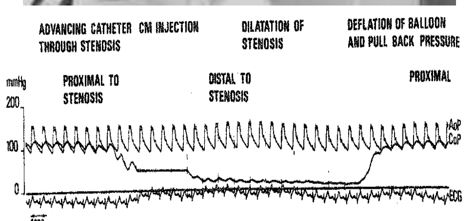
Similarities and Dissimilarities of FFR, iFR and resting Pd/Pa

Bon-Kwon Koo, MD, PhD

Seoul National University Hospital, Seoul, Korea

From resting pressure gradient,
to hyperemic gradient, FFR

1977



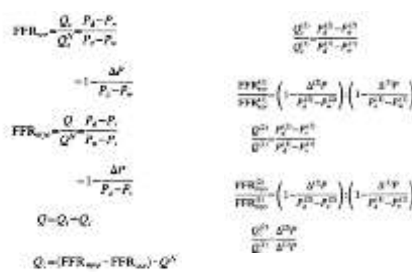
Tried, but failed due to

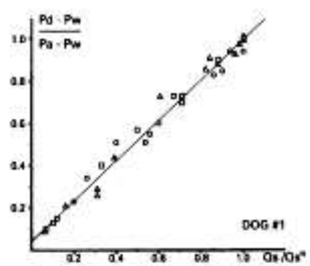
- Large OTW balloon
- Resting pressure only (no hyperemia)

1993

Experimental Basis of Determining Maximum Coronary, Myocardial, and Collateral Blood Flow by Pressure Measurements for Assessing Functional Stenosis Severity Before and After Percutaneous Transluminal Coronary Angioplasty

Nico H.J. Pijls, MD; Jacques A.M. van Son, MD; Richard L. Kirkeeide, PhD; Bernard De Bruyne, MD; and K. Lance Gould, MD



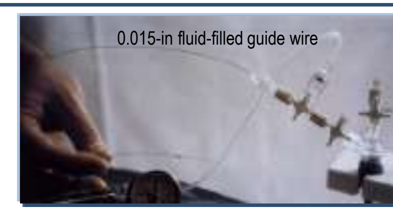


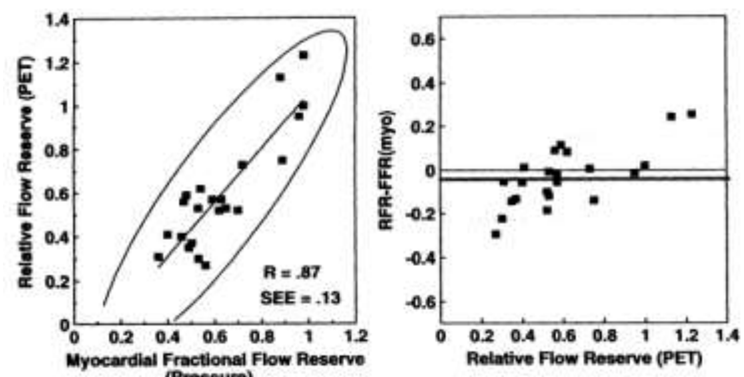
1994

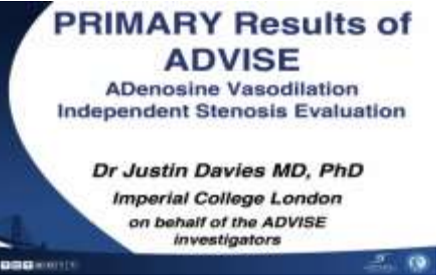
Coronary Flow Reserve Calculated From Pressure Measurements in Humans

Validation With Positron Emission Tomography

Bernard De Bruyne, MD; Thierry Baudhuin, MD†; Jacques A. Melin, MD, PhD; Nico H.J. Pijls, MD, PhD; Stanislas U. Sys, MD, PhD; Anne Bol, PhD; Walter J. Paulus, MD; Guy R. Heyndrickx, MD, PhD; William Wijns, MD, PhD

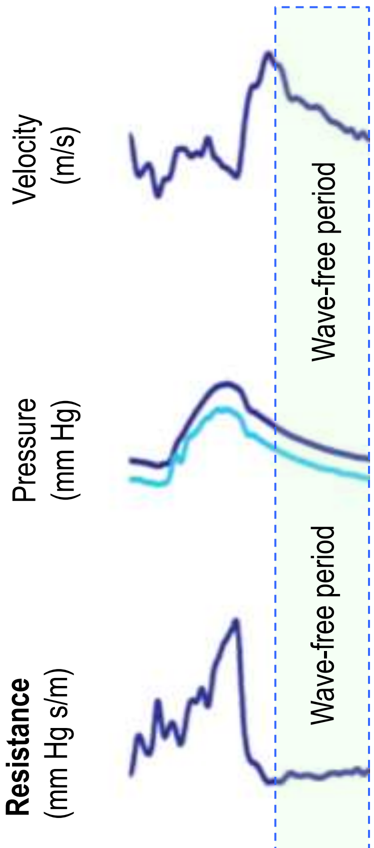


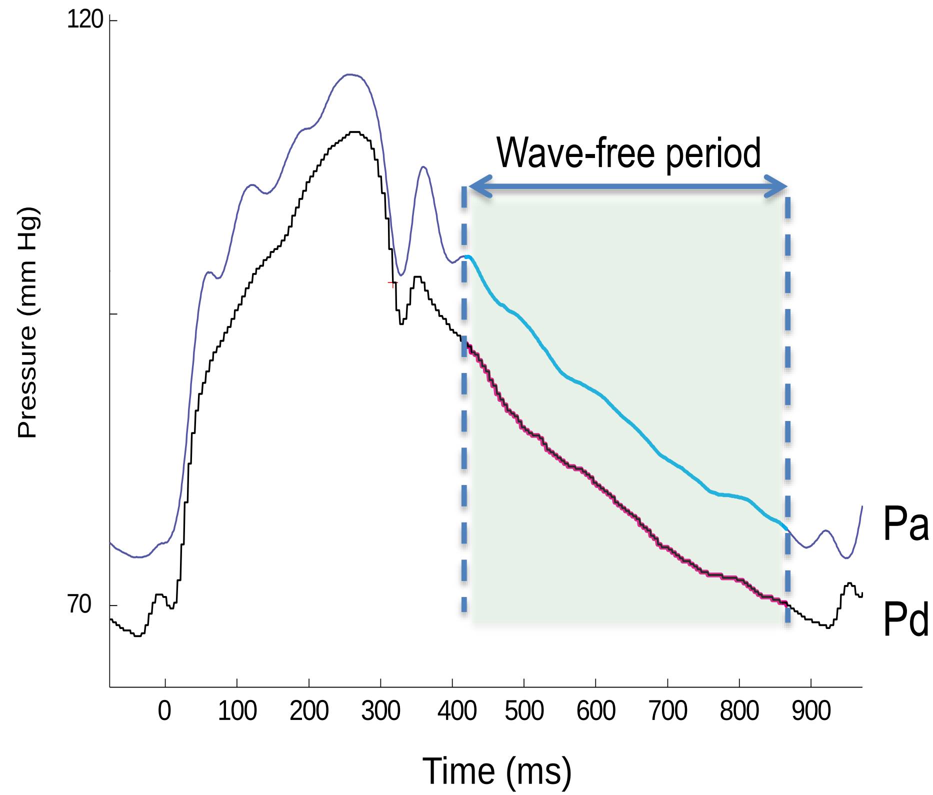




Return of a forgotten "Resting Pressure Index"

iFR = **i**nstantaneous wave-**F**ree **R**atio

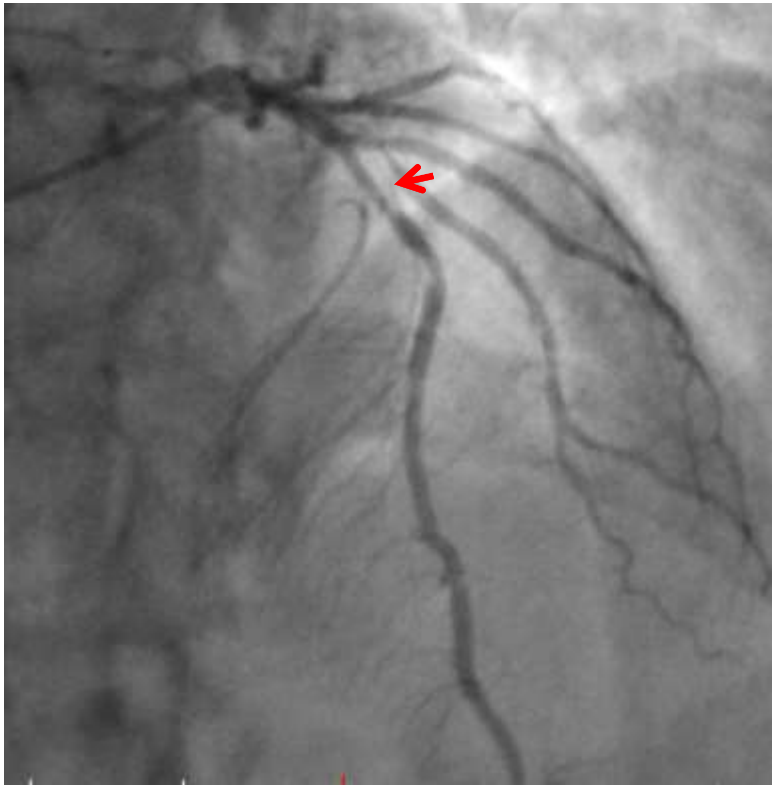




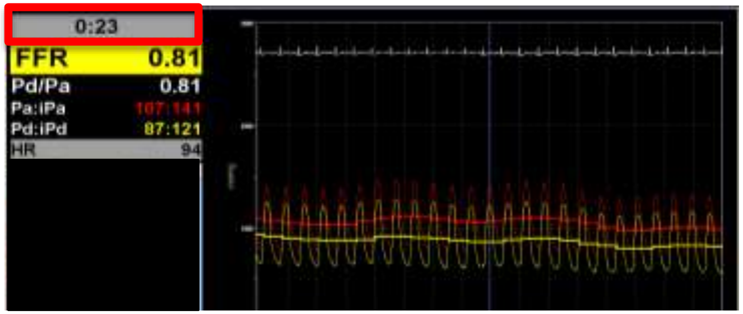
iFR: Pd/Pa ratio during the ***resting*** wave-free period

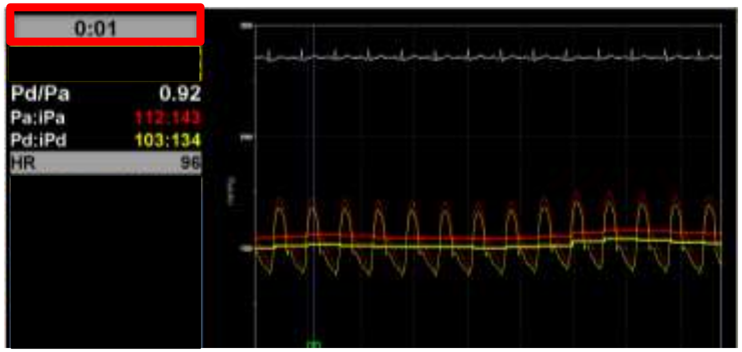
iFR doesn't need hyperemia and measurement is instantaneous.

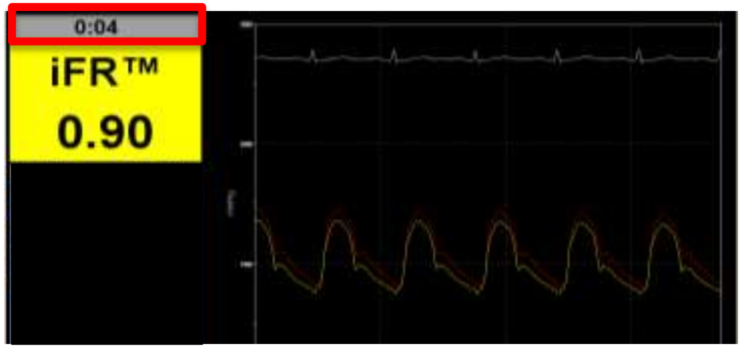
iFR, How easy?



20 sec with adenosine, chest discomfort…..

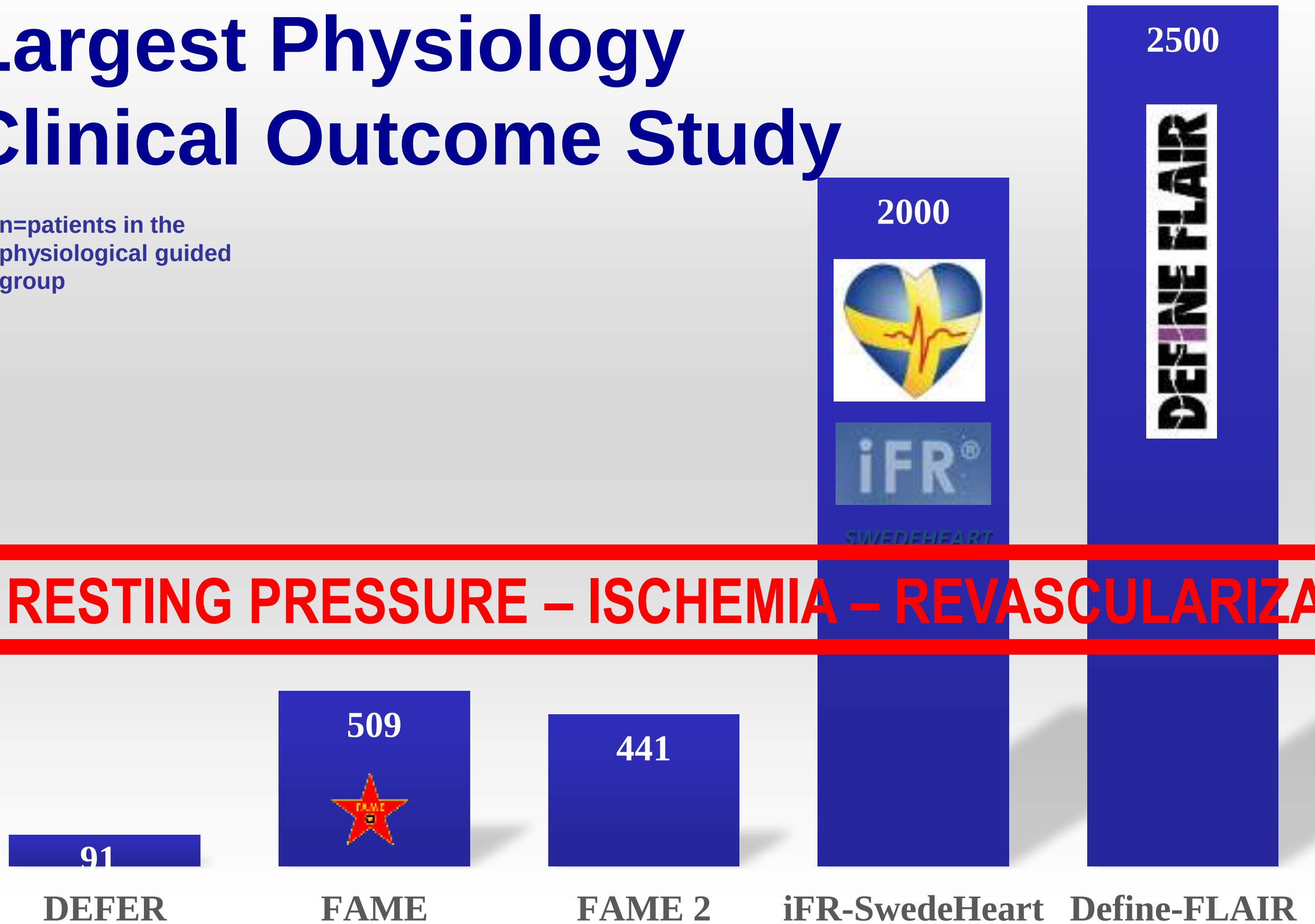






DEFINE-FLAIR
Largest Physiology Clinical Outcome Study

n=patients in the physiological guided group



RESTING PRESSURE – ISCHEMIA – REVASCULARIZATION - OUTCOMES

Modified from Dr Escaned's presentation

iFR vs. FFR

"*equivalent*" and "*comparable*"

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Cardiac Imaging

Diagnostic Classification of the Instantaneous Wave-Free Ratio Is Equivalent to Fractional Flow Reserve and Is Not Improved With Adenosine Administration

Results of CLARIFY (Classification Accuracy of Pressure-Only Ratios Against Indices Using Flow Study)

Sayan Sen, MBBS,* Kaleab N. Asress, MA, BM, BCh,† Sukhjinder Nijjer, MB ChB,* Ricardo Petraco, MD,* Iqbal S. Malik, MBBS, PhD,*‡ Rodney A. Foale, MD,* Ghada W. Mikhail, MBBS, MD,*‡ Nicolas Foin, PhD,* Christopher Broyd, MBBS,* Nearchos Hadjiloizou, MBBS, PhD,*‡ Amarjit Sethi, MBBS, PhD,‡ Mahmud Al-Bustami, MD,‡ David Hackett, MD,‡ Masood A. Khan, MB, BChir, MA,‡ Muhammed Z. Khawaja, MBBS,† Christopher S. Baker, MBBS, PhD,‡ Michael Bellamy, MBBS, MD,‡ Kim H. Parker, PhD,§ Alun D. Hughes, MBBS, PhD,* Darrel P. Francis, MB, BChir, MA,* Jamil Mayet, MBChB, MD, MBA,* Carlo Di Mario, MD, PhD,§ Javier Escaned, MD, PhD,‖ Simon Redwood, MD,† Justin E. Davies, MBBS, PhD*
London, United Kingdom; and Madrid, Spain

Conclusions iFR and FFR had equivalent agreement with classification

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ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.09.065

VERIFY (VERification of Instantaneous Wave-Free Ratio and Fractional Flow Reserve for the Assessment of Coronary Artery Stenosis Severity in EverydaY Practice)

A Multicenter Study in Consecutive Patients

Colin Berry, MBChB, PhD,*† Marcel van 't Veer, MSc, PhD,‡ Nils Witt, MD, PhD,§ Petr Kala, MD,‖ Otakar Bocek, MD,‖ Stylianos A. Pyxaras, MD,¶ John D. McClure, MSc, PhD,* William F. Fearon, MD,# Emanuele Barbato, MD, PhD,¶ Pim A. L. Tonino, MD, PhD‡

Conclusions iFR correlates weakly with FFR and is not independent of hyperemia. sion making in patients with coronary artery disease. (Comparison of

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ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.11.003
FOCUS ISSUE: TRANSCATHETER CARDIOVASCULAR THERAPEUTICS
Coronary Disease

Development and Validation of a New Adenosine-Independent Index of Stenosis Severity From Coronary Wave–Intensity Analysis

Results of the ADVISE (ADenosine Vasodilator Independent Stenosis Evaluation) Study

Sayan Sen, MBBS,* Javier Escaned, MD, PhD,† Iqbal S. Malik, MBBS, PhD,‡
...Mikhail, MBBS, MD,‡ Rodney A. Foale, MD,* Rafael Mila, MD,† Jason Tarkin, MBBS,*
...aco, MD,* Christopher Broyd, MBBS,* Richard Jabbour, MBBS,*

Conclusions

resistance is naturally constant and minimized during the wave-free period. The instantaneous
o calculated over this period produces a drug-free index of stenosis severity comparable to FFR.
ree Measure of Fractional Flow Reserve [ADVISE]; NCT01118481) (J Am Coll Cardiol 2012;59:

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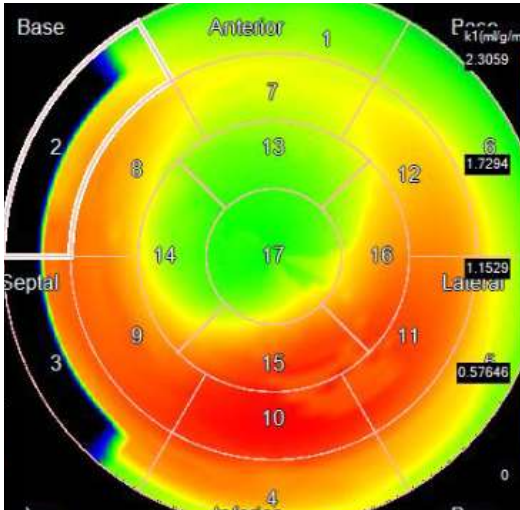
Vol. 61, No. 13, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.09.064

Does the Instantaneous Wave-Free Ratio Approximate the Fractional Flow Reserve?

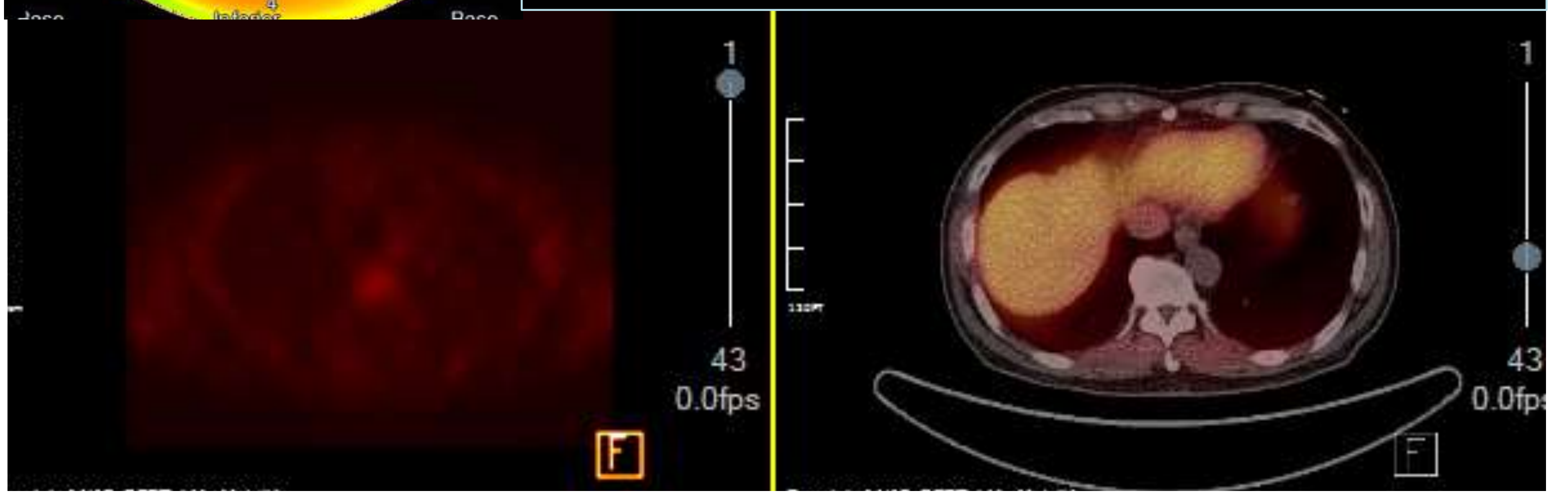
Nils P. Johnson, MD, MS,* Richard L. Kirkeeide, PhD,* Kaleab N. Asress, MA, BM, BCh,† William F. Fearon, MD,‡ Timothy Lockie, MB, ChB, PhD,†§ Koen M. J. Marques, MD, PhD,‖ Stylianos A. Pyxaras, MD,¶ M. Cristina Rolandi, MSc,# Marcel van 't Veer, MSc, PhD,**†† Bernard De Bruyne, MD, PhD,¶ Jan J. Piek, MD, PhD,§ Nico H. J. Pijls, MD, PhD,**††

Conclusions iFR provides both a biased estimate of FFR, on average, Diastolic resting myocardial resistance does not equal m

iFR vs. FFR: **Who can be the judge?**



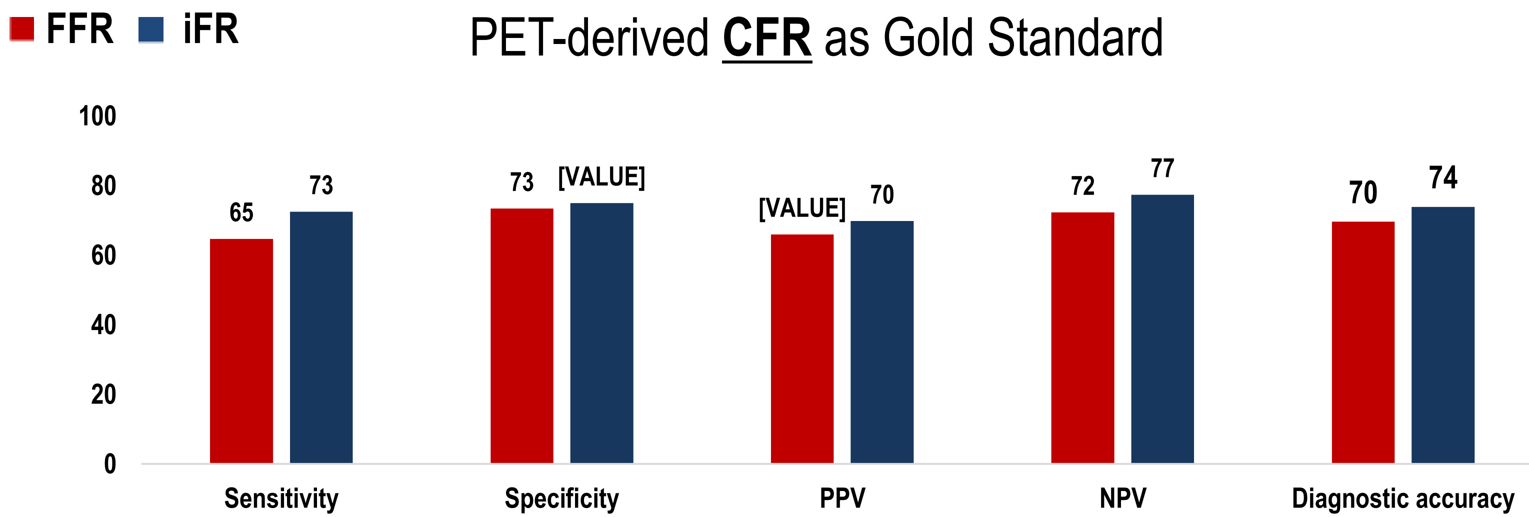
	Flow (ml/g/min)				Reserve	
	Stress		Rest			
	mean	std dev.	mean	std dev.	mean	std dev.
LAD	1.51	0.30	0.86	0.14	1.77	0.28
LCX	1.74	0.35	0.82	0.16	2.09	0.21
RCA	1.77	0.44	0.85	0.21	2.06	0.19
Global	1.63	0.37	0.84	0.16	1.92	0.29



N13-Ammonia PET perfusion scan

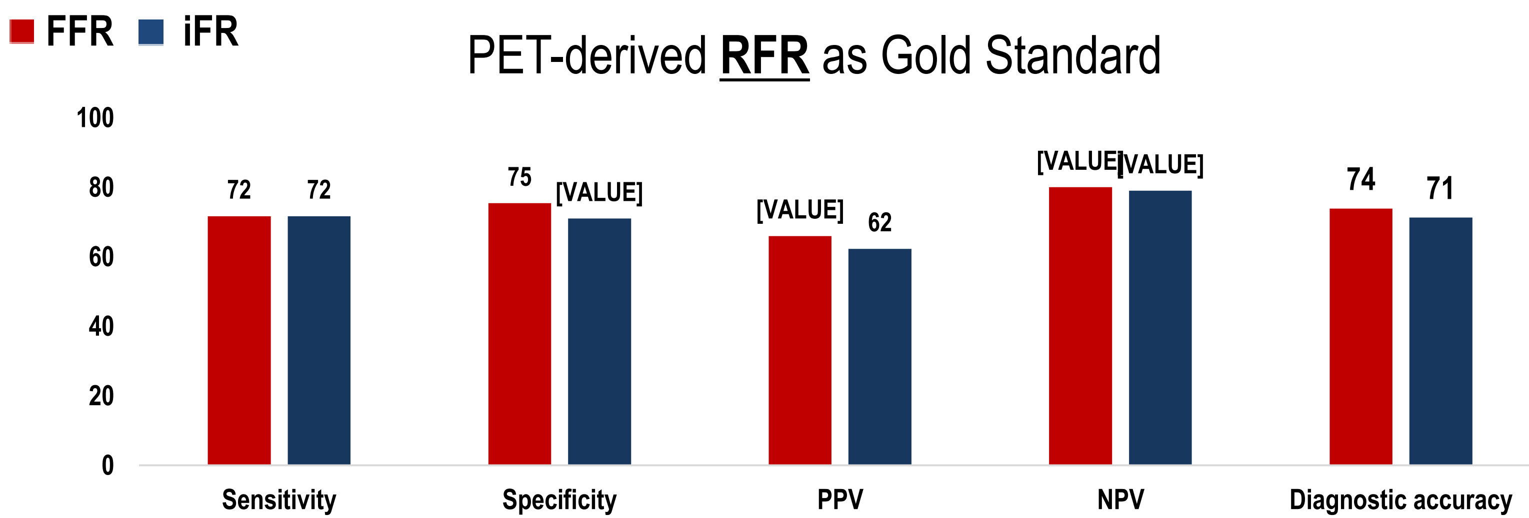
Diagnostic Performance of FFR and iFR

PET-derived **CFR** as Gold Standard



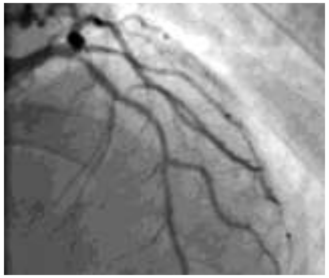
CFR = coronary flow reserve, RFR = relative flow reserve

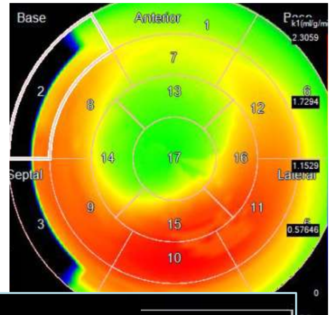
PET-derived **RFR** as Gold Standard



Hwang D, Lee JM, Koo BK, et al. JACC interv 2016

Coronary Circulatory Response to Stenosis
: Combined PET flow and invasively measured pressure





FLOW(ml/g/min)	Stress		Rest		Reserve	
	mean	std dev.	mean	std dev.	mean	std dev.
LAD	1.51	0.30	0.86	0.14	1.77	0.28
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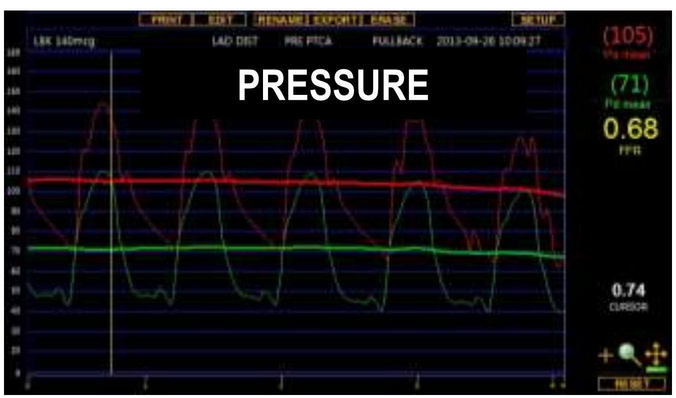
Global	1.63	0.37	0.84	0.16	1.92	0.29

+



Myocardial blood flow (MBF, ml/min/g)	
Resting MBF	0.830
Hyperemic MBF	2.087

+

Coronary Pressure (mmHg)	
Resting Pa	90
Resting Pd	86
Hyperemic Pa	85
Hyperemic Pd	68

$$\text{Resting microvascular resistance} = \frac{\text{Resting Pd}}{\text{Resting MBF}}(\text{mmHg}\cdot\text{min}\cdot\text{g}\cdot\text{ml}^{-1}) = \frac{86}{0.830} = 103.6$$

$$\text{Hyperemic microvascular resistance} = \frac{\text{Hyperemic Pd}}{\text{Hyperemic MBF}}(\text{mmHg}\cdot\text{min}\cdot\text{g}\cdot\text{ml}^{-1}) = \frac{68}{2.087} = 32.6$$

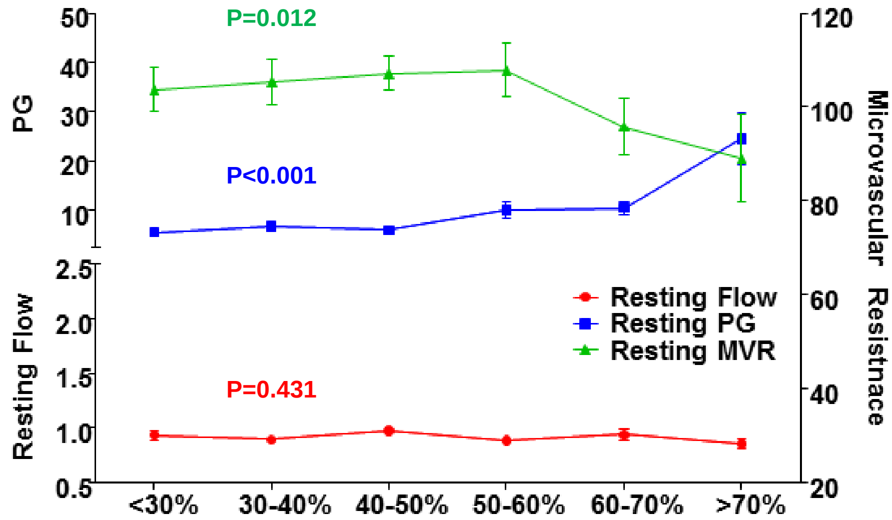
$$\text{Basal stenosis resistance (BSR)} = \frac{\text{Resting (Pa−Pd)}}{\text{Resting MBF}}(\text{mmHg}\cdot\text{min}\cdot\text{g/ml}) = \frac{90-86}{0.830} = 4.8$$

$$\text{Hyperemic stenosis resistance (HSR)} = \frac{\text{Hyperemic (Pa−Pd)}}{\text{Hyperemic MBF}}(\text{mmHg}\cdot\text{min}\cdot\text{g/ml}) = \frac{85-68}{2.087} = 8.14$$

Lee JM…..Koo BK Circulation 2017

Coronary Circulatory Responses to Epicardial Stenosis

Resting

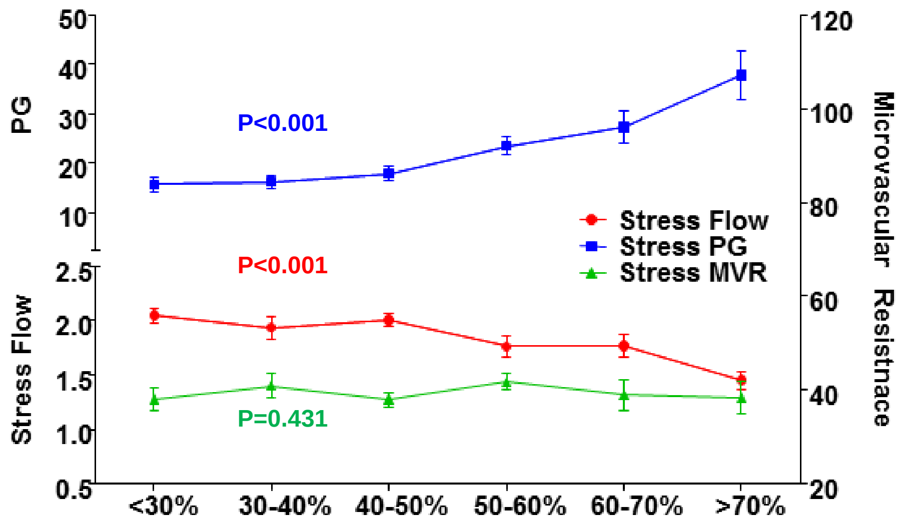


As stenosis severity (epicardial resistance) increases

- No change in resting flow
- MV resistance ▼
- Resting pressure gradient ▲

*MV, microvascular; PG, pressure gradient

Hyperemia



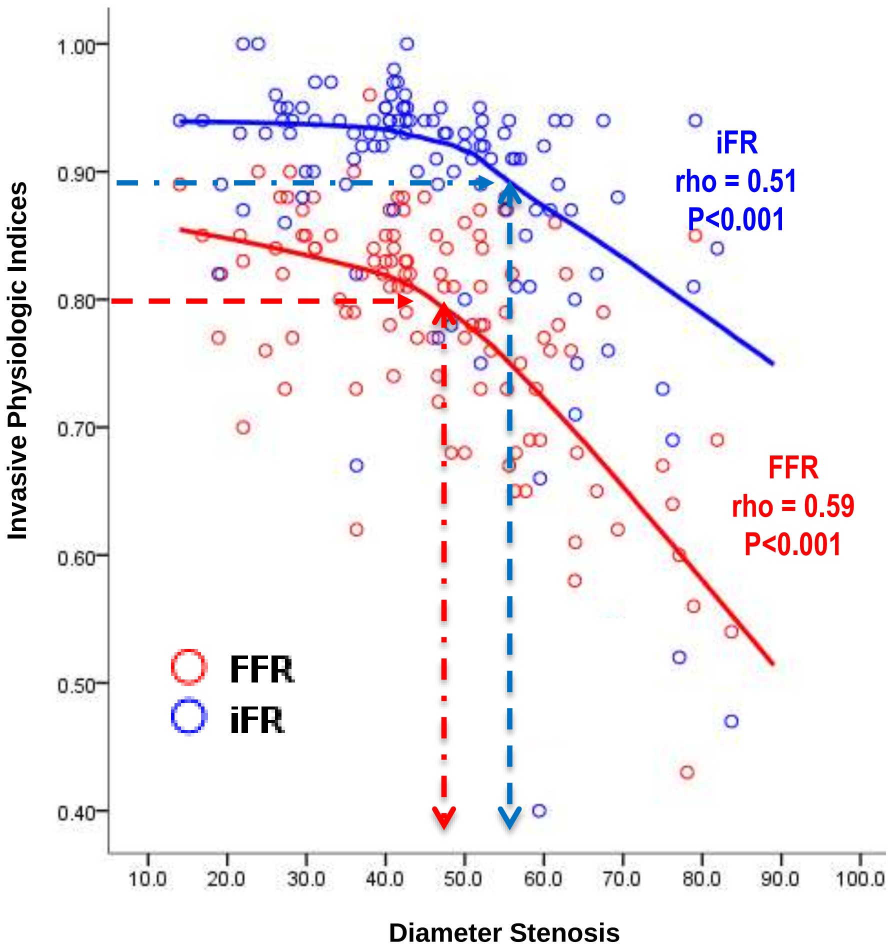
As stenosis severity (epicardial resistance) increases

- Minimal and stable MV resistance
- Hyperemic flow ▼
- Hyperemic pressure gradient ▲

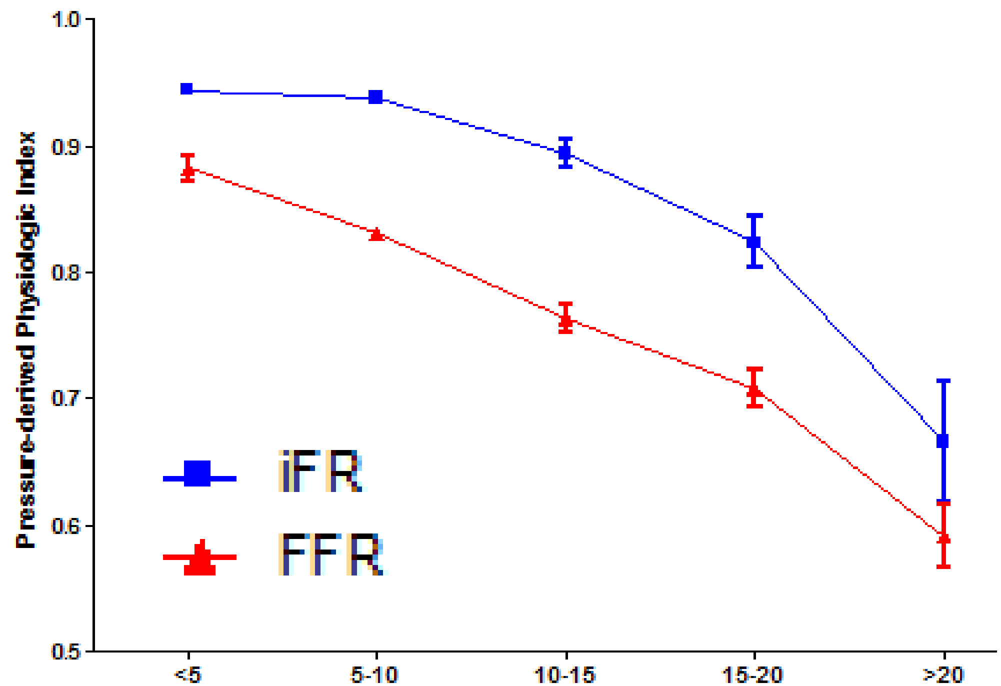
JM Lee, BK Koo et al. Circulation 2017

Invasive Physiologic Indices vs. Stenosis, Resistance and Flow

Angiographic stenosis



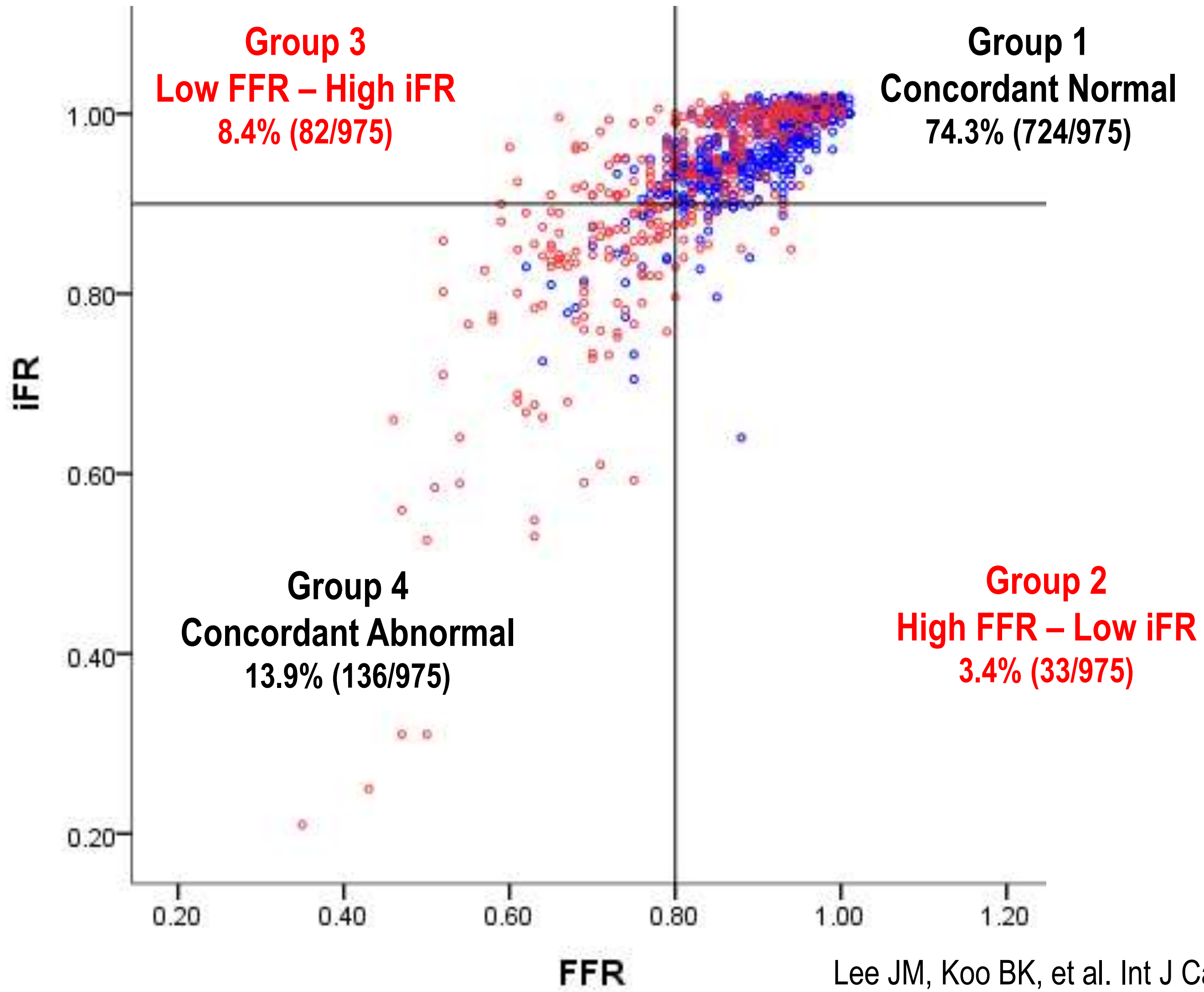
Hyperemic Stenosis Resistance



Lee JM ,Koo BK, et al Circulation 2017

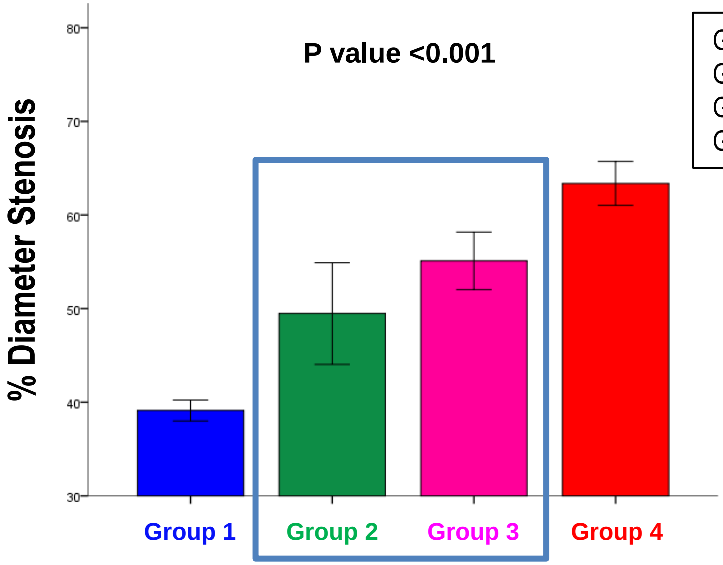
Clinical relevance of iFR/FFR discordance?

(from 3V-FFR FRIENDS study)

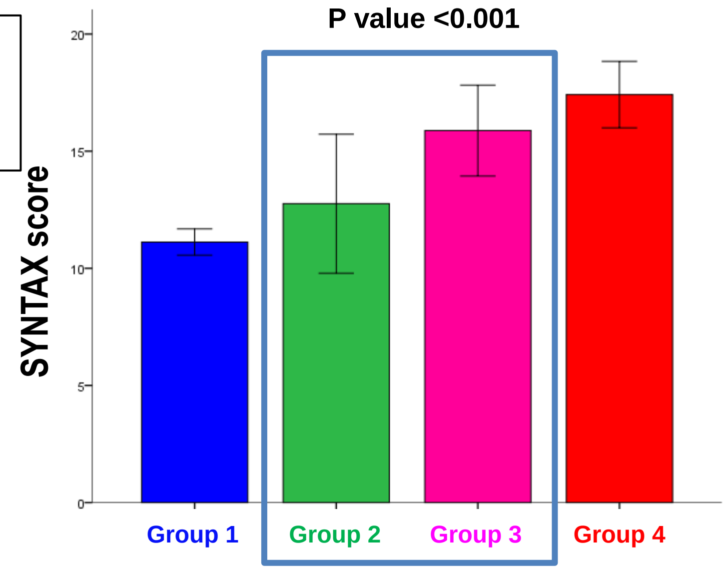


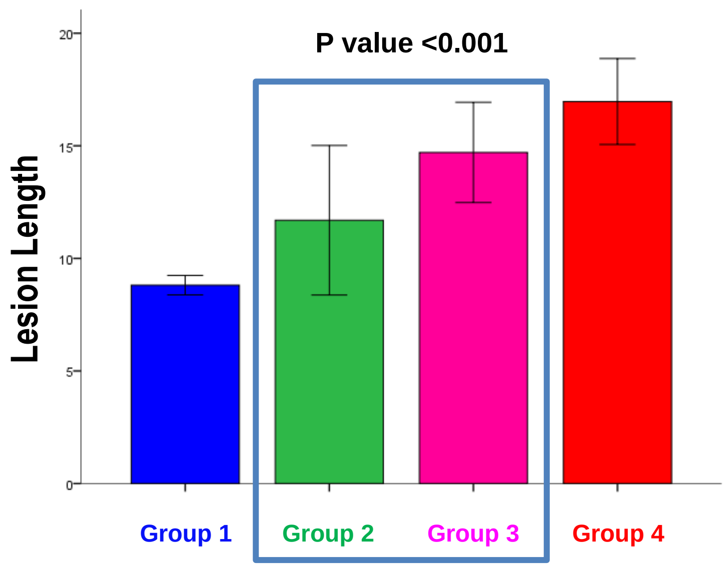
Lee JM, Koo BK, et al. Int J Cardiol 2017
Lee JM, Koo BK, et al. Eur Heart J 2018

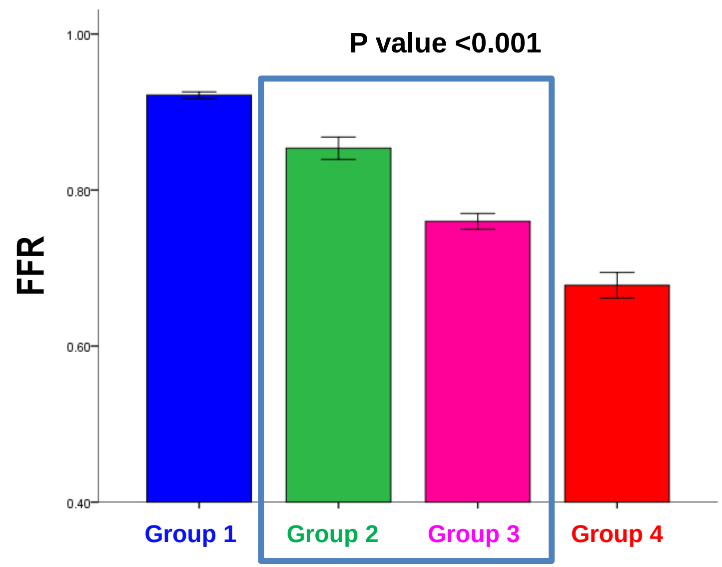
Clinical relevance of iFR/FFR discordance



Group 1: Both high
Group 2: High FFR & Low iFR
Group 3: Low FFR & High iFR
Group 4: Both low







Lee JM, Koo BK, et al. Int J Cardiol 2017

Independent Predictors of iFR/FFR Discordance

Low iFR among High FFR lesions		
	OR (95% CI)	P value
Female	**2.1** (1.01-4.47)	0.046
Diabetes mellitus	**2.14** (1.02-4.49)	0.045
Reference diameter	**0.41** (0.23-0.75)	0.003
% Diameter stenosis	**1.03** (1.00-1.05)	0.024
High iFR among Low FFR lesions		
	OR (95% CI)	P value
Male	**3.25** (1.32-8.00)	0.011
Diabetes mellitus	**0.47** (0.25-0.90)	0.022
% Diameter stenosis	**0.96** (0.94-0.98)	<0.001

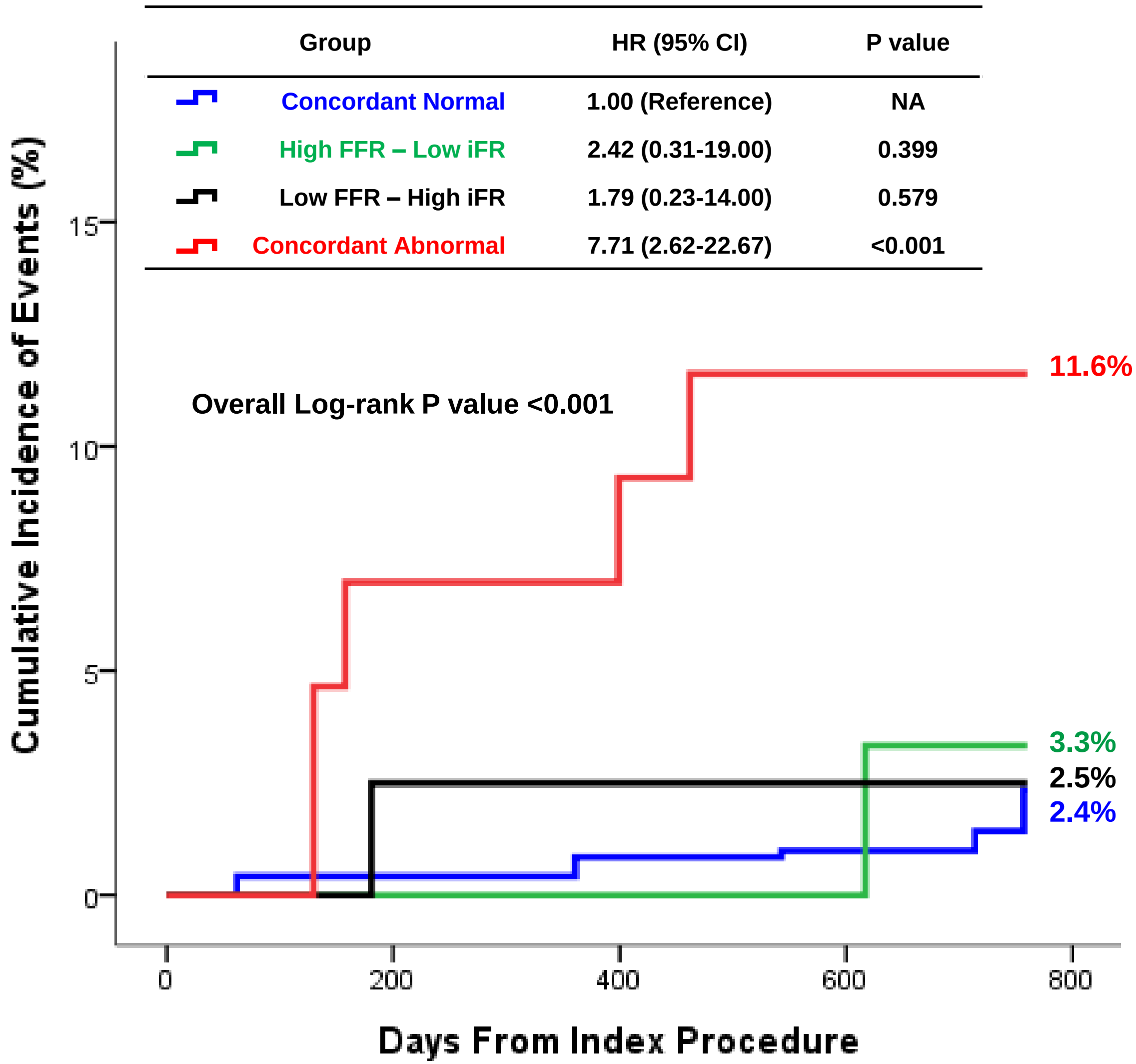
Lee JM, Koo BK, et al. Int J Cardiol 2017

Physiologic relevance of discordance in low FFR

	High iFR	Low iFR	p
Diameter stenosis, %	**47.4 ± 11.8**	57.9 ± 17.1	0.025
FFR	**0.77 (0.76 - 0.78)**	0.68 (0.61 - 0.73)	< 0.001
iFR	0.92 (0.91 - 0.94)	0.81 (0.71 - 0.87)	< 0.001
CFR	**2.27 ± 0.50**	1.76 ± 0.33	0.001
Resting			
Myocardial blood flow	0.87 ± 0.20	0.92 ± 0.15	0.360
Microvascular resistance	**114.5 ± 25.0**	90.6 ± 21.4	0.001
Stenosis resistance	**7.9 ± 2.7**	18.4 ± 12.9	< 0.001
Stress			
Myocardial blood flow	**1.94 ± 0.45**	1.60 ± 0.33	0.003
Microvascular resistance	38.8 ± 10.6	41.0 ± 10.0	0.474
Stenosis resistance	**12.2 ± 4.3**	21.3 ± 8.9	< 0.001

Lee JM, Koo BK, et al. Int J Cardiol 2017:243:91-94

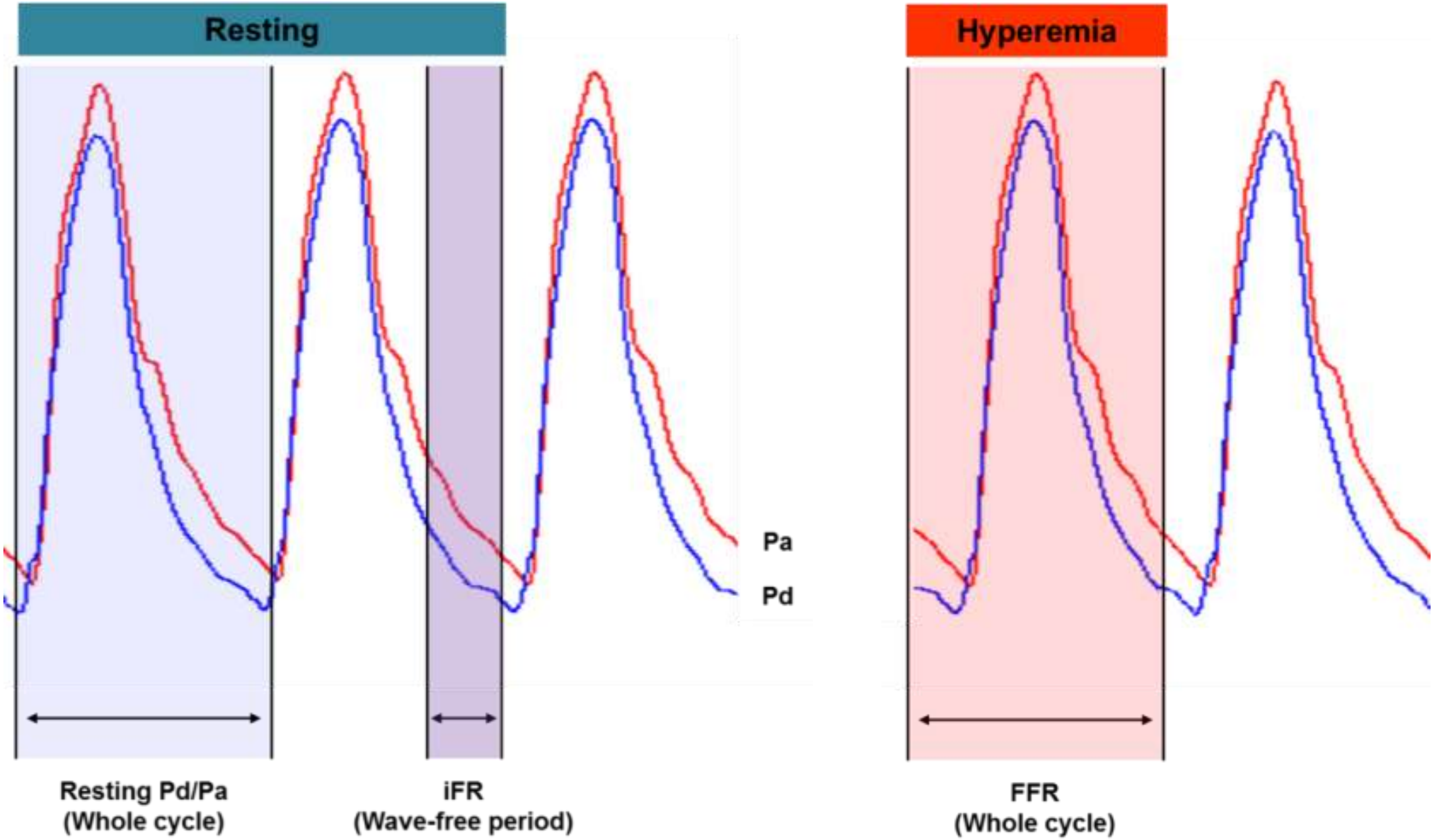
Clinical outcomes according to FFR/iFR classification



Group	HR (95% CI)	P value
Concordant Normal	1.00 (Reference)	NA
High FFR – Low iFR	2.42 (0.31-19.00)	0.399
Low FFR – High iFR	1.79 (0.23-14.00)	0.579
Concordant Abnormal	7.71 (2.62-22.67)	<0.001

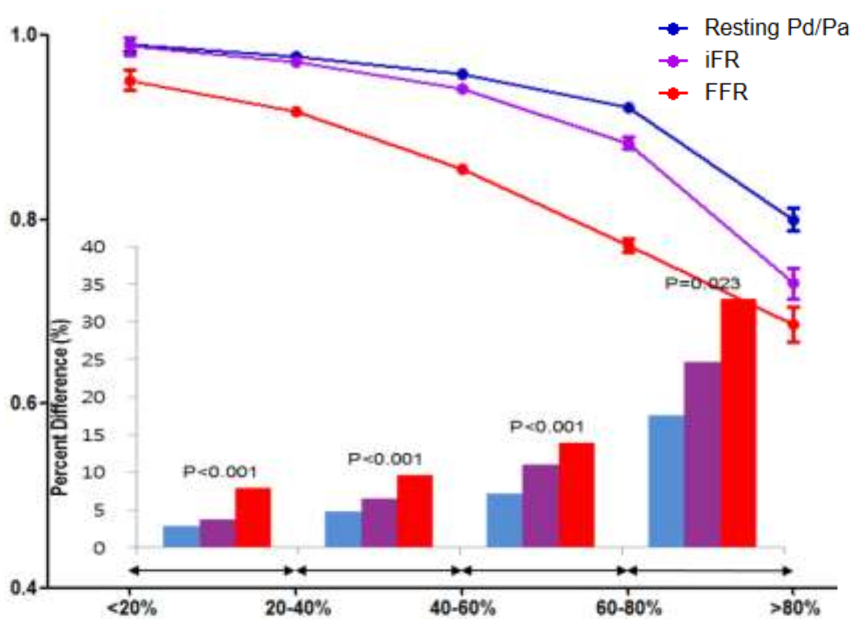
Lee JM, Koo BK, et al. JACC: Cardiovasc Interv 2018

Similarity and Difference between Resting and Hyperemic indexes

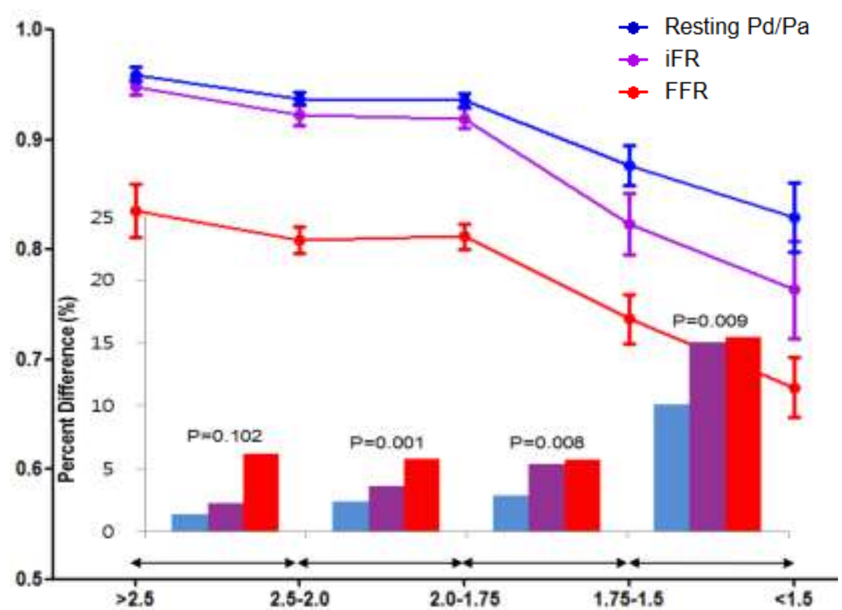


Similarity and Difference between Resting and Hyperemic indexes

Stenosis severity vs. Pressure indexes



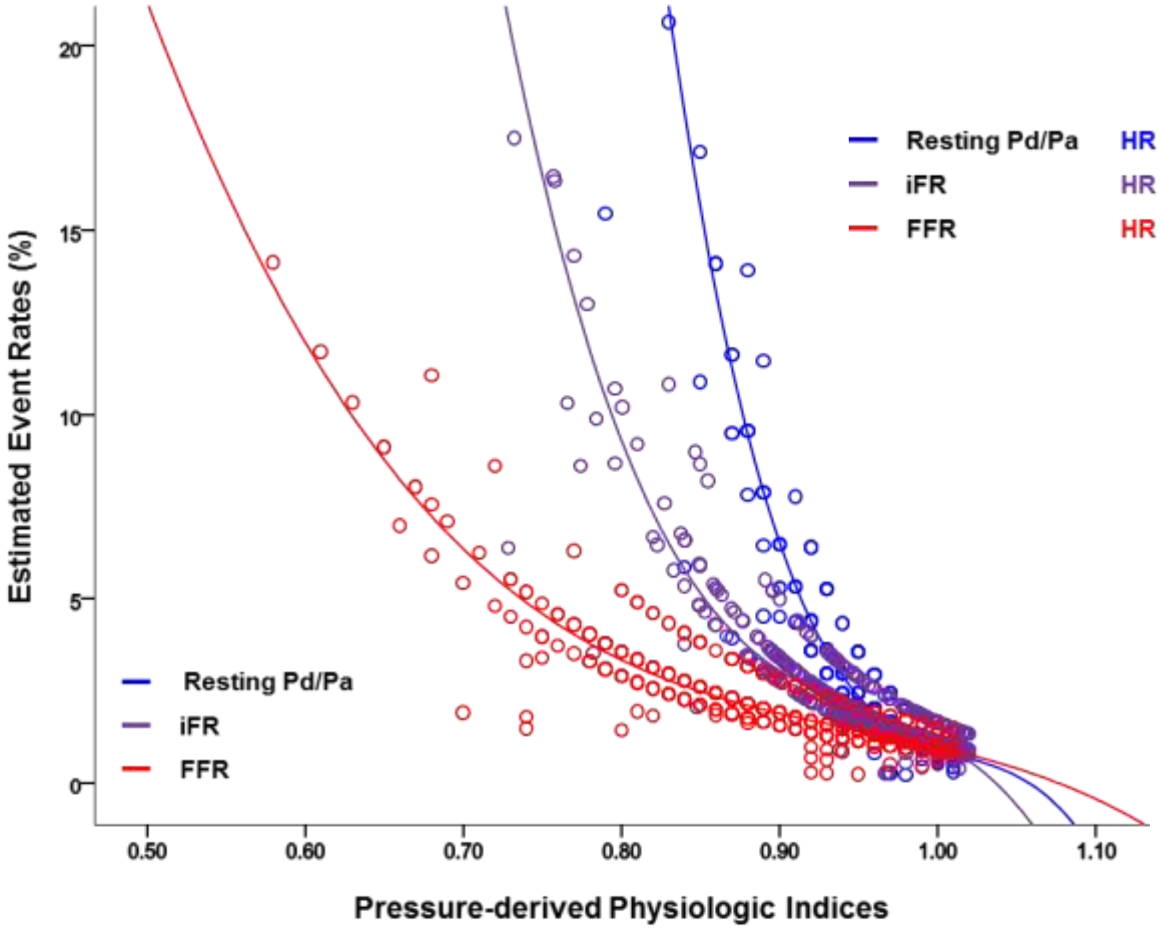
Angiographic % diameter stenosis



Hyperemic Stenosis Resistance

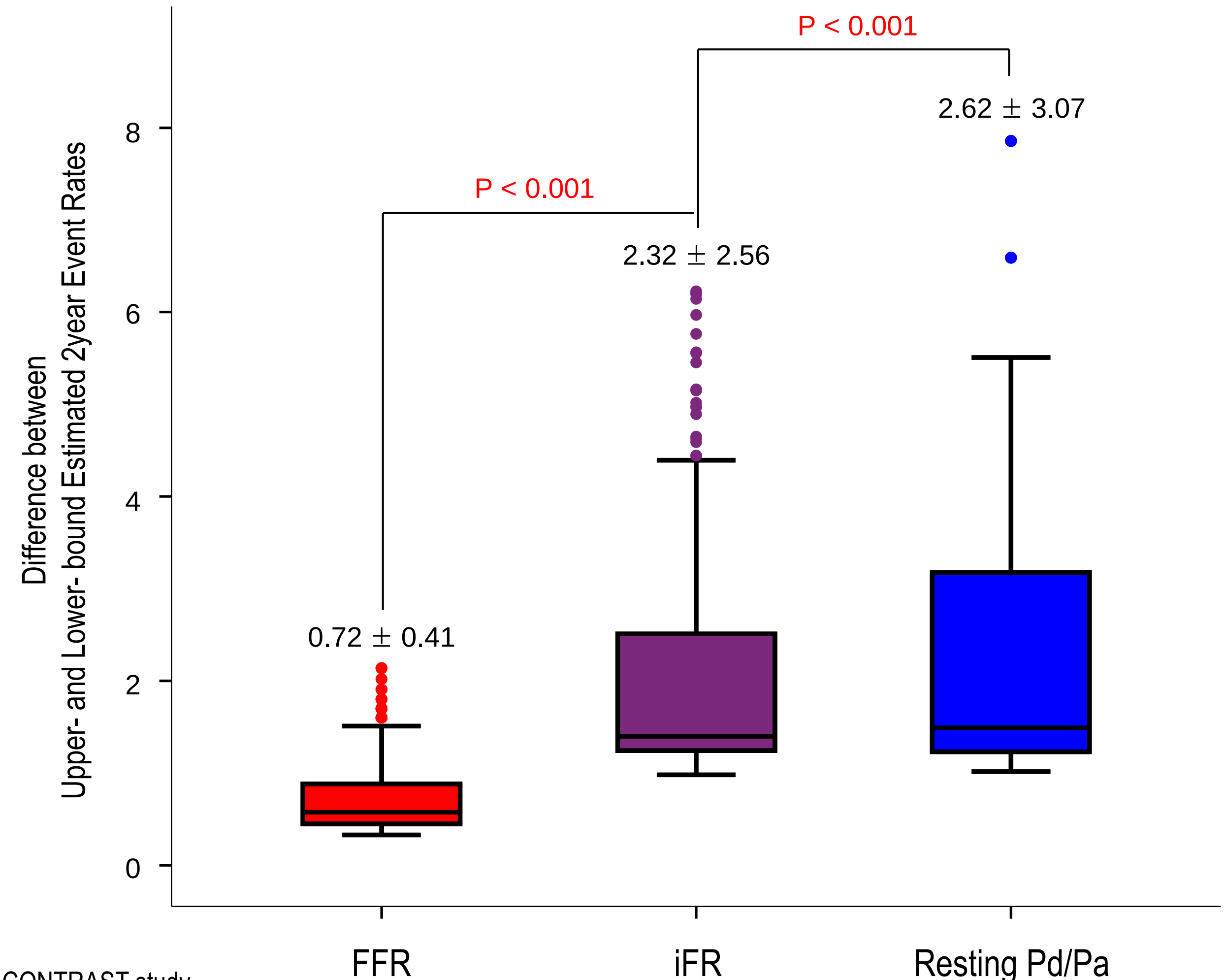
Lee JM, ……, Koo BK, J Am Coll Cardiol 2017

Association with Clinical outcomes



Lee JM, Koo BK, et al. Circulation 2017
Lee JM, Koo BK, et al. JACC 2017

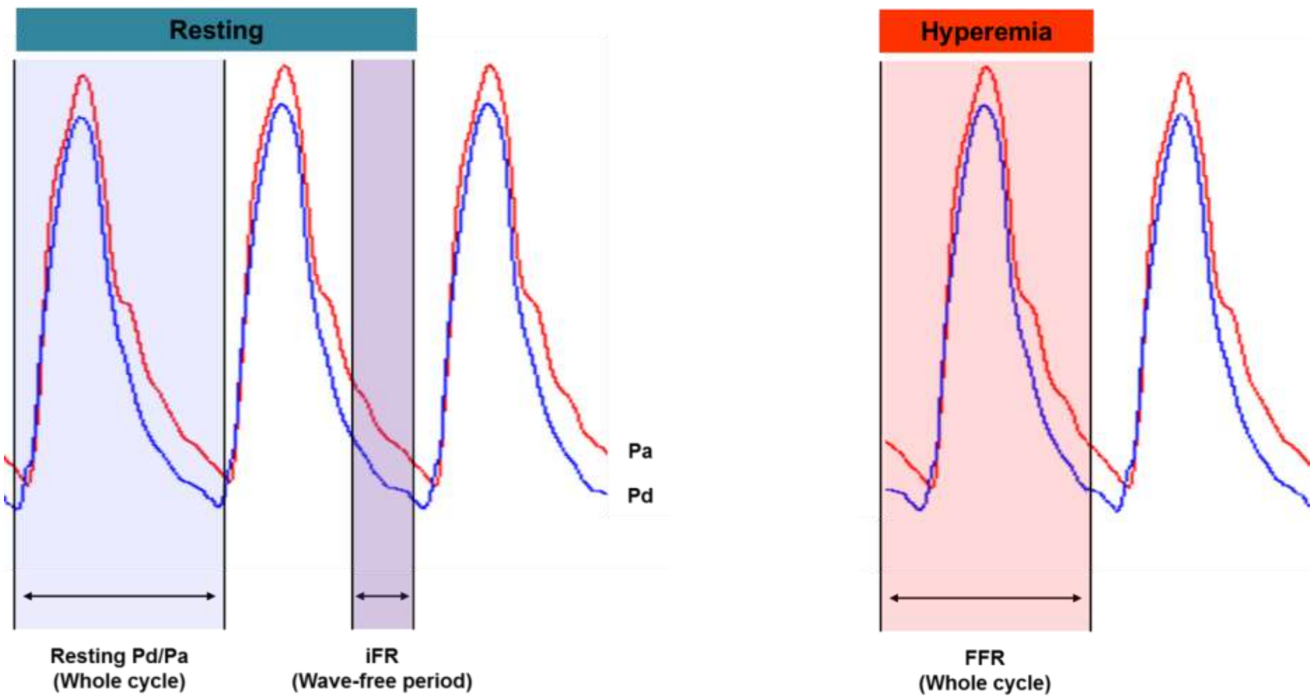
Estimated event rates according to measurement variability



* Measurement variability from CONTRAST study

Lee JM, Koo BK, et al. Circulation 2017
Lee JM, Koo BK, et al. JACC 2017

Similarity and Difference between Resting and Hyperemic indexes



Response to anatomical or hemodynamic stenosis severity	Resting Pd/Pa	<	iFR	<	FFR
Diagnostic accuracy for ISCHEMIA, Vulnerability Association with MACE	Resting Pd/Pa	=?	iFR	=?	FFR
Vulnerability to measurement variability	Resting Pd/Pa	>	iFR	>	FFR

Summary

- Resting pressure index represents the degree of exhausted flow reserve and hyperemic index, reduced hyperemic flow due to stenosis.
- Both resting and hyperemic indexes have prognostic implications.
- Discordance between resting and hyperemic indexes itself has clinical relevance.
- Hyperemic index is more sensitive to stenosis severity and resting index, to measurement variability.
- Integrated use will maximize the benefit of invasive physiologic assessment.