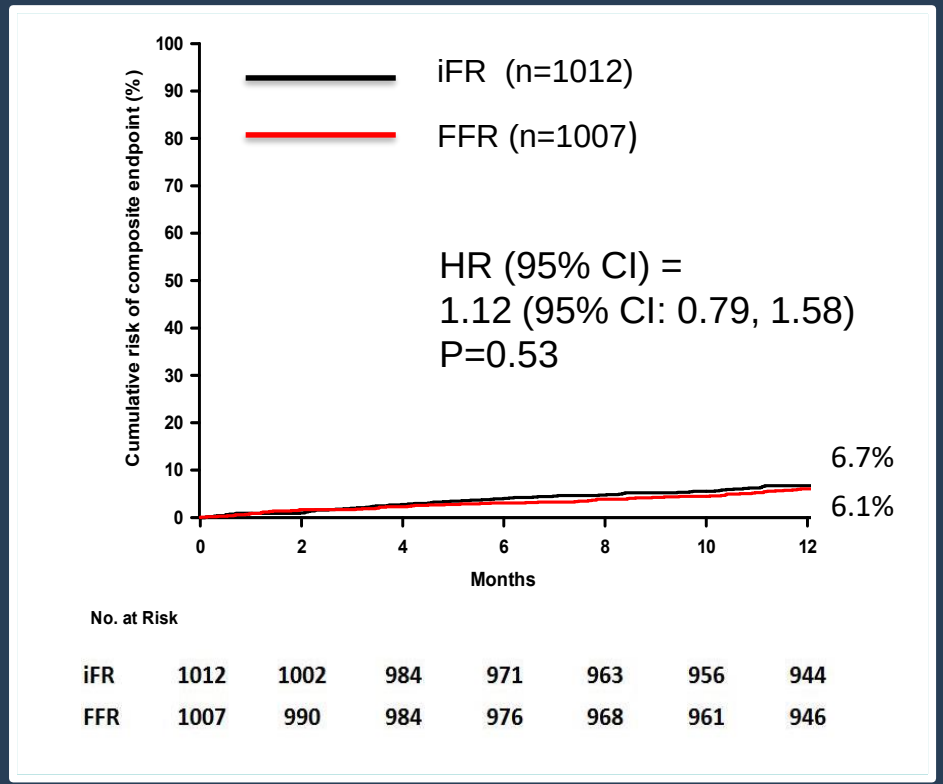
iFR is Non-Inferior to FFR to Guide Revascularization Decision

DEFINE-FLAIR



N Engl J Med. 2017 May 11;376(19):1824-1834

iFR-SWEDEHEART



N Engl J Med. 2017 May 11;376(19):1813-1823

Guidelines

ESC Guideline 2018

Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis.[15,17,18,39]	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI.[29,31]	IIa	B
IVUS should be considered to assess the severity of unprotected left main lesions.[35–37]	IIa	B

ACC/AHA Guideline 2021

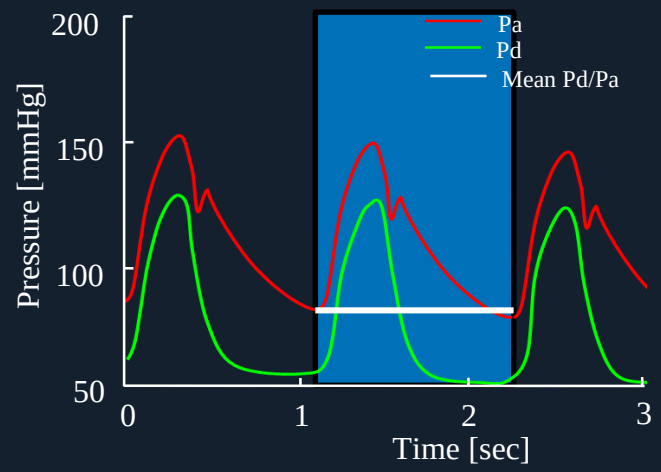
Recommendations for the Use of Coronary Physiology to Guide Revascularization With PCI
Referenced studies that support the recommendations are summarized in Online Data Supplement 5.

COR	LOE	Recommendations
1	A	1. In patients with angina or an anginal equivalent, undocumented ischemia, and angiographically intermediate stenoses, the use of fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) is recommended to guide the decision to proceed with PCI.[1-6]
3: No benefit	B-R	2. In stable patients with angiographically intermediate stenoses and FFR >0.80 or iFR >0.89, PCI should not be performed.[7-10]

Since 2017,
Many Non-Hyperemic Pressure Ratios (NHPR)

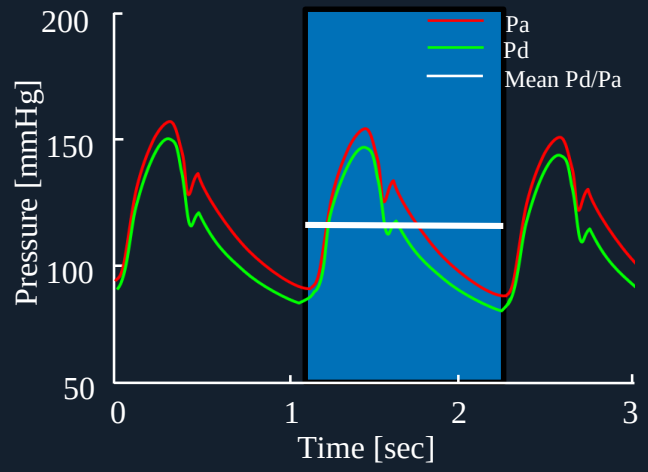
Definition of Physiologic Indices

(A) FFR (≤0.80)



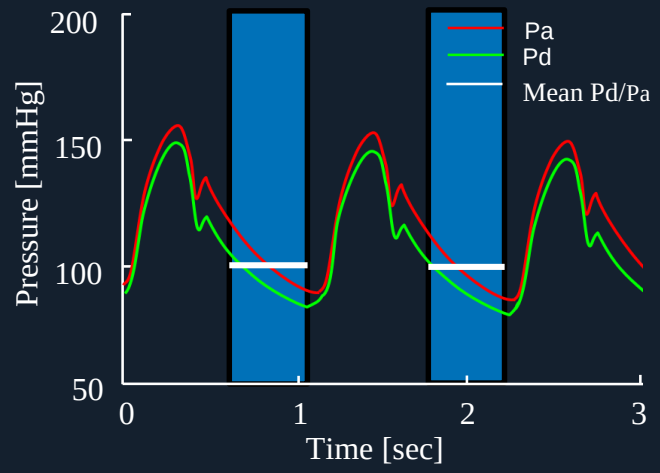
Mean Pd/Pa at hyperemia during the entire cardiac cycle

(B) Resting Pd/Pa (≤0.91/0.92)



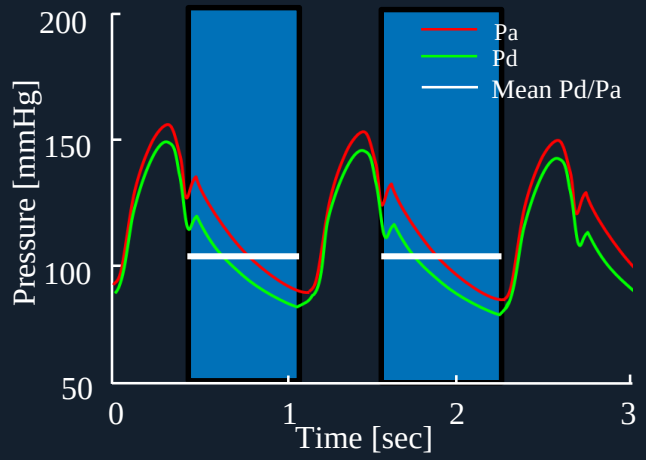
Mean Pd/Pa at rest during the entire cardiac cycle

(C) iFR (≤0.89)



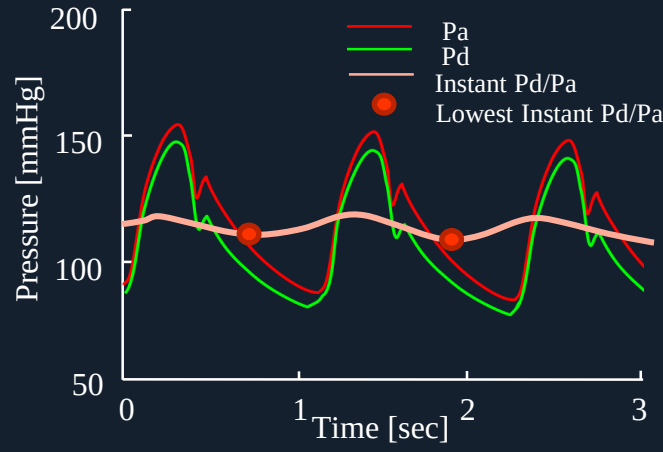
Mean Pd/Pa at rest during wave free period (WFP)

(D) dPR (≤0.89)



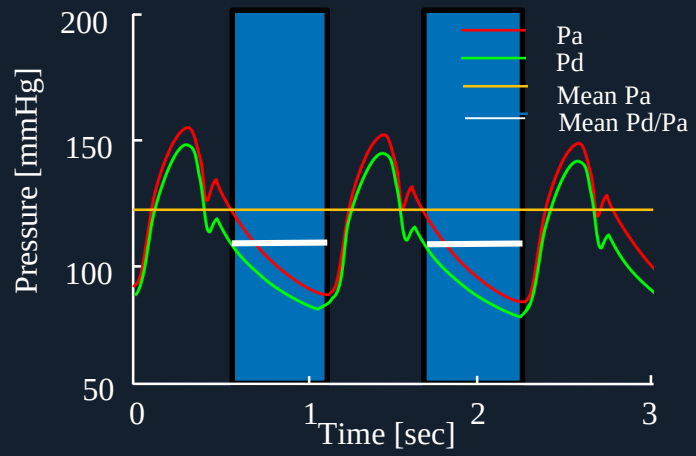
Mean Pd/Pa at rest during the entire diastole

(E) RFR (≤0.89)

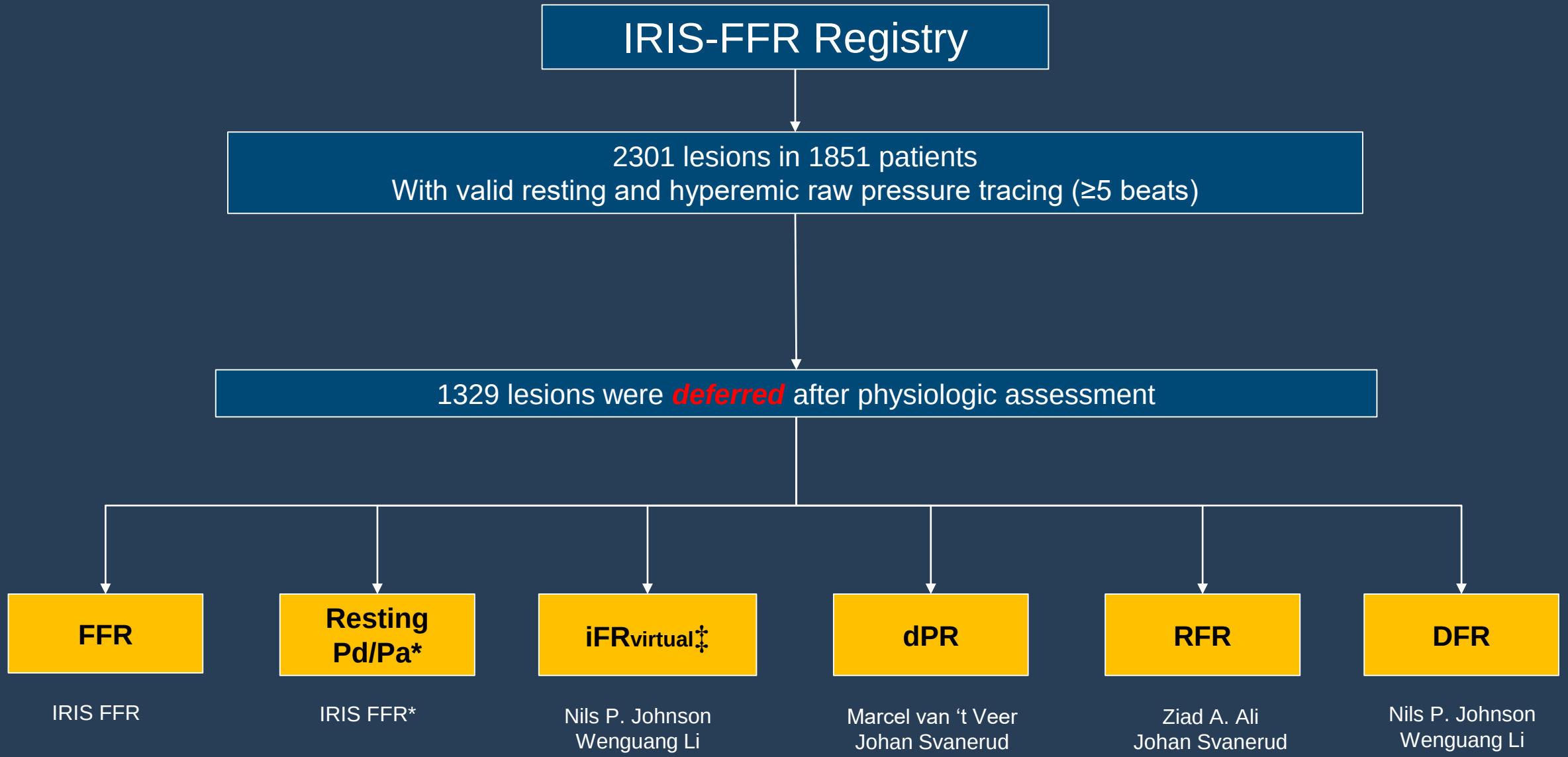


Lowest Instant Pd/Pa at rest during the entire cardiac cycle

(F) DFR (≤0.89)



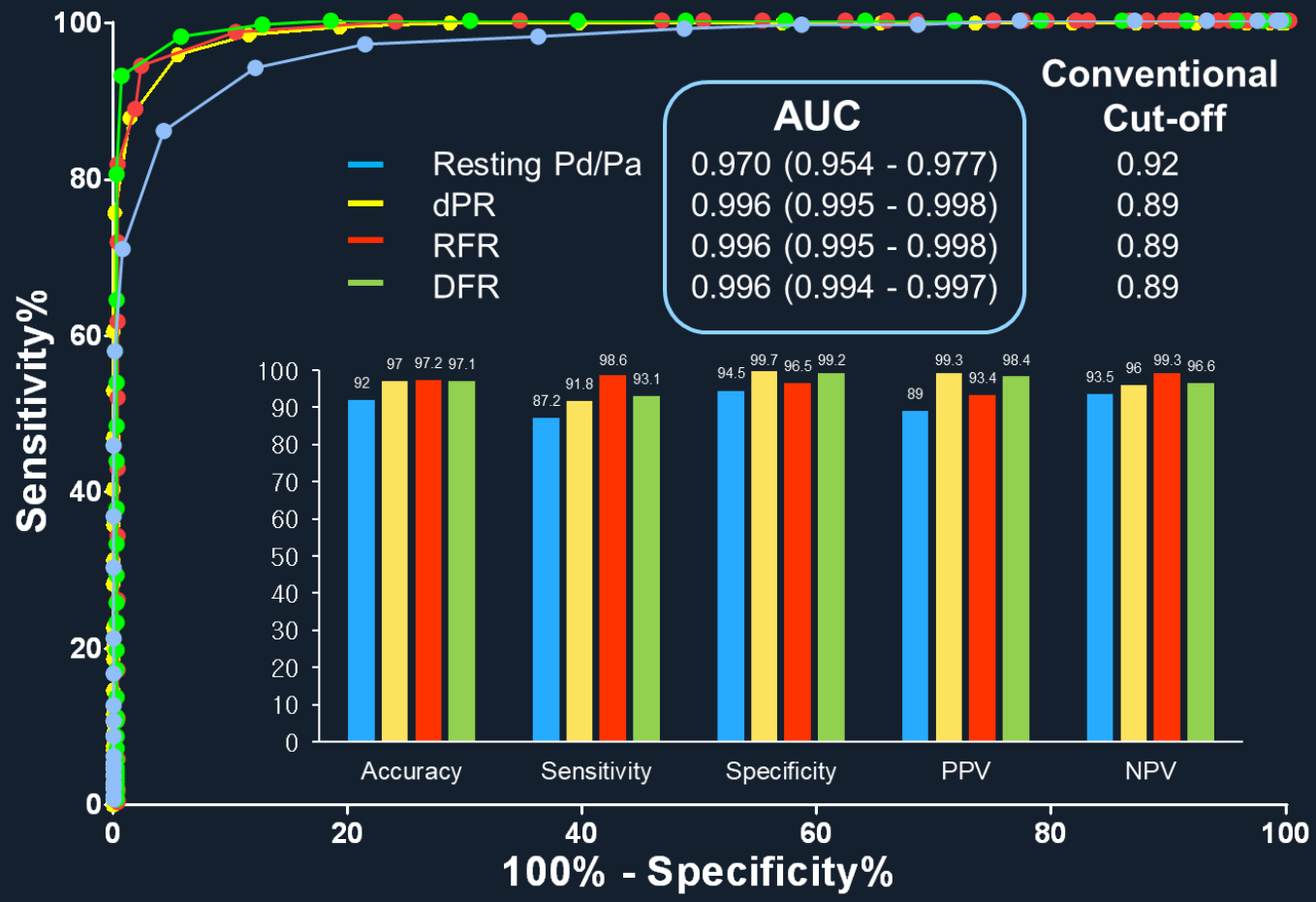
Mean Pd/Pa at rest during the period
Between Pa < mean Pa AND down-sloping Pa



*All resting tracings were confirmed by Wenguang Li during virtual iFR and DFR calculation
‡calculated using the proprietary software (Volcano Corporation)

NHPR vs. iFR

Prediction of iFR ≤0.89

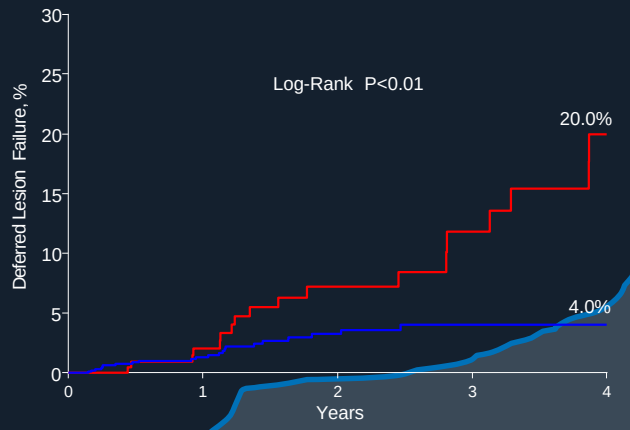


80-85% Accuracy

97% Accuracy

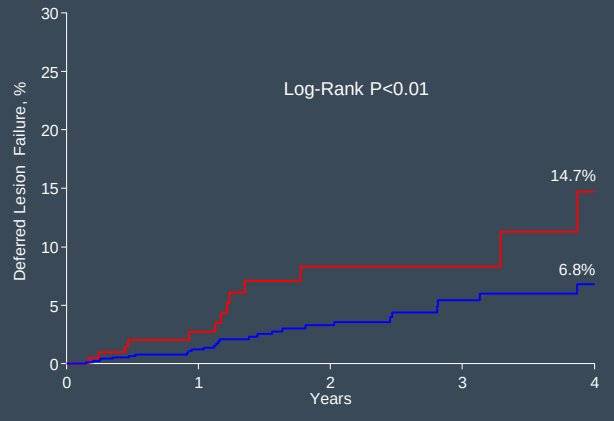
Kaplan-Meier Curves

(A) FFR



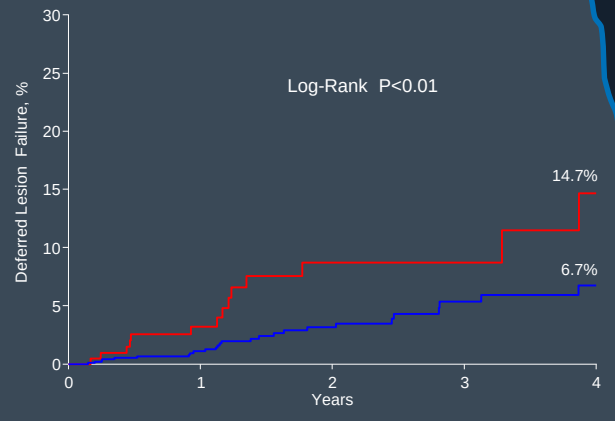
At risk				
FFR≤0.80	256	96	35
FFR>0.80	1073	297	100

(B) Resting Pd/Pa



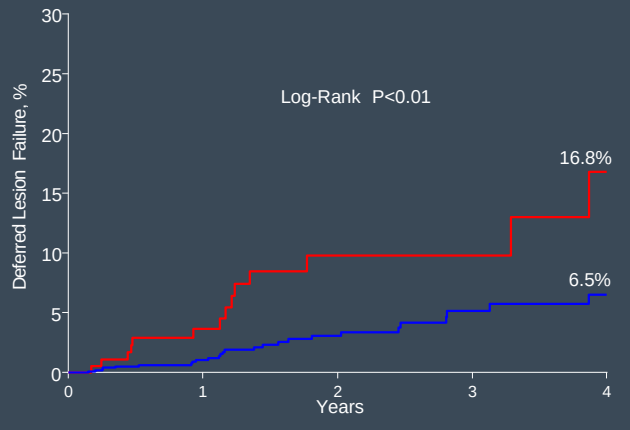
At risk				
Pd/Pa≤0.92	238	64	24
Pd/Pa>0.92	1091	329	111

(C) iFR



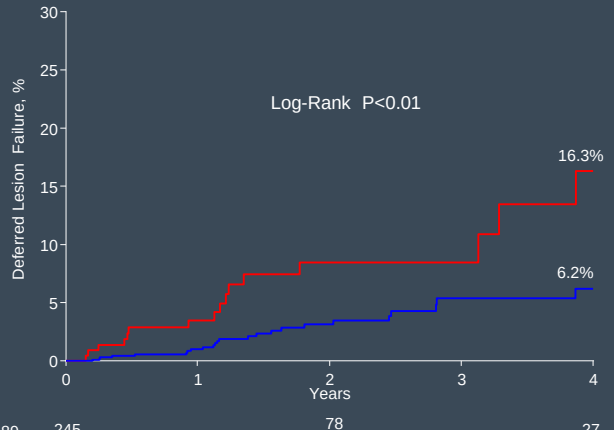
At risk				
iFR≤0.89	231	70	25
iFR>0.89	1098	323	110

(D) dPR



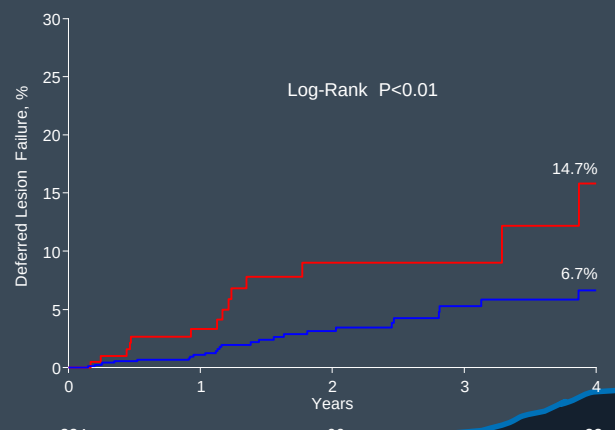
At risk				
dPR≤0.89	204	61	21
dPR>0.89	1125	332	114

(E) RFR



At risk				
RFR≤0.89	245	78	27
RFR>0.89	1084	315	108

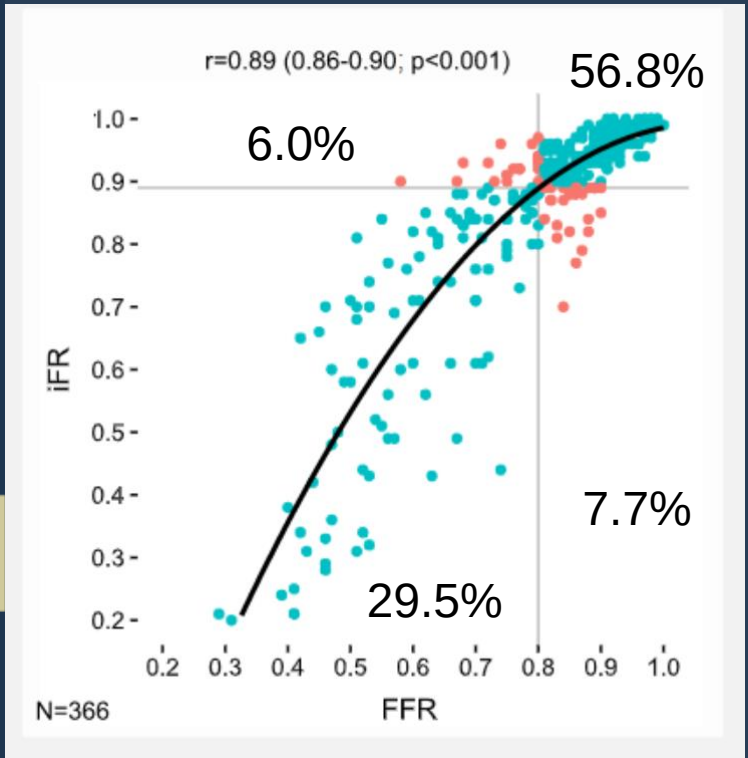
(F) DFR



At risk				
DFR≤0.89	224	66	22
DFR>0.89	1105	327	113

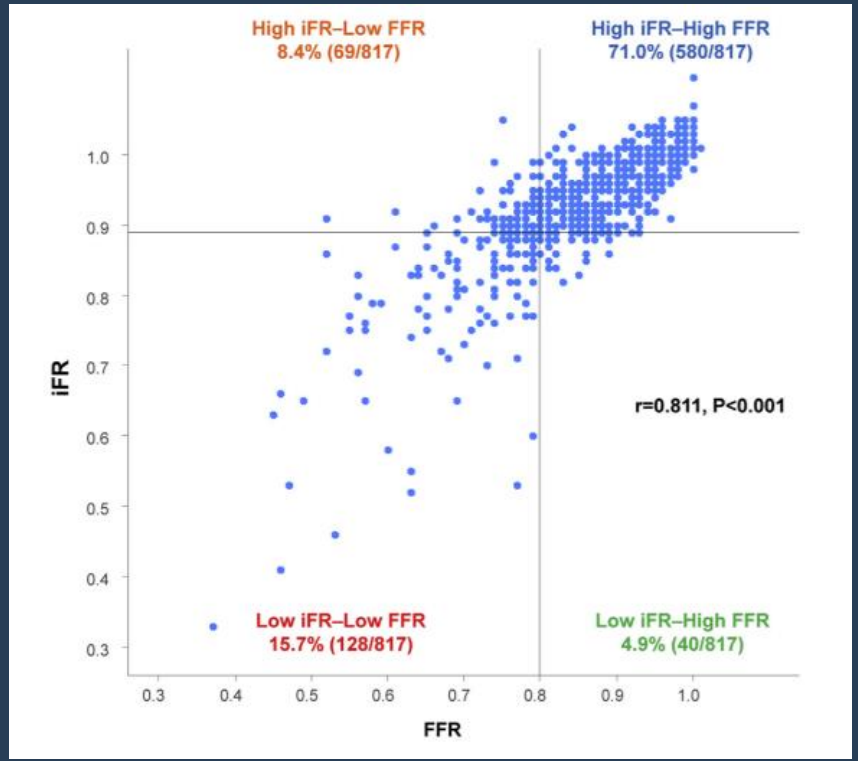
Frequency of FFR/iFR Discordance

13.7 %



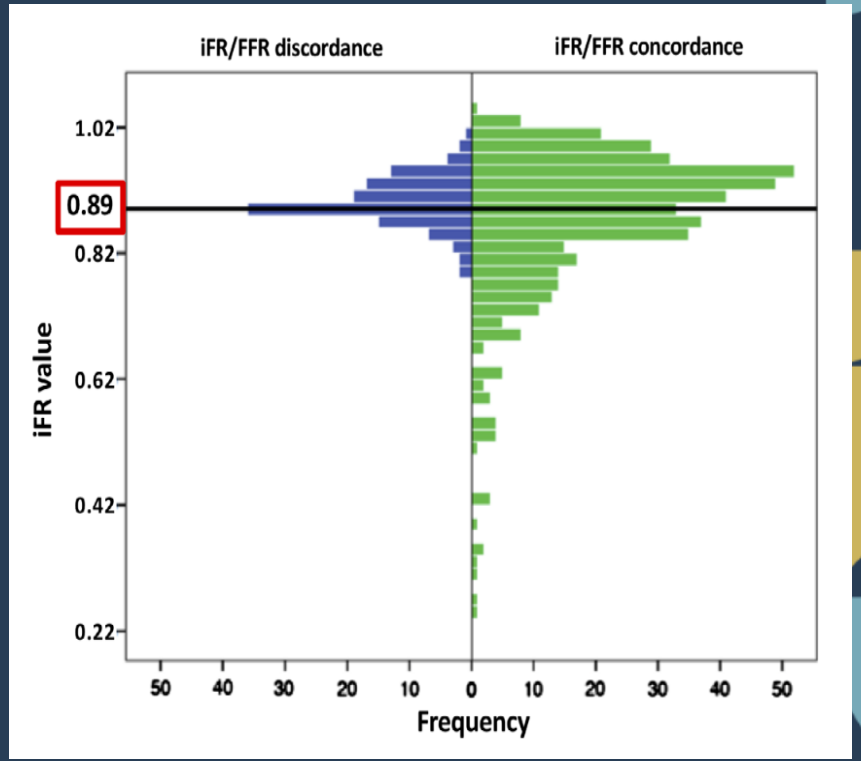
Cook CM et al.
JACC Cardiovasc Interv. 2017;10(24):2514-2524

13.3 %



SH Lee et al.
JACC Cardiovasc Interv. 2019;12(20):2018-2031

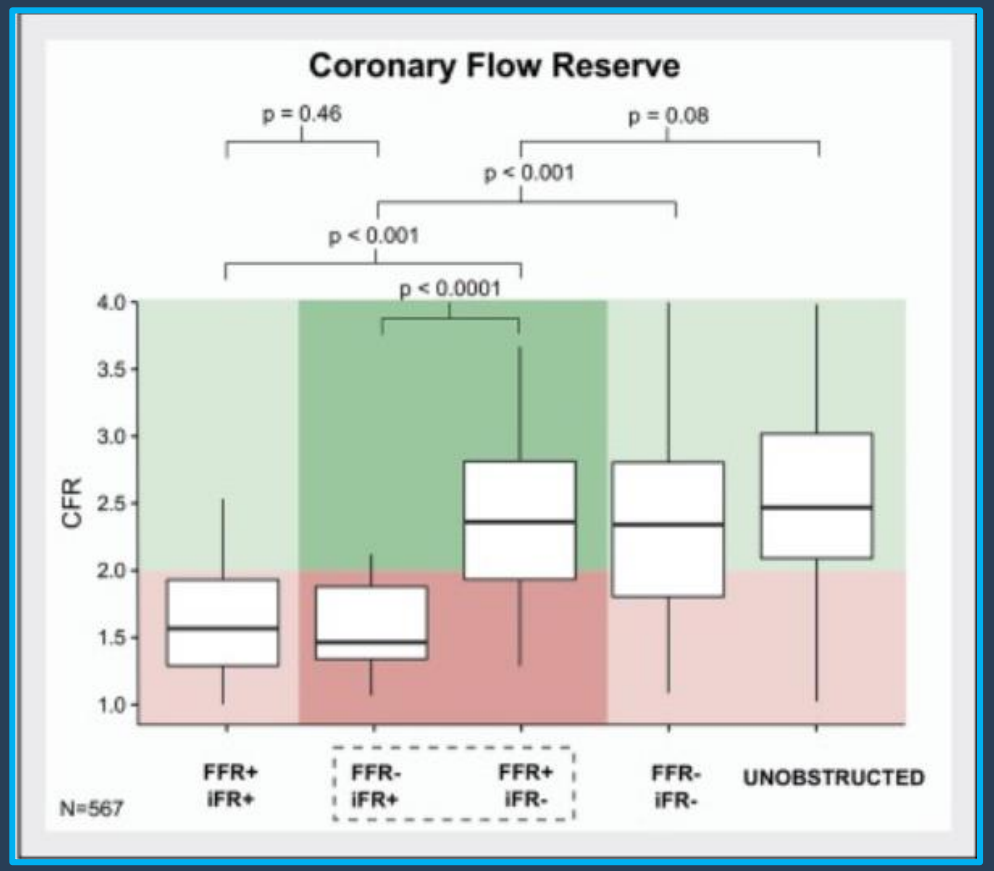
20.6 %



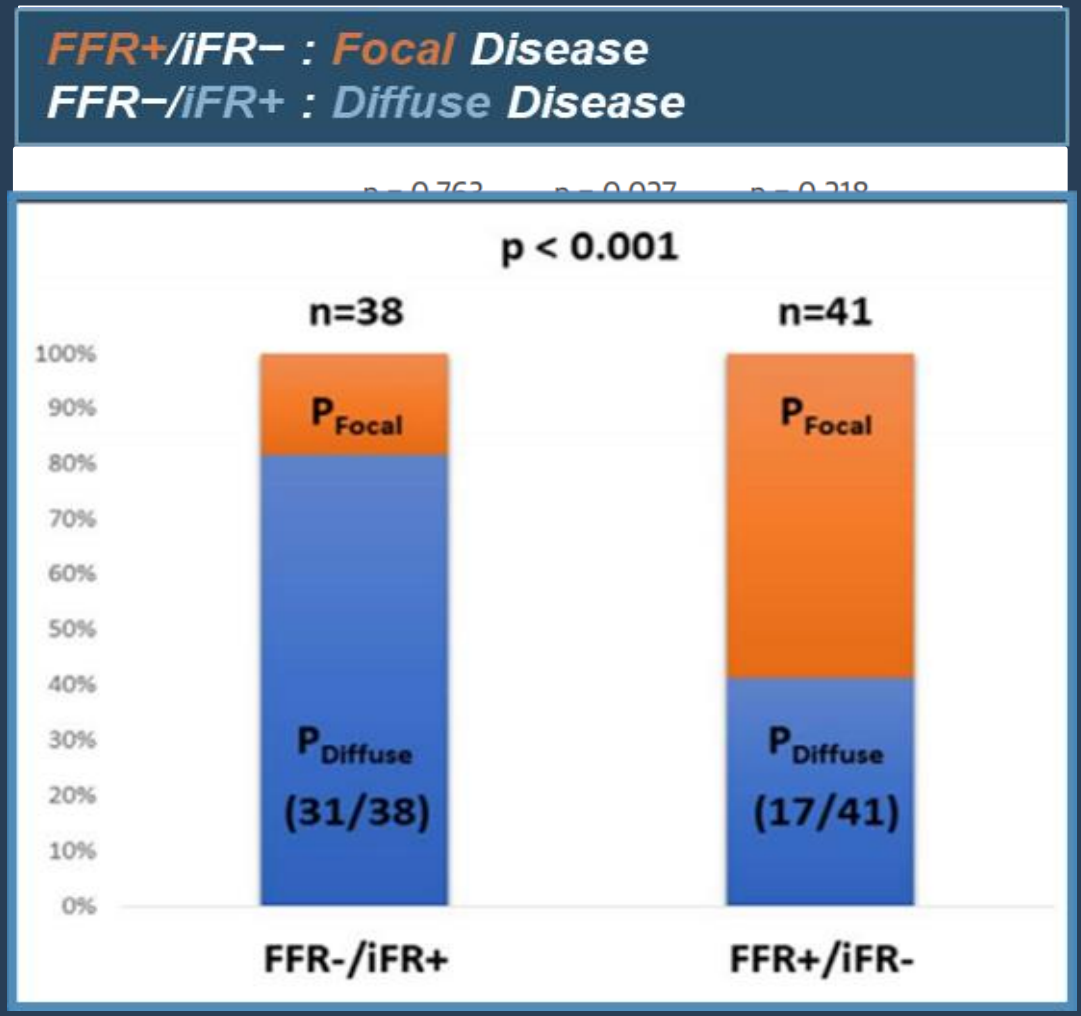
Derimay F et al.
Catheter Cardiovasc Interv. 2019 Sep 1;94(3):356-363

Physiologic and Anatomic Characteristics of Discordant Lesions

Differences in Coronary Flow Reserve



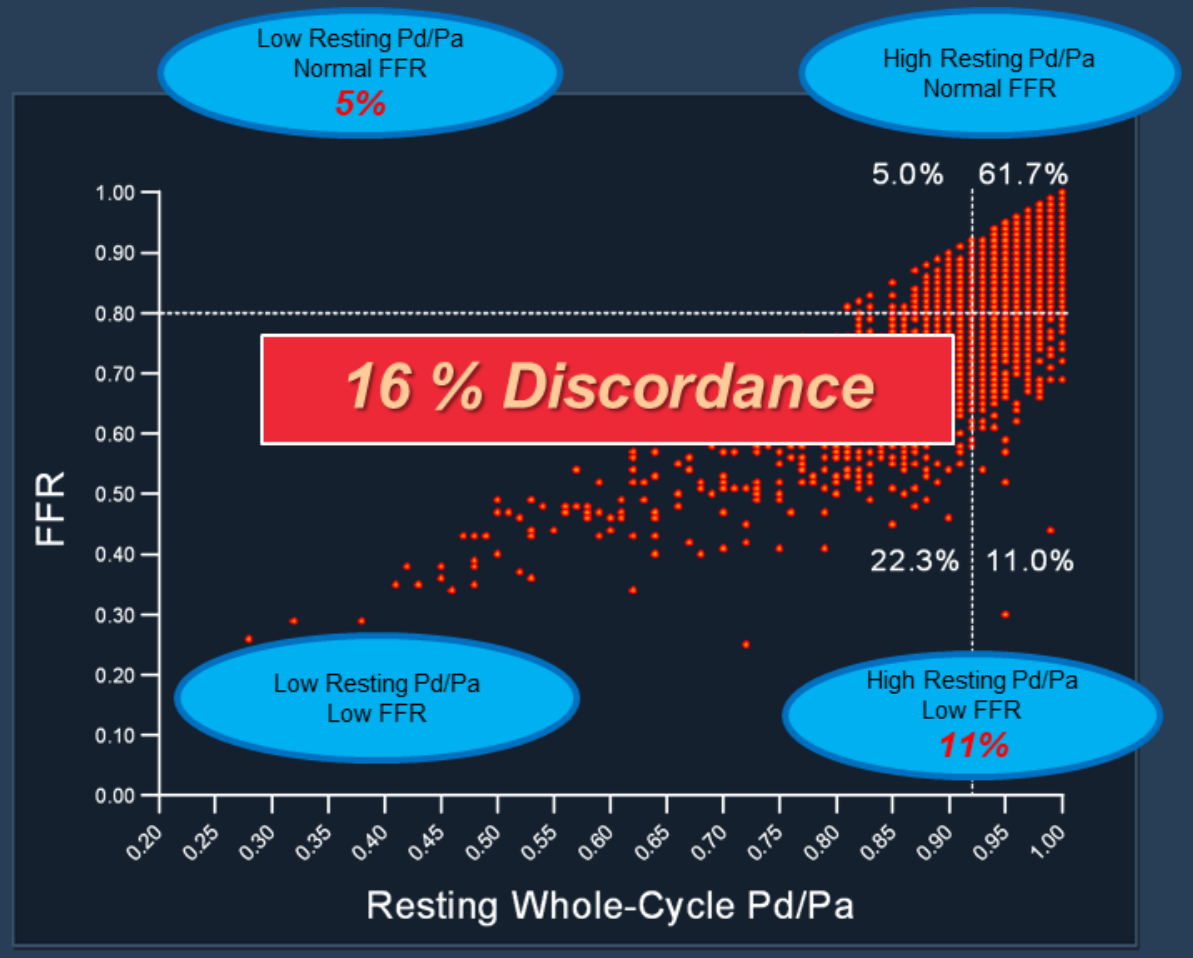
Cook CM et al.
JACC Cardiovasc Interv. 2017;10(24):2514-2524



JACC Cardiovasc Imaging. 2020 Mar;13(3):746-756.
Circ Cardiovasc Interv. 2019;12:e007494

*Adverse plaque characteristics include low-attenuation plaque, positive remodeling, spotty calcification, and napkin risk sign

Clinical Characteristics of Discordant Lesions



	Odds Ratio	95% CI	P Value
Resting Pd/Pa≤0.92 and FFR>0.80 **Very Small Hyperemic Pressure Drop**			
Age	1.02	1.01-1.03	0.004
Gender (Male)	74	0.59-0.94	0.012
Diabetes	1.50	1.19-1.89	0.001
Hyperlipidemia	0.72	0.57-0.91	0.005
Proximal location (vs. mid to distal)	0.60	0.49-0.78	<0.001
Resting Pd/Pa>0.92 and FFR≤0.80 **Very Big Hyperemic Pressure Drop**			
Age	0.98	0.97-0.99	<0.001
Gender (Male)	1.79	1.45-2.22	<0.001
Diabetes		0.66-0.96	0.016
Family history		0.50-0.87	0.003
Chronic renal failure	0.32	0.14-0.75	0.008
Diameter stenosis (≥50%)	4.06	3.16-5.21	<0.001
AHA/ACC B2C lesion	1.44	1.20-1.71	<0.001

Low CFR phenotype

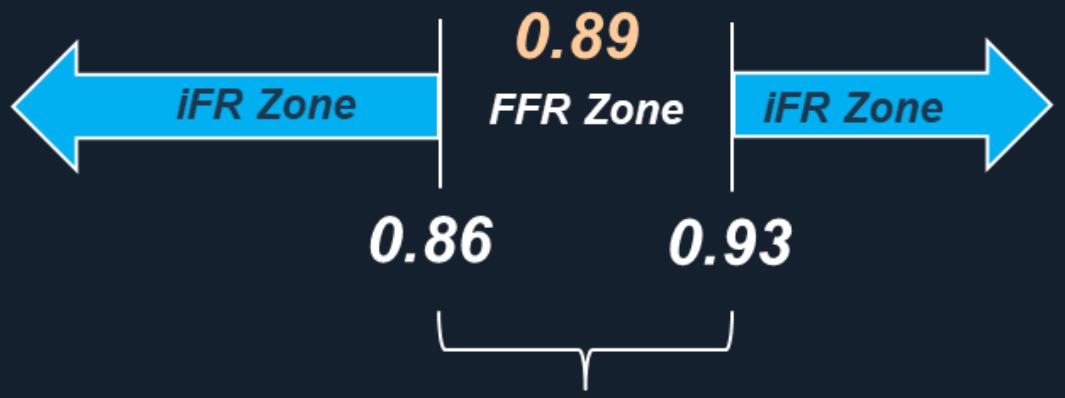
LM/pLAD

Super normal CFR phenotype

Ahn JM, Park SJ et al. Circ Cardiovasc Interv. 2020 May;13(5):e007868

How To Compromise the Discordance

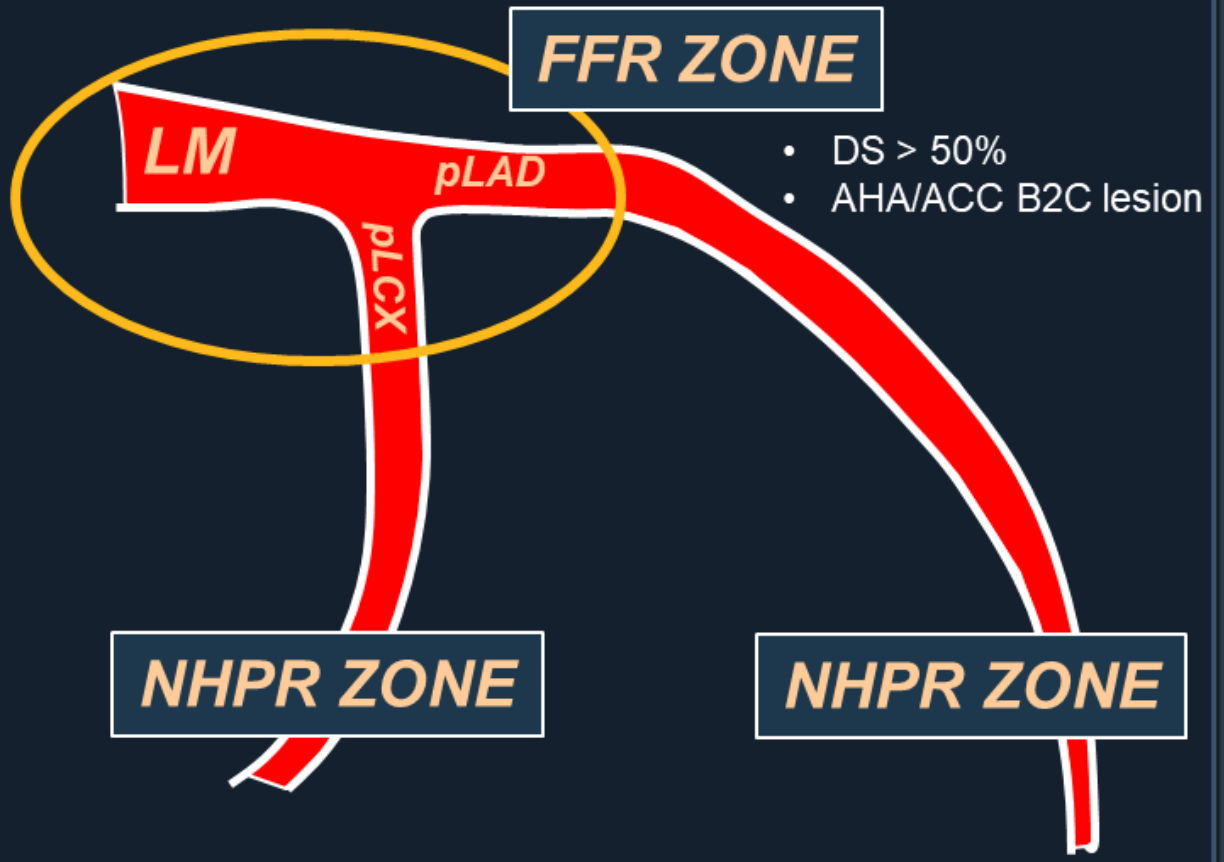
Physiologic Consideration



Clinical Consideration

- Young age
- Male
- Diabetes

Anatomical Consideration



- DS > 50%
- AHA/ACC B2C lesion

Summary

- Current guideline widely endorsed intracoronary physiology, both FFR and iFR.
- iFR could be used in the revascularization decision-making, particularly when hyperemic agents are not easily available.
- FFR would be preferred in lesions which was proximally located or showed angiographically tight or complex.
- All NHPR (resting Pd/Pa, iFR, dPR, RFR, DFR) are the same. Physicians can apply other NHPRs in daily practice in the same manner as iFR.
- In the post-ISCHEMIA era, FFR≤0.80 (or iFR ≤0.89) would be a minimum requirement for coronary revascularization and stenting on the stenosis with FFR>0.80 (or iFR >0.89) is never justified. Please defer.