Synergetic Approach for Discordant Lesions Between FFR and Hyperemia Free Indexes

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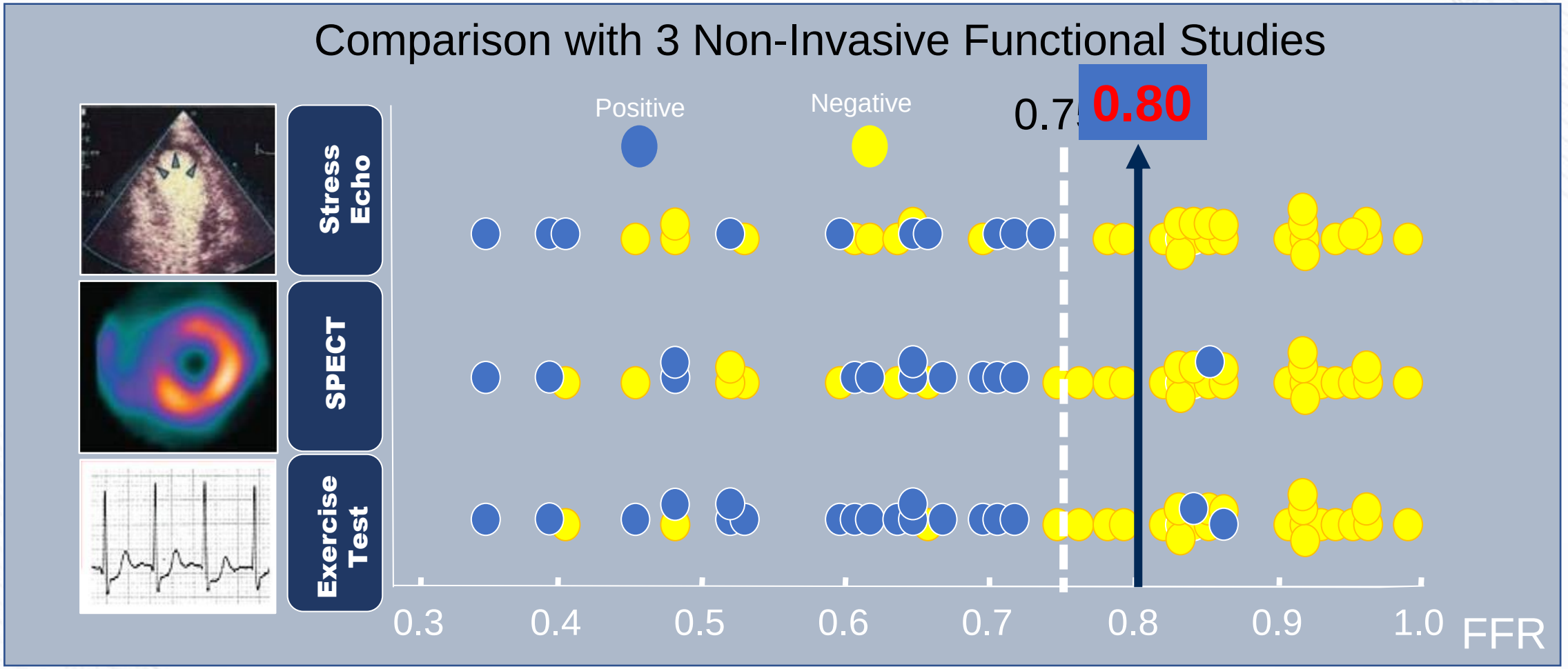
N H Pijls et al. N Engl J Med 1996;334:1703-8,

FFR (0.80) as A Non-Invasive Functional Study In Cath Lab



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

Since TCT 2011,

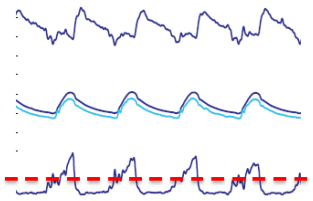
iFR, Instantaneous wave-free ratio (0.89)

Non-hyperemic surrogate index to predict FFR of 0.80

Hypothesis 1

Resistance measured at rest during
free period is similar to mean resis
hyperaemia.

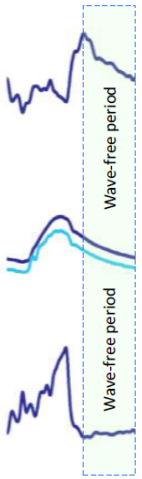
Hyperaemic mean resistance

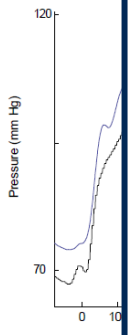


ADVISE study

Hypothesis 2

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



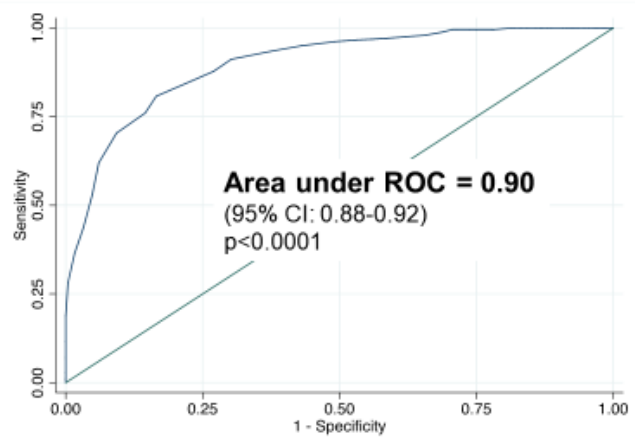


ADVISE study

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

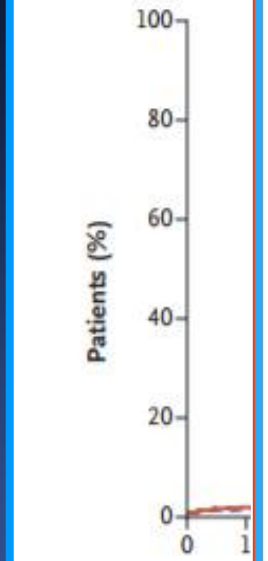
ACC 2017,

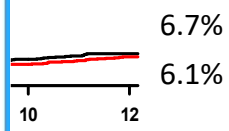
i

e

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





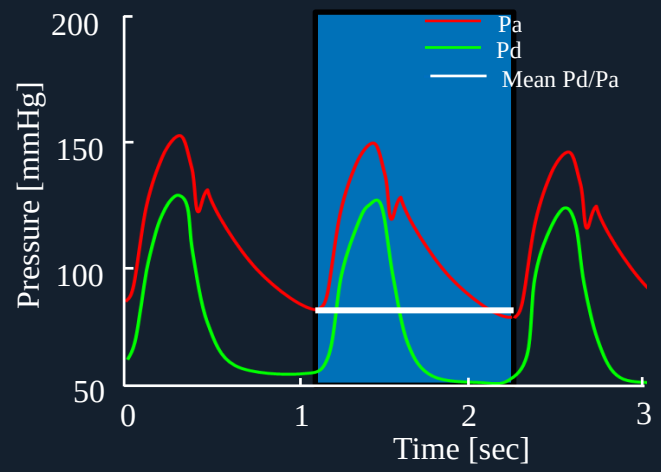
12)
07)
CI) =
0.79, 1.58)
53
956 944
961 946

N Engl J 1813-1823

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

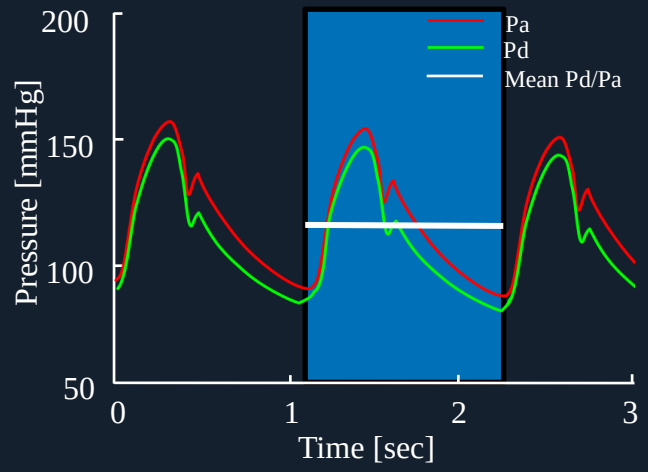
Definition of Physiologic Indices

(A) FFR (≤0.80)



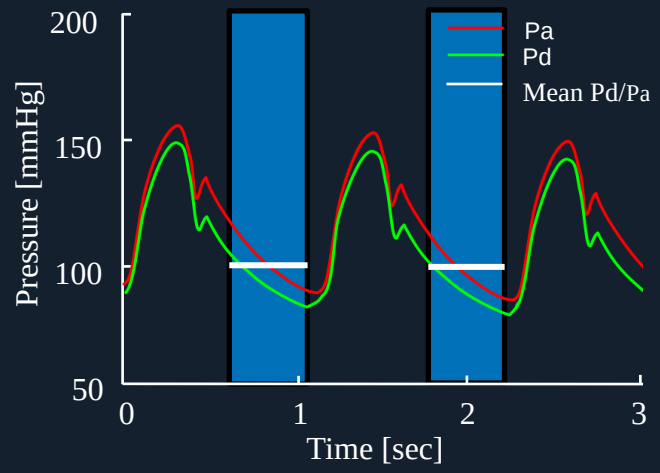
Mean Pd/Pa at hyperemia during the entire cardiac cycle

(B) Resting Pd/Pa (≤0.91/0.92)



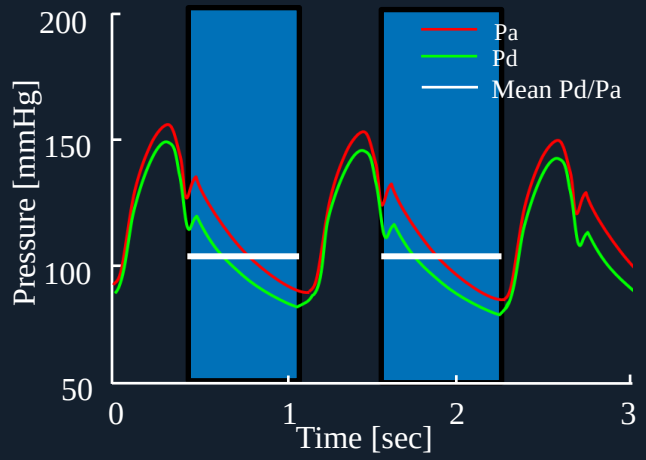
Mean Pd/Pa at rest during the entire cardiac cycle

(C) iFR (≤0.89)



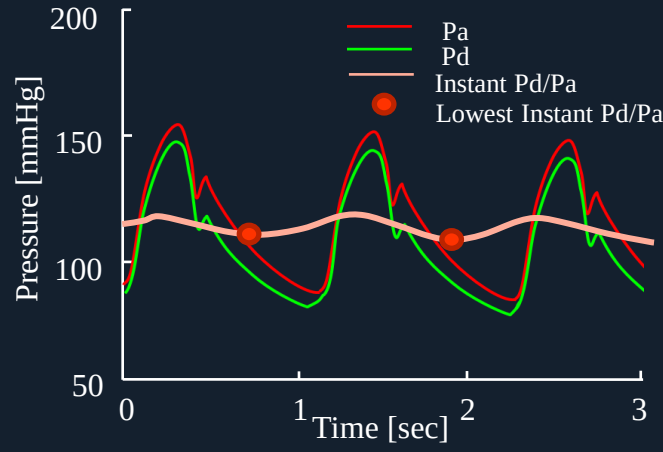
Mean Pd/Pa at rest during wave free period (WFP)

(D) dPR (≤0.89)



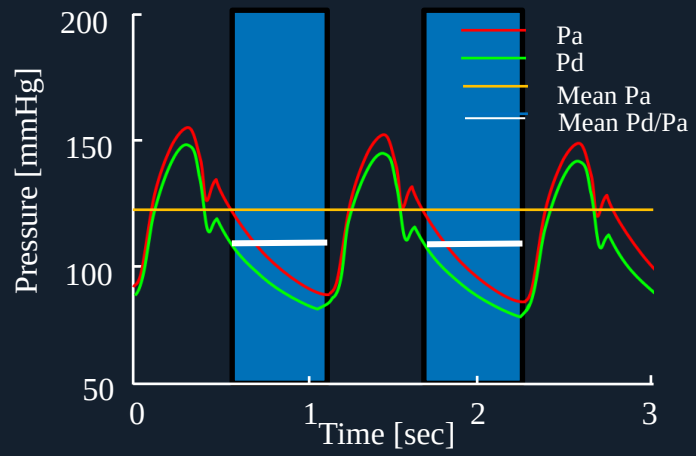
Mean Pd/Pa at rest during the entire diastole

(E) RFR (≤0.89)



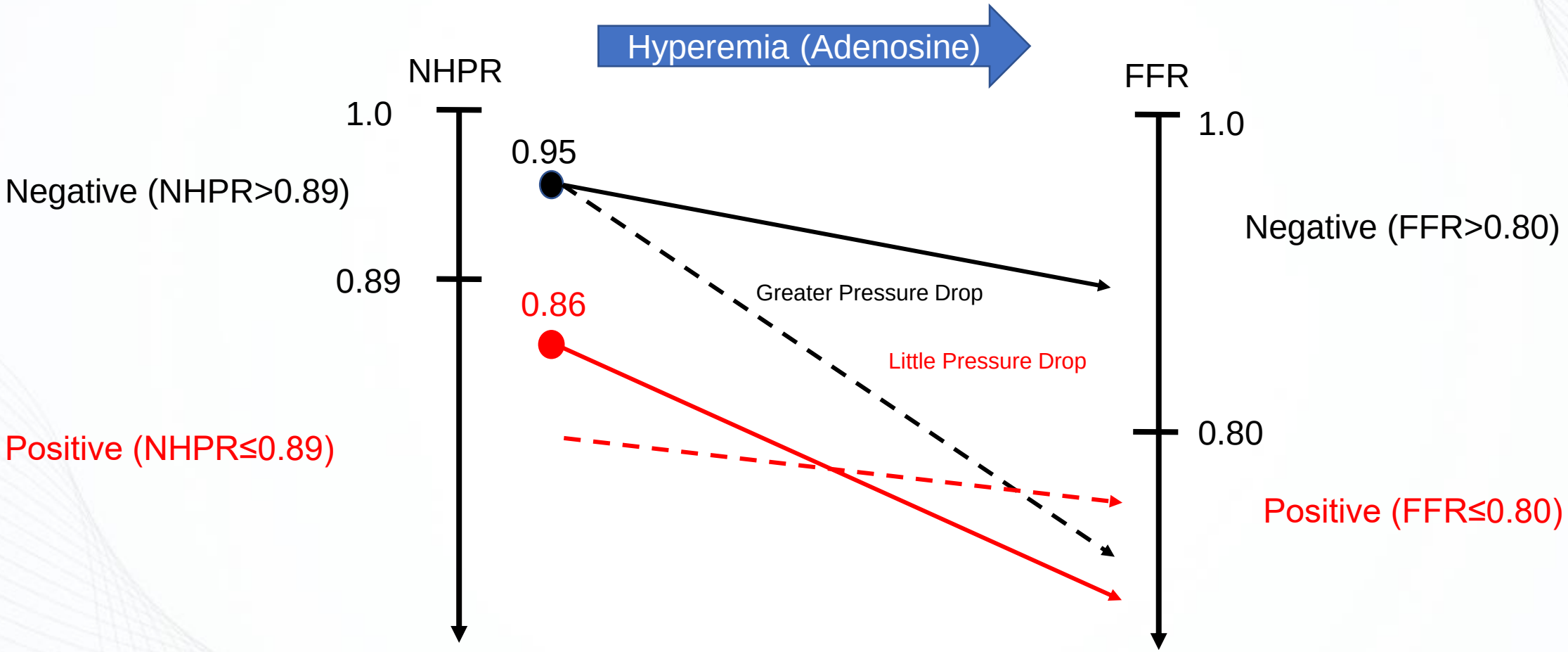
Lowest Instant Pd/Pa at rest during the entire cardiac cycle

(F) DFR (≤0.89)

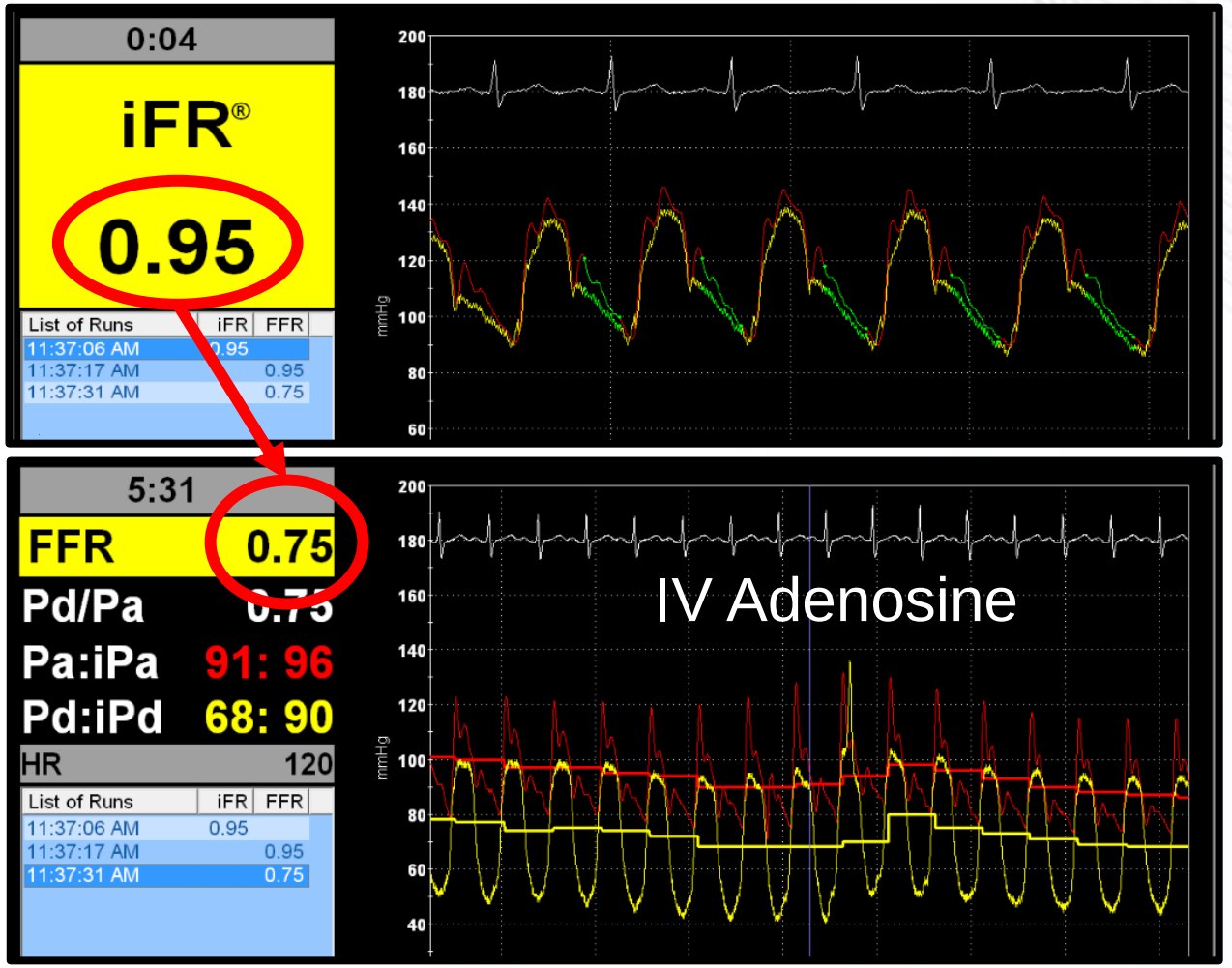


Mean Pd/Pa at rest during the period
Between Pa < mean Pa AND down-sloping Pa

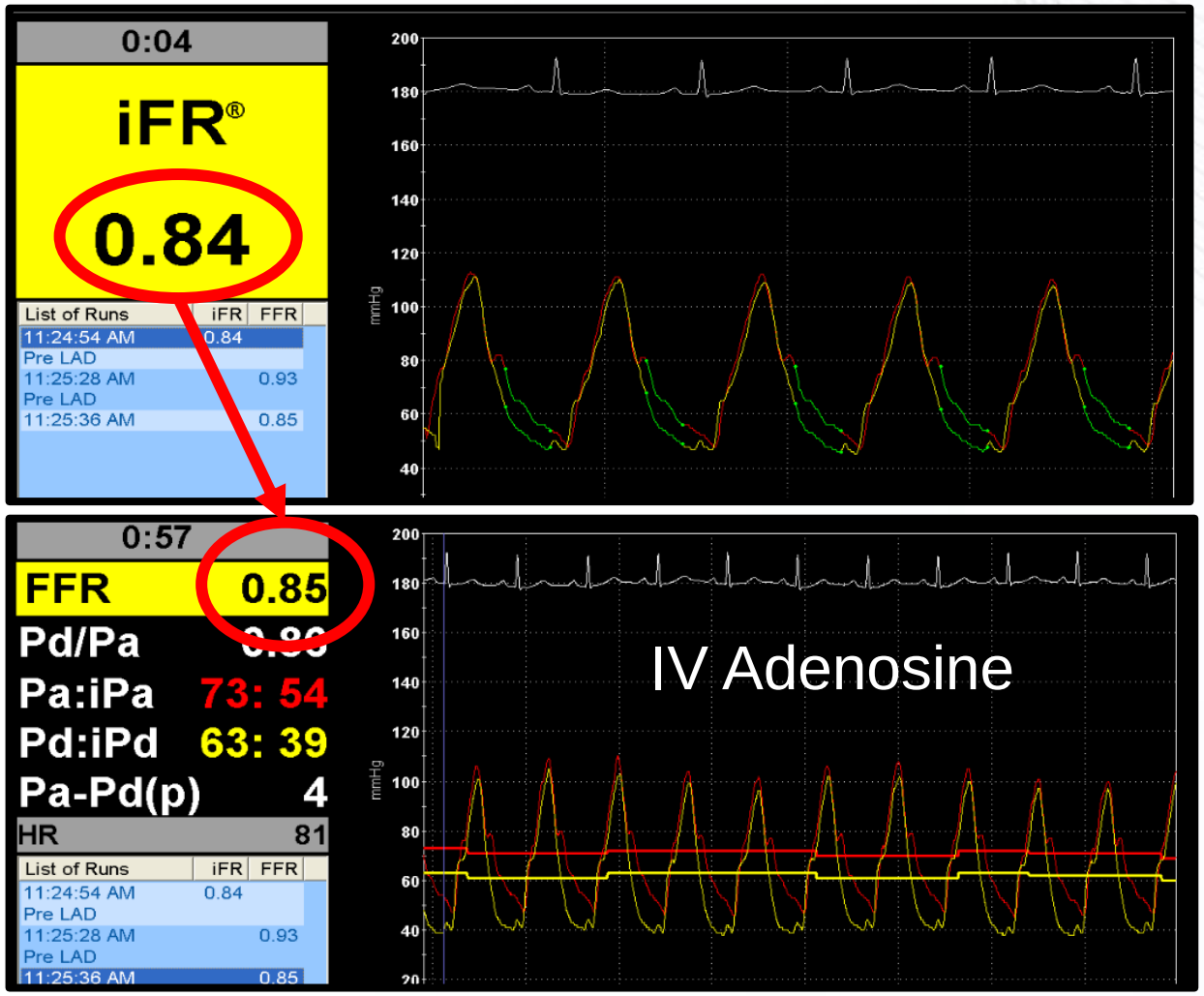
FFR and NHPR Discordance



61 YO/Male with Effort Related Chest Pain (iFR 0.95 ➡ FFR 0.75)

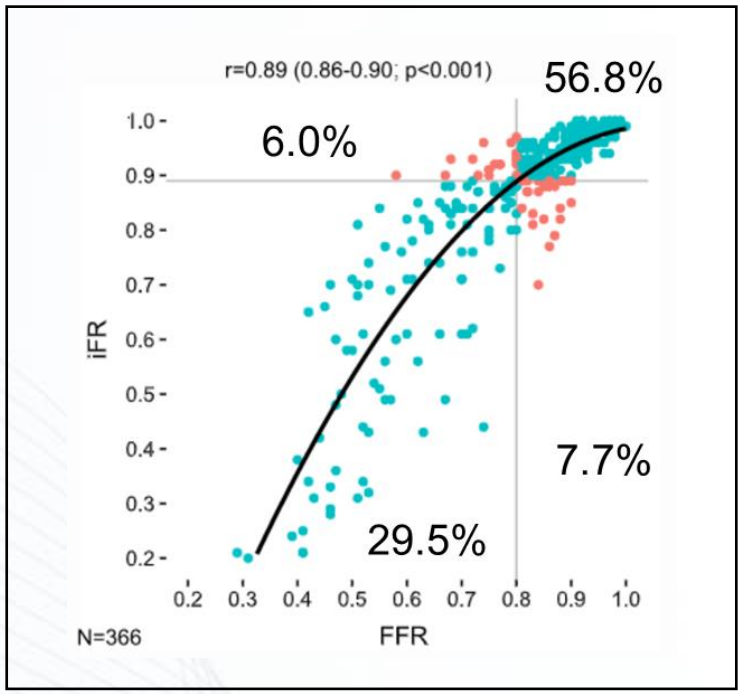


83 YO/Male with Severe AS (iFR 0.84 ➡ FFR 0.85)



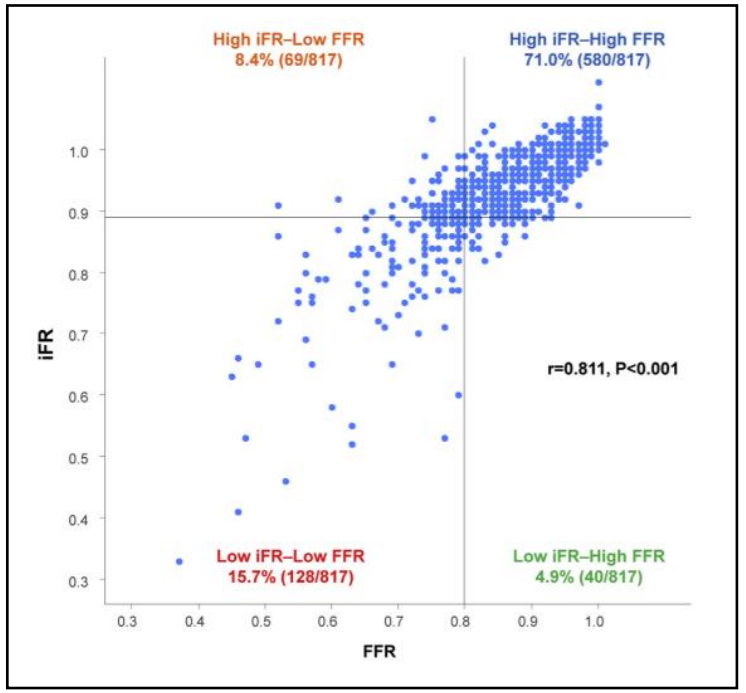
Incidence (1)

13.7 %



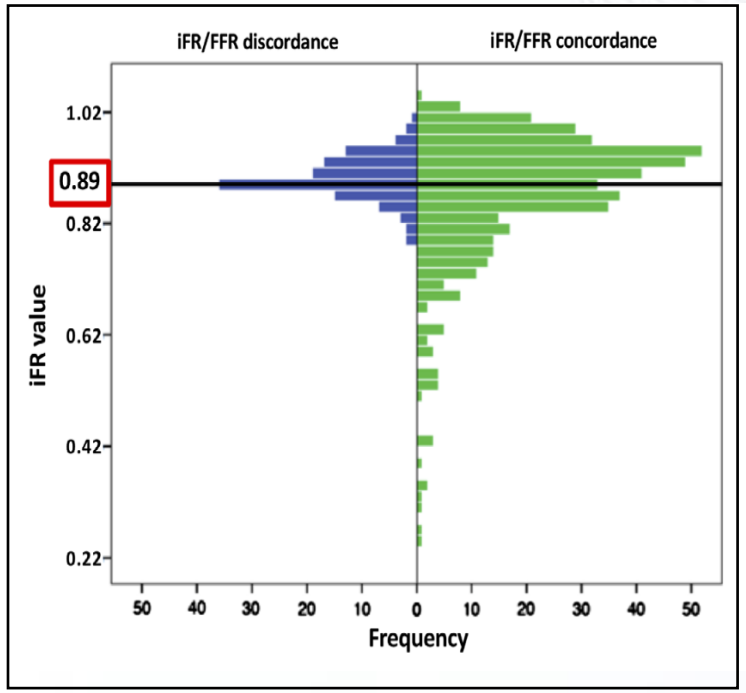
Cook CM et al.
JACC Cardiovasc Interv. 2017;10(24):2514-2524

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

Incidence (2)

Meta-analysis
from 16 studies comprising 5756

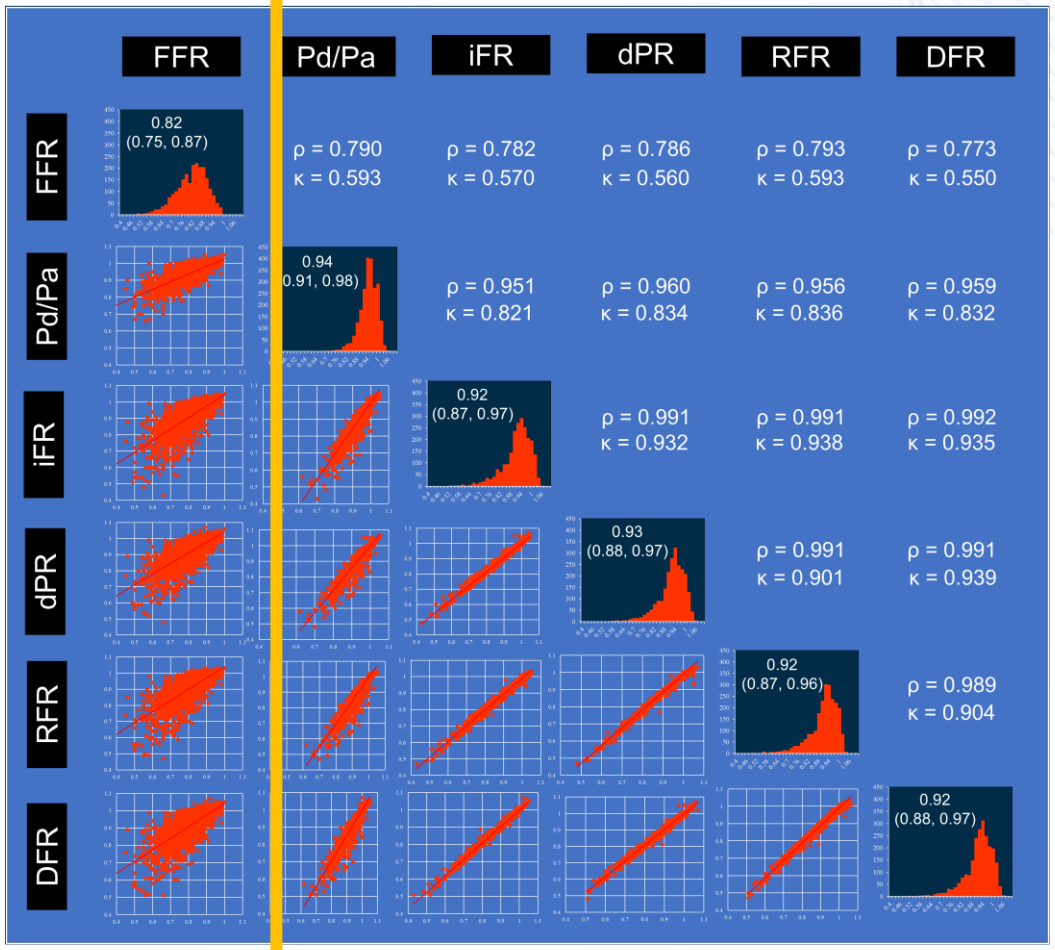
Diagnostic Accuracy: 81%

Measure	Value (95% CI[c])
Diagnostic accuracy	0.81 (0.78–0.84)
Sensitivity	0.78 (0.76–0.79)
Specificity	0.83 (0.81–0.84)
Positive likelihood ratio	4.54 (3.85–5.35)
Negative likelihood ratio	0.28 (0.24–0.32)
Diagnostic odds ratio	17.38 (14.16–21.34)

About 20% Discordance

Cardiovasc Revasc Med. Jul-Aug 2018;19(5 Pt B):613-620

82% Accuracy



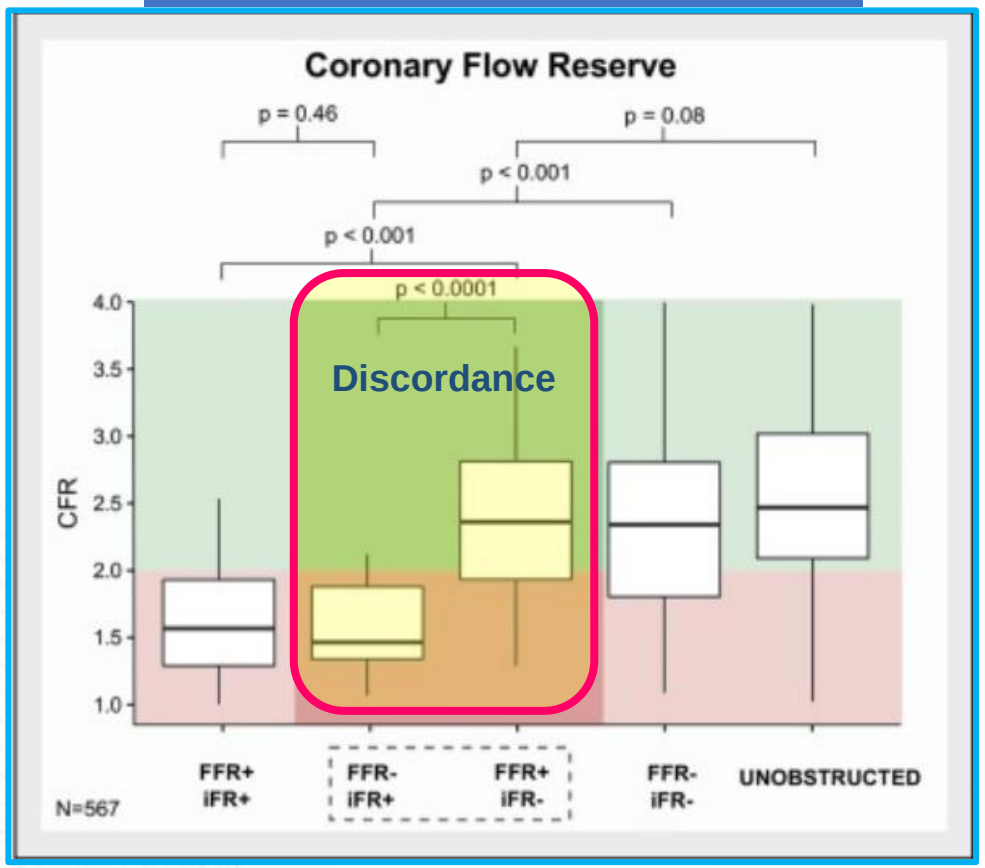
Unpublished Data From IRIS FFR Registry

Incidence (3)

15-20%

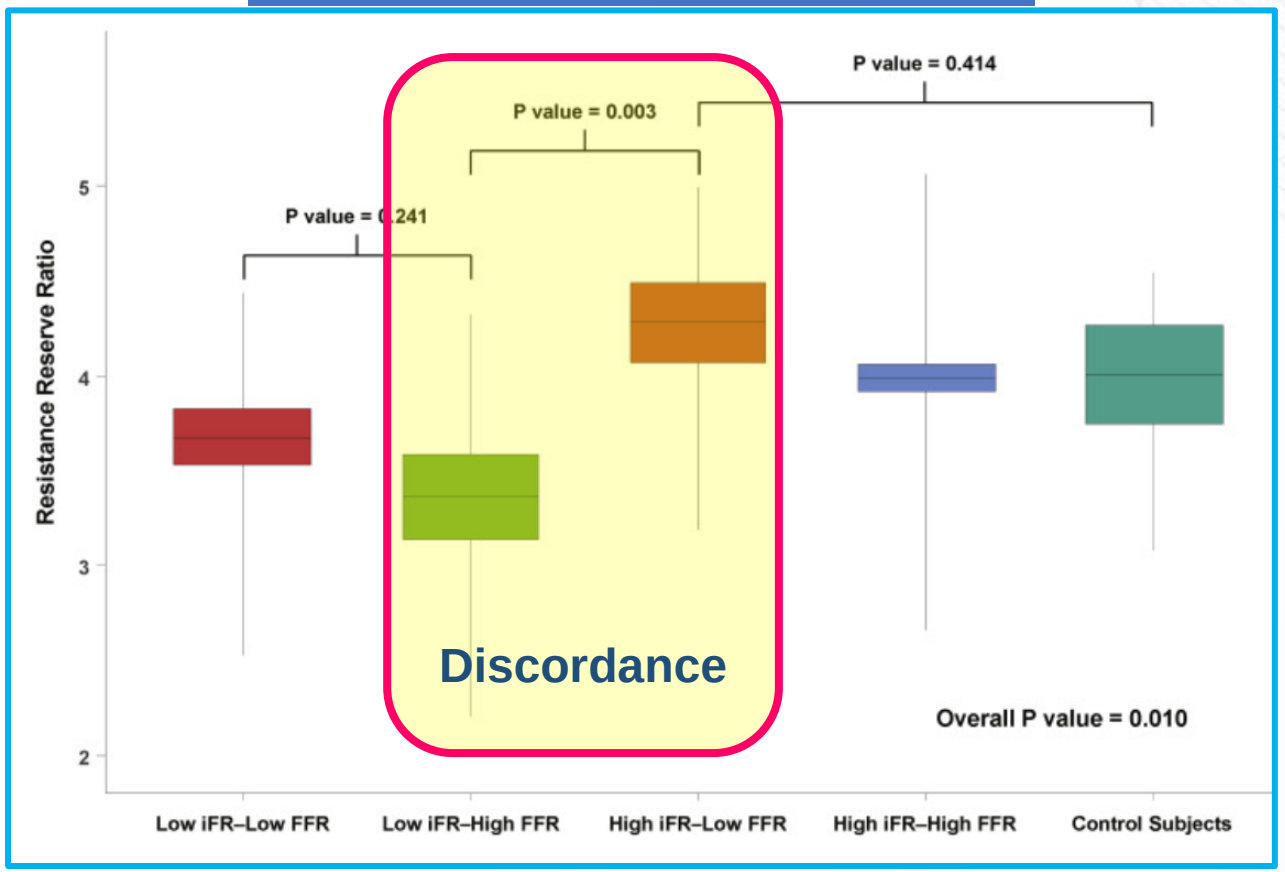
Underlying Mechanism (1) Physiologic Characteristics

Coronary Flow Reserve



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

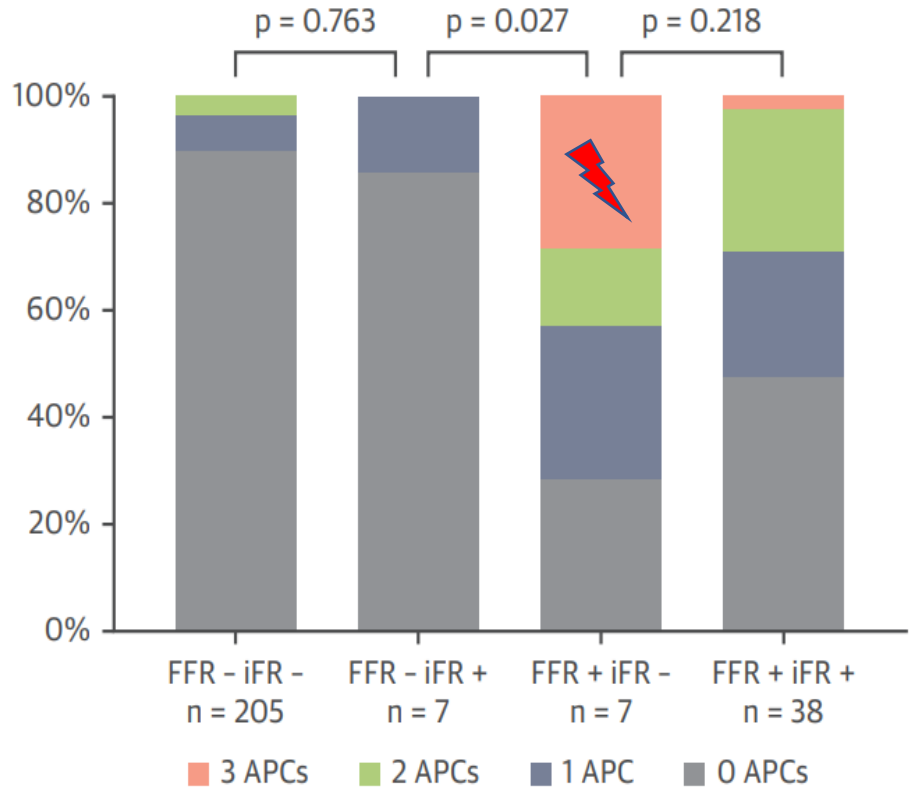
Resistance Reserve Ratio



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

Underlying Mechanism (2) Anatomical Characteristics

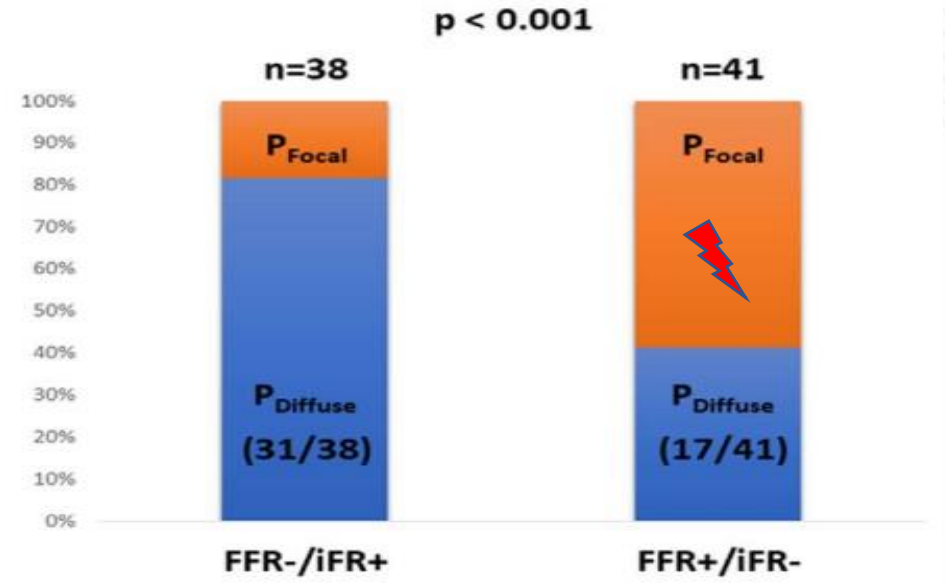
Adverse Plaque Characteristics* Relate More Strongly With FFR than iFR

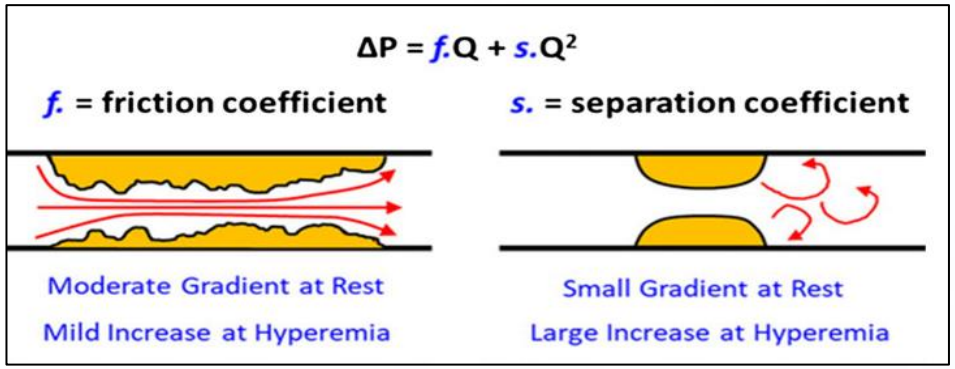


JACC Cardiovasc Imaging. 2020 Mar;13(3):746-756.

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

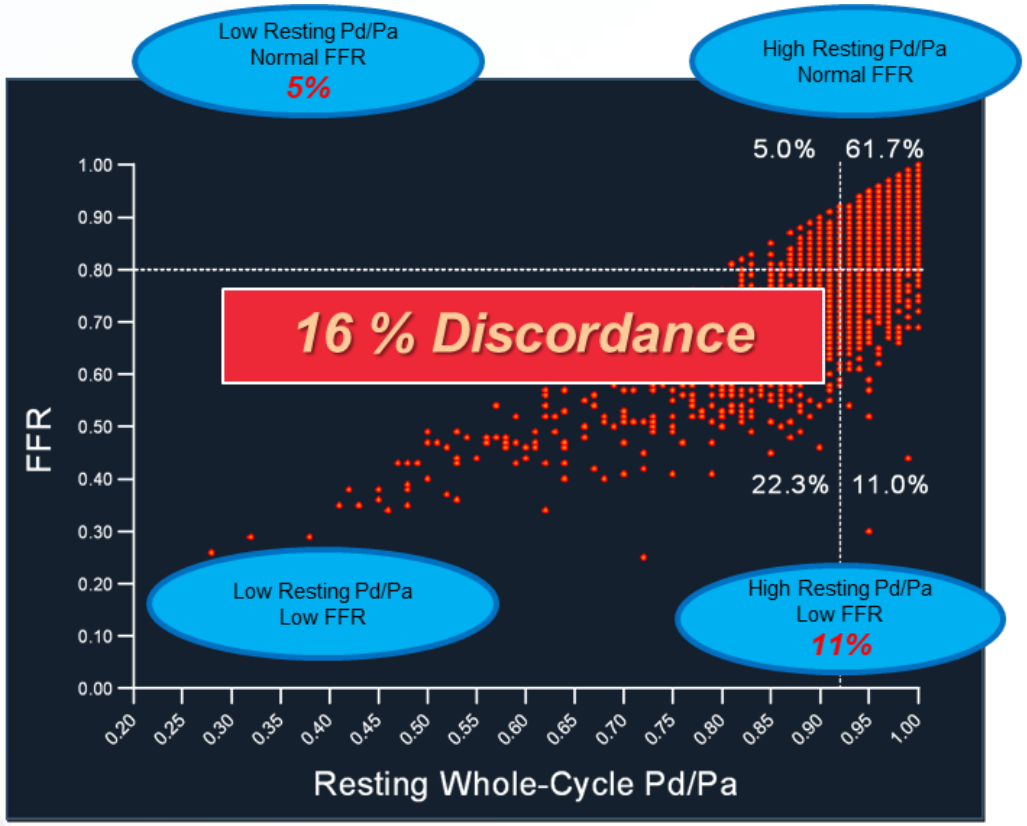
FFR+ iFR− : Focal Disease
FFR− iFR+ : Diffuse Disease





Circ Cardiovasc Interv. 2019;12:e007494

Underlying Mechanism (3) Clinical Characteristics



	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

Super normal CFR phenotype

Old Age, Male Sex, DM, Hyperlipidemia, Family Hx, Chronic renal failure, Proximal Location, Severe Stenosis, AHA/ACC B2C lesion

Red: Pd/Pa- FFR+, **Blue**: Pd/Pa+ FFR-

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

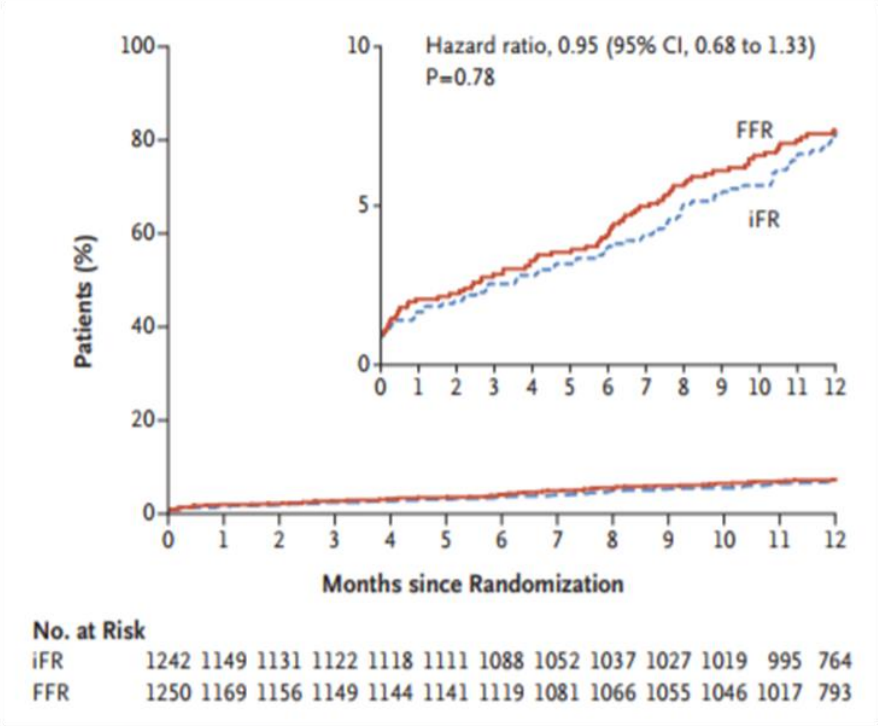
Underlying Mechanism: Summary

NHPR/FFR Discordance

	NHPR+ FFR-	NHPR- FFR+
Coronary physiology	**Un**-Healthy Vascular Status	**More** Complex Atherosclerosis
Coronary anatomy		
Clinical Characteristics		

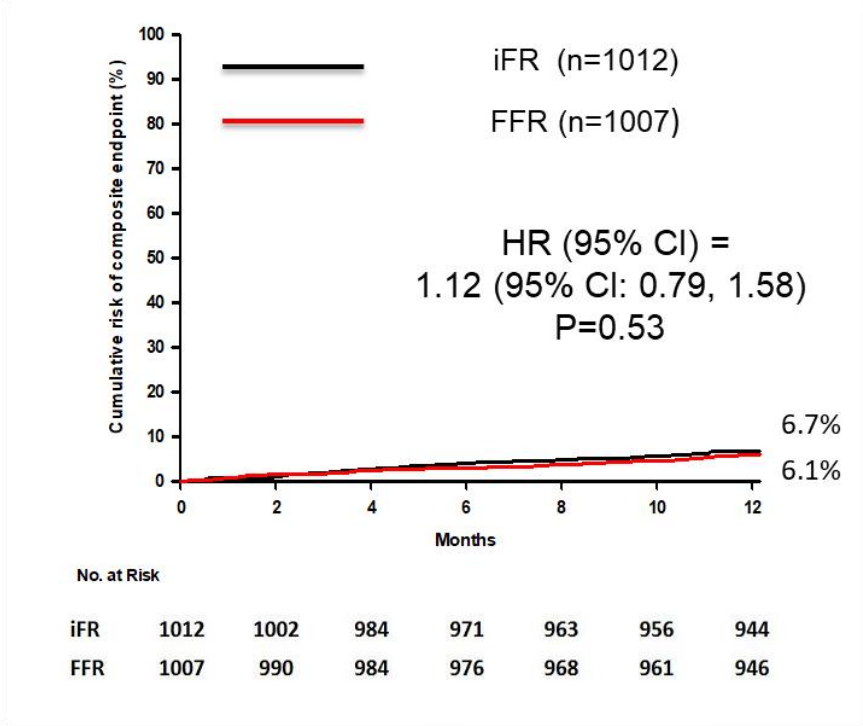
‘One-Size-Fits-All’ 0.89 iFR threshold ?

DEFINE-FLAIR



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

iFR-SWEDEHEART

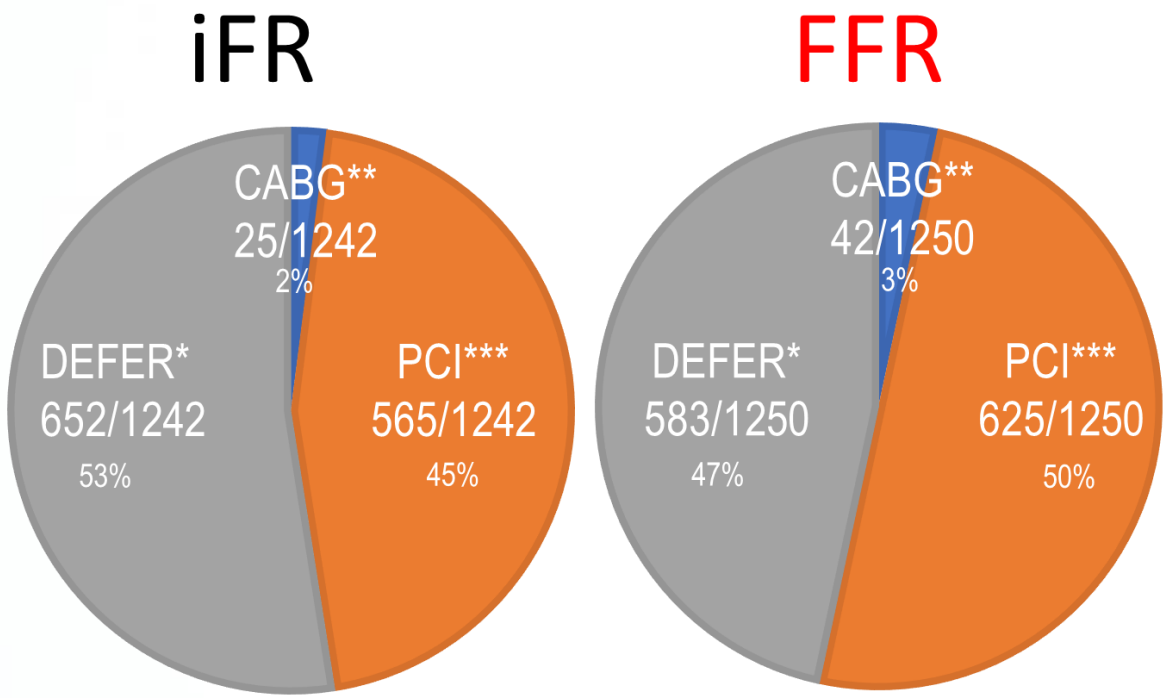


N Engl J Med. 2017 May 11;376(19):1813-1823

Physiologic Perspective, Underpowered Studies

Different Treatment Due to Discordance

Treatment allocation with iFR and FFR



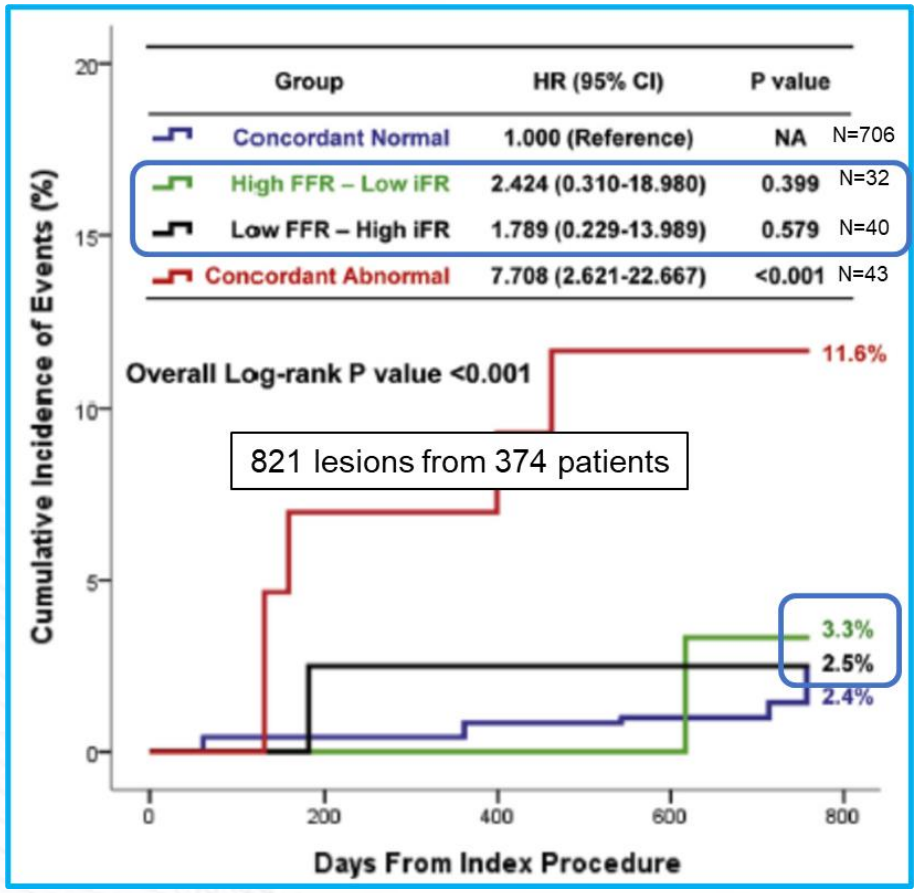
p for comparison between patients randomized to iFR and FFR

DEFER* p=0.003
CABG** p=0.04
PCI*** p=0.02

Significantly less revascularization based on iFR interrogation

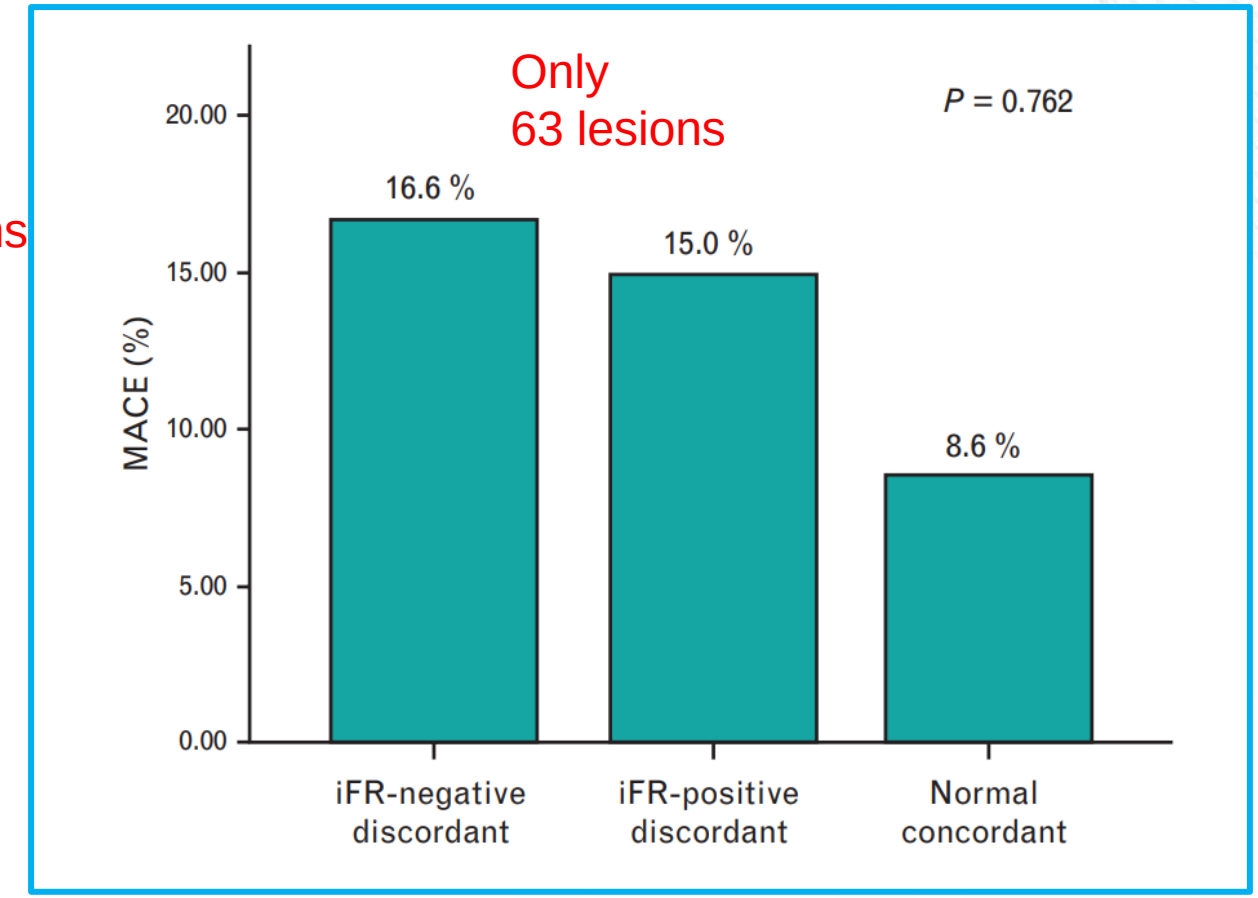
DEFINE FLAIR

Prognosis of Discordant Lesion…..Very Limited Data



Only
72 lesions

Only
63 lesions



J Am Coll Cardiol Intv 2017, 10: 2502

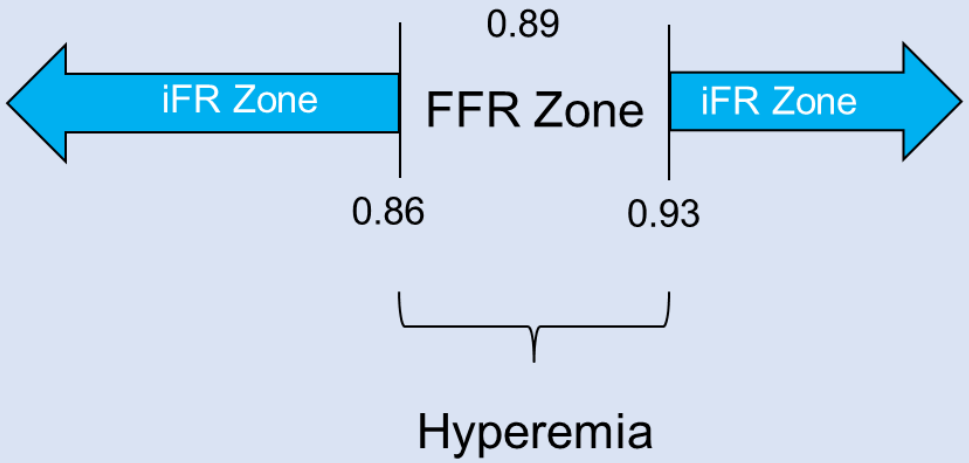
Journal of Cardiovascular Medicine 23(2):p 106-115, February 2022

FFR and iFR value of Discordant Lesions

	FFR		iFR	
	iFR+ FFR-	iFR- FFR+	iFR+ FFR-	iFR- FFR+
Cook CM et al. JACC Cardiovasc Interv. 2017;10(24):2514-2524	0.86 (0.84-0.88)	0.77 (0.74-0.80)	0.88 (0.84-0.89)	0.92 (0.91-0.93)
SH Lee et al. JACC Cardiovasc Interv. 2019;12(20):2018-2031	0.85 (0.84-0.86)	0.76 (0.75-0.78)	0.88 (0.87-0.88)	0.93 (0.92-0.93)
Derimay F et al. Catheter Cardiovasc Interv. 2019;94(3):356-363	0.84±0.03	0.77±0.04	0.87±0.03	0.92±0.03
Filippo et al. J Cardiovasc Med. 2022;23(2):106-115	0.87±0.03	0.76±0.05	0.86±0.02	0.92±0.02
Aoi et al. Cardiovasc Revasc Med. 2021;24:57-64.	0.85±0.04	0.77±0.04	0.85±0.04	0.88±0.04

How To Rectify the Discordance

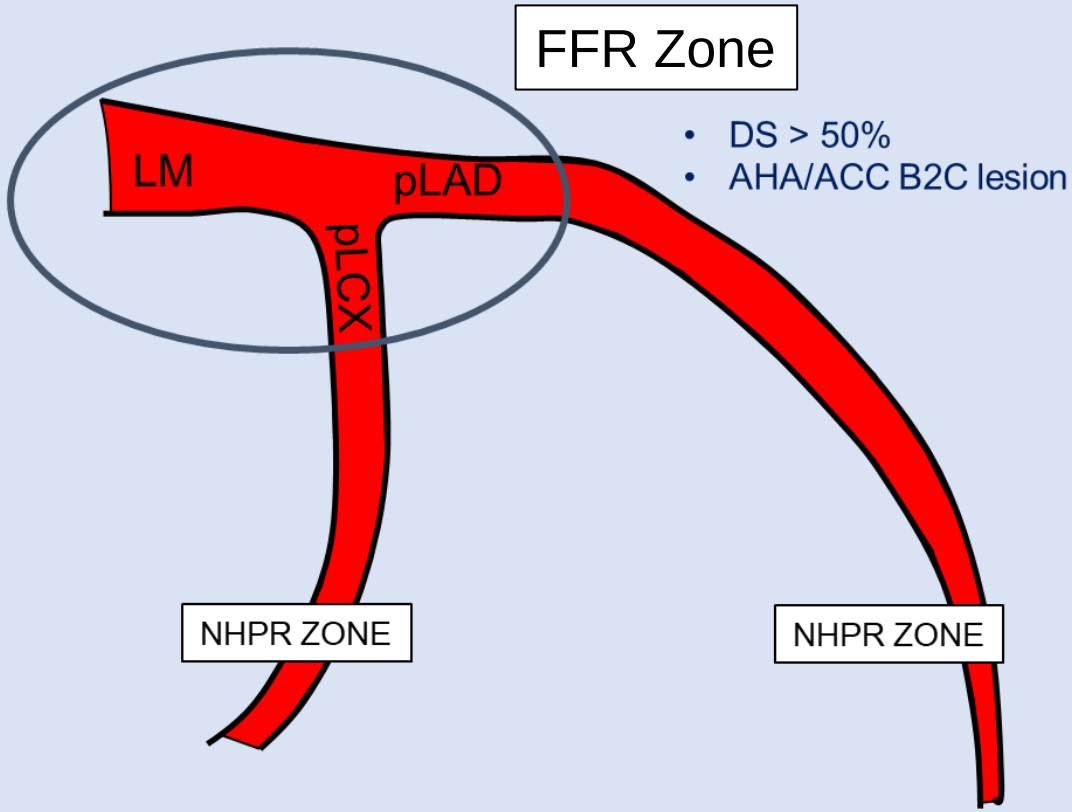
Physiologic Consideration



Clinical Consideration

- Young age
- Male
- Diabetes, Chronic Kidney Disease

Anatomical Consideration



- DS > 50%
- AHA/ACC B2C lesion

Summary

- Incidence of FFR-NHPR discordance = 15-20%
- The FFR-NHPR discordance is associated with distinct physiologic, anatomic and clinical characteristics.
- However, there is currently no evidence (only limited number of studies with very small population) to suggest any prognostic differences between the two discordant patterns. In addition, FFR values in FFR+NHPR- discordant lesion are located in “grey-zone” FFR, indicating that the clinical implications may be less critical.
- Nevertheless, FFR should be preferred in stenoses of LM or pLAD, where FFR+ iFR- discordance is more common, and where revascularization has been shown to impact survival.
- Further study focusing on discordant lesions including larger population with long-term follow-up would be necessary.