

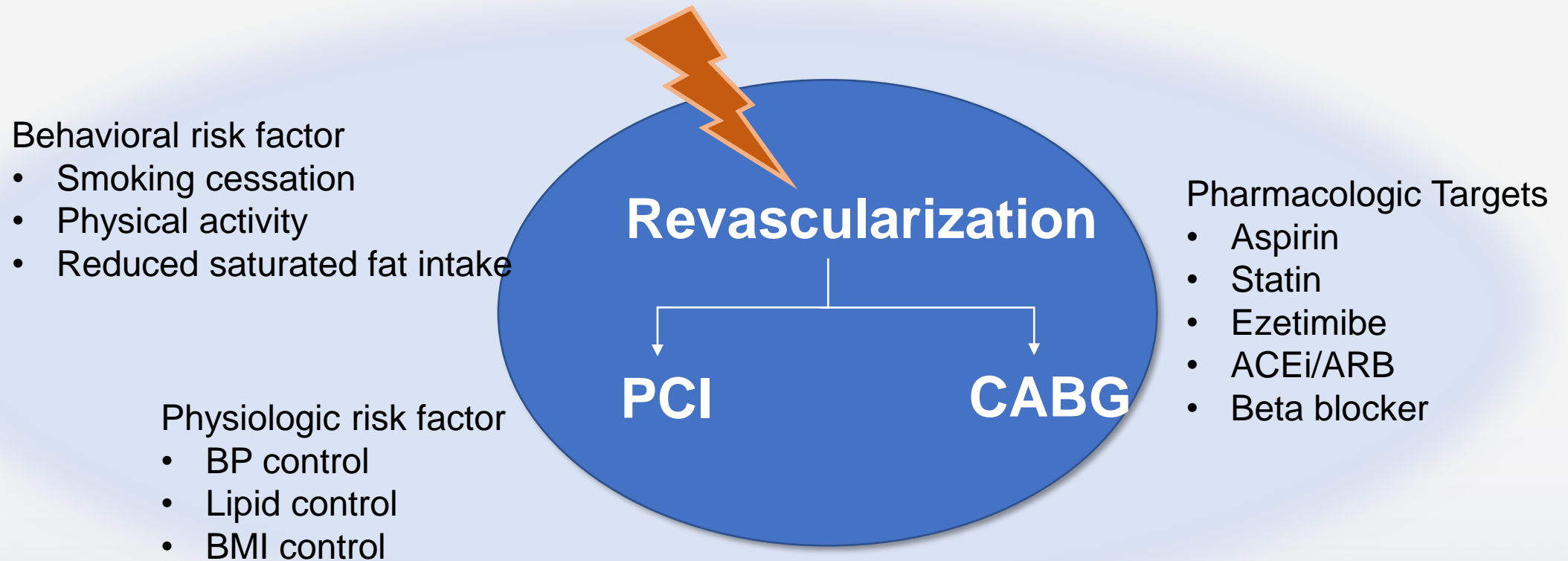
Synergetic Approach for Discordant Lesions Between FFR and Non-Hyperemic Indexes

Jung-Min Ahn, MD.

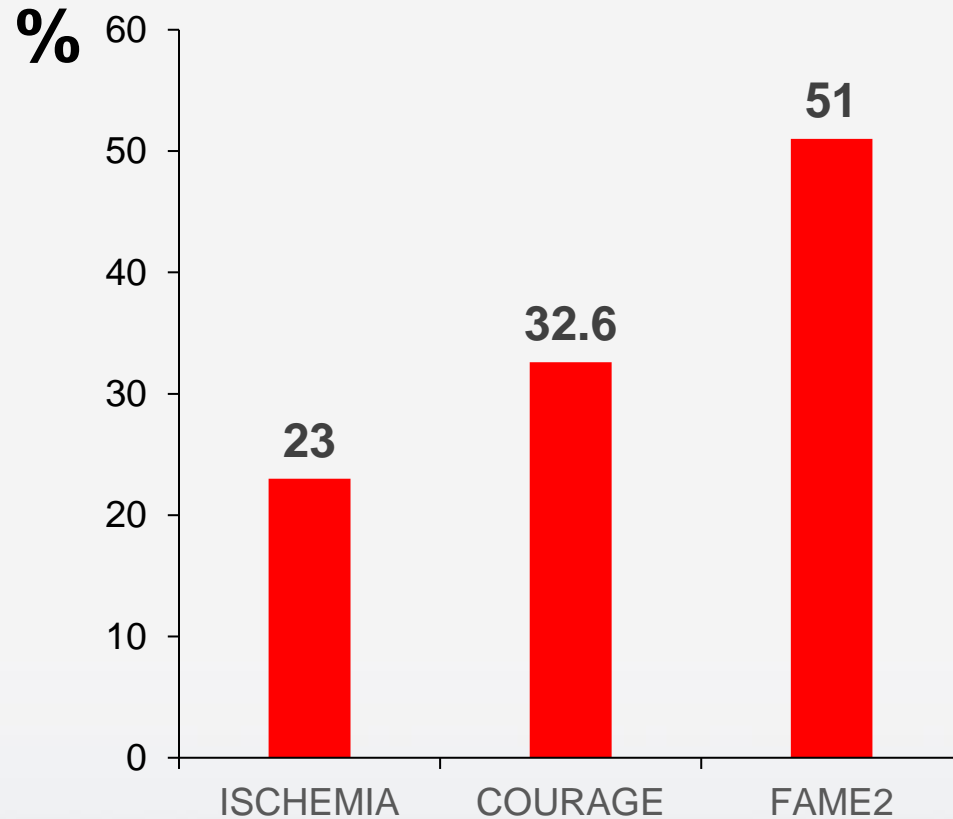
Division of Cardiology, Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea

Treatment of SIHD

OMT plus Risk Factor Modification (Default Treatment)



Revascularization in Medication Group



Reduction of Spontaneous MI

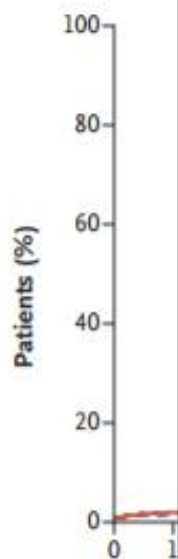
	Hazard Ratio
COURAGE Trial	≈ 0.89 (?)
FAME2 Trial	0.62 (0.39-0.99)
Meta*	0.59 (0.42-0.83)
ISCHEMIA Trial	0.67 (0.53-0.83)
COMPLETE Trial	0.68 (0.53-0.86)

Non culprit lesion revascularization
in STEMI with MV

* Meta-analysis from FAME2, DANAMI, COMPARE-Acute
Eur Heart J . 2019 Jan 7;40(2):180-186.

ESC Guideline 2018

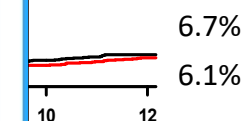
Recommendations	Class ^a	Level ^b
When evidence of ischaemia is not available, FFR or iwFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis. ^{15,17,18,39}	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI. ^{29,31}	IIa	B
IVUS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



No. at Risk	
IFR	1242 114
FFR	1250 116

12)
07)

, CI) =
0.79, 1.58)
53



956 944
961 946

1813-1823

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

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ORIGINAL INVESTIGATION

Agreement of to Aortic Coronary the Instantaneous

Yuhei Kobayashi, MD,^{a,b} Nils P. Johnson^{a,b},
Colin Berry, MBChB, PhD,^{a,b} Allen J. Jen
Gilles Rioufol, MD, PhD,^c Seung-Jung
Keith G. Oldroyd, MBChB, MD,^d Emma
Bernard De Bruyne, MD, PhD,^e William

ABSTRACT

BACKGROUND Recently, 2 randomised
resting coronary physiological index, i
distal to aortic coronary pressure (P_a/P_r)
catheterization laboratory, however, i

OBJECTIVES The goal of this study

METHODS A total of 763 patients we
rested conditions. Using iFR ≤ 0.89 a
assessed.

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

CONCLUSIONS P_a/P_r was analyzabl
agreement with iFR, suggesting that i
Approximate FFR Compared to Pure Re
© 2017 by the American College of Car



Listen to this manuscript's
audio summary by
JACC Editor-in-Chief
Dr. Valentin Fuster.



From the ^aStanford University School of Medicine,
^bMcGovern Medical School at UTHealth and Me
Netherlands; ^cKarolinska Institutet, Södersjuk
Johannes National Hospital, Copenhagen, Sweden;
Cardiovascular and Medical Sciences, Universit
Brook University Medical Center, Stony Brook,
National University Hospital, Seoul, South Kore
CARMEN, Lyon, France; ^dUniversity of Orlan
Center Aulh, Aulh, Belgium; and the ^eStederve
was an investigator-initiated study sponsored by

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COLLEGE OF CARDIOLOGY FOUNDATION
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Comparison Diastolic Res Are They All Equal

Marcel van't Veer, MSc, PhD,^{a,b}
Stuart Watkins, MBChB, MD,^{c,d},
Lokien X. van Nunen, MD, PhD,

ABSTRACT

BACKGROUND Pressure mea
resting-state physiological asse

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 l
differences, Spearman correlatio
diagnostic performance with res

RESULTS Median iFR in 197 pa
differences (± SD) with iFR we
0.009 (FFR_{rest}), 0.003 ± 0.01
>0.99 ($p < 0.001$ for all). Area
accuracy compared with FFR wa

CONCLUSIONS All diastolic r
agreement with FFR. A numeric
guidelines, and clinical recomm
Unselected Population Referred
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From the ^aDepartment of Cardiology, C
Engineering, Eindhoven University of T
cular Research Centre, University of Gl
Golden Jubilee National Hospital, Clyde
York; ^bCardiovascular Center Aulh, Aulh
Naples, Italy; ^cSan Vito has received
has equity in Philips, GE, HeartFlow, and
Judo Medical and Cardiovascular System
Boston Scientific; ^dDr. De Bruyne is shan
Omega Pharma; his institution, the Card
track, and St. Jude Medical; and his in
Opens, and Boston Scientific outside of
has received speaker and consultancy fe
of Glasgow hold research and consultan
Abbott, and has received research suppo
relevant to the contents of this paper to
Manuscript received September 7, 2017;



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JACC Editor-in-Chief
Dr. Valentin Fuster.



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



Johan Svanerud¹, MSc; Jung-Min Ah
Ankita Gore^{2,3}, BS, MSc; Akiko Maeh
Bernard De Bruyne⁴, MD, PhD; Nils F
Stuart Watkins⁵, MD; Colin Berry^{6,11},
Seung-Jung Park⁶, MD, PhD; Ziad A.

1. Corvenit Research AB, Uppsala, Sweden; 2. Asan Medi
Research Foundation, New York, NY, USA; 4. St. Francis Ho
the Netherlands; 6. Eindhoven University of Technology, De
7. New York Presbyterian Hospital/Columbia University Med
Hospital, Aulh, Belgium; 9. Weatherhead PET Center, Divis
at UTHealth and Memorial Hermann Hospital, Houston, TX
Kingdom; 11. Institute of Cardiovascular and Medical Scien
This paper also includes supplementary data published online at:

KEYWORDS

- fractional flow reserve
- innovation
- other imaging modalities

Abstract

Aims: Randomised controlled t
fractional flow reserve (FFR) fo
by sensitive landmarking of the
resistance occur during a fixed
a novel non-hyperaemic index o
distal coronary pressure to aor
timing within the cardiac cy

Methods and results: VALID
RFR. The primary endpoint was
in 651 waveforms in which iFR
correlated to iFR ($R=0.99$, $p<$
0.020). The diagnostic performa
specificity 96.9%, positive predi
operating characteristic curve of
95% CI: -0.009 to 0.006, $p=0.0$
diastolic cycles and 32.4% (167/516
compared to FFR was lowest (4

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

*Corresponding author: Columbia University Medical C
New York, NY 10019, USA. E-mail: zxa2112@columbia.edu

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European Heart Journal (2019) 40, 2585–2
doi:10.1093/eurheartj/ehz230

Diastolic pressure ratio validation vs. the instan

Nils P. Johnson¹, Wenguang Li², Xi Chen²
Colin Berry^{3,4}, William F. Fearon⁵, and K

¹Weatherhead PET Center, Division of Cardiology, Department of Medicine, McGov
²Boston Scientific Corporation, CA, USA; ³British Heart Foundation Glasgow Cardio
Glasgow, Glasgow, UK; ⁴West of Scotland Heart and Lung Centre, Golden Jubilee Na
Cardiology, Stanford University, Stanford, CA, USA

Received 14 December 2017; revised 16 February 2018; editorial decision 12 February 2018

Aims

The instantaneous wave-free ratio (iFR)
non-hyperaemic conditions. To test for uni
coronary pressure measurements, we comp
numerical similarity and test/retest repeatab

Methods and results

Eight hundred and ninety-three lesions from
ies. Diastolic pressure ratio and a linear tra
Mean difference between dPR and iFR [Δ =
(ROC) curve (AUC) = 0.997] mirrored t
<0.001 ± 0.004, r^2 = 0.998, AUC = 1.00),
over a broad range of the cardiac cycle. Δ
(Δ = -0.012 ± 0.031, r^2 = 0.927, AUC = 0.1
matched almost exactly (average Δ = <0.00

Conclusions

Our dPR offers numerical equivalency to
period of diastole, the agreement between
analysis further confirm numerical equivalency

Keywords

Instantaneous wave-free ratio • Coronary

Introduction

Resting coronary physiology to guide revascularization 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 aP was

*Corresponding author. Tel: +44-141-951 5180. Email: keth.ahm@birc.nyu.edu
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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.

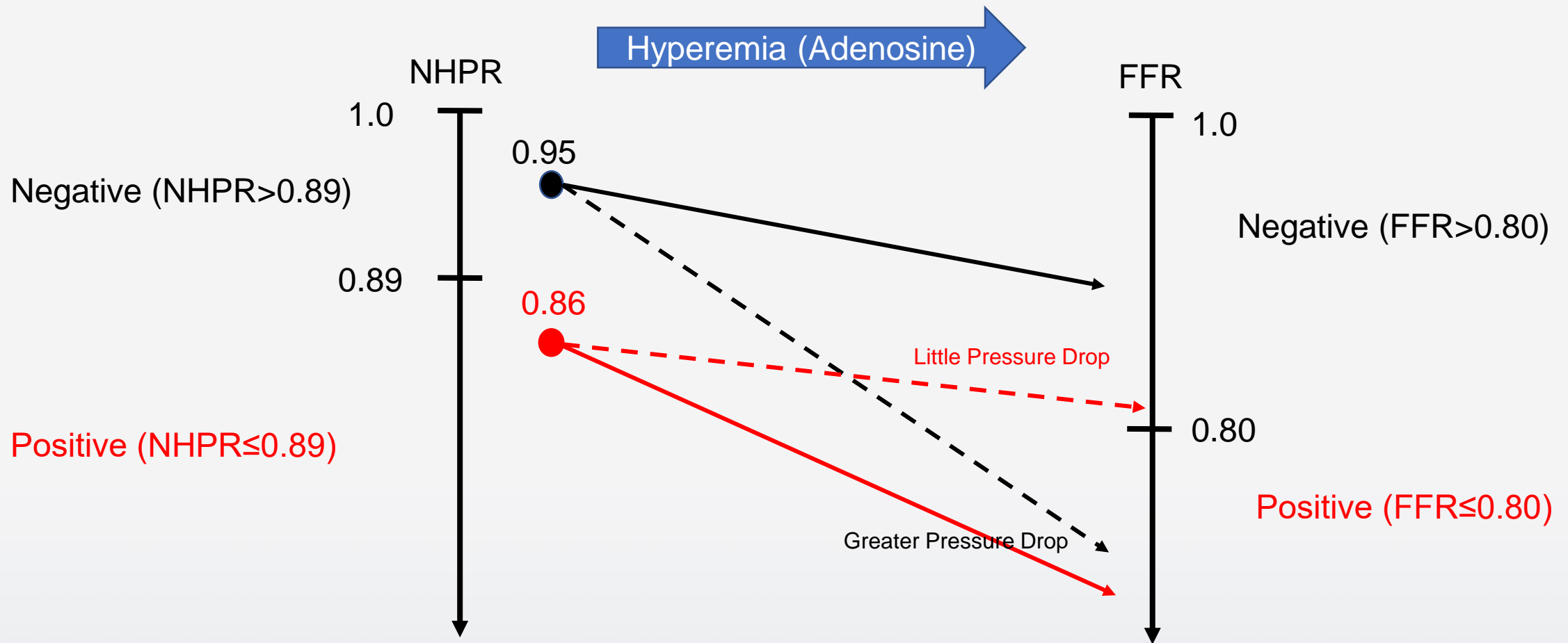
Jurgen Ligthart, RT*
Kanesha Masdjedi, MD*
Karen Witberg, RN
Frits Mastik, BSc
Laurens van Zandvoort,
BSc
Miguel E. Lemmert, MD,
PhD
Jeroen Wilschut, MD
Roberto Diletti, MD, PhD
Peter de Jaegere, MD,
PhD
Felix Zijlstra, MD, PhD
Isabella Kardys, MD, PhD
Nicolas M Van Mieghem,
MD, PhD
Joost Daemen, MD, PhD

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

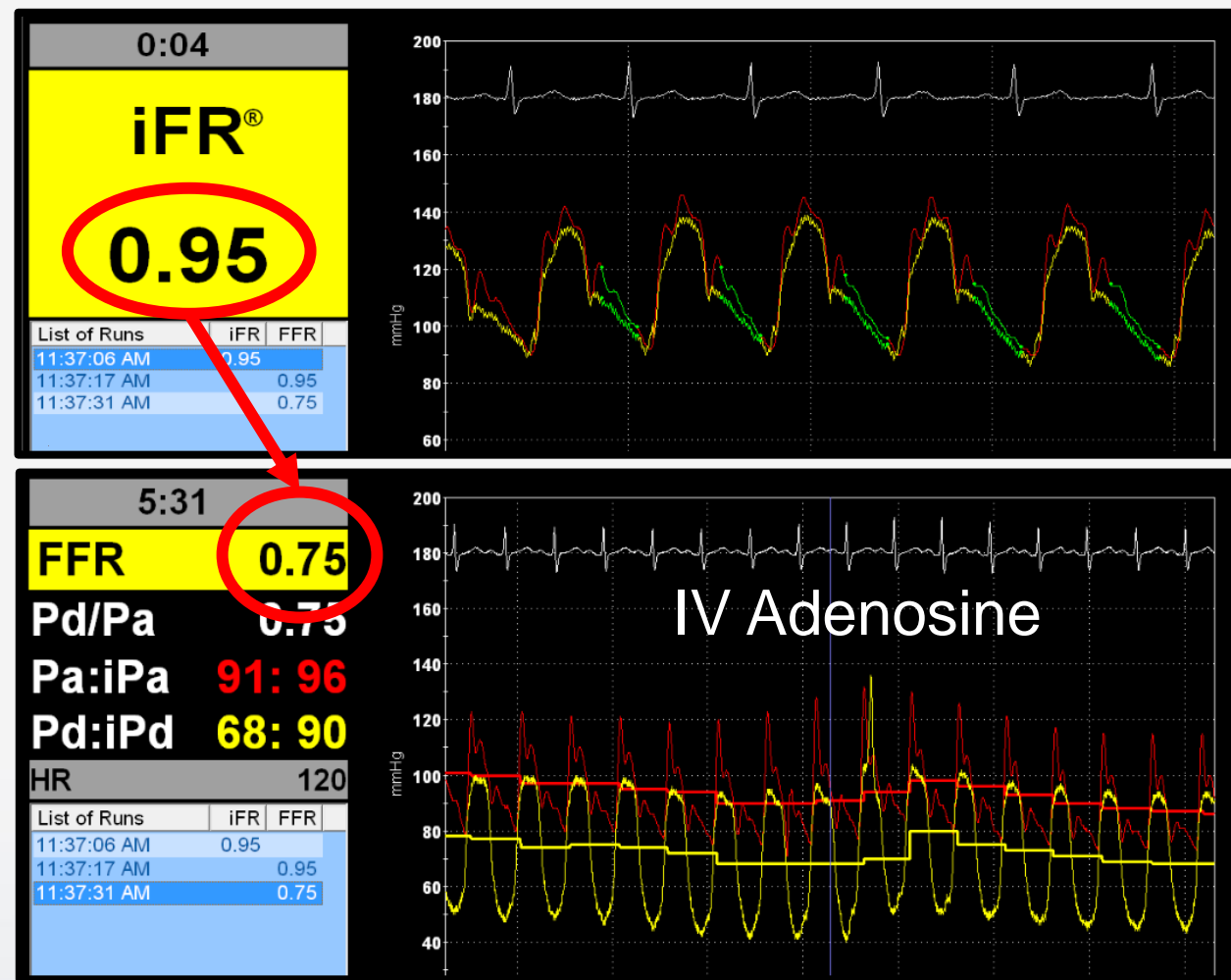
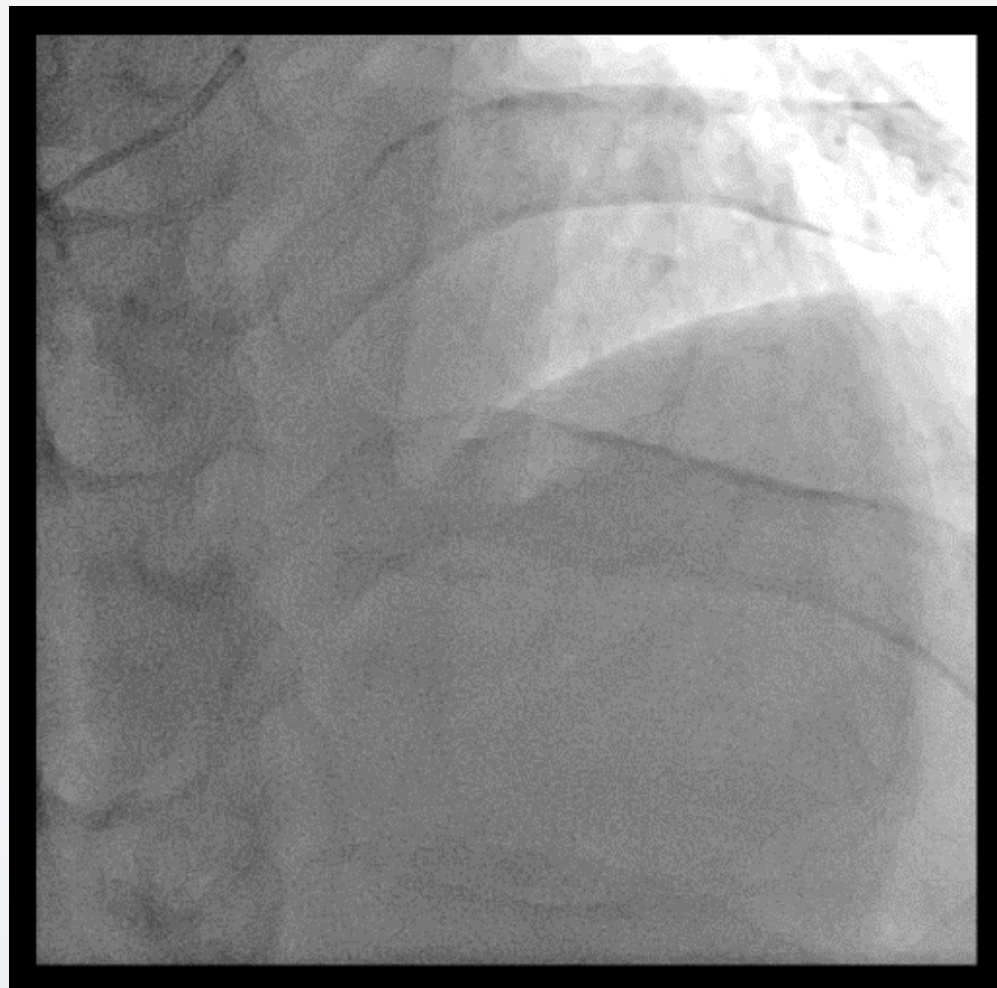
Key Words: catheter • methods
• physiology • software • software
validation

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

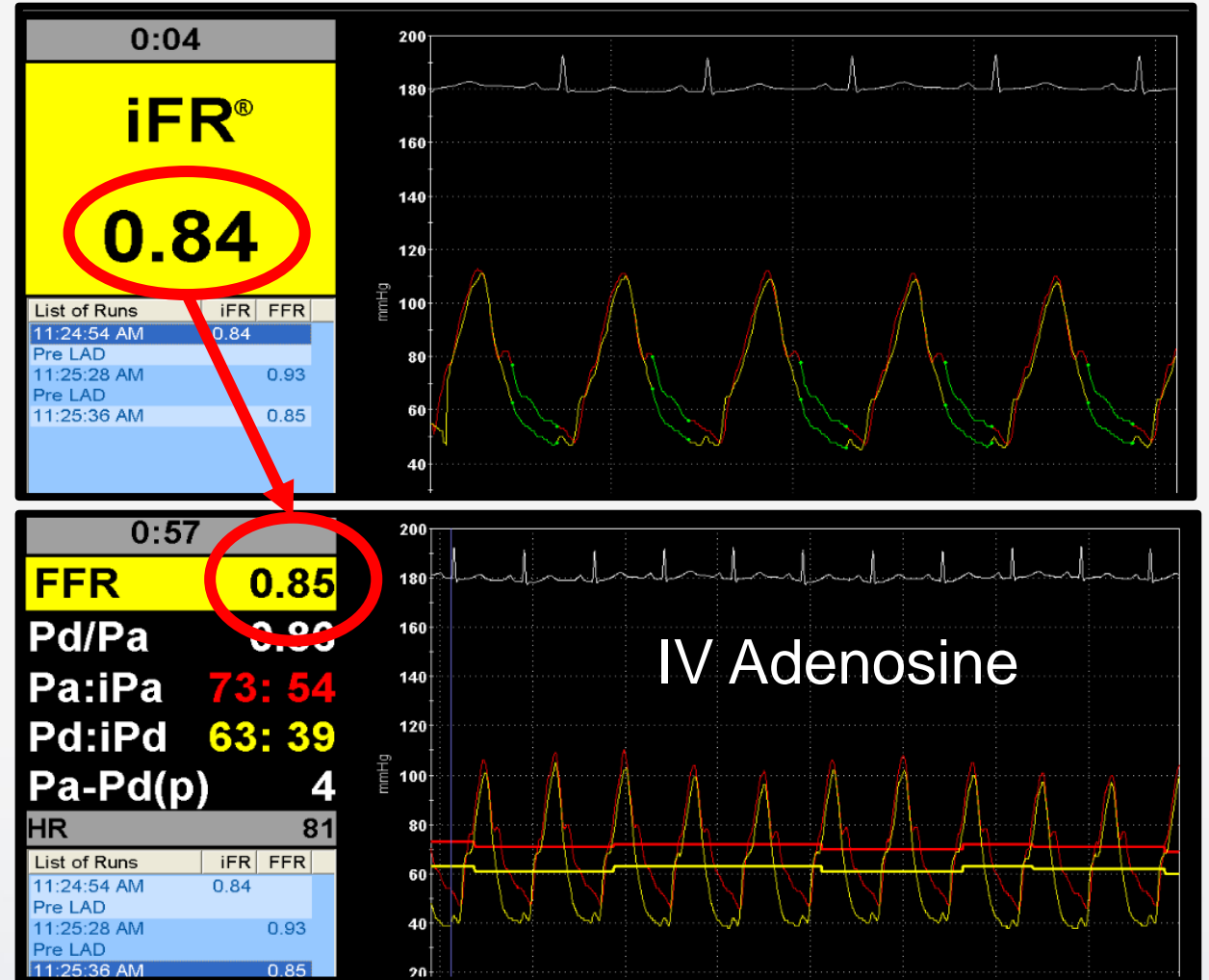
FFR and NHPR Discordance



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

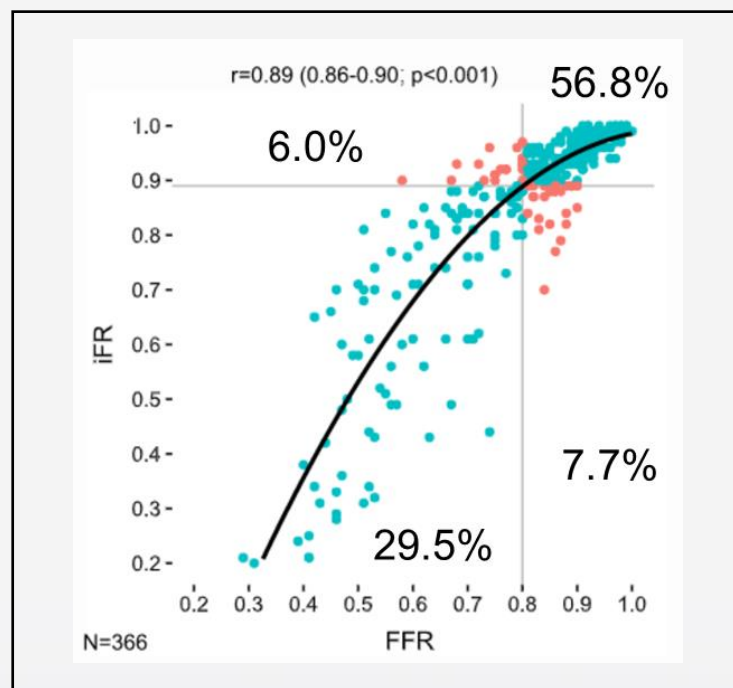


83 YO/Male with Severe AS (iFR 0.84 → FFR 0.85)



Incidence (1)

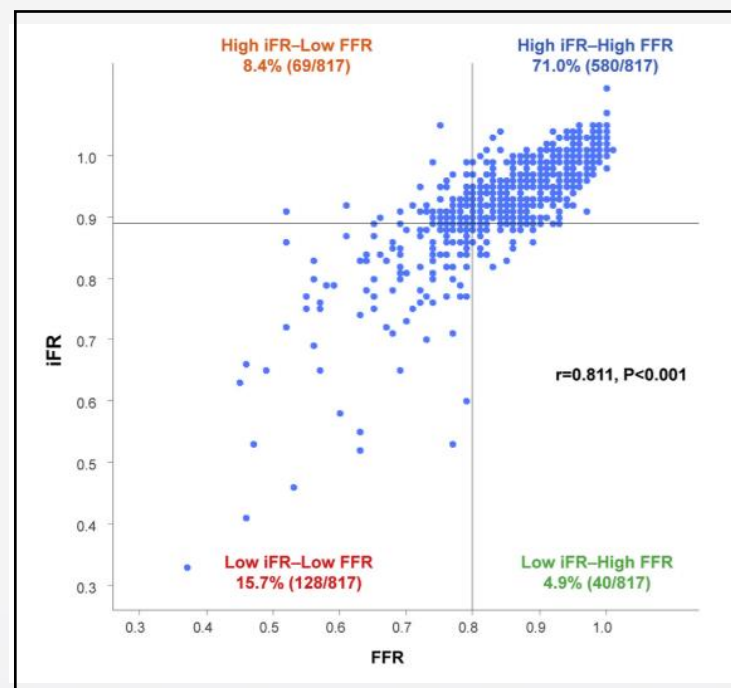
13.7 %



Cook CM et al.

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

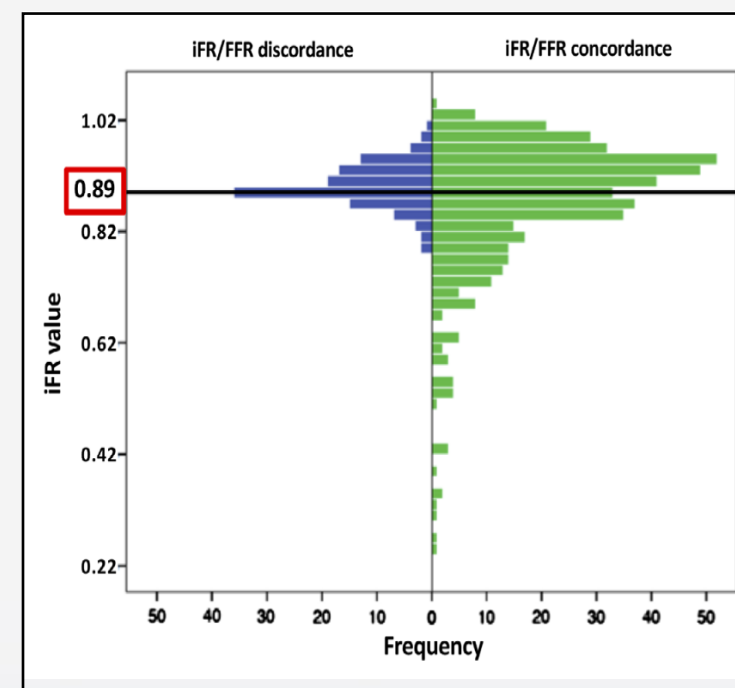
13.3 %



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

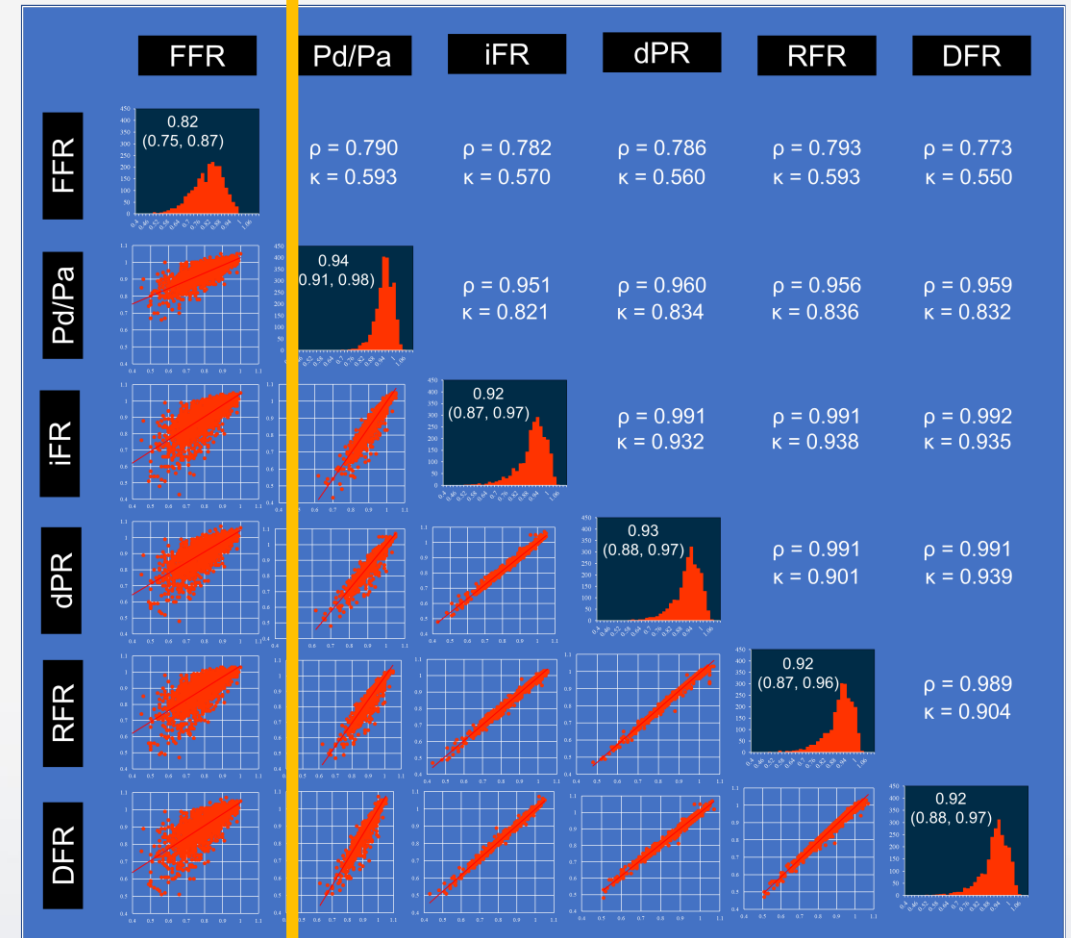
Diagnostic Accuracy: 81%

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



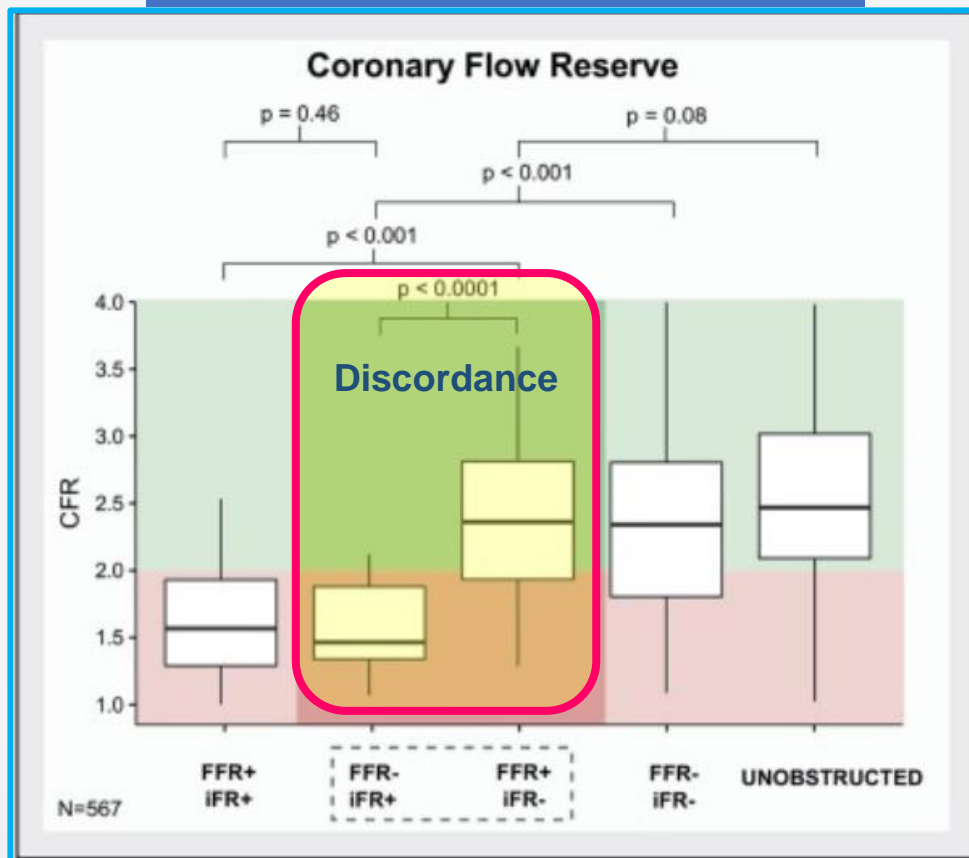
Unpublished Data From IRIS FFR Registry

Incidence (3)

15-20%

Underlying Mechanism (1) Physiologic Characteristics

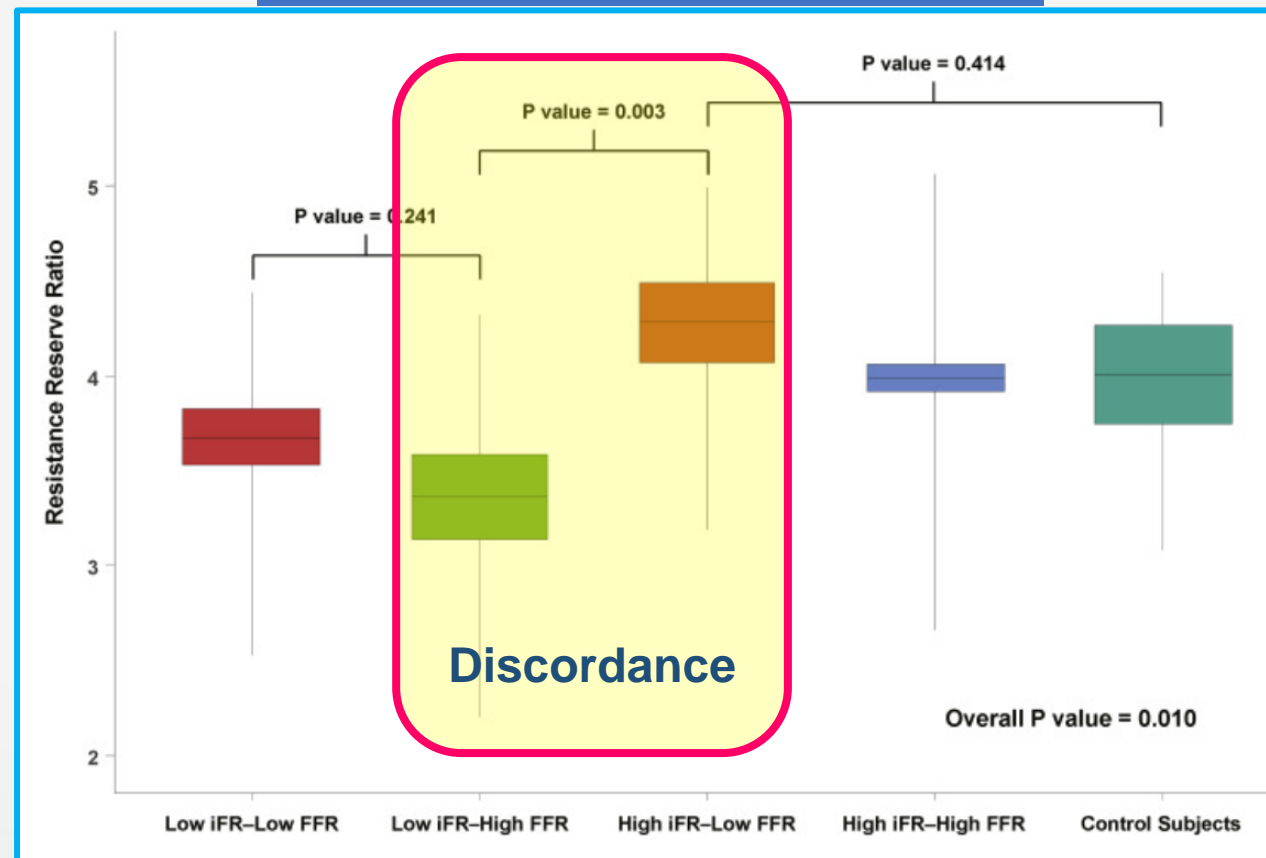
Coronary Flow Reserve



Cook CM et al.

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

Resistance Reserve Ratio

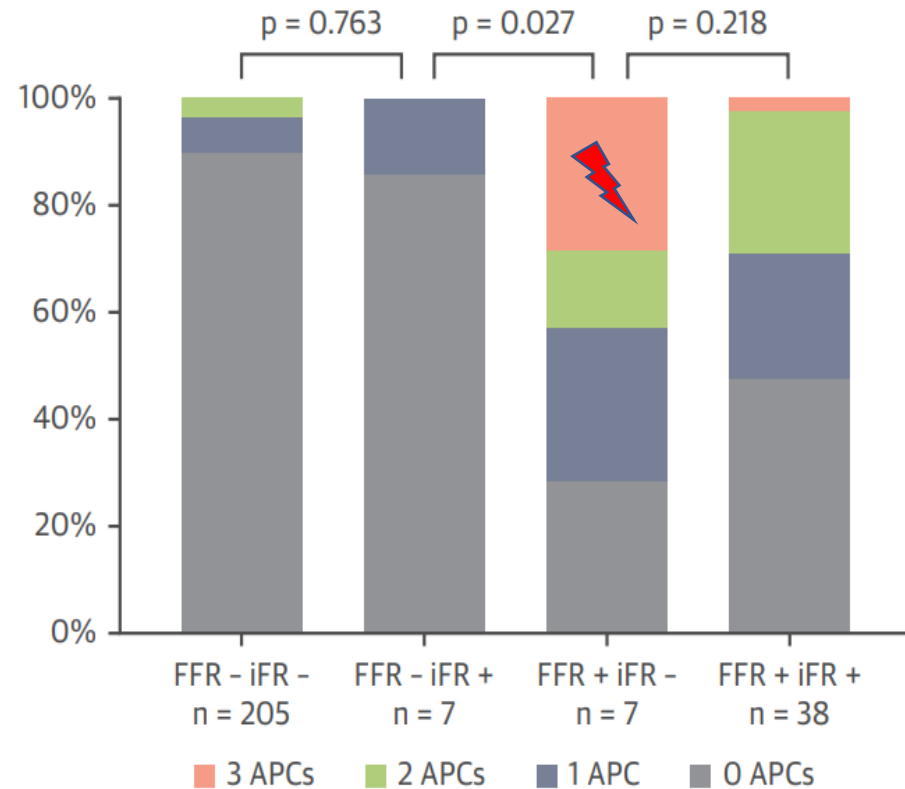


SH Lee et al.

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

Underlying Mechanism (2) Anatomical Characteristics

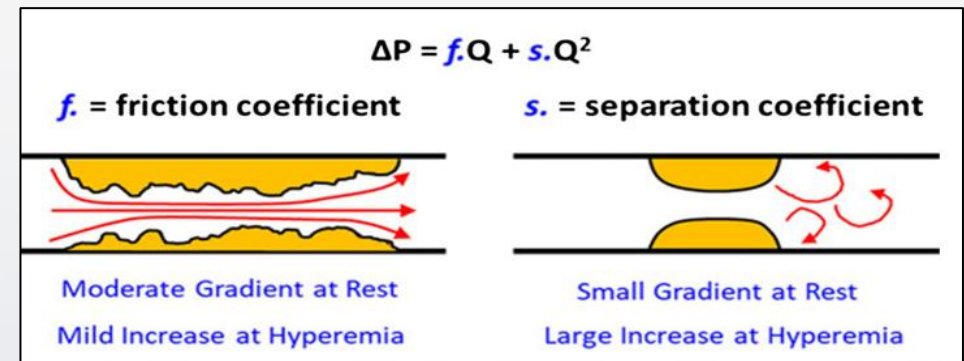
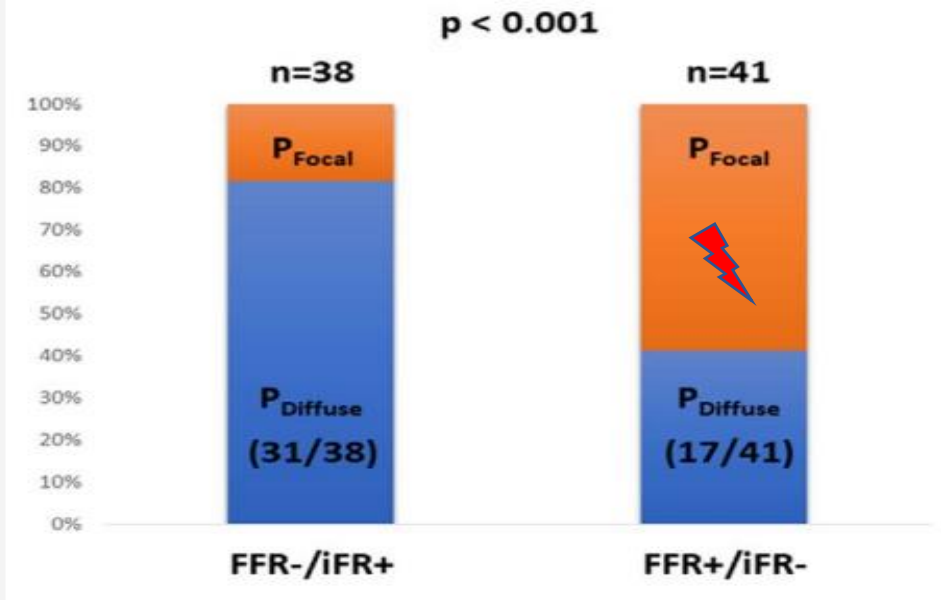
Adverse Plaque Characteristics* Relate More Strongly With FFR than iFR



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

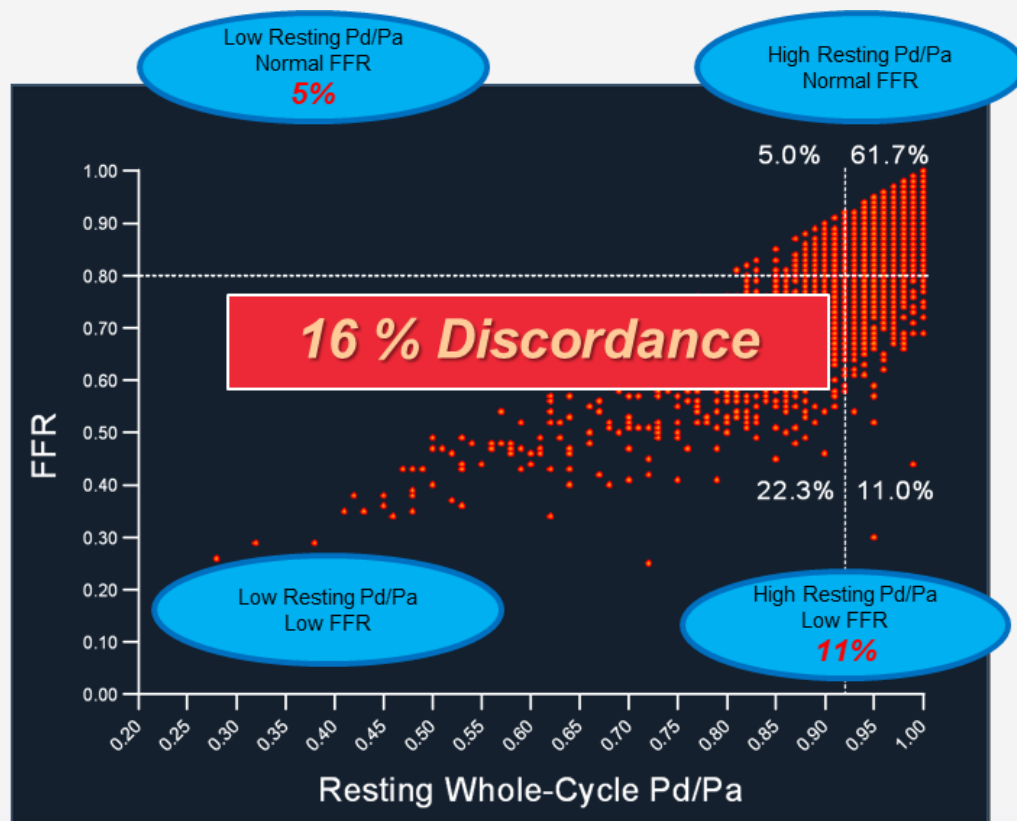
*Adverse plaque characteristics include low-attenuation plaque, positive remodeling, spotty calcification, and napkin risk sign

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 <i>Very Small Hyperemic Pressure Drop</i>			
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
Resting Pd/Pa > 0.92 and FFR ≤ 0.80 <i>Very Big Hyperemic Pressure Drop</i>			
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

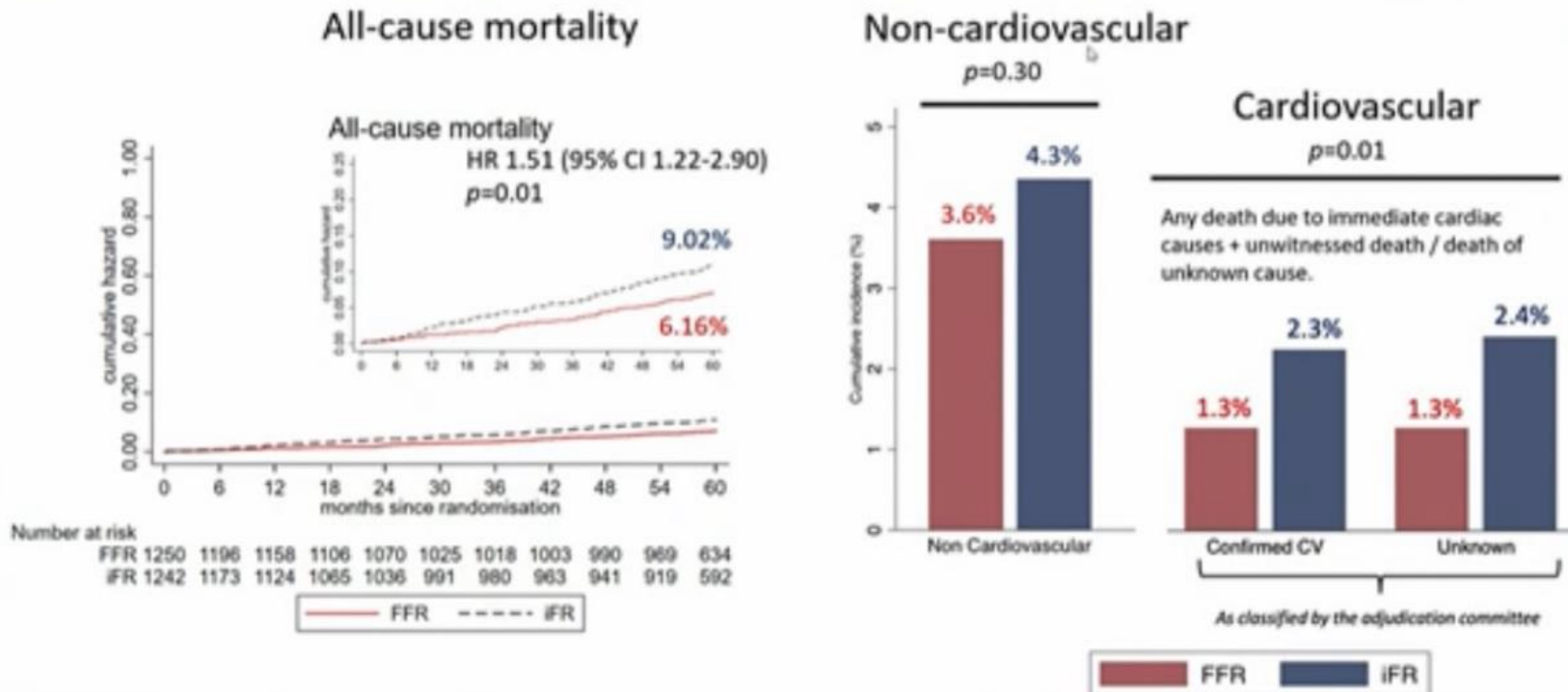
Underlying Mechanism: Summary

NHPR/FFR Discordance

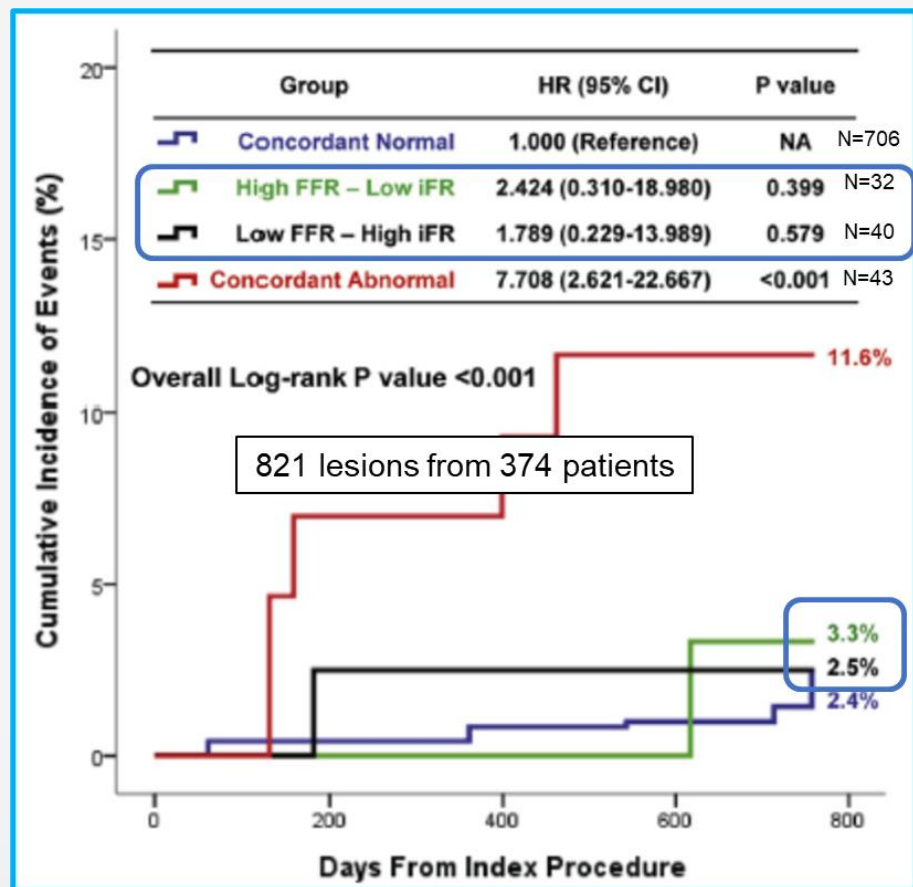
	NHPR+ FFR-	NHPR- FFR+
<i>Coronary physiology</i>	Un-Healthy Vascular Status	More Complex Atherosclerosis
<i>Coronary anatomy</i>		
<i>Clinical Characteristics</i>		

DEFINE FLARE 5-year FU

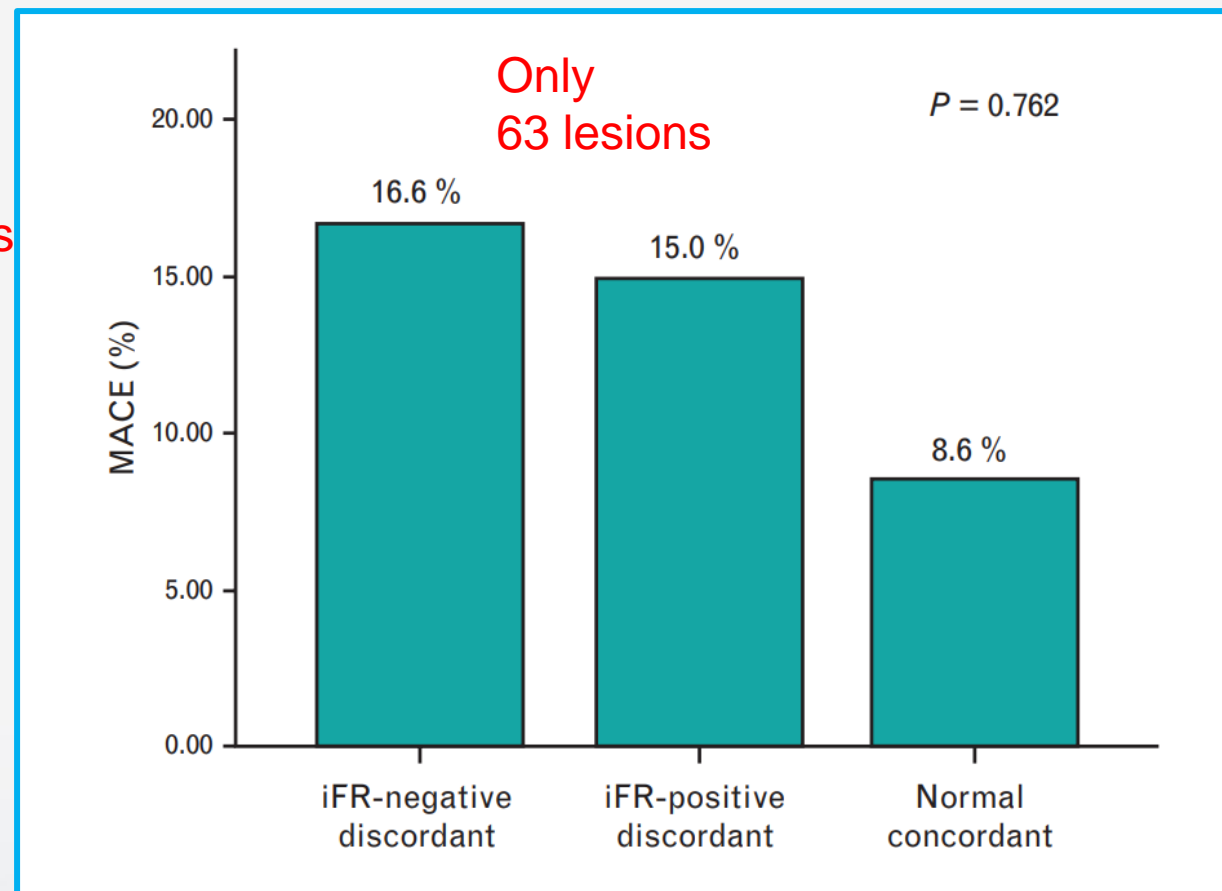
5-year results: Mortality



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



Only
72 lesions



J Am Coll Cardiol Interv 2017, 10: 2502

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

FFR and iFR value of Discordant Lesions

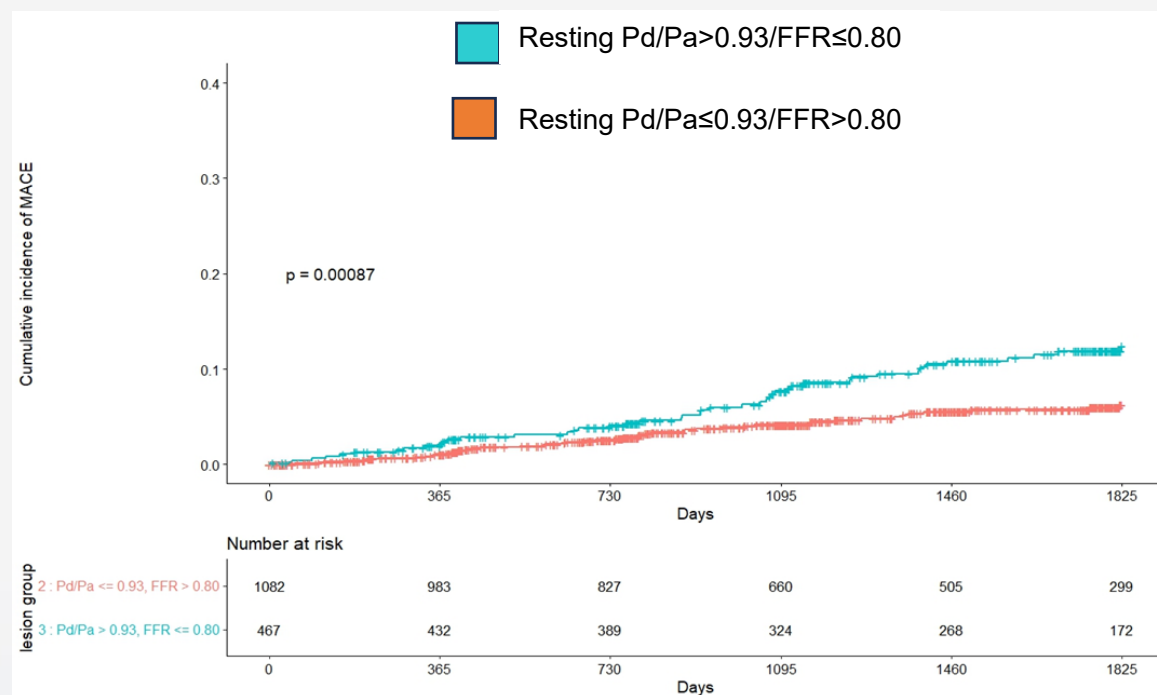
	FFR		iFR	
	iFR+ FFR-	iFR- FFR+	iFR+ FFR-	iFR- FFR+
Cook CM et al. JACC Cardiovasc Interv. 2017;10(24):2514-2524	0.86 (0.84-0.88)	0.77 (0.74-0.80)	0.88 (0.84-0.89)	0.92 (0.91-0.93)
SH Lee et al. JACC Cardiovasc Interv. 2019;12(20):2018-2031	0.85 (0.84-0.86)	0.76 (0.75-0.78)	0.88 (0.87-0.88)	0.93 (0.92-0.93)
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



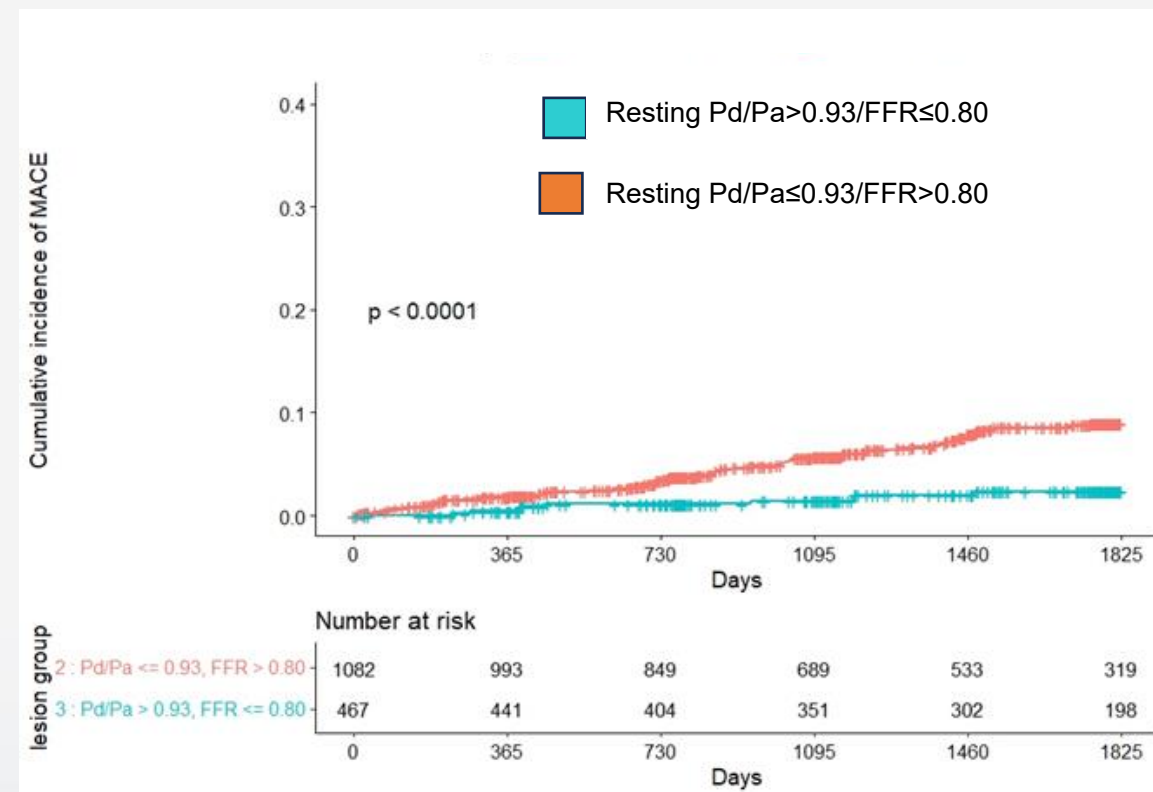
“Grey Zone” FFR

Contrasting Prognostic Value of Discordant Lesion/Patient Outcome

Target Vessel **MI** and **RR**



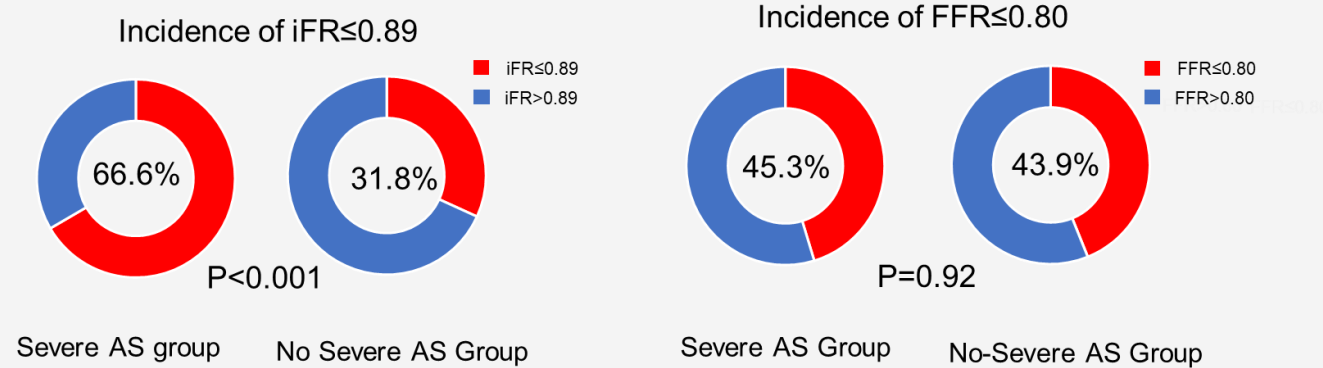
Death From Any Cause



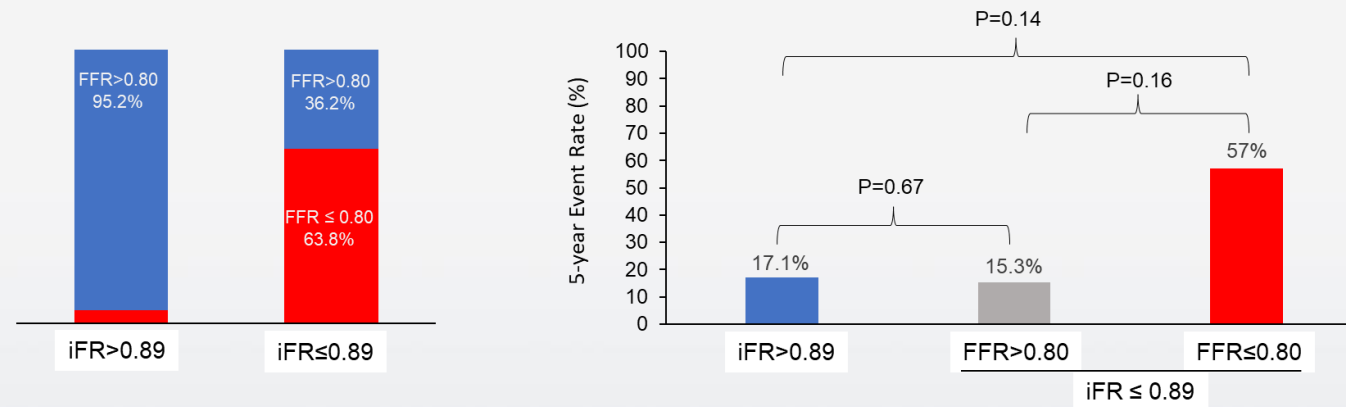
Unpublished Data from IRIS-FFR

IRIS-FFR Registry – Severe AS Subgroup

Incidence of Hemodynamically Significant Stenosis in Severe AS Group and No Severe AS Group

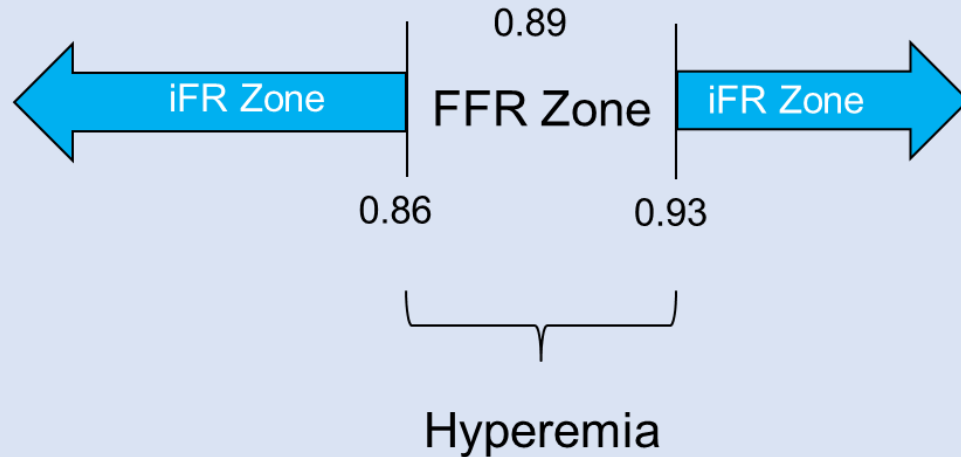


Prognostic Value of iFR and FFR in Severe AS Group



When To Use Hyperemia

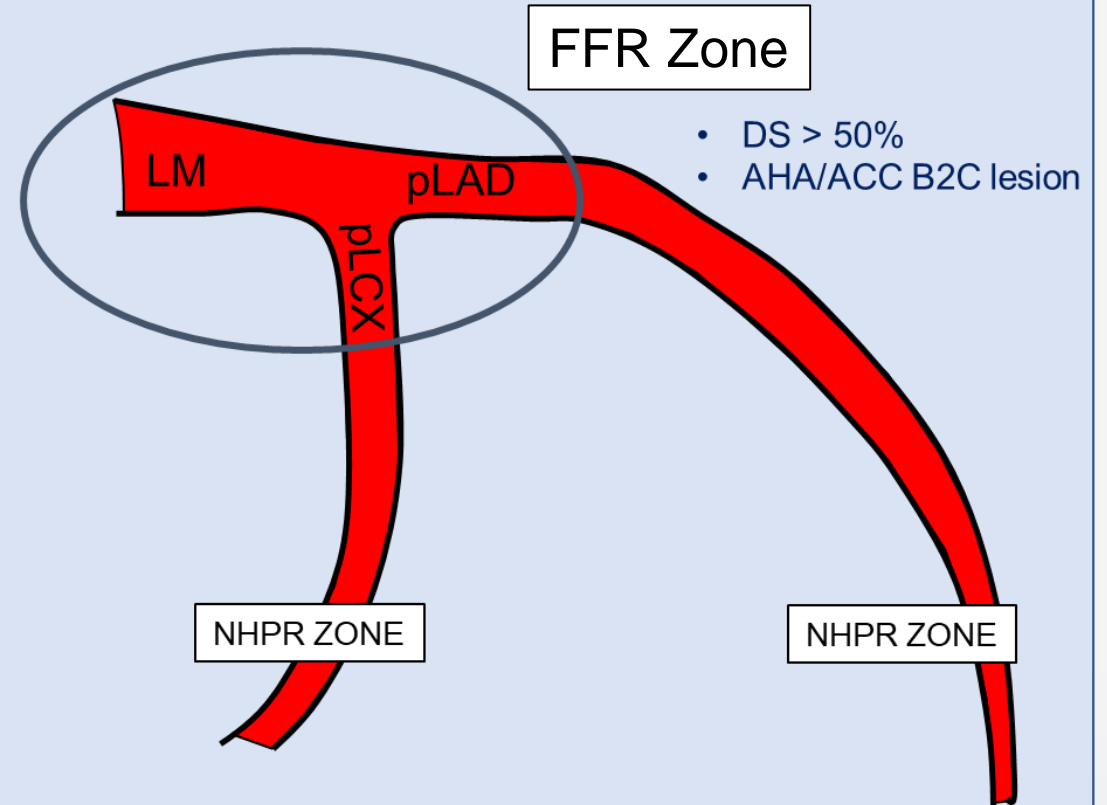
Physiologic Consideration



Clinical Consideration

- Young age
- Male
- Diabetes, Chronic Kidney Disease

Anatomical Consideration



Is iFR the Same as FFR? - Still?

NHPR/FFR Discordance

	NHPR+ FFR-	NHPR- FFR+
<i>Coronary physiology</i>	Un -Healthy Patient Status Related with Death	More Complex Atherosclerosis Related with TV-MI and RR
<i>Coronary anatomy</i>		
<i>Clinical Characteristics</i>		

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.