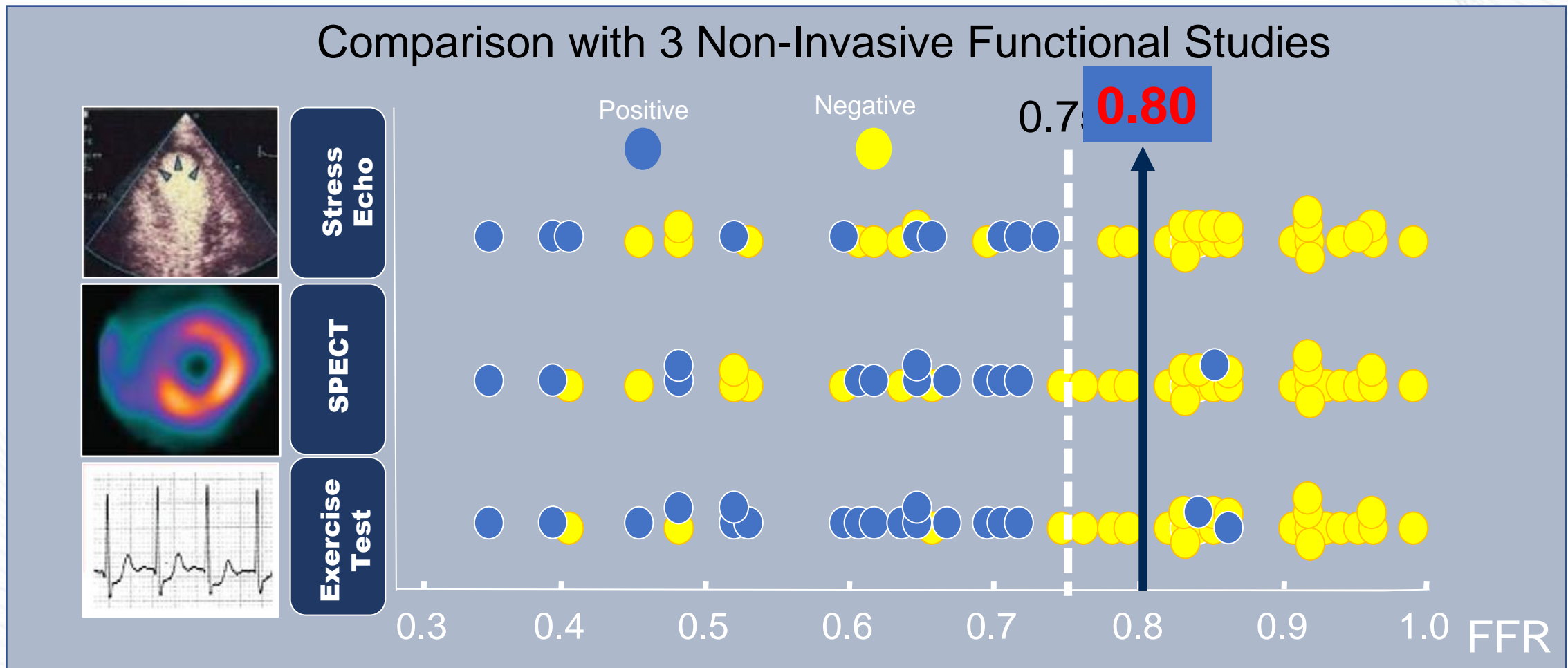


Synergetic Approach for Discordant Lesions Between FFR and Hyperemia Free Indexes

Jung-Min Ahn, MD.

Division of Cardiology, Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea

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,

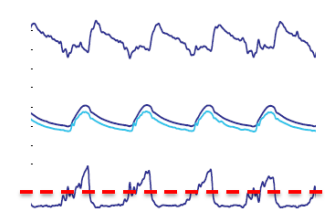
iFR, Instantaneous wave-free ratio (0.89)

Non-hyperemic surrogate index to predict FFR of 0.80

Hypothesis 1

Resistance measured at rest during wave-free period is similar to mean resistance during **hyperaemia**.

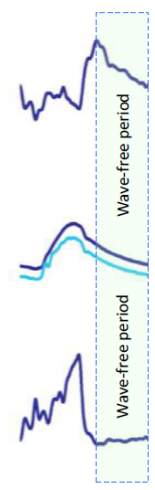
Hyperaemic mean resistance



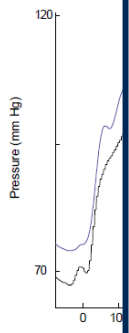
ADVISE study

Hypothesis 2

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

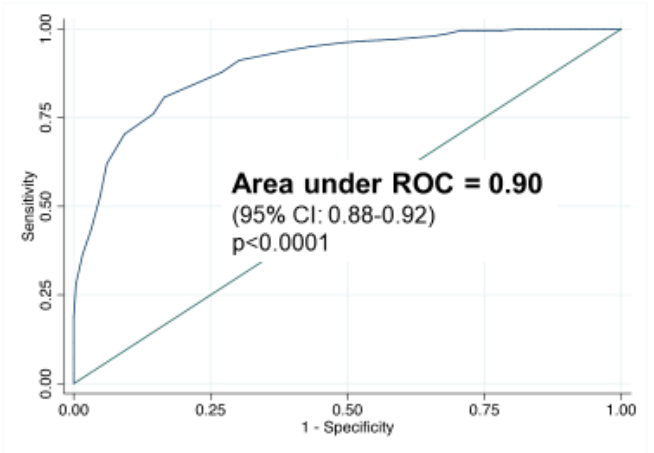


ADVISE study



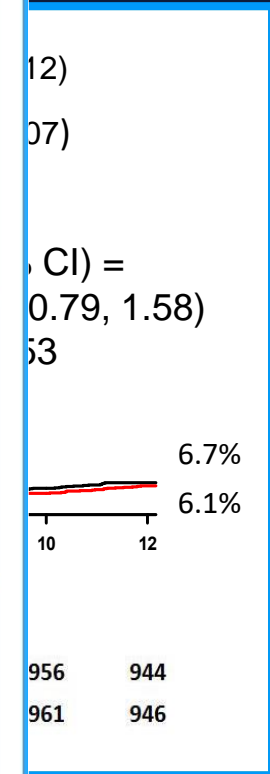
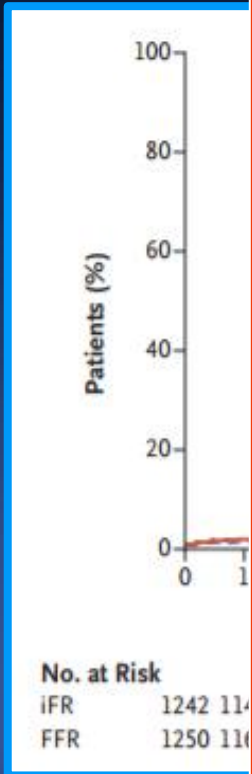
Diagnostic accuracy of iFR Compared with FFR, 0.80

- 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%**



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



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

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PUBLISHED BY ELSEVIER

ORIGINAL INVESTIGATION

Agreement of to Aortic Coronary Pressure the Instantaneous

Yuhei Kobayashi, MD,^{1,2} Nils P. Johnson,³ Colin Berry, MBChB, PhD,^{4,5} Allen J. Giles Rioufol, MD, PhD,⁶ Seung-Jung Keith G. Oldroyd, MBChB, MD,⁷ Emma Bernard De Bruyne, MD, PhD,⁸ William

ABSTRACT

BACKGROUND Recently, 2 randomised resting coronary physiological index, i.e. distal to aortic coronary pressure (Pd/Pa) catheterization laboratory; however, i

OBJECTIVES The goal of this study

METHODS A total of 763 patients were assessed. Using iFR = 0.89 ± 0.08 ± 0.09 (FR_{mean}), 0.003 ± 0.001 > 0.99 (p < 0.001 for all). Area accuracy compared with FFR was

RESULTS According to the independence (82.2% vs 96.1%; p < 0.001), respectively (interquartile range: 0.88 to 0.95), and according to the receiver-operating characteristic curve: 0.98; 95% confidence interval: accuracy, sensitivity, specificity, positive and 92.7%, respectively. These results

CONCLUSIONS Pd/Pa was analyzable agreement with iFR, suggesting that Approximate FFR Compared to Pure Res

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From the ¹Stanford University School of Medicine, ²McGovern Medical School at UTHealth and the Netherlands; ³Kanazawa Institute, Södergård Jubilee National Hospital, Clydebank, Scotland; ⁴Cardiovascular and Medical Sciences, University Book University Medical Center, Stony Brook, National University Hospital, Seoul, South Korea; ⁵CARMEN, Lyon, France; ⁶University of Osnabrück Center Aachen, Aachen, Belgium; and the ⁷Cardflow was an investigator-initiated study sponsored by

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Comparison Diastolic Res Are They All Equal

Marcel van't Veer, MSc, PhD,^{1,2} Stuart Watkins, MBChB, MD,^{3,4} Lolkien X. van Nunen, MD, PhD,

ABSTRACT

BACKGROUND Pressure mea resting-state physiological as

OBJECTIVES The aim of this

METHODS In the population of study, iFR calculated by propri compared with the ratio of resti (dPR), 25% to 75% of diastole (d iFR-like indexes shortening the I differences, Spearman correlatio diagnostic performance with res

RESULTS Median iFR in 197 pa differences (± SD) with iFR we 0.009 (FR_{mean}), 0.003 ± 0.00 > 0.99 (p < 0.001 for all). Area accuracy compared with FFR wa

CONCLUSIONS All diastolic re agreement with FFR. A numeric guidelines, and clinical recom Unselected Population Referred © 2017 The Authors. Published access article under the CC BY-N

From the ¹Department of Cardiology, C Engineering, Eindhoven University of T cular Research Centre, University of G Golden Jubilee National Hospital, Clyde York; ²Cardiovascular Center Aachen, Aachen, Italy; ³van't Veer has received has equity in Philips, GE, HeartFlow, and Jude Medical and Cardiovascular System Boston Scientific, Dr. De Bruyne is Share Omega Pharma; his institution, the Card track, and St. Jude Medical, and his ins Openess, and Boston Scientific outside of has received speaker and consultancy fo of Glasgow hold research and consultant Abbott; and has received research support relevant to the contents of this paper to

Manuscript received September 2, 2017;



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euro PCR 2018 LATE BREAKING TRIALS

Validation of a novel non-hyperemic artery stenosis severity: the (VALIDATE RFR) study



Johan Svanerud¹, MSc; Jung-Min Ahn, Ankit Gore^{2,3}, BS, MSc; Akiko Maebe, Bernard De Bruyne⁴, MD, PhD; Nils P. Smart Watkins⁵, MD; Colin Berry^{6,7,8,9,10,11}, Seung-Jung Park², MD, PhD; Ziad A.

1. Corvallis Research AB, Uppsala, Sweden; 2. Asian Medical Research Foundation, New York, NY, USA; 3. St. Francis Hospital the Netherlands; 4. Eindhoven University of Technology, Dept. the Netherlands; 5. NewYork-Presbyterian Hospital/Columbia University Medical Hospital, Aachen, Belgium; 6. Weatherhead PET Center, Division at UTHealth and Memorial Hermann Hospital, Houston, TX, Kingdom; 7. Institute of Cardiovascular and Medical Science

This paper also includes supplementary data published online at

KEYWORDS

- fractional flow reserve
- innovation
- other imaging modalities

Abstract
Aims: Randomised controlled fractional flow reserve (FFR) for by sensitive landmarking of the resistance occur during a fixed p novel non-hyperemic index o distal coronary pressure to aortic timing within the cardiac cycle

Methods and results: VALIDATE RFR. The primary endpoint was in 651 waveforms in which iFR correlated to iFR (R=0.99, p<0.020). The diagnostic performance specificity 96.9%, positive predictive operating characteristic curve of 95% CI: -0.009 to 0.006, p=0.002, and 32.4% (167/516) compared to FFR was lowest (4

Conclusions: RFR is diagnostic Pd/Pa during the full cardiac cycle would be missed by assessment

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European Heart Journal (2019) 40, 2585–2592
doi:10.1093/eurheartj/ehz230

Diastolic pressure ratio validation vs. the instantaneous

Nils P. Johnson¹, Wenguang Li², Xi Chen³, Colin Berry^{3,4}, William F. Fearon⁵, and K

¹Weatherhead PET Center, Division of Cardiology, Department of Medicine, McGovern Medical School, Baylor College of Medicine, Houston, TX, USA; ²British Heart Foundation Glasgow Cardiovascular Research Centre, Glasgow, UK; ³West of Scotland Heart and Lung Centre, Golden Jubilee National Hospital, Glasgow, UK; ⁴St. Francis Hospital, New York, NY, USA; ⁵Stanford University School of Medicine, Stanford, CA, USA

Aims

The instantaneous wave-free ratio (iFR) non-hyperemic conditions. To test for unique coronary pressure measurements, we compared numerical similarity and test/retest repeatability

Methods and results

Eight hundred and ninety-three lesions from 100 patients. Diastolic pressure ratio and a linear trend. Mean difference between dPR and iFR (Δ) = (ROC curve (AUC) = 0.997) mirrored that of iFR (Δ) = -0.012 ± 0.031, r² = 0.927, AUC = 0.997, p < 0.001, indicating excellent agreement. Average Δ = -0.002 ± 0.001, r² = 0.998, AUC = 1.000, indicating perfect agreement.

Conclusions

Our dPR offers numerical equivalency to iFR. The agreement between dPR and iFR during the period of diastole, the agreement between dPR and iFR during the period of diastole, the agreement between dPR and iFR during the period of diastole further confirm numerical equivalency

Keywords

Instantaneous wave-free ratio • Coronary

Introduction

Resting coronary physiology to guide revascularisation procedures dates to the very advent of percutaneous coronary intervention (PCI). In the first reported series of coronary balloon angioplasties in 1979, Andreas Grüntzig measured the pressure drop across the stenosis (ΔP) at baseline and again after dilation, although biased by the acknowledged iatrogenic gradient generated by the device itself.¹ Pressure gradient assessment was a routine component of interventional procedures in the initial years, until catheters became too small to obtain reliable signals through the central channel. In some early clinical cases at Emory University, measurement of resting ΔP was

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ORIGINAL ARTICLE

Validation of Resting Diastolic Pressure Ratio Calculated by a Novel Algorithm and Its Correlation With Distal Coronary Artery Pressure to Aortic Pressure, Instantaneous Wave-Free Ratio, and Fractional Flow Reserve

The dPR Study

See Editorial by Kern and Seto

BACKGROUND: Instantaneous wave-free ratio (iFR) offers a reliable non-hyperemic assessment of coronary physiology but requires dedicated proprietary software with a fully automated algorithm. We hypothesized that dPR (diastolic pressure ratio), calculated with novel universal software, has a strong correlation with iFR, similar diagnostic accuracy relative to resting distal coronary artery pressure/aortic pressure and fractional flow reserve (FFR).

METHODS AND RESULTS: The dPR study is an observational, retrospective, single-center cohort study including patients who underwent iFR or FFR. Dedicated software was used to calculate the dPR from Digital Imaging and Communications in Medicine (DICOM) pressure waveforms. The flat period on the pressure difference between sample (dP) to the time difference between the same sample points (dt) signal was used to detect automatically the period, where the resistance is low and constant, and to calculate the dPR, which is an average over 5 consecutive heartbeats. The software was validated by correlating iFR results with dPR. Software validation was done by comparing 78 iFR measurements in 44 patients who underwent iFR. Mean iFR and dPR were 0.91 ± 0.10 and 0.92 ± 0.10, respectively, with a significant linear correlation (R = 0.997; P < 0.001). Diagnostic accuracy was tested in 100 patients who underwent FFR. Mean FFR, resting distal coronary artery pressure/aortic pressure, and dPR were 0.85 ± 0.09, 0.94 ± 0.05, and 0.93 ± 0.07, respectively. There was a significant linear correlation between dPR and FFR (R = 0.77; P < 0.001). Both distal coronary artery pressure/aortic pressure and dPR had good diagnostic accuracy in the identification of lesions with an FFR ≤ 0.80 (area under the curve, 0.84; 95% CI, 0.76–0.92 and 0.86; 95% CI, 0.78–0.93, respectively).

CONCLUSIONS: dPR, calculated by a novel validated software tool, showed a strong linear correlation with iFR. dPR correlated well with FFR with a good diagnostic accuracy to identify positive FFR.

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Frits Mastik, BSc
Laurens van Zandvoort, BSc
Miguel E. Lemmert, MD, PhD
Jeroen Wilschut, MD
Roberto Diletti, MD, PhD
Peter de Jaegere, MD, PhD
Felix Zijlstra, MD, PhD
Isabella Kardys, MD, PhD
Nicolas M Van Mieghem, MD, PhD
Joost Daemen, MD, PhD

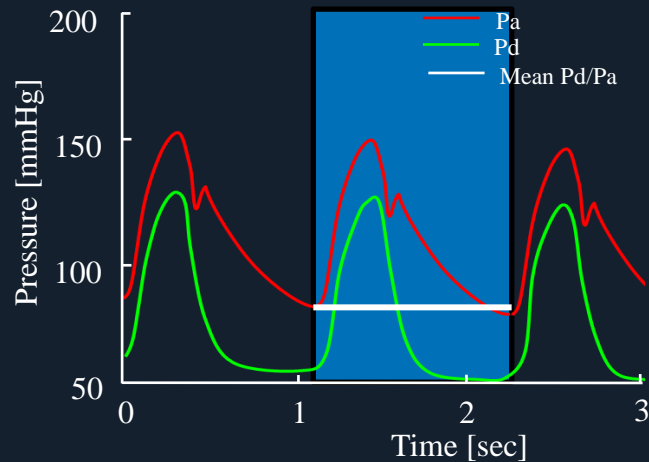
*J. Ligthart and Dr Masdjedi contributed equally to this paper.

Key Words: catheter • methods • physiology • software • software validation

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https://www.ahajournals.org/journal/circinterventions

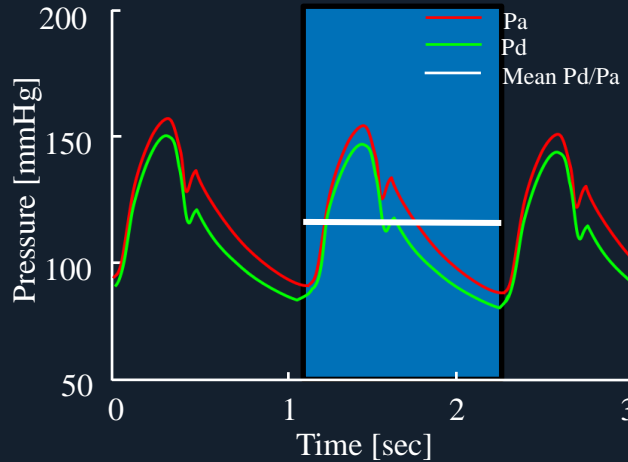
Definition of Physiologic Indices

(A) FFR (≤ 0.80)



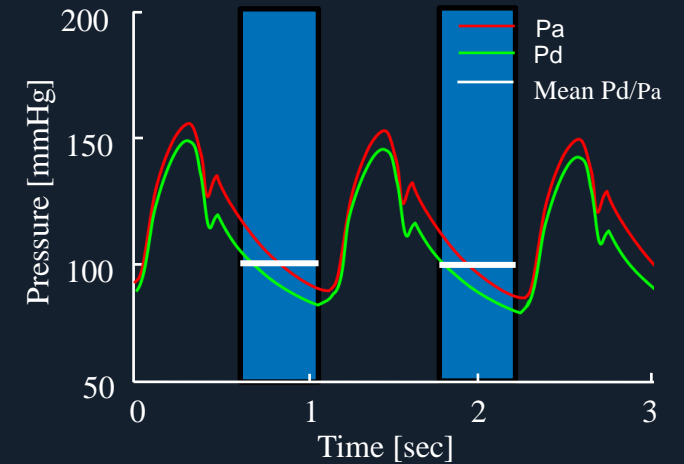
Mean Pd/Pa at hyperemia during the entire cardiac cycle

(B) Resting Pd/Pa ($\leq 0.91/0.92$)



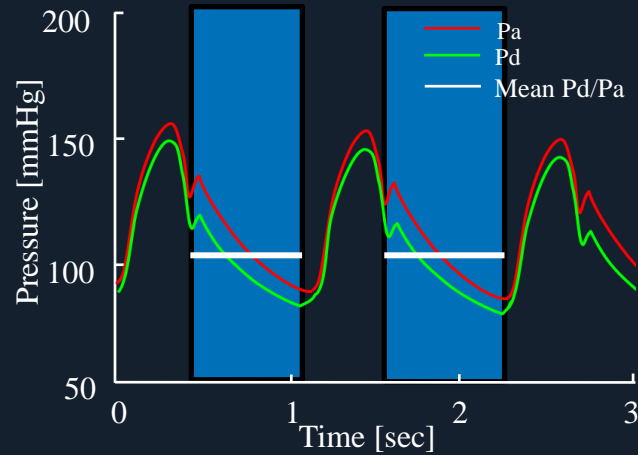
Mean Pd/Pa at rest during the entire cardiac cycle

(C) iFR (≤ 0.89)



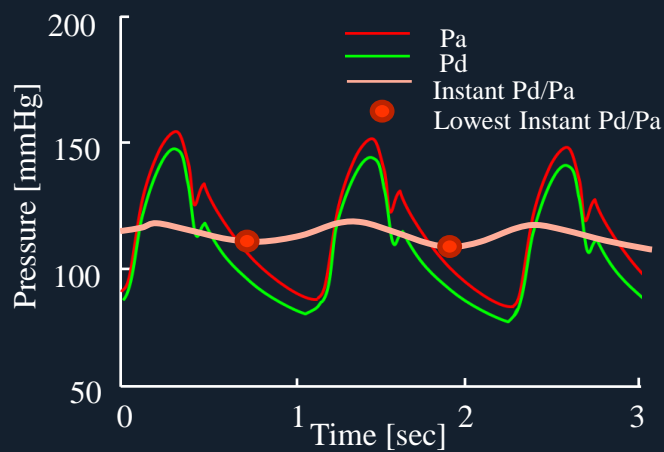
Mean Pd/Pa at rest during wave free period (WFP)

(D) dPR (≤ 0.89)



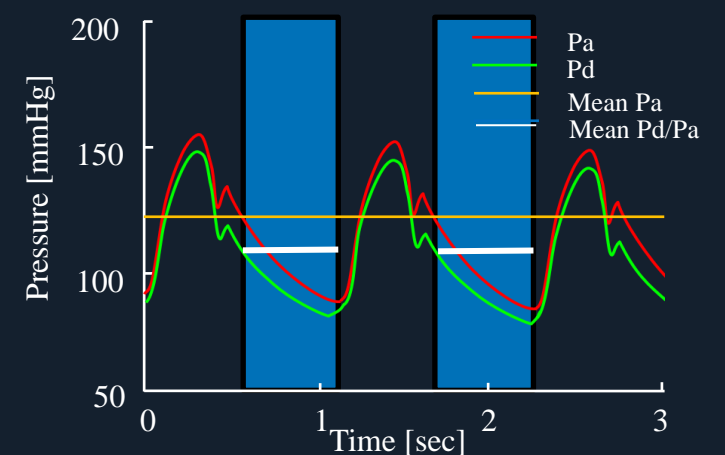
Mean Pd/Pa at rest during the entire diastole

(E) RFR (≤ 0.89)



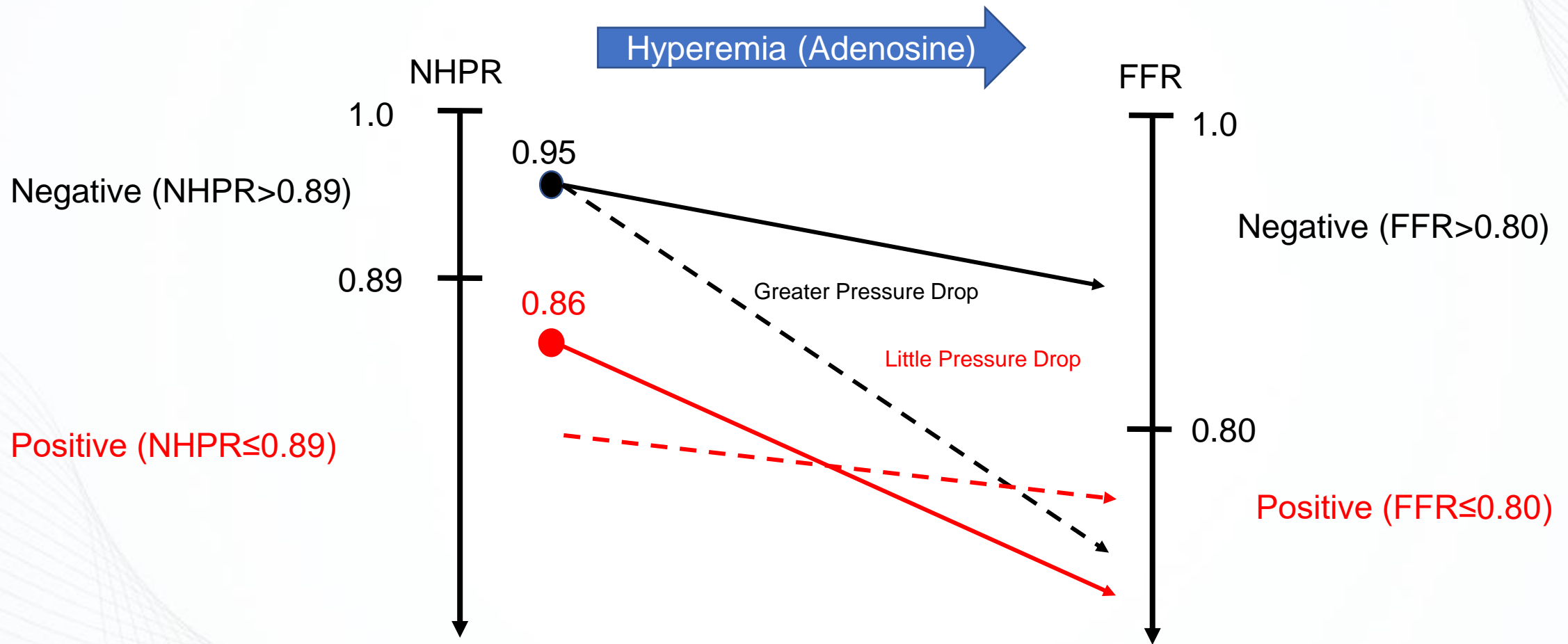
Lowest Instant Pd/Pa at rest during the entire cardiac cycle

(F) DFR (≤ 0.89)

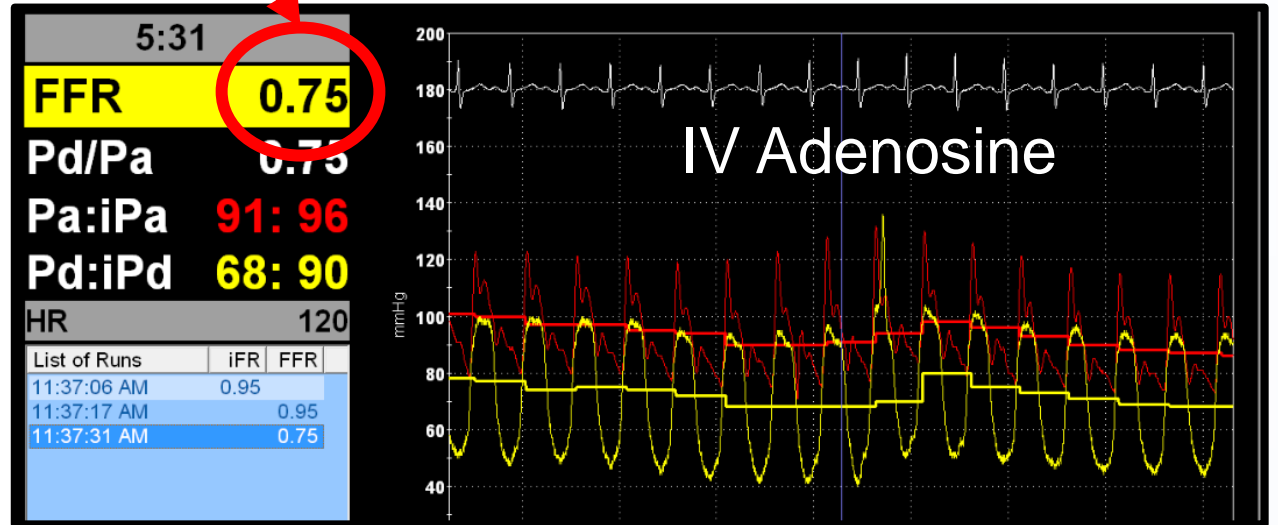
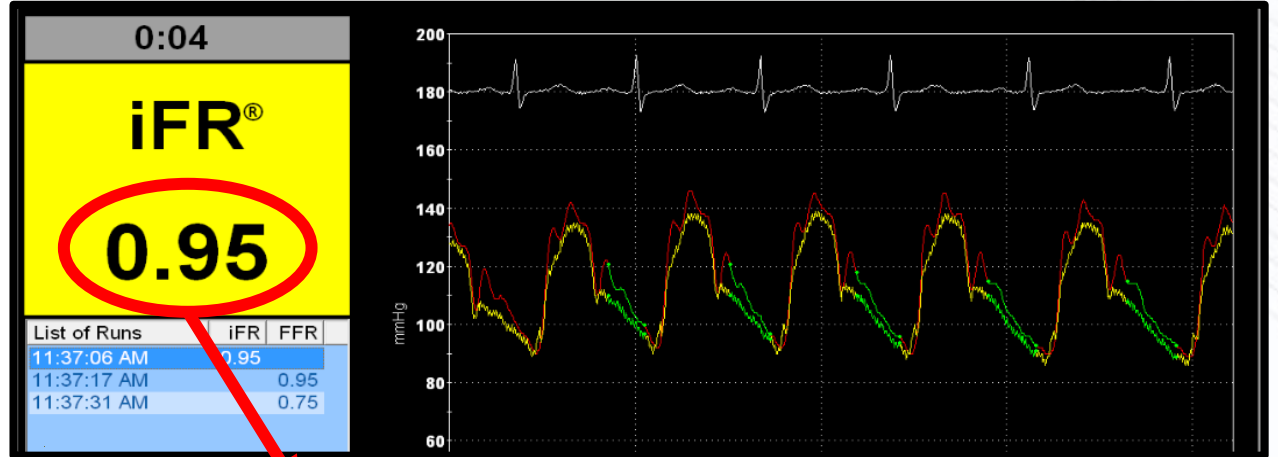
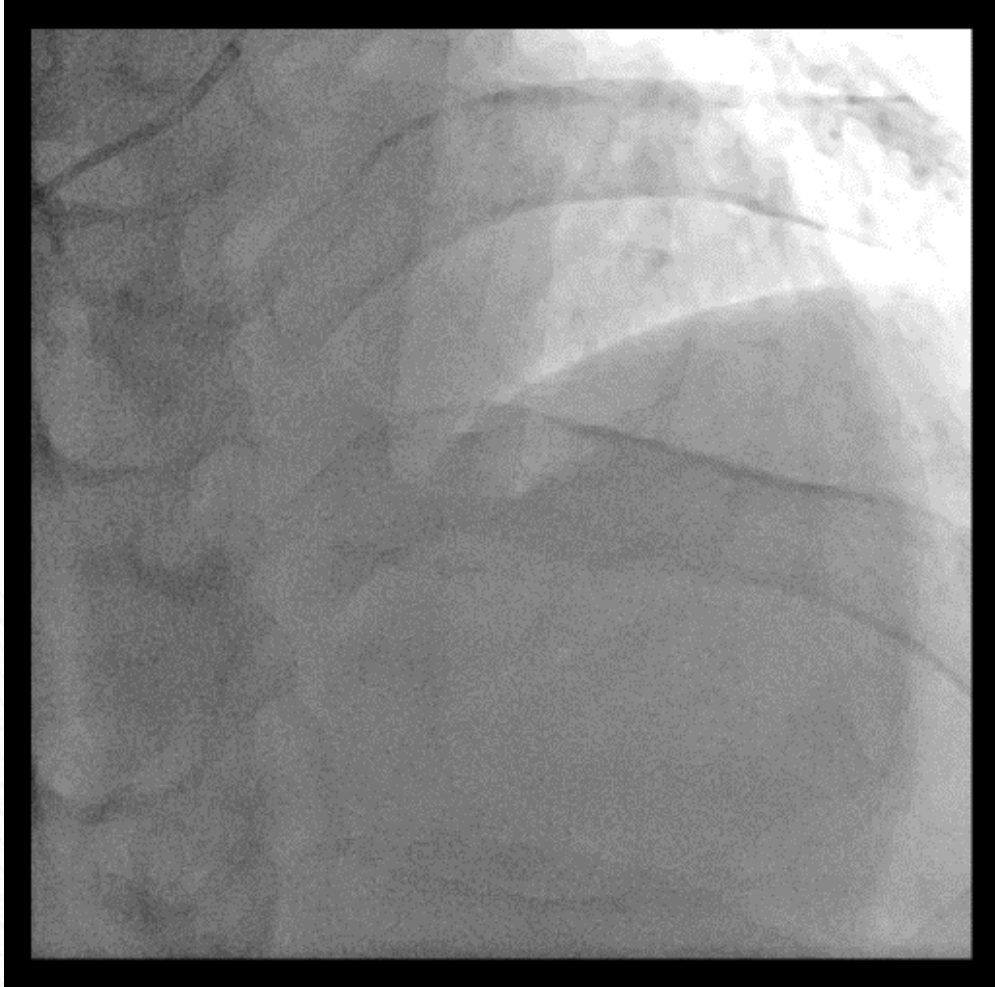


Mean Pd/Pa at rest during the period Between Pa < mean Pa AND down-sloping Pa

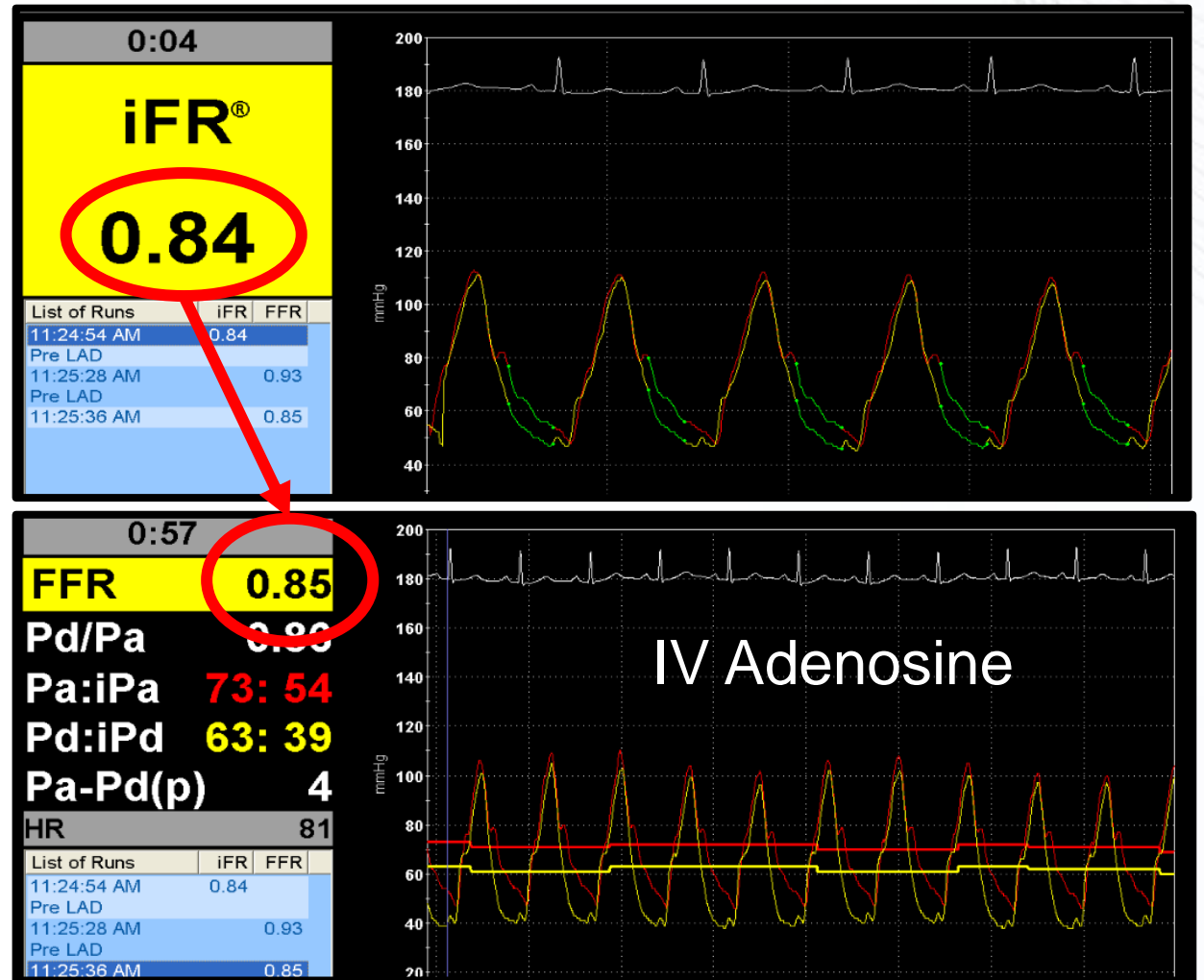
FFR and NHPR Discordance



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

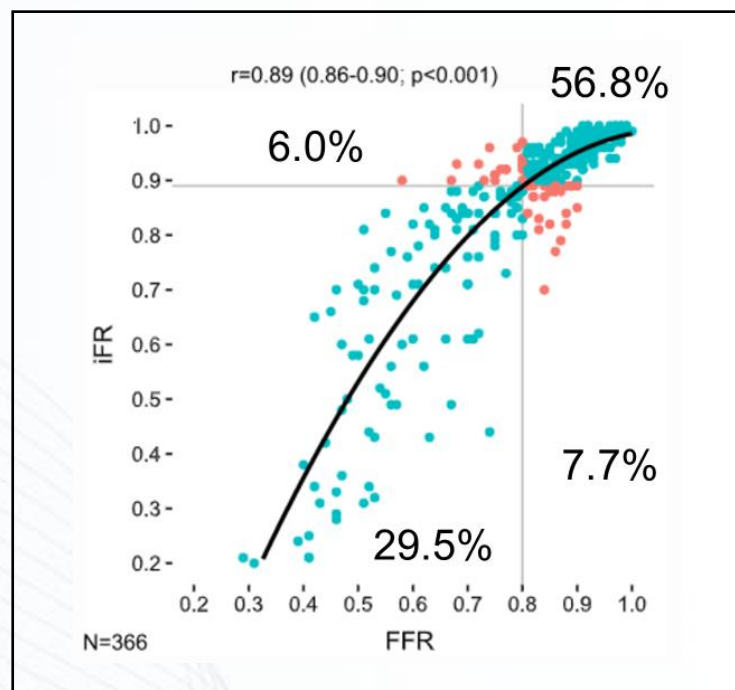


83 YO/Male with Severe AS (iFR 0.84 → FFR 0.85)



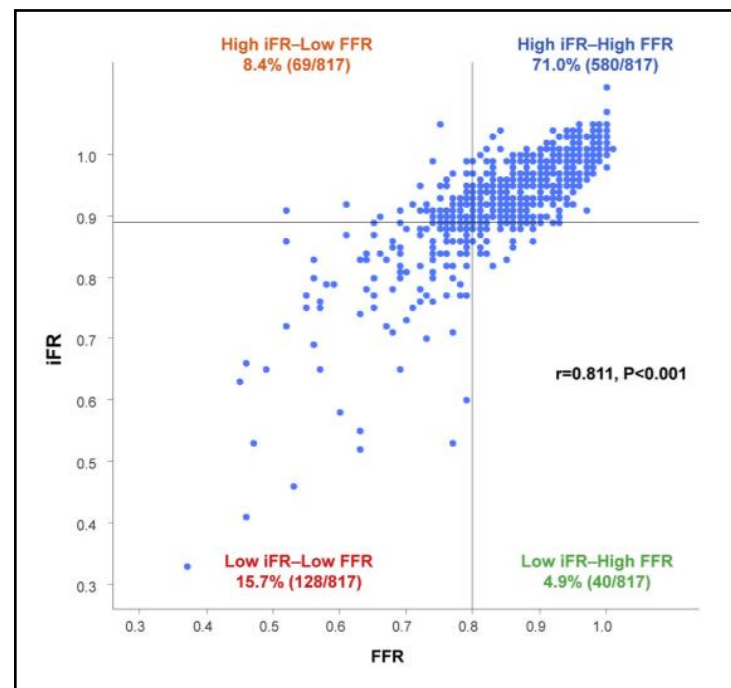
Incidence (1)

13.7 %



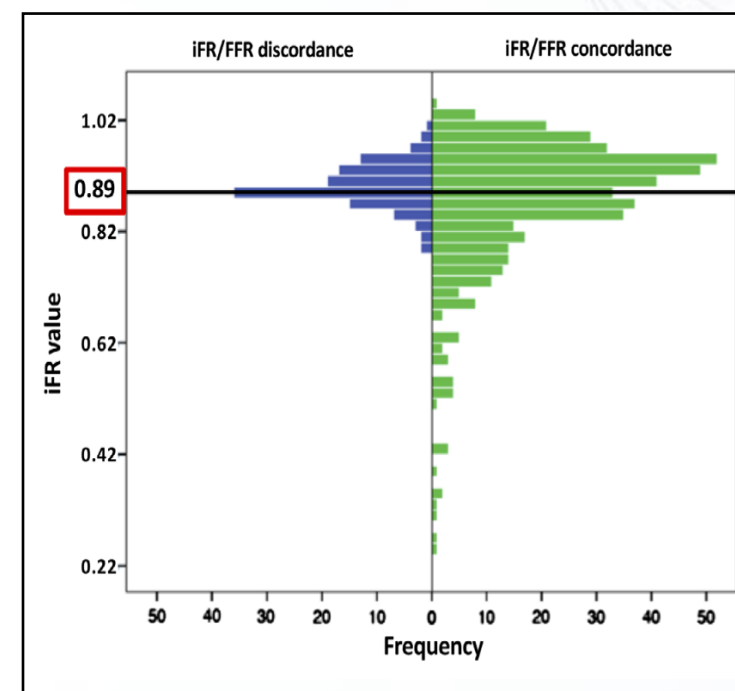
Cook CM et al.
JACC Cardiovasc Interv. 2017;10(24):2514-2524

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

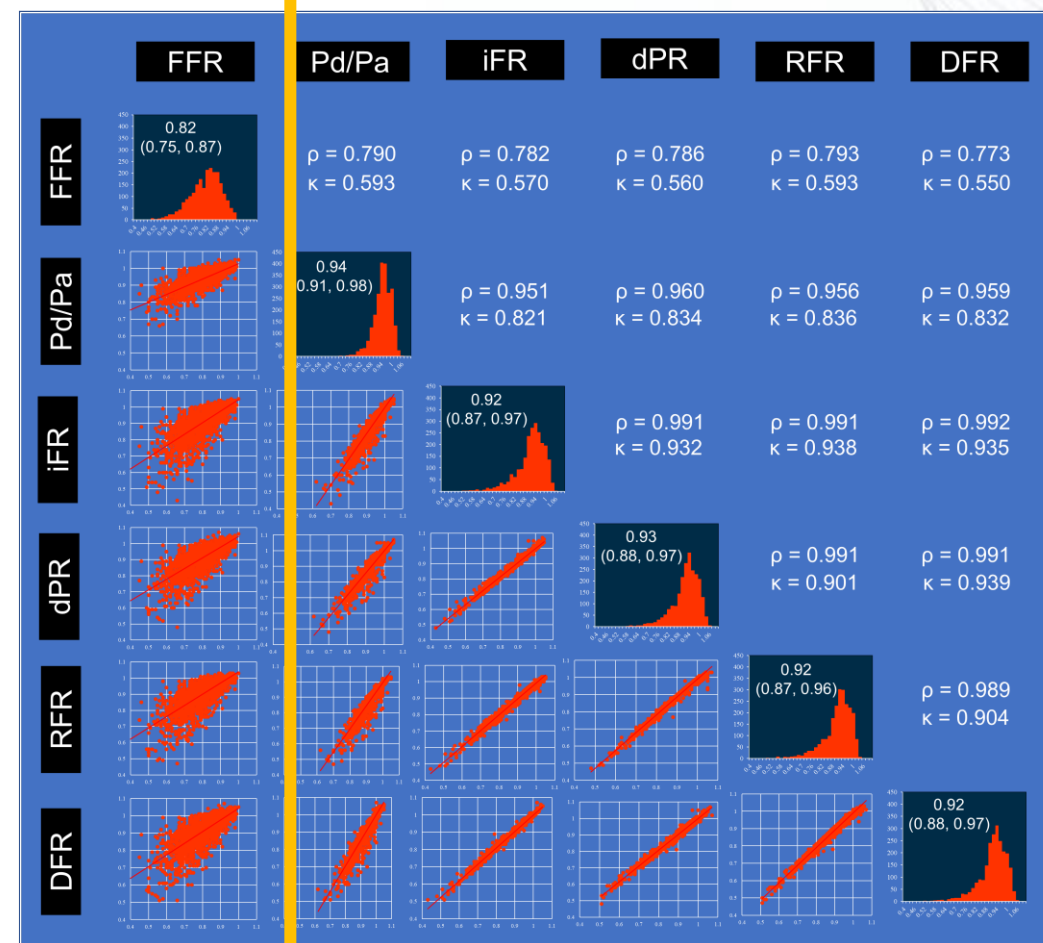
Diagnostic Accuracy: 81%

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



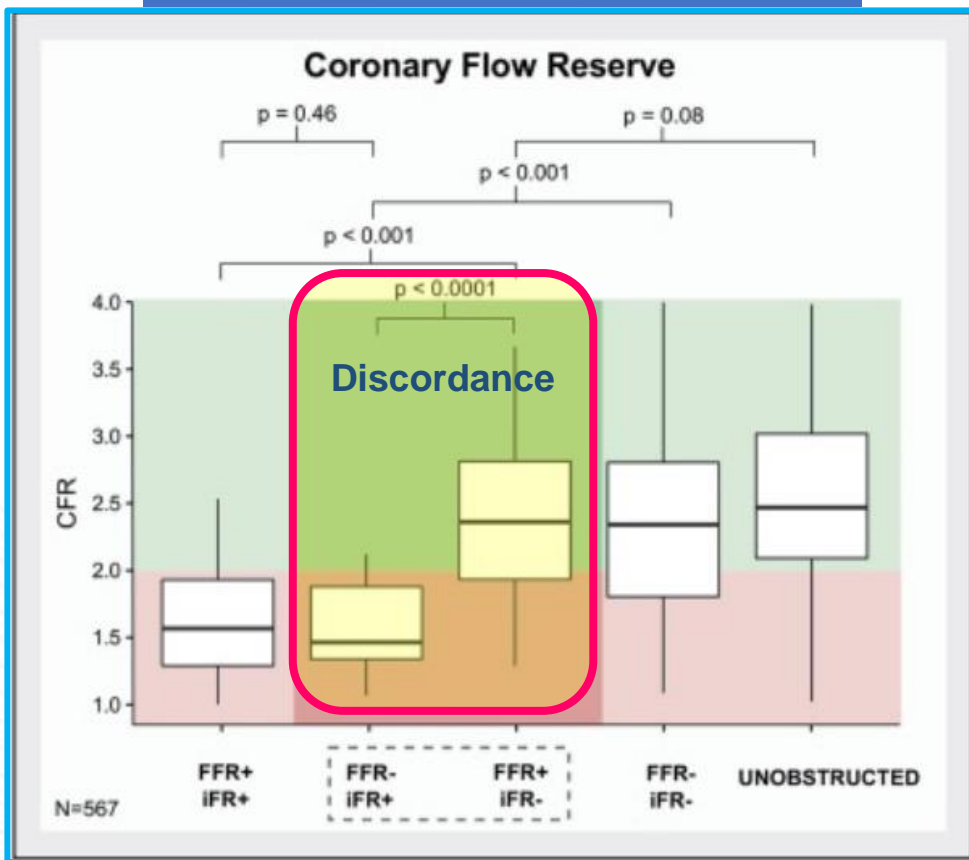
Unpublished Data From IRIS FFR Registry

Incidence (3)

15-20%

Underlying Mechanism (1) Physiologic Characteristics

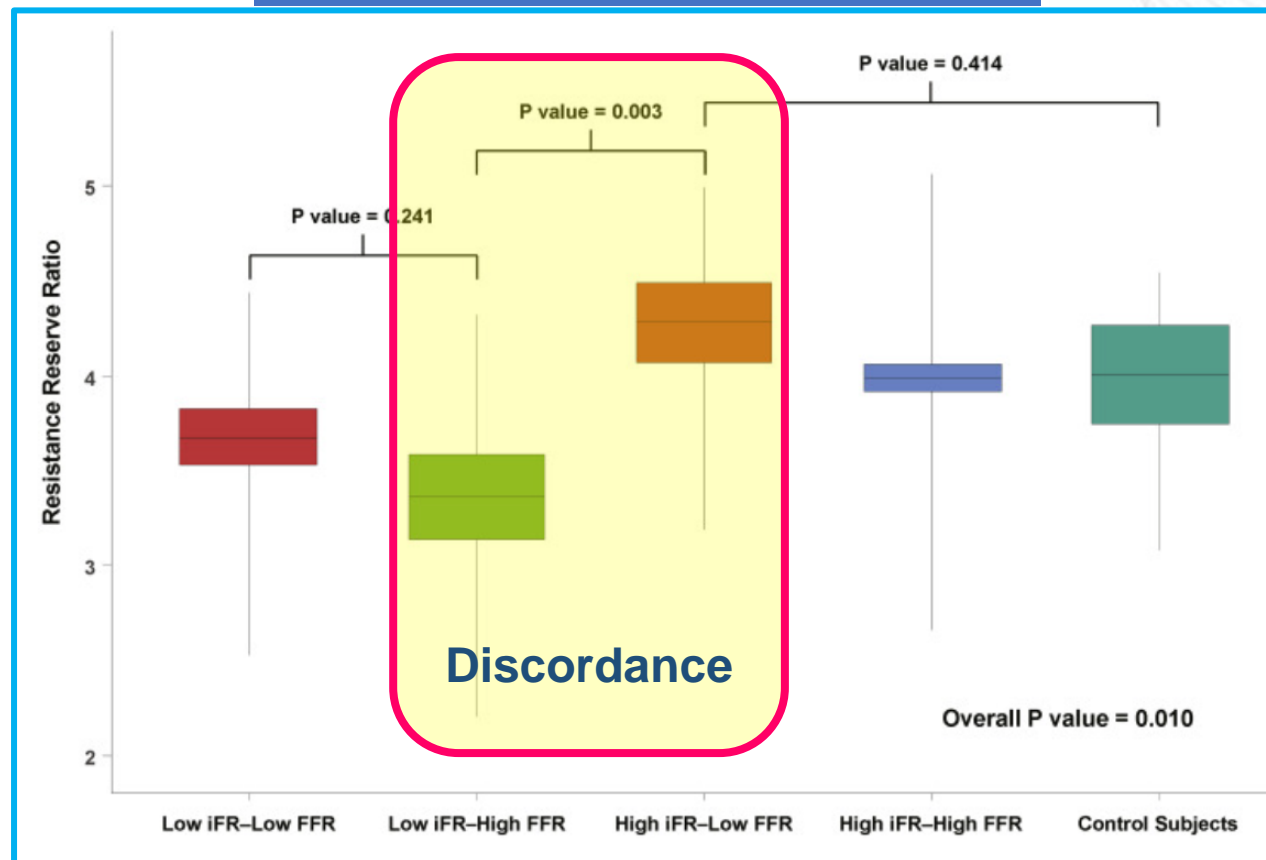
Coronary Flow Reserve



Cook CM et al.

JACC Cardiovasc Interv. 2017;10(24):2514-2524

Resistance Reserve Ratio

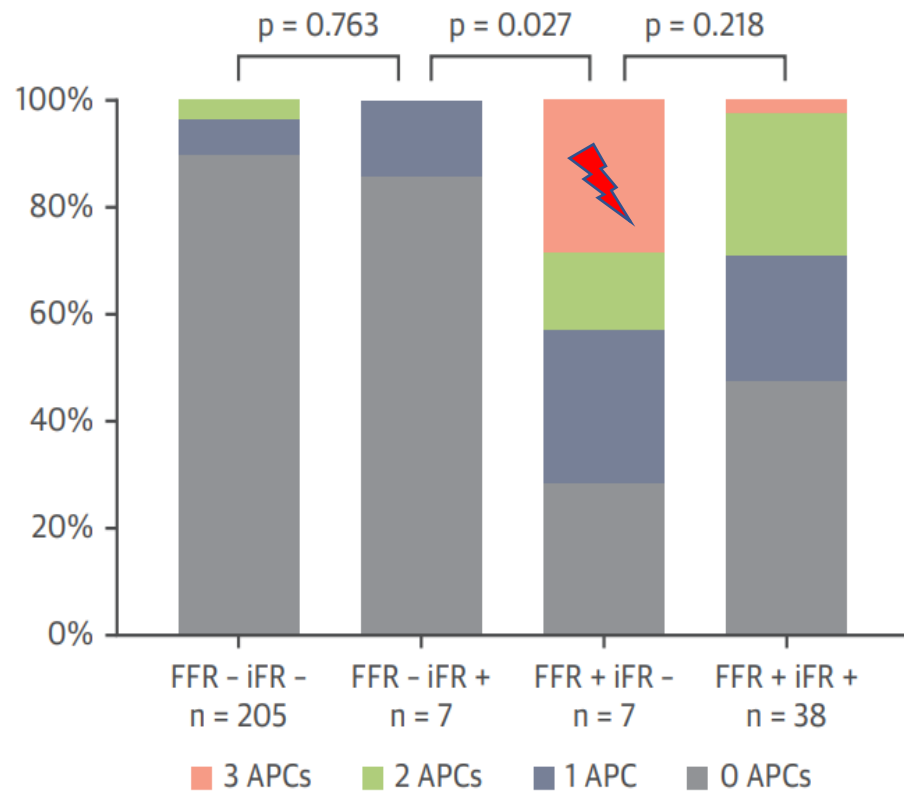


SH Lee et al.

JACC Cardiovasc Interv. 2019;12(20):2018-2031

Underlying Mechanism (2) Anatomical Characteristics

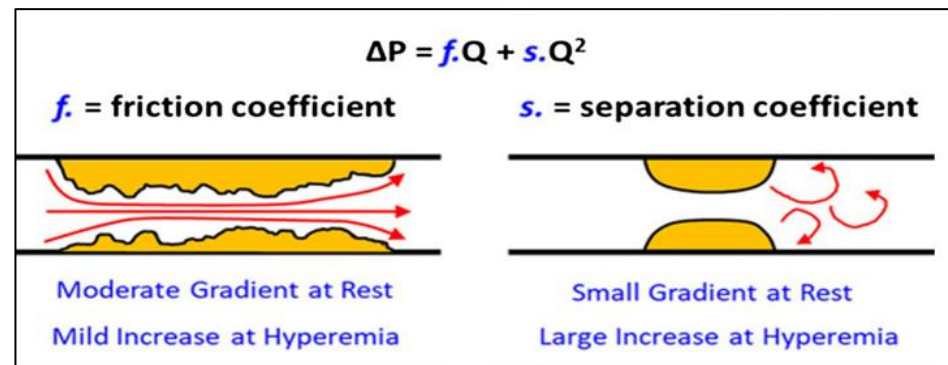
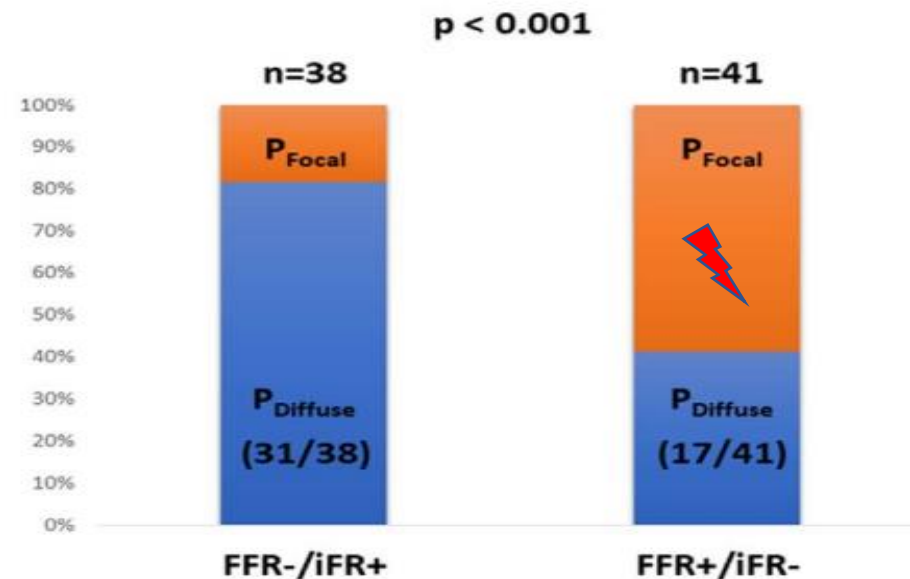
Adverse Plaque Characteristics* Relate More Strongly With FFR than iFR



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

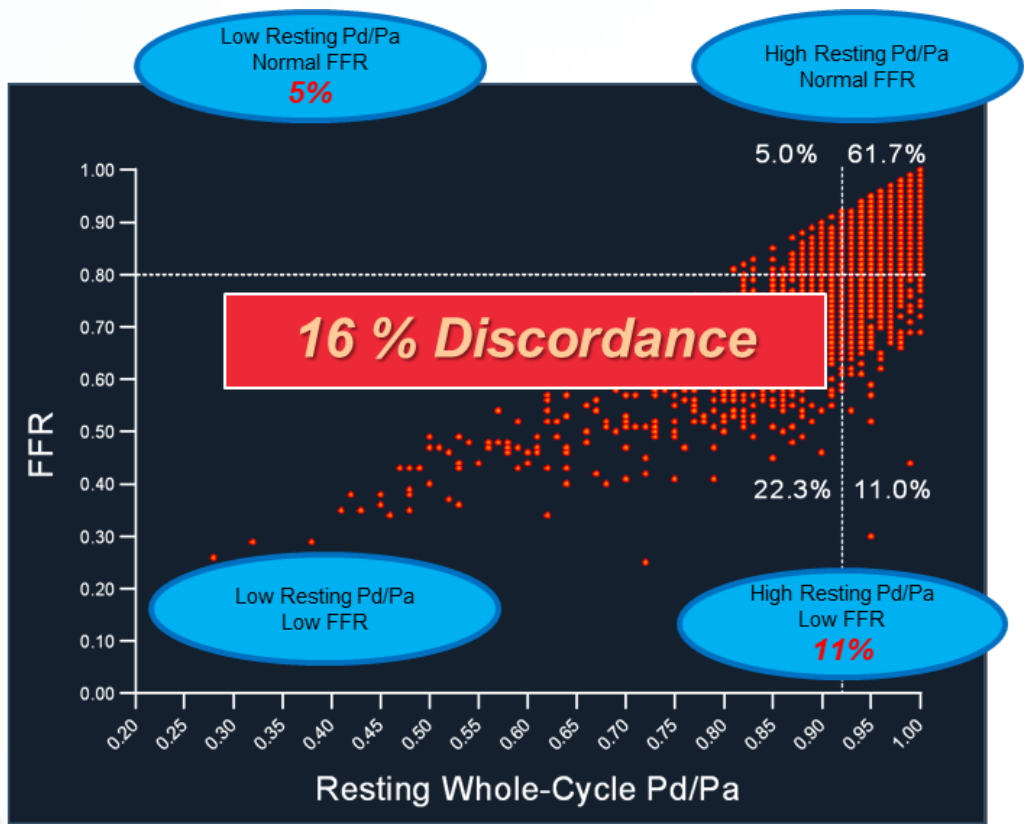
*Adverse plaque characteristics include low-attenuation plaque, positive remodeling, spotty calcification, and napkin risk sign

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
<i>Resting Pd/Pa</i> ≤ 0.92 and <i>FFR</i> > 0.80	Very Small Hyperemic Pressure Drop		
Age	1.02	1.01-1.03	0.004
Gender (Male)	0.74	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
<i>Resting Pd/Pa</i> > 0.92 and <i>FFR</i> ≤ 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	0.88	0.66-0.96	0.016
Family history	0.88	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

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

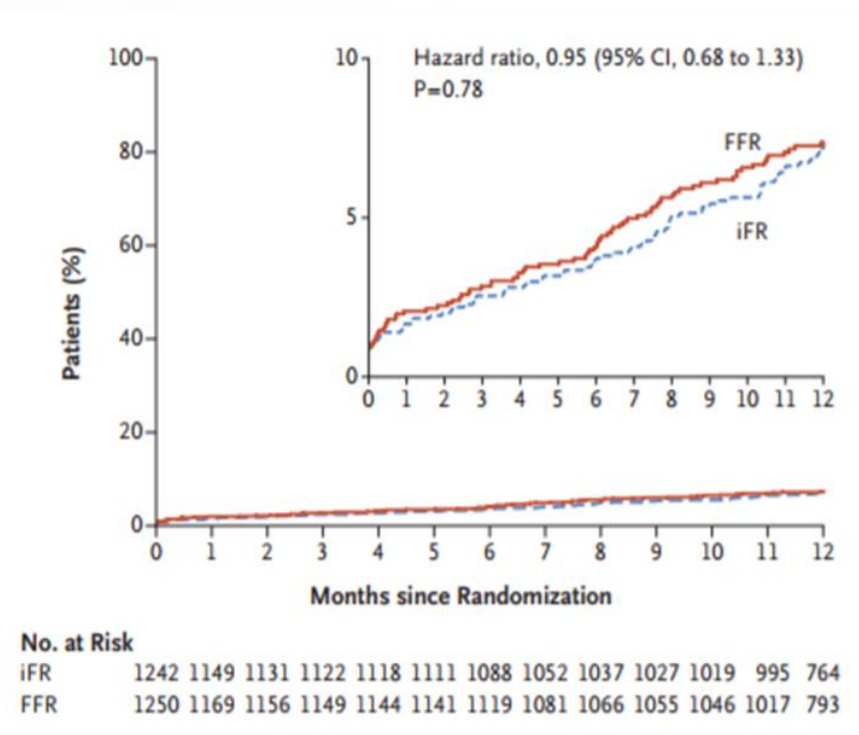
Underlying Mechanism: Summary

NHPR/FFR Discordance

	NHPR+ FFR-	NHPR- FFR+
<i>Coronary physiology</i>	Un-Healthy Vascular Status	More Complex Atherosclerosis
<i>Coronary anatomy</i>		
<i>Clinical Characteristics</i>		

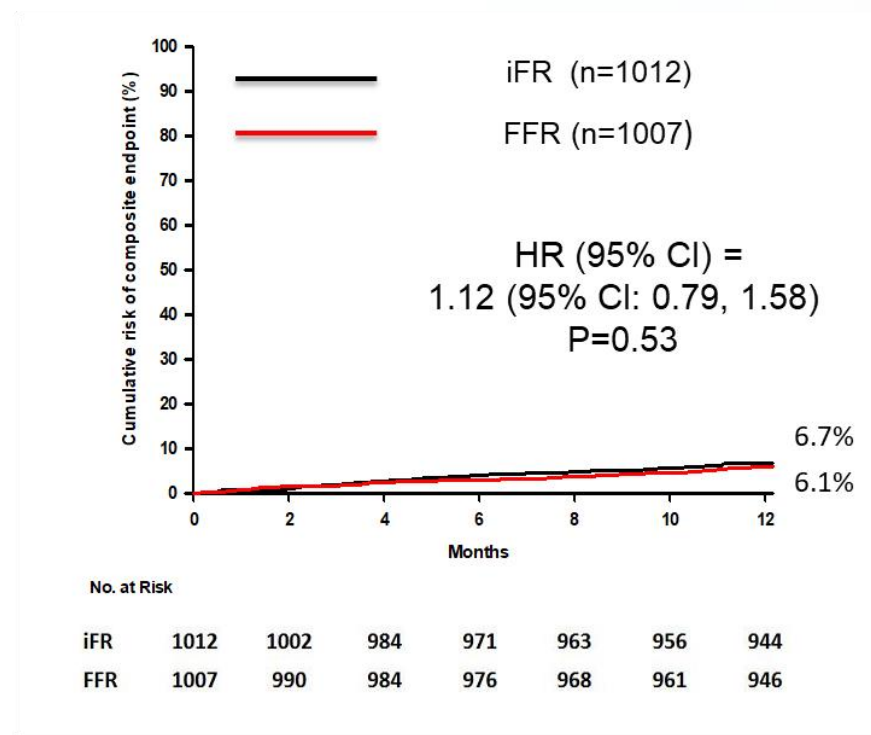
'One-Size-Fits-All' 0.89 iFR threshold ?

DEFINE-FLAIR



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

iFR-SWEDEHEART

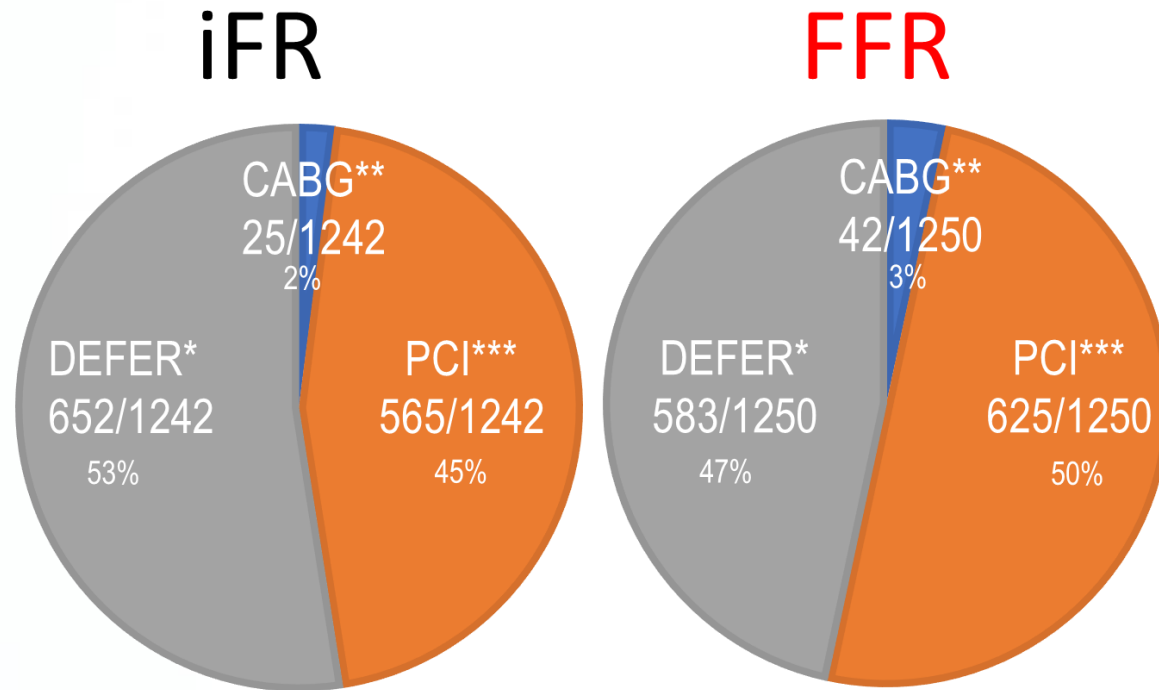


N Engl J Med. 2017 May 11;376(19):1813-1823

Physiologic Perspective, Underpowered Studies

Different Treatment Due to Discordance

Treatment allocation with iFR and FFR



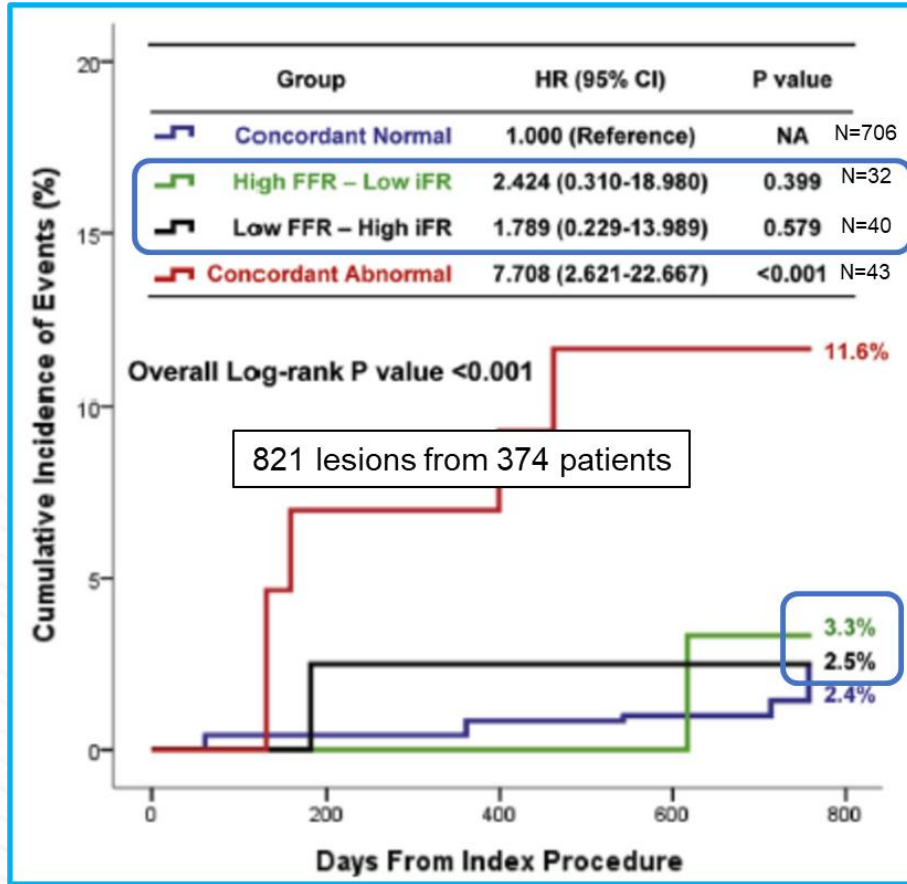
p for comparison between patients randomized to iFR and FFR

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

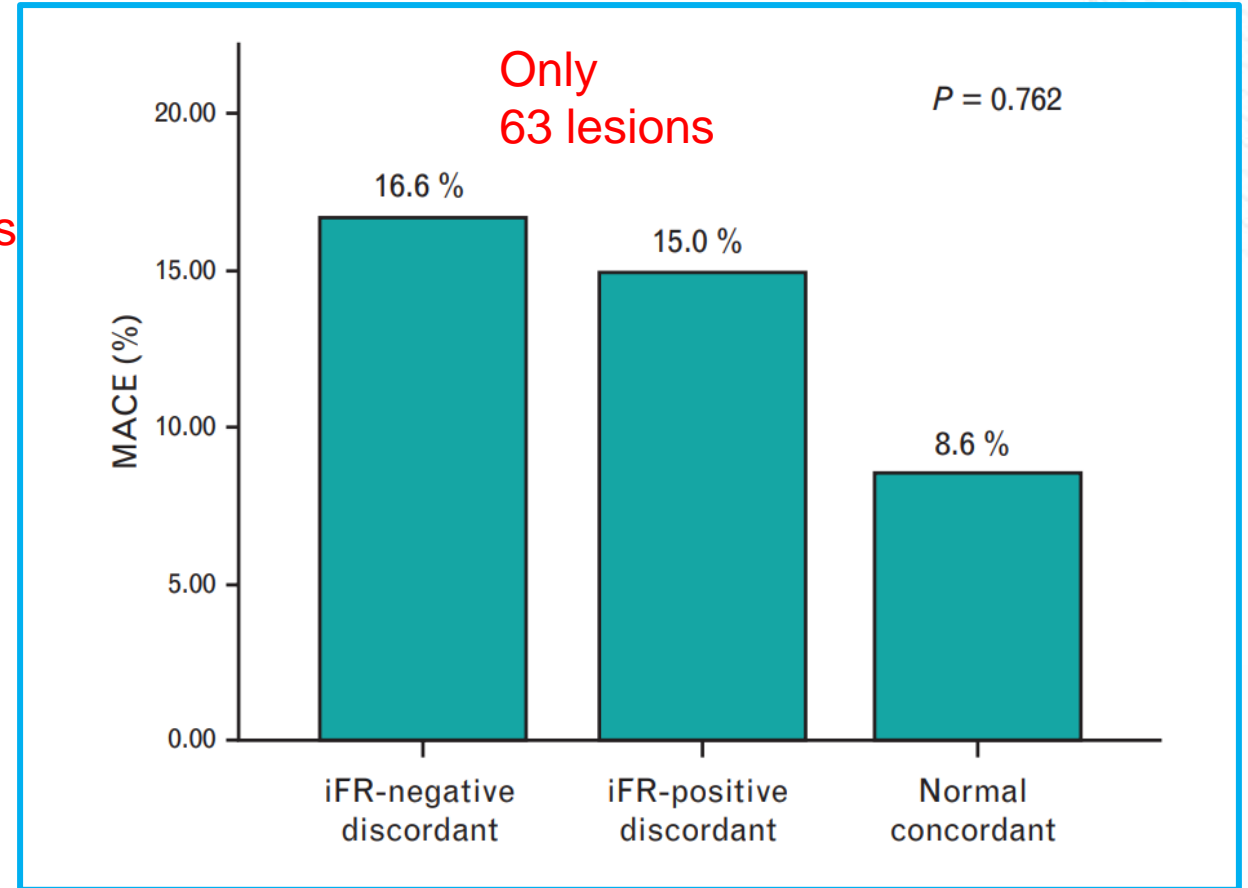
Significantly less revascularization based on iFR interrogation

DEFINE FLAIR

Prognosis of Discordant Lesion.....Very Limited Data



Only 72 lesions



J Am Coll Cardiol Intv 2017, 10: 2502

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

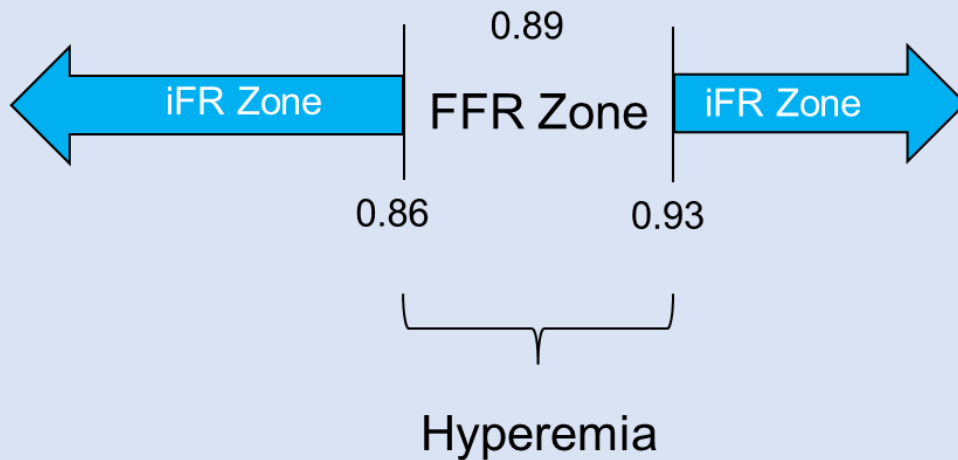
FFR and iFR value of Discordant Lesions

	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

“Grey Zone” FFR

How To Rectify the Discordance

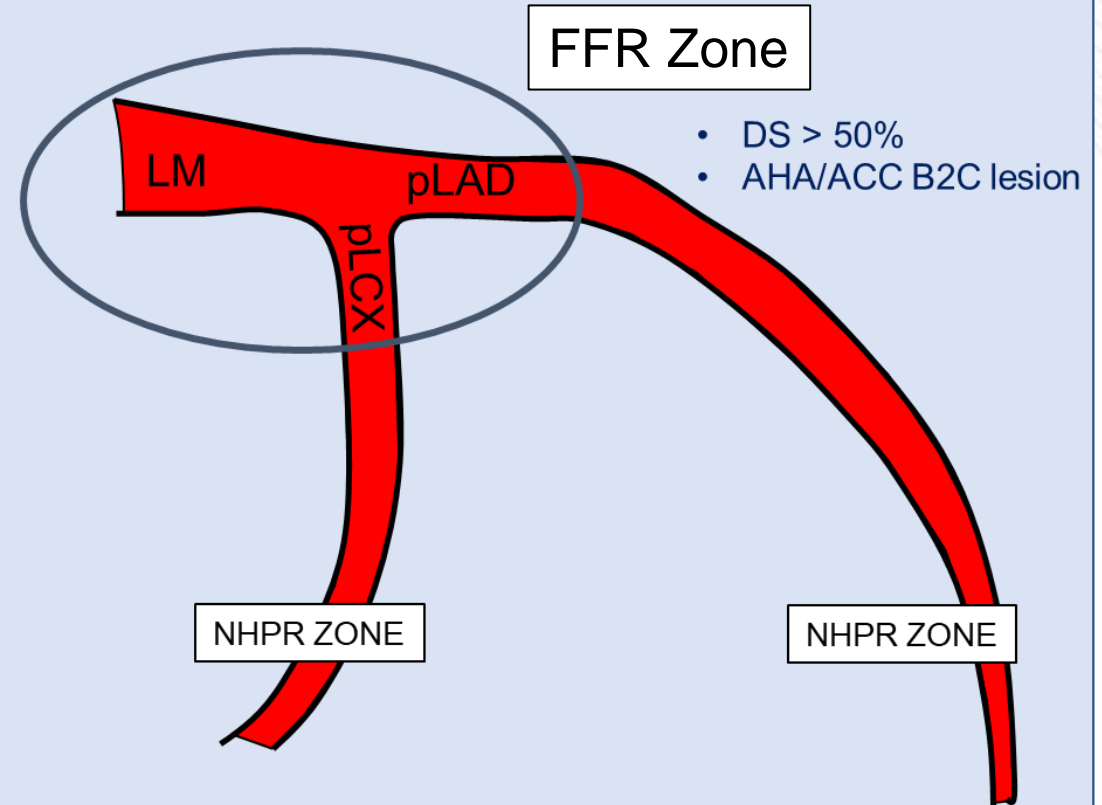
Physiologic Consideration



Clinical Consideration

- Young age
- Male
- Diabetes, Chronic Kidney Disease

Anatomical Consideration



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.