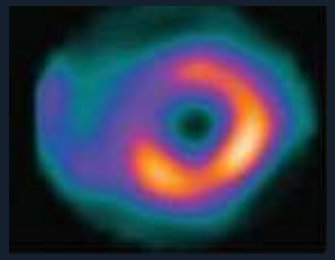
Synergetic Approach for Discordant Lesions Between FFR and Hyperemia Free Index

Jung-Min Ahn, MD

Heart Institute, University of Ulsan College of Medicine
Asan Medical Center, Seoul, Korea

How To Detect Objective Ischemia

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



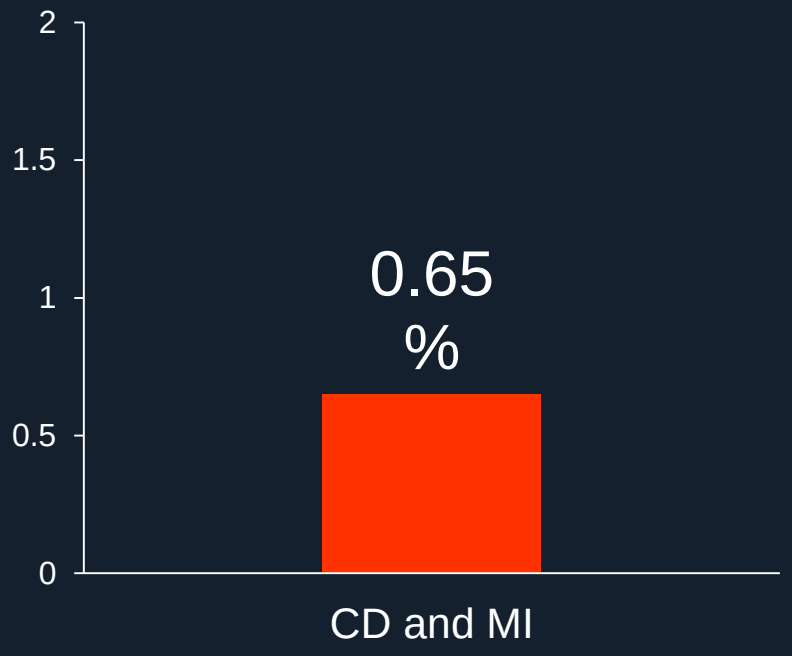
Myocardial Perfusion Abnormality

Contractile Abnormality

Electrical Abnormality

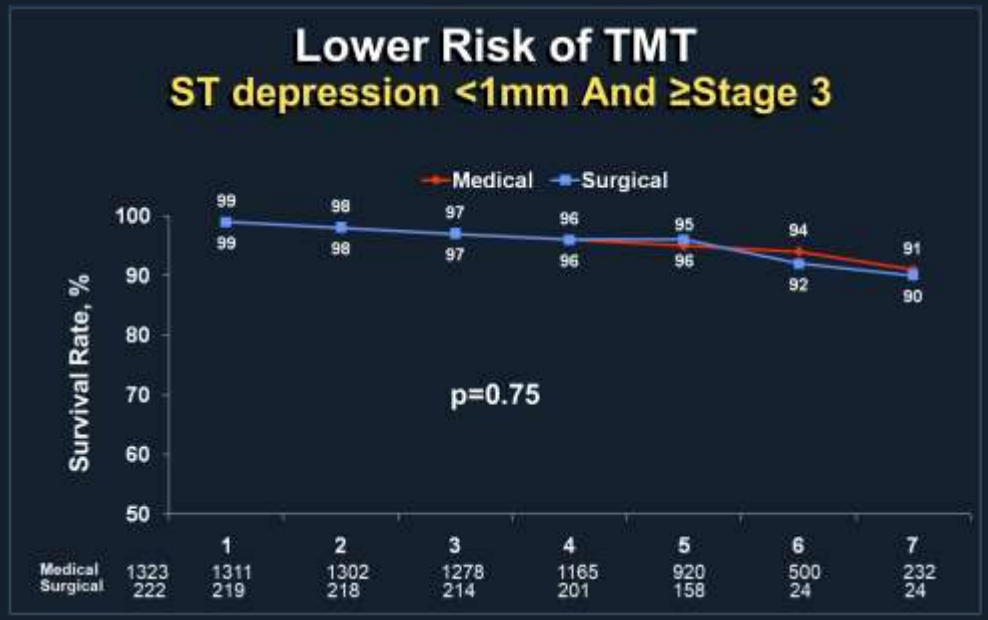
Negative Test, Excellent Prognosis

Negative Exercise Myocardial Perfusion



Journal of Nuclear Cardiology, 11(5), 551-561

Survival Benefit of CABG Over Med.



DONALD AW et al. J Am Coll Cardiol 1986;8:741-8

Non-Invasive Functional Study

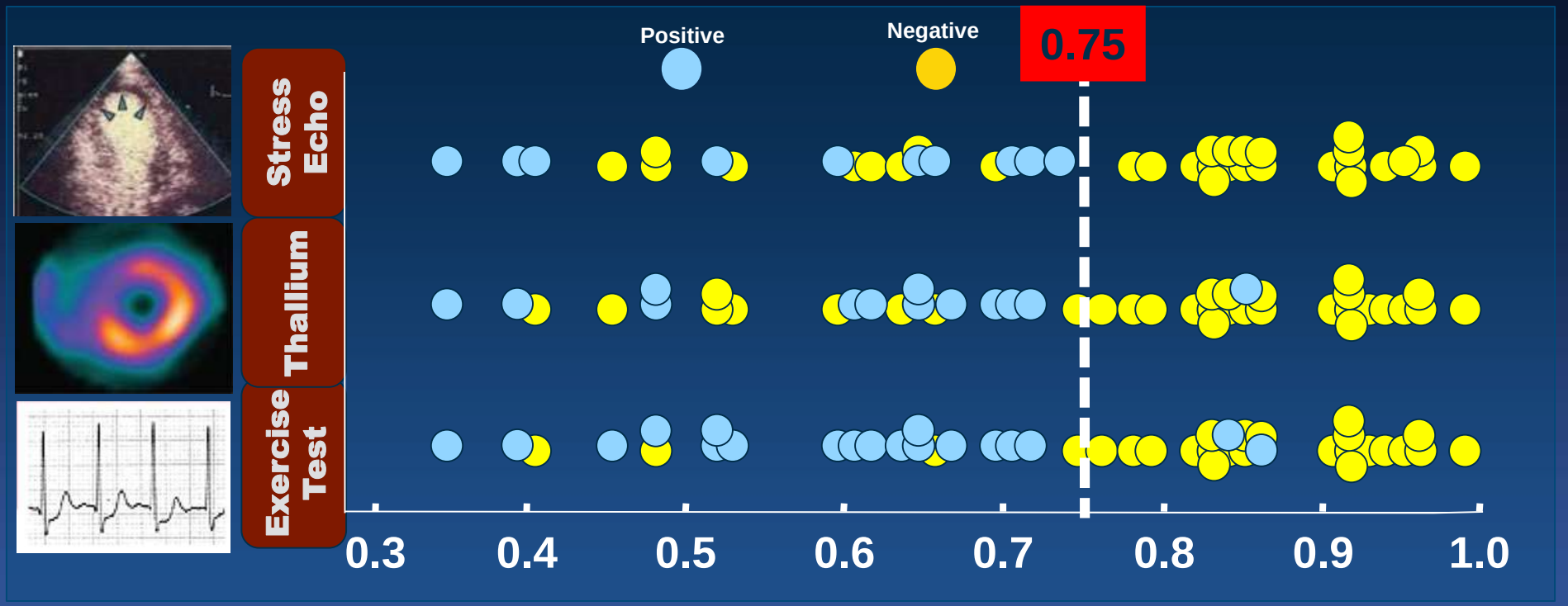
Limitations

- Low frequency of performing stress test
- False negative or positive results
- Low spatial resolution
- Limited in the multivessel assessment
- Limited in the non-culprit lesion assessment in ACS
- Further resources and experts are necessary

N Engl J Med 1996;334:1703-8

Non-Invasive Study In Cath Lab

Comparison with 3 non-invasive functional studies



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

FFR Guided PCI (FAME I)

≤ 0.80 (*FAME II*)

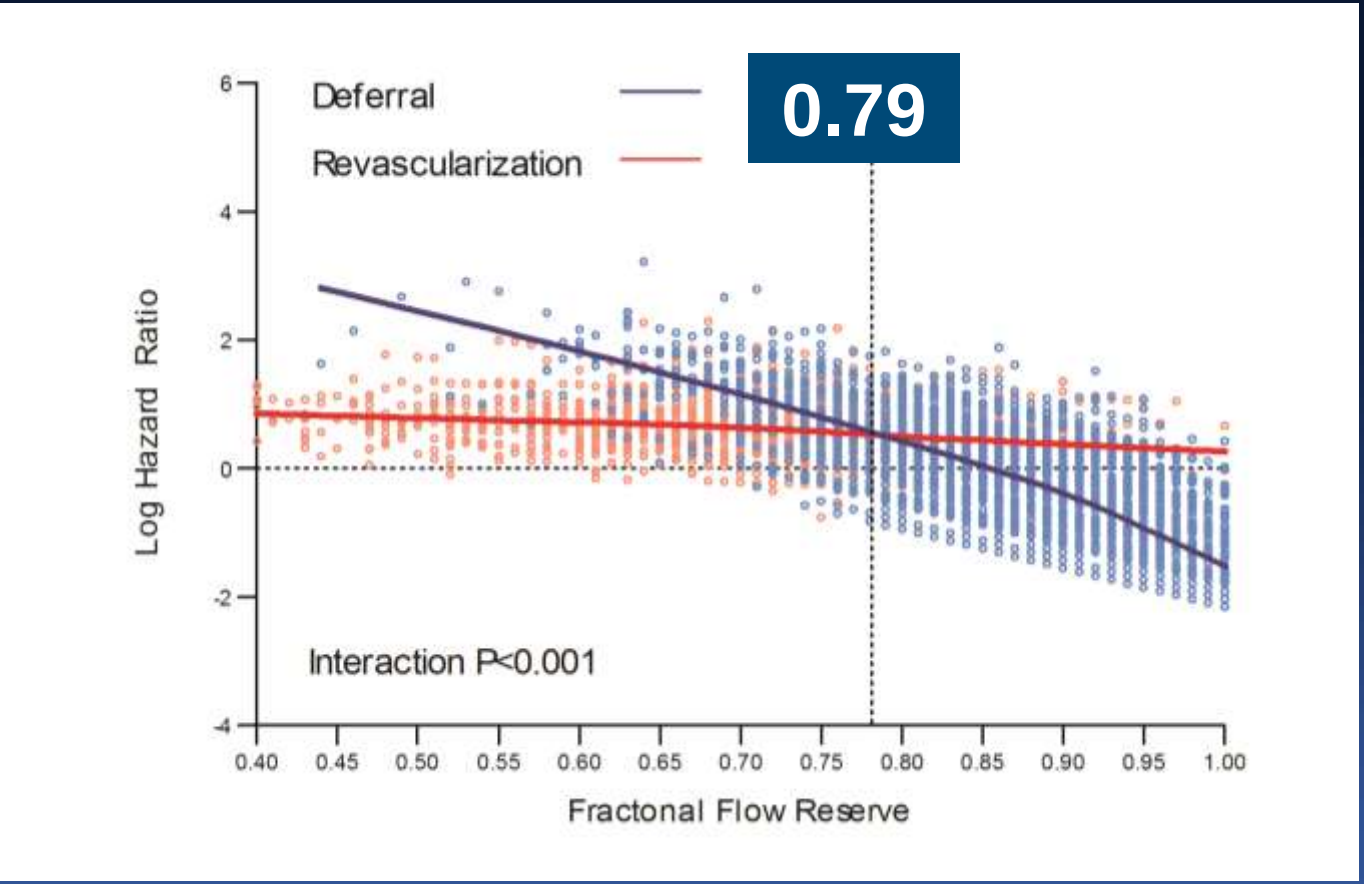
- ✓Myocardial Ischemia producing
- ✓Stenting

>0.80 (*DEFER, >0.75*)

- ✓Not Myocardial Ischemia producing
- ✓Optimal Medical Treatment
- ✓Deferral of Stenting

Lokien X van Nuen et al. LANCET 7–13 November 2015, Pages 1853–1860
De Bruyne, et al. New Engl J Med 2014;371:1208-17.

Outcome Derived Revascularization Threshold



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

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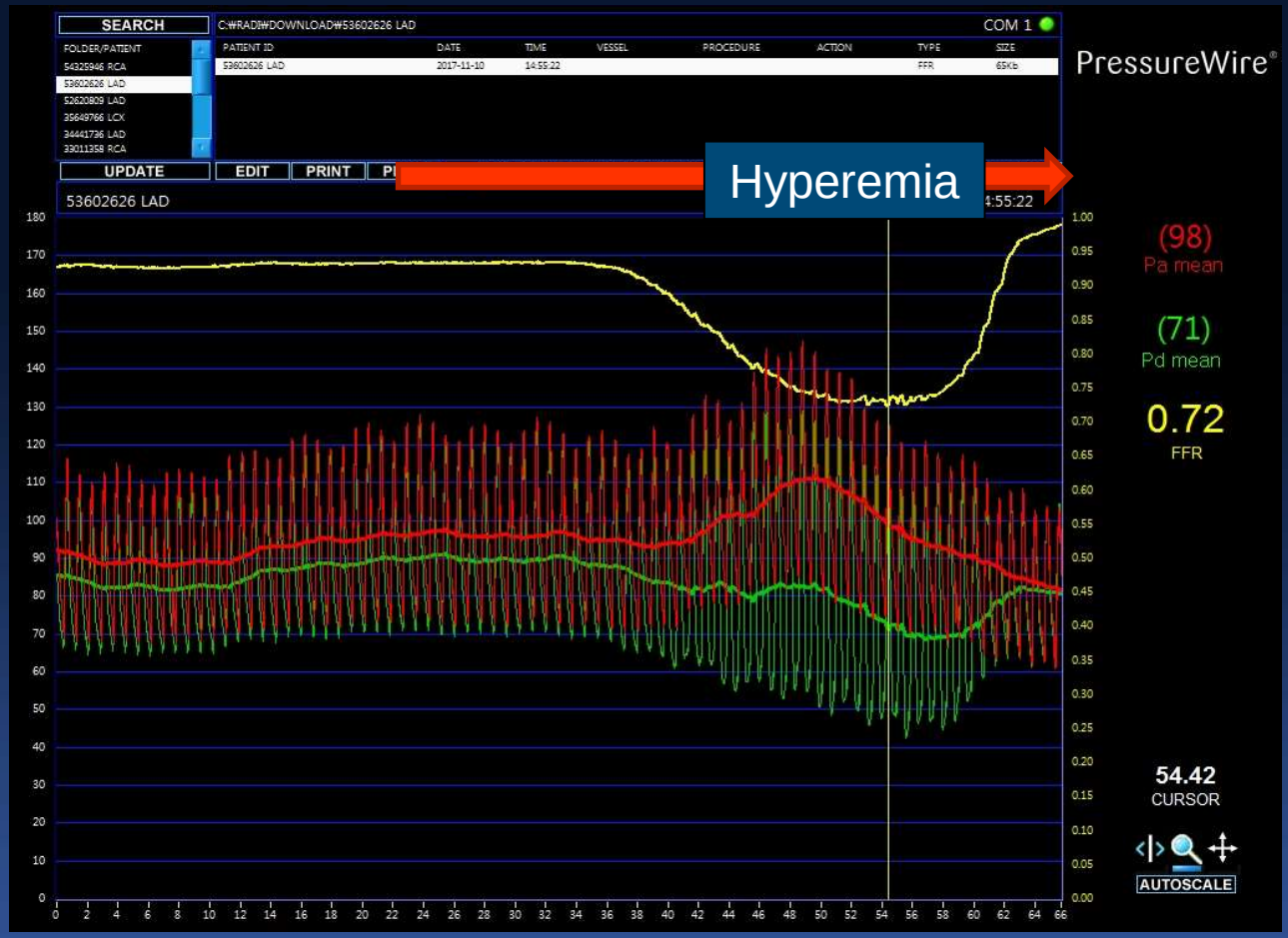
Adenosine, Hyperemia



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

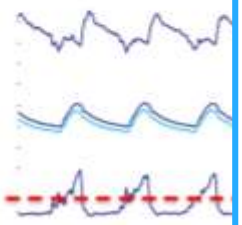
Since TCT 2011,

iFR, Instantaneous wave-free ratio

Hypothesis 1

Resistance mea
free period is si
hyperaemia.

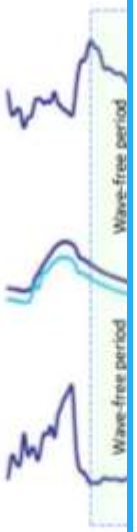
Hyperaemic mean re



ADVISE study

Hypothesis 2

The Pd/Pa ratio
period was simi

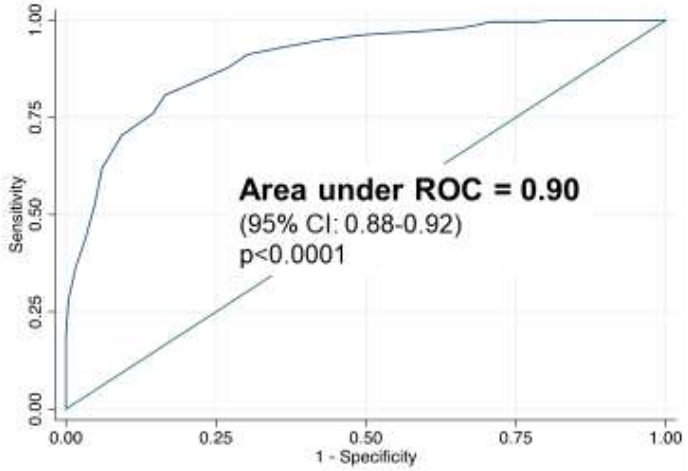


ADVISE study

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

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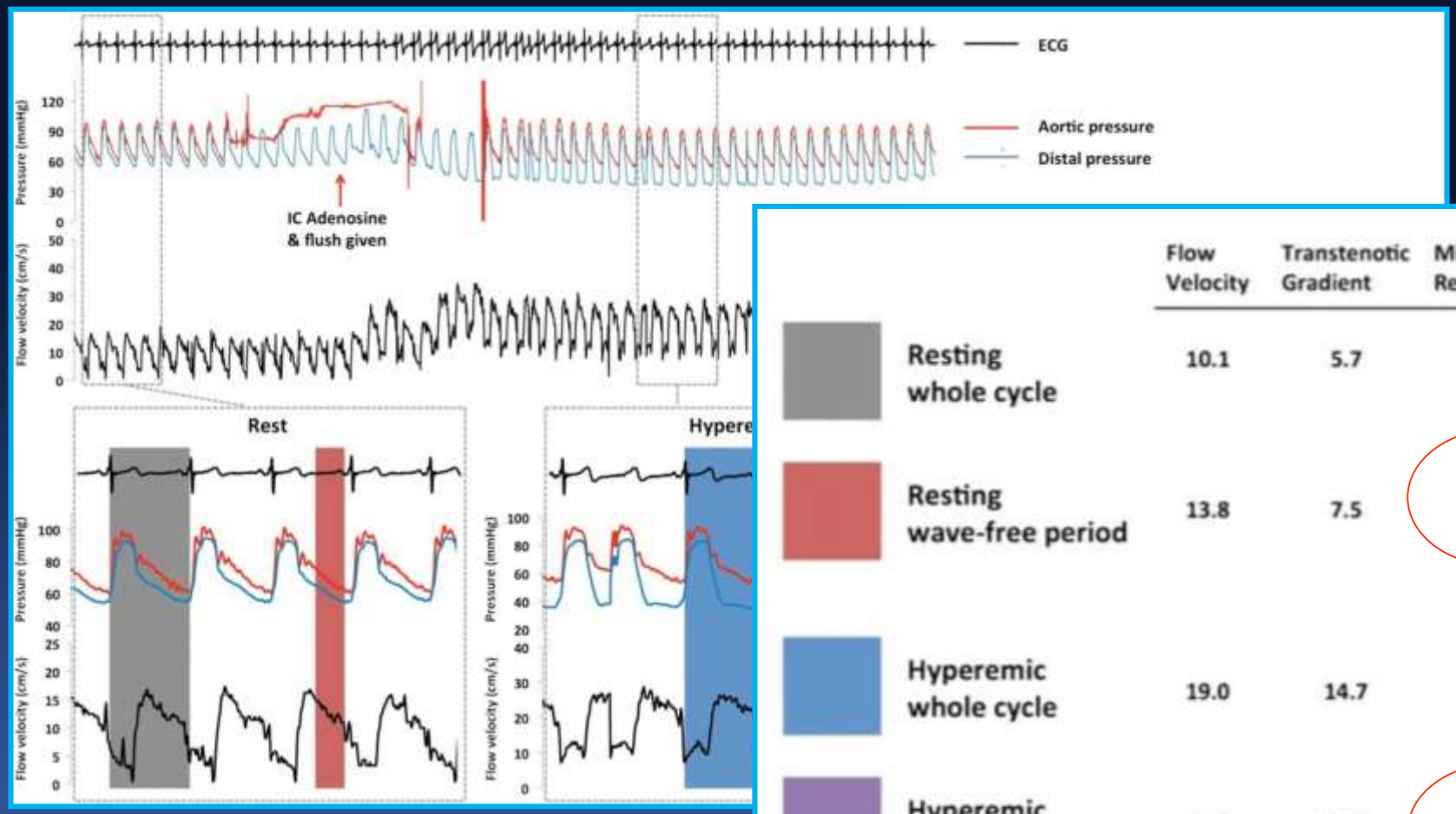
Minimal Resistance in wFP ?

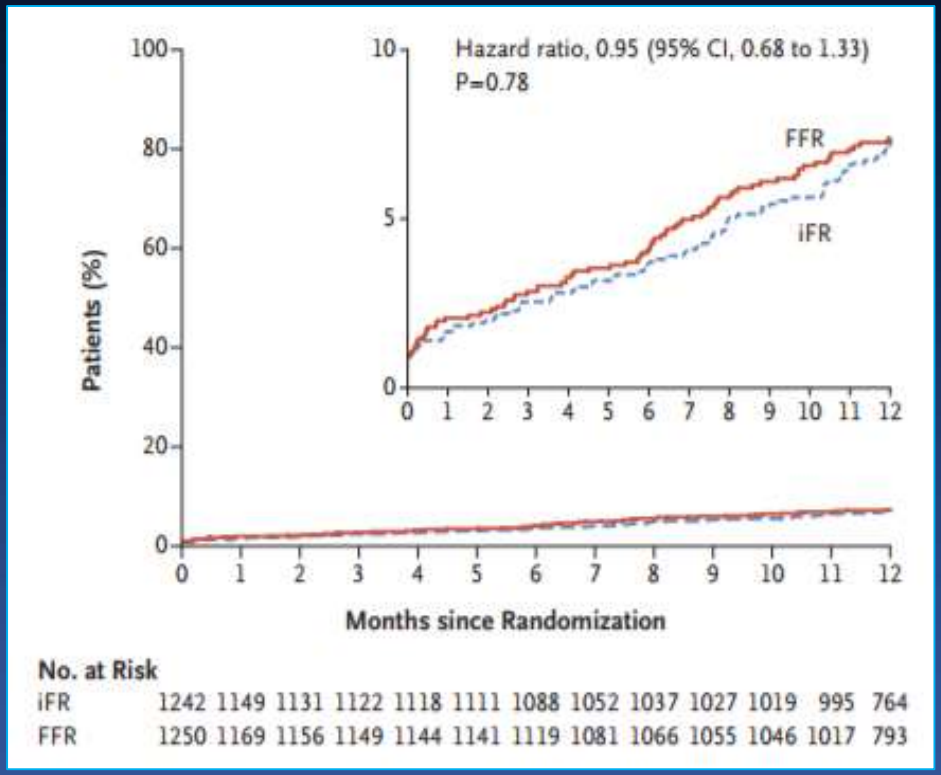


	Flow Velocity	Transtenotic Gradient	Microvascular Resistance
Resting whole cycle	10.1	5.7	7.0
Resting wave-free period	13.8	7.5	4.5
Hyperemic whole cycle	19.0	14.7	
Hyperemic wave-free period	24.9	20.9	1.6

Eur Heart J 2016 Jul 7;37(26):2069-80

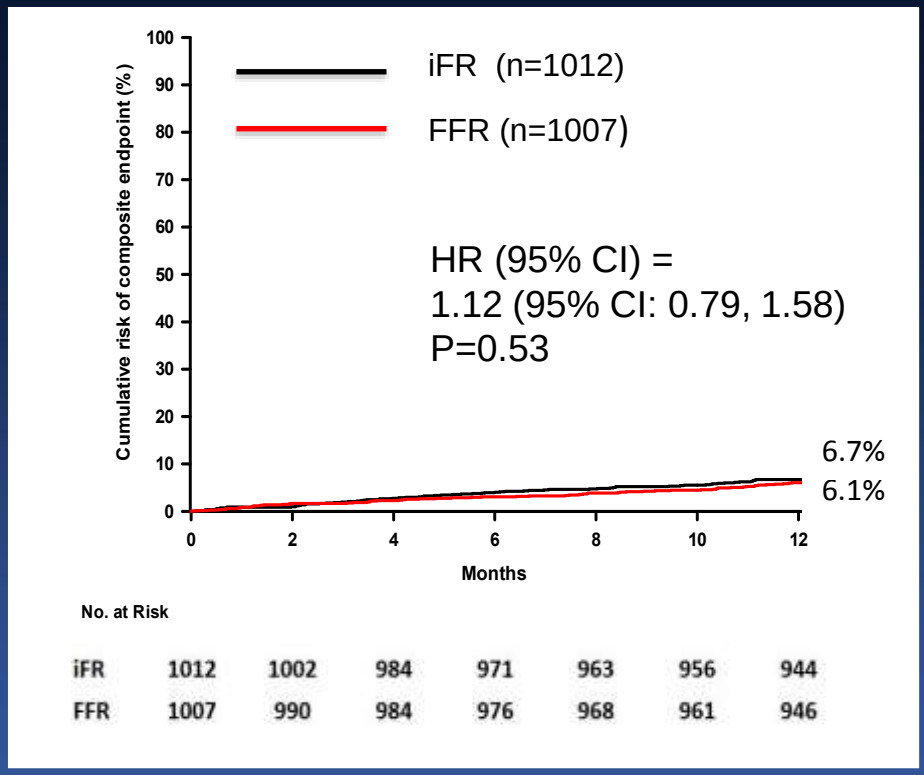
iFR is non-inferior to FFR

DEFINE-FLAIR



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

iFR-SWEDEHEART

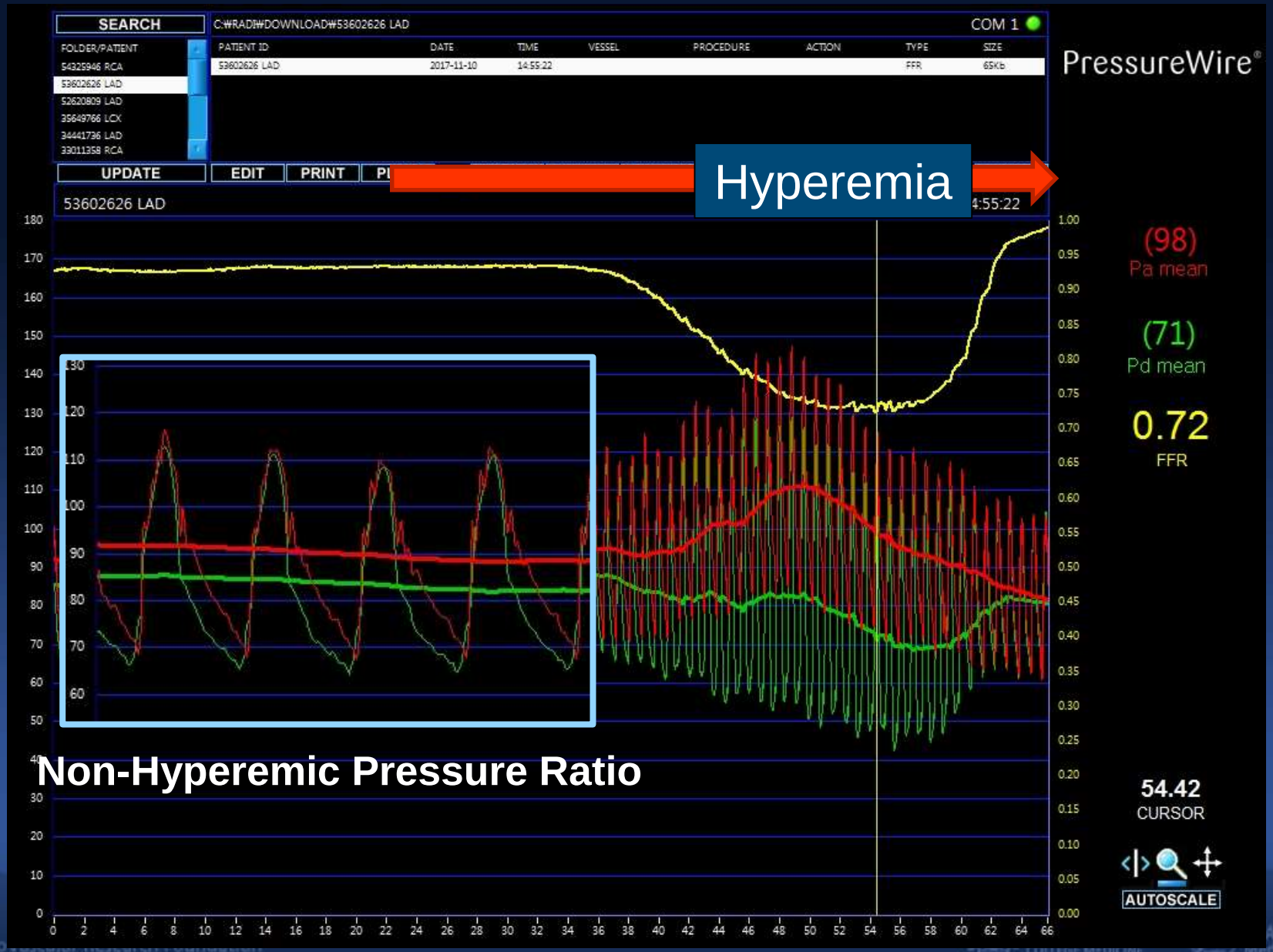


N Engl J Med. 2017 May 11;376(19):1813-1823

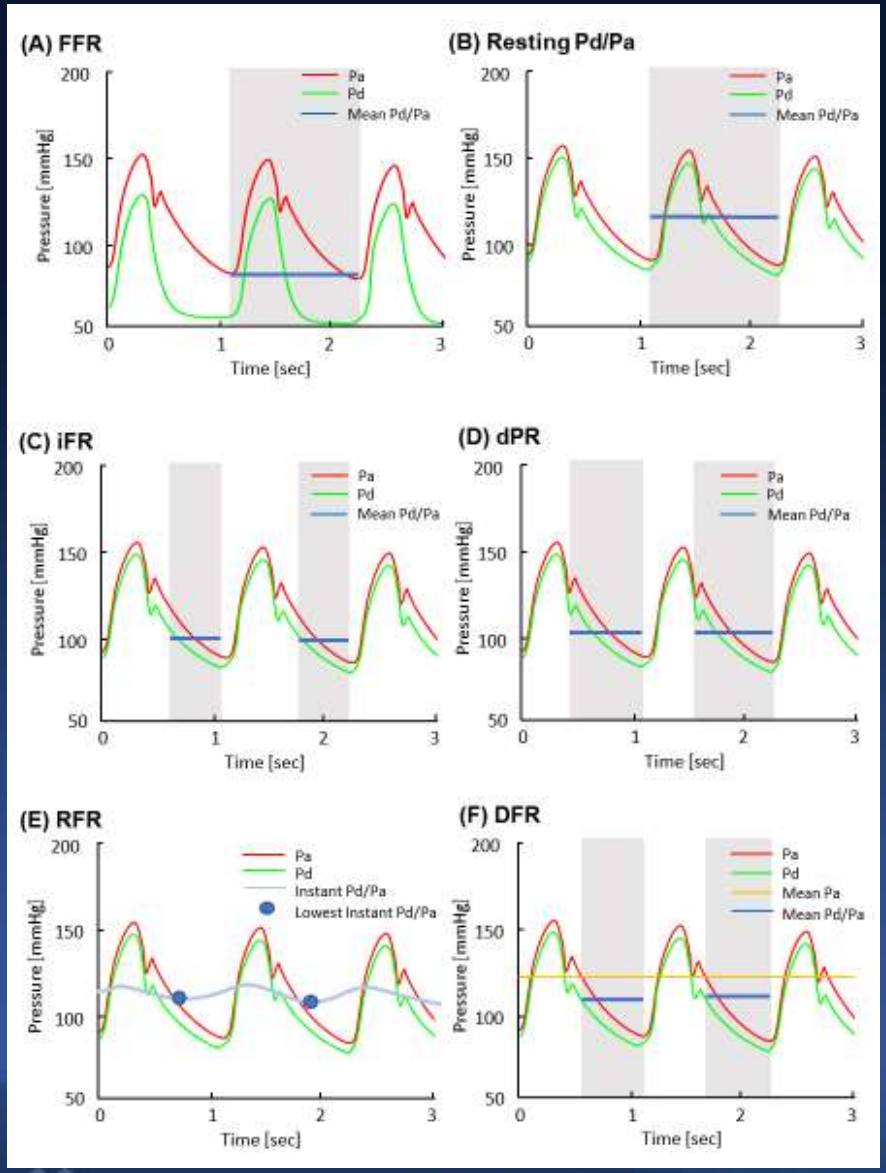
ESC Guideline 2018

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

Non-Hyperemic Pressure Ratio (NHPR)



Pressure Derived Physiologic Index, 2019

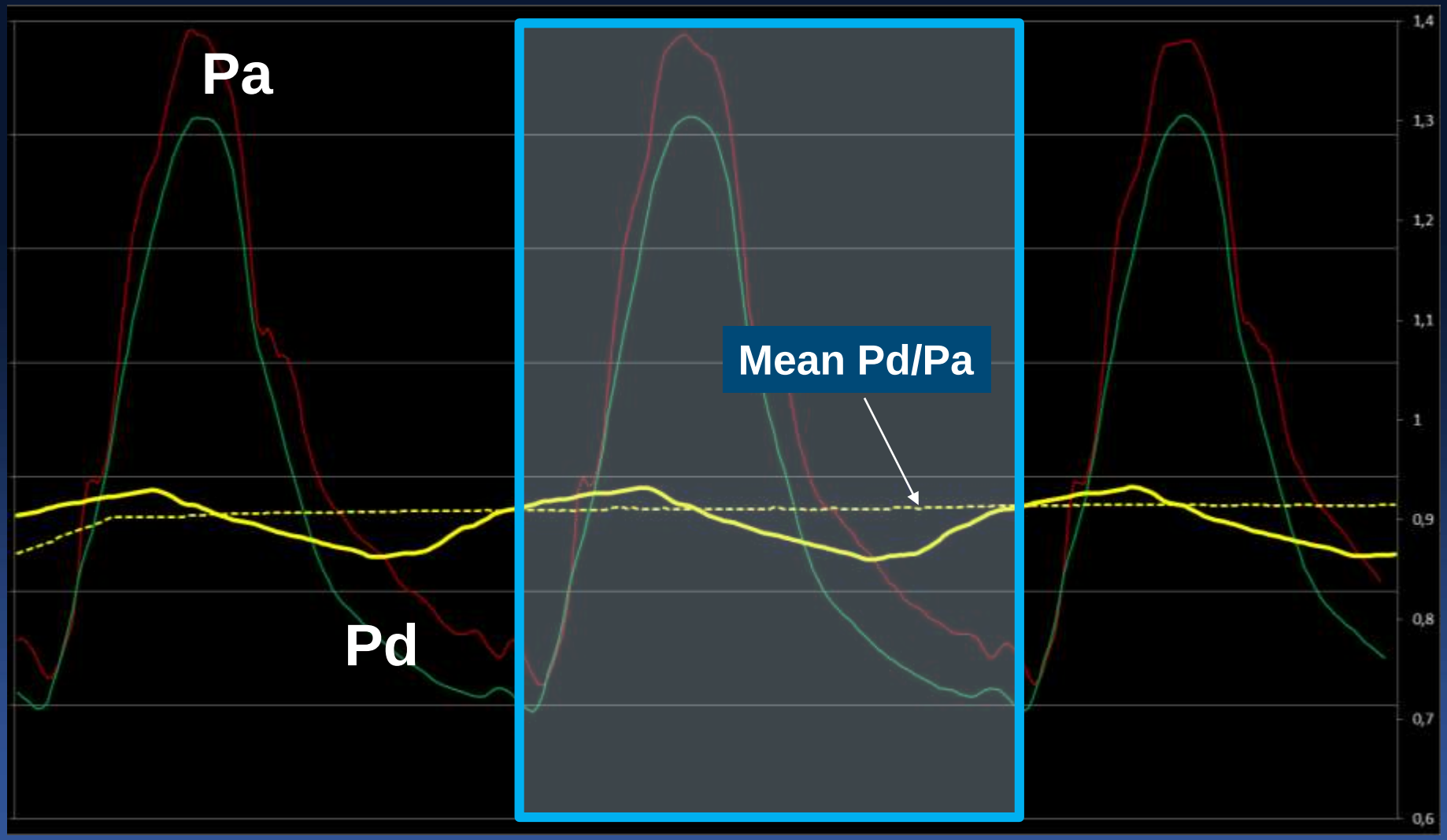


Hyperemic Index: FFR

Non-Hyperemic Pressure Ratio (NHPR)

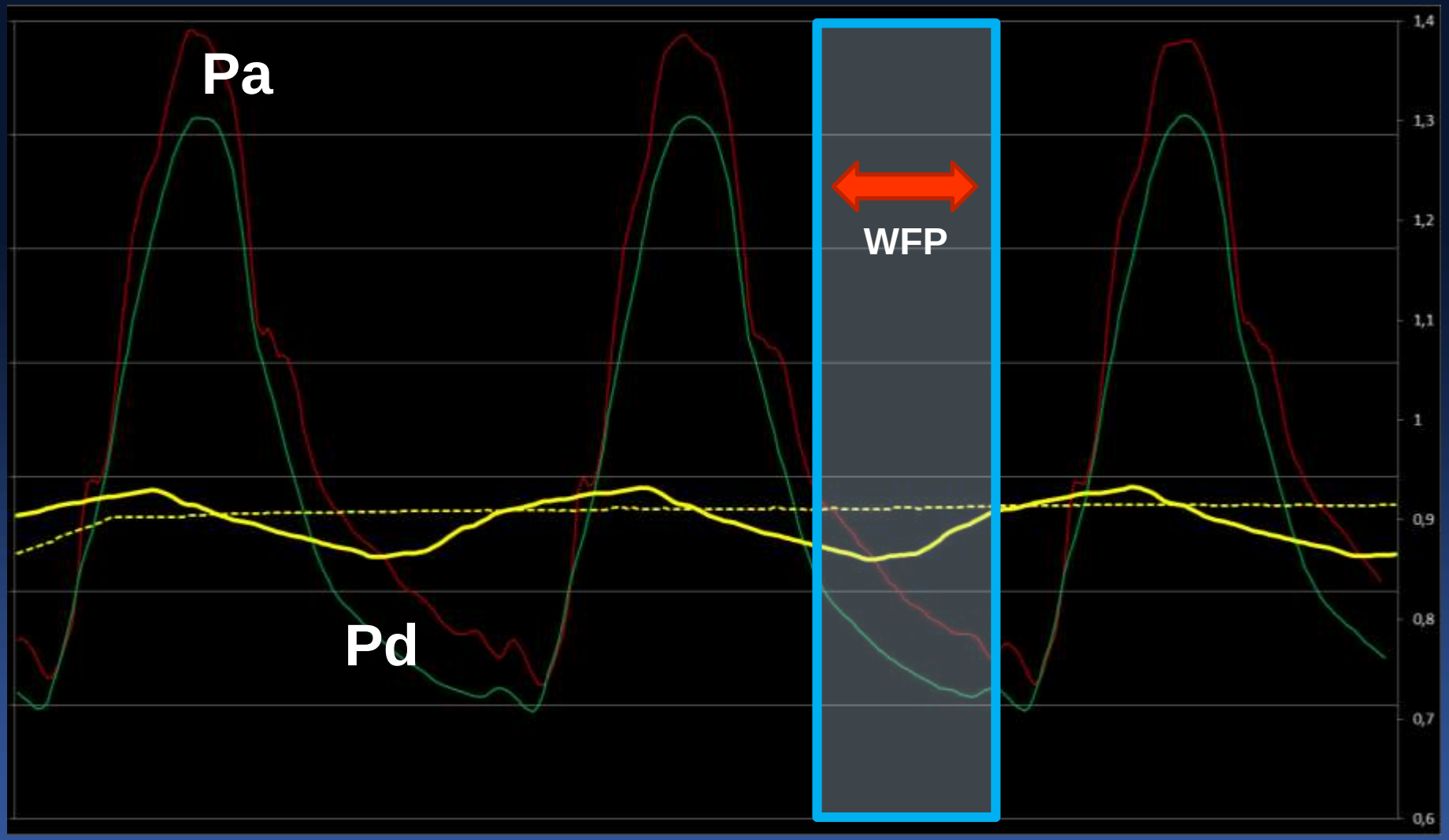
- Resting Pd/Pa: 0.91(or 0.92)
- iFR: 0.89
- dPR (Diastolic pressure ratio): 0.89
- RFR (Resting full-cycle ratio): 0.89
- DFR (Diastolic hyperemia-free index): 0.89

Resting Whole Cycle Pd/Pa



Average Pd/Pa during the entire cardiac cycle

iFR (instantaneous Wave-Free Ratio)

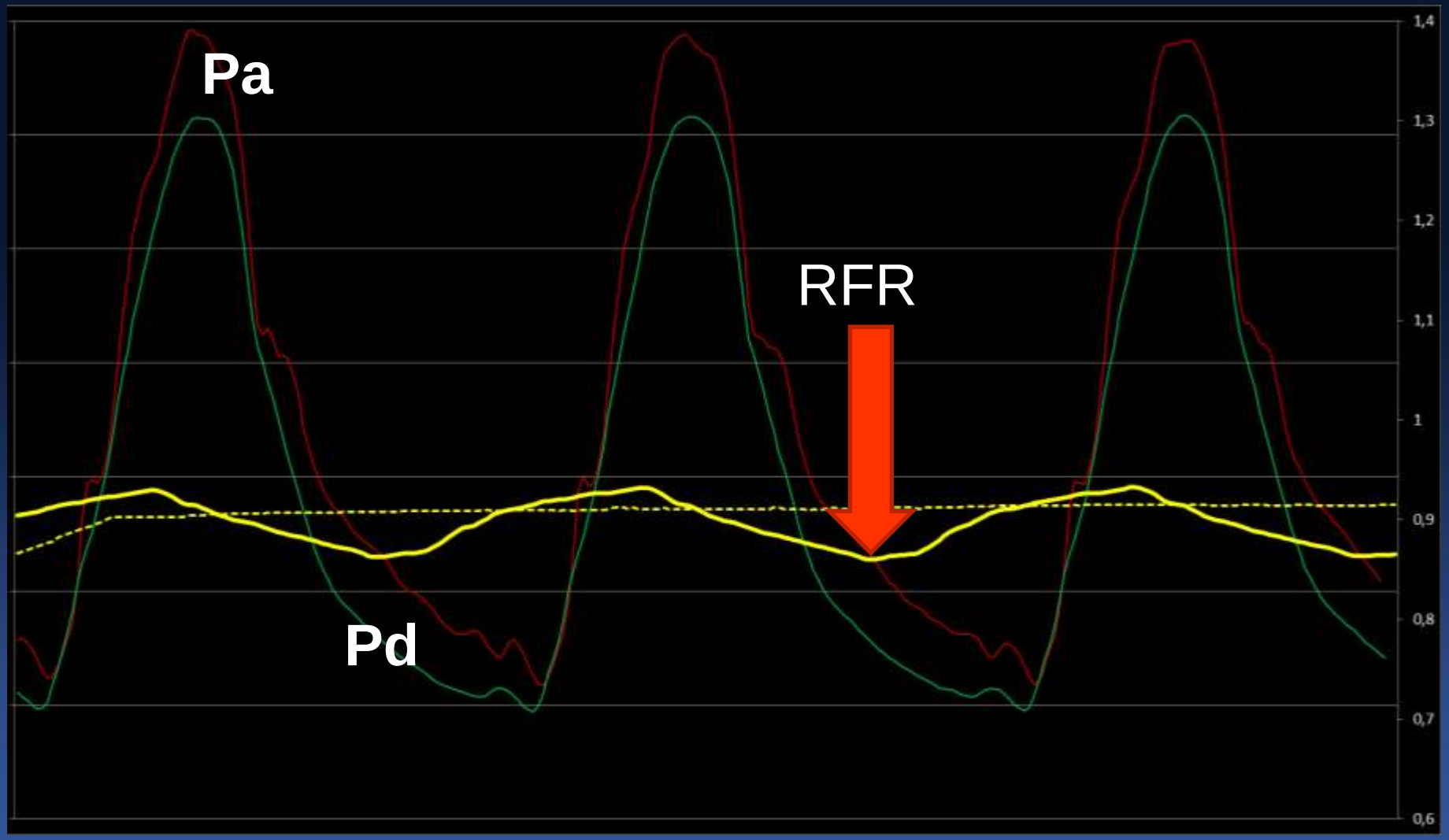


Average Pd/Pa during wave free period (WFP)

dPR_{dia} (Diastolic Pressure Ratio)

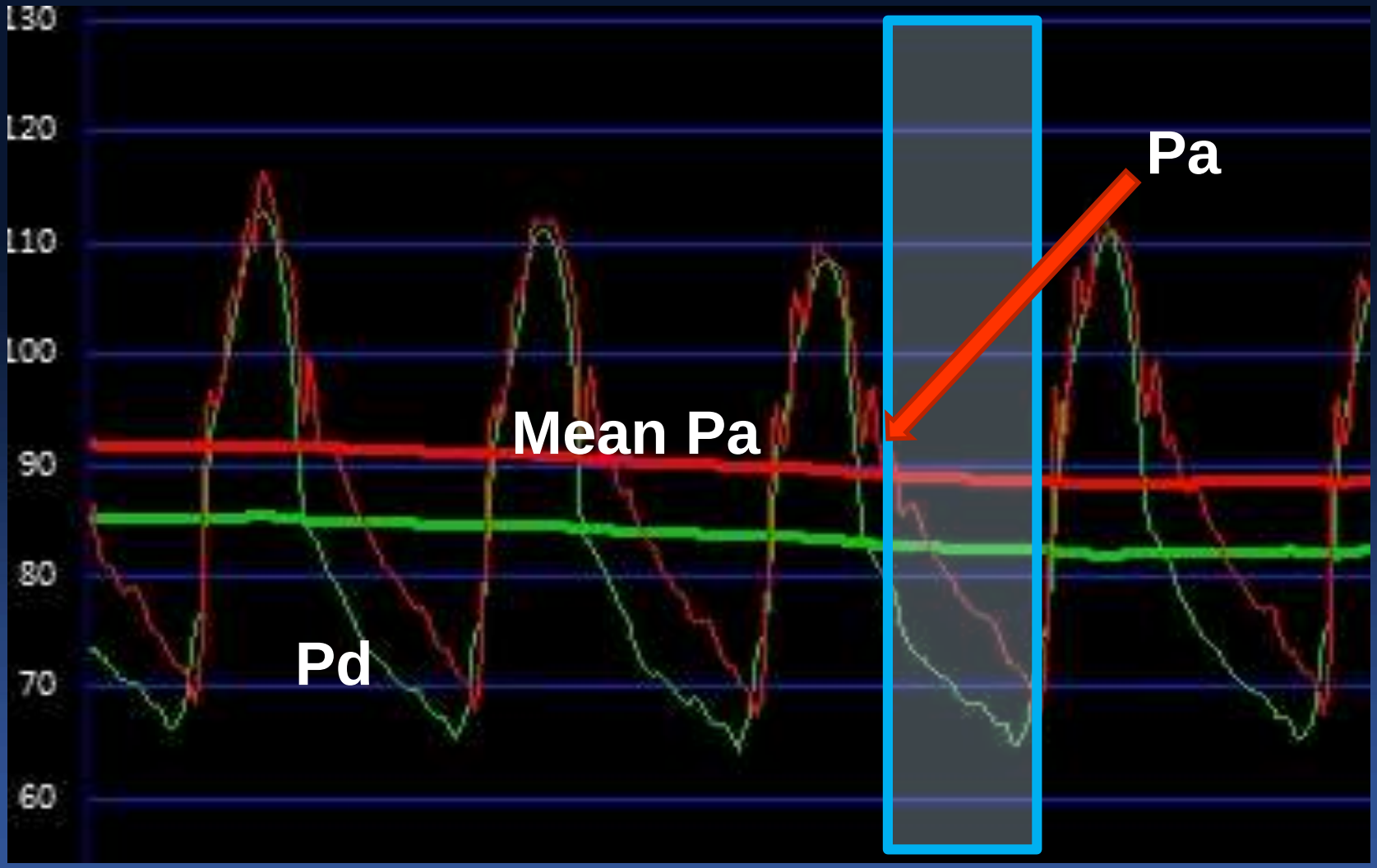
Average Pd/Pa during the entire diastole

RFR (Resting Full-cycle Ratio)



Lowest Instant Pd/Pa ratio during the entire cardiac cycle

DFR (Diastolic Hyperemia Free Ratio)



Average Pd/Pa during the period

Between Pa < mean Pa AND down-sloping Pa

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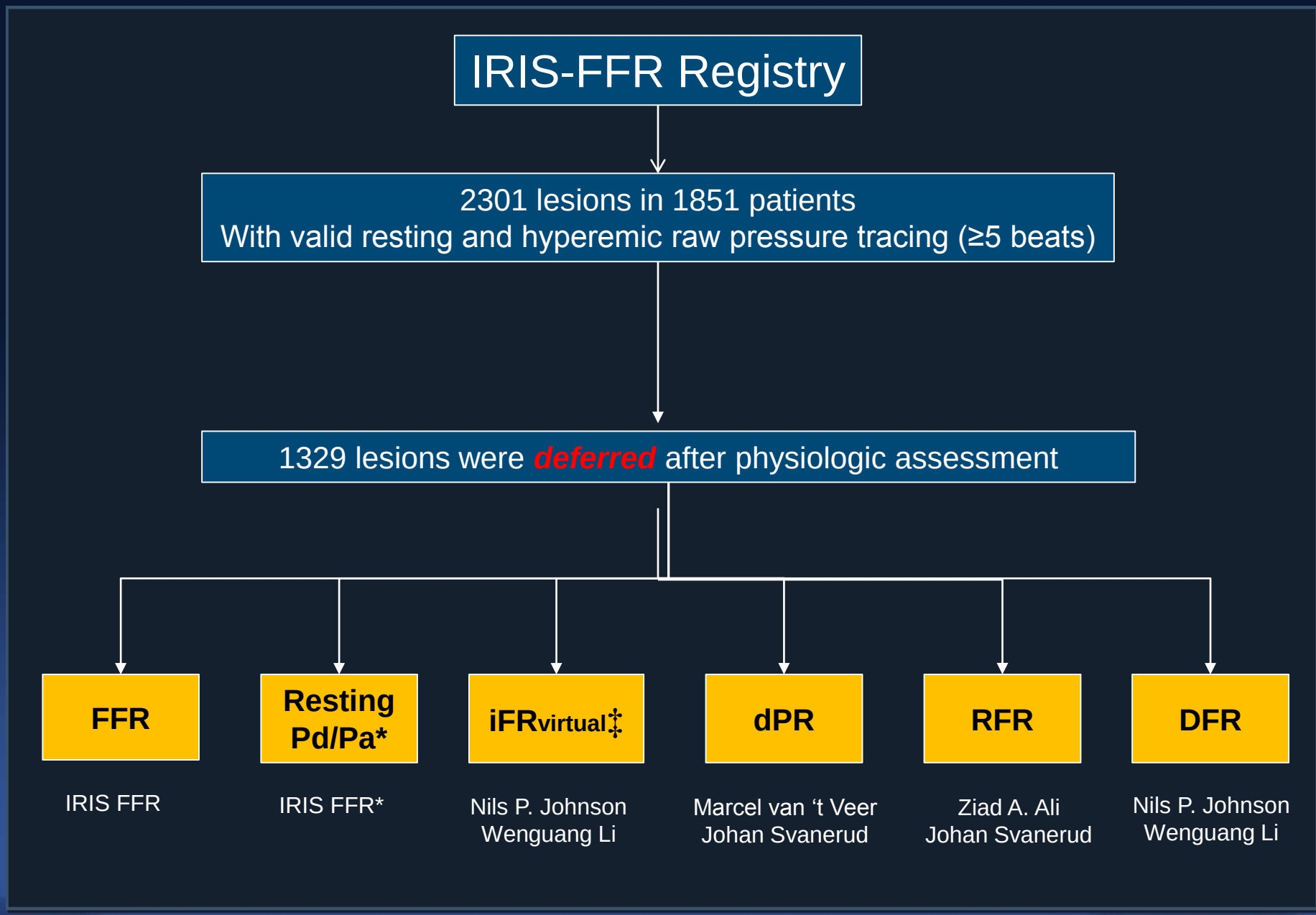
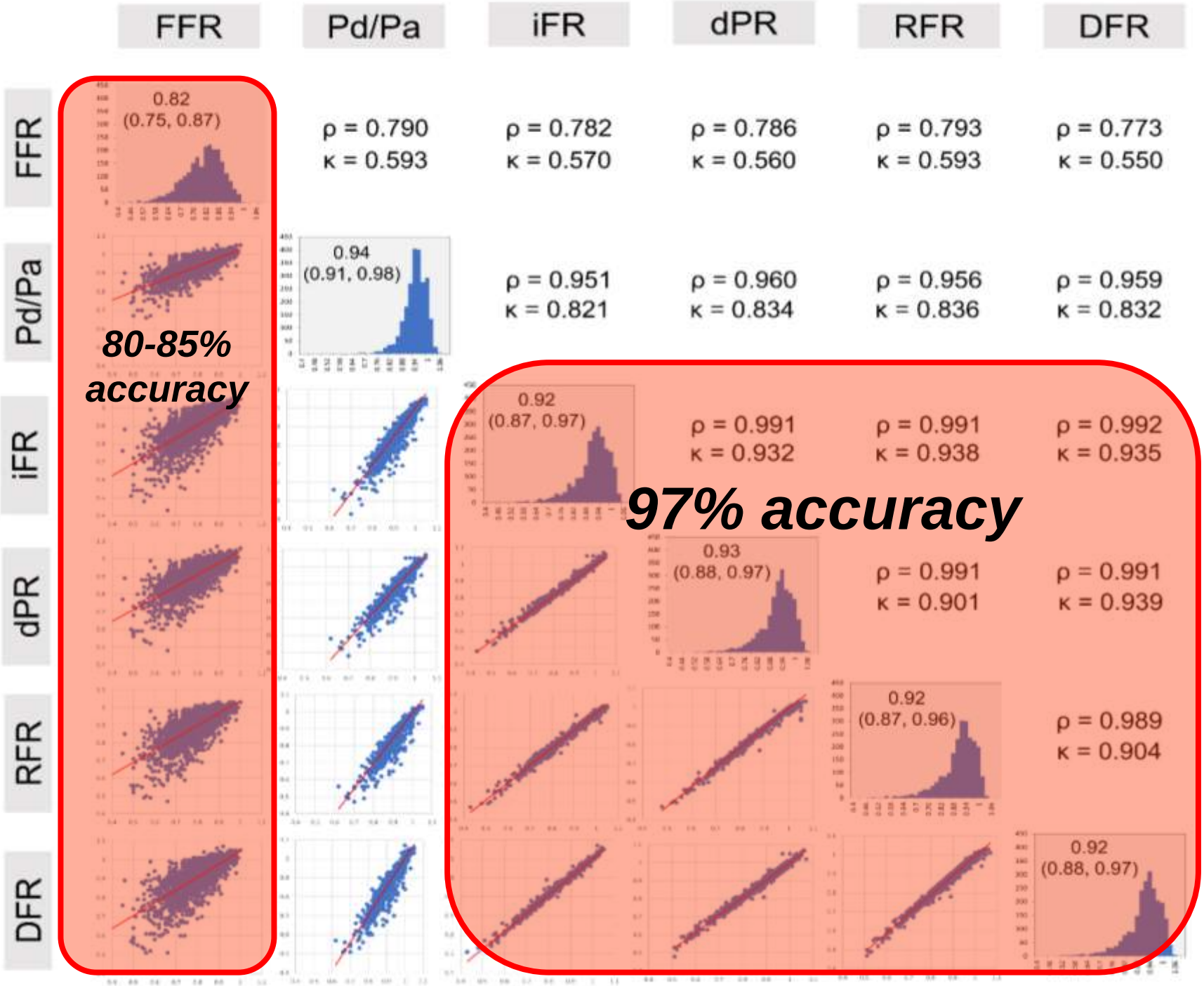
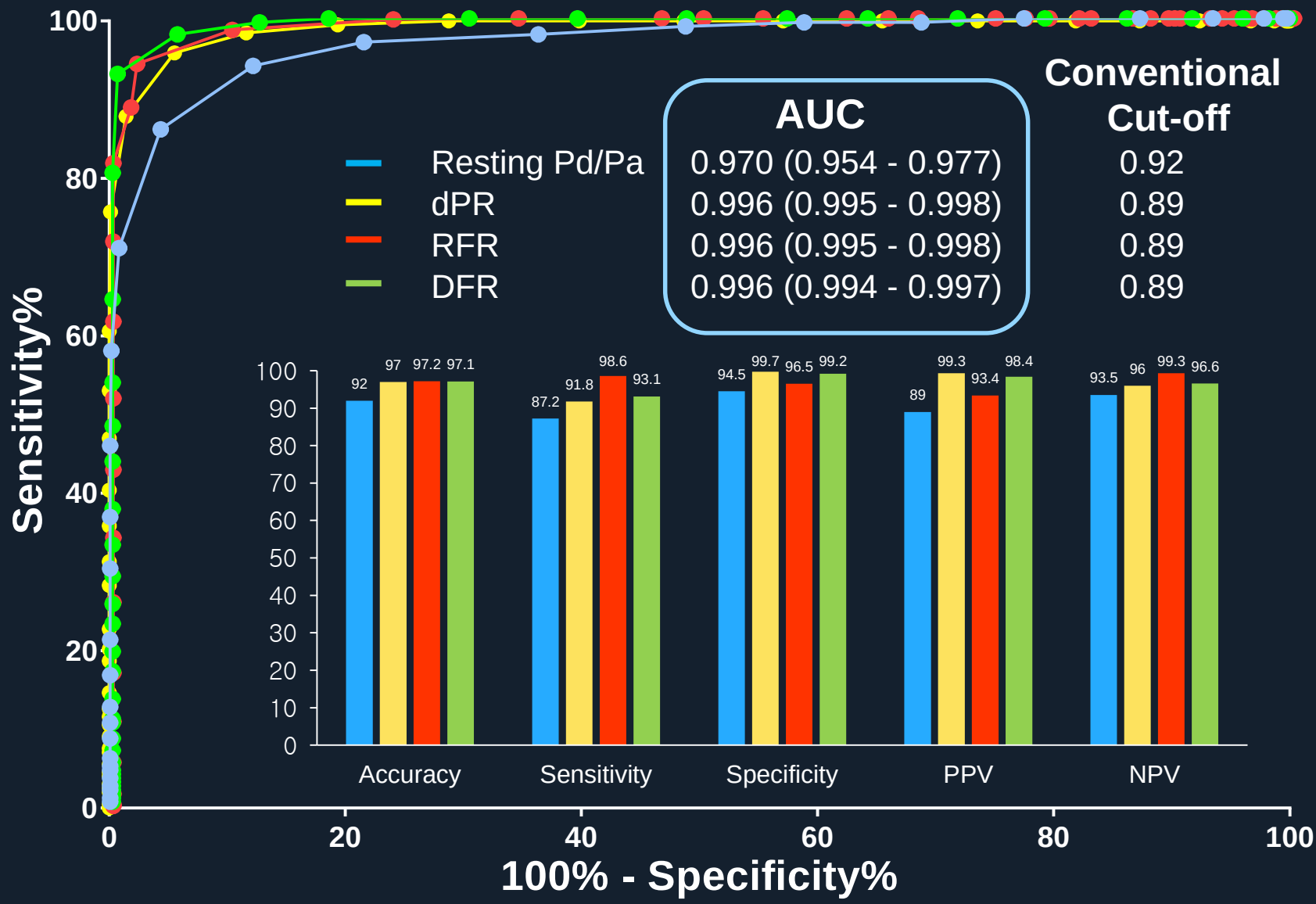


*All resting tracings were confirmed by Wenguang Li during virtual iFR and DFR calculation
‡calculated using the proprietary software (Volcano Corporation)


FFR
Pd/Pa
iFR
dPR
RFR
DFR
0.82
(0.75, 0.87)
ρ = 0.790
κ = 0.593
ρ = 0.782
κ = 0.570
ρ = 0.786
κ = 0.560
ρ = 0.793
κ = 0.593
ρ = 0.773
κ = 0.550
0.94
(0.91, 0.98)
ρ = 0.951
κ = 0.821
ρ = 0.960
κ = 0.834
ρ = 0.956
κ = 0.836
ρ = 0.959
κ = 0.832
80-85% accuracy
0.92
(0.87, 0.97)
ρ = 0.991
κ = 0.932
ρ = 0.991
κ = 0.938
ρ = 0.992
κ = 0.935
97% accuracy
0.93
(0.88, 0.97)
ρ = 0.991
κ = 0.901
ρ = 0.991
κ = 0.939
0.92
(0.87, 0.96)
ρ = 0.989
κ = 0.904
0.92
(0.88, 0.97)

Prediction of iFR 0.89



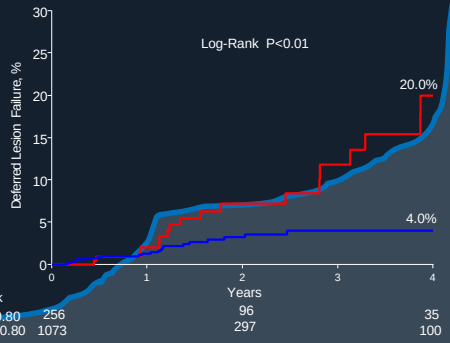
Deferred Lesion Failure

- During a median FU of 1.2 year
- Deferred Lesion Failure: 47 cases

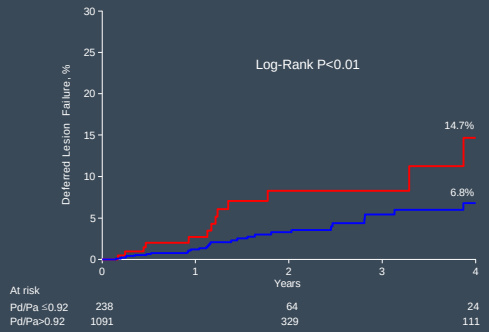
  Cardiac Death: 5 cases
  Myocardial Infarction: 3 cases
  Repeated Revascularization: 43 cases

Kaplan-Meier Curves

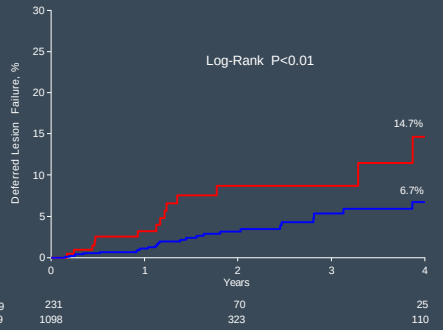
(A) FFR



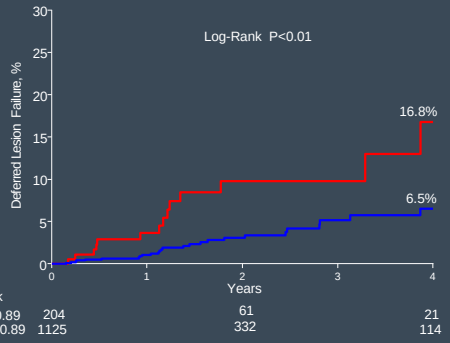
(B) Resting Pd/Pa



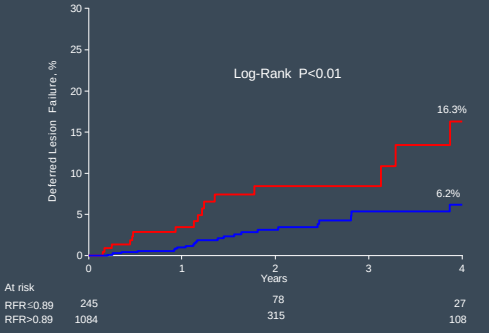
(C) iFR



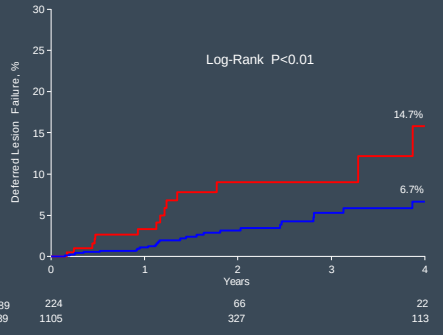
(D) dPR



(E) RFR



(F) DFR

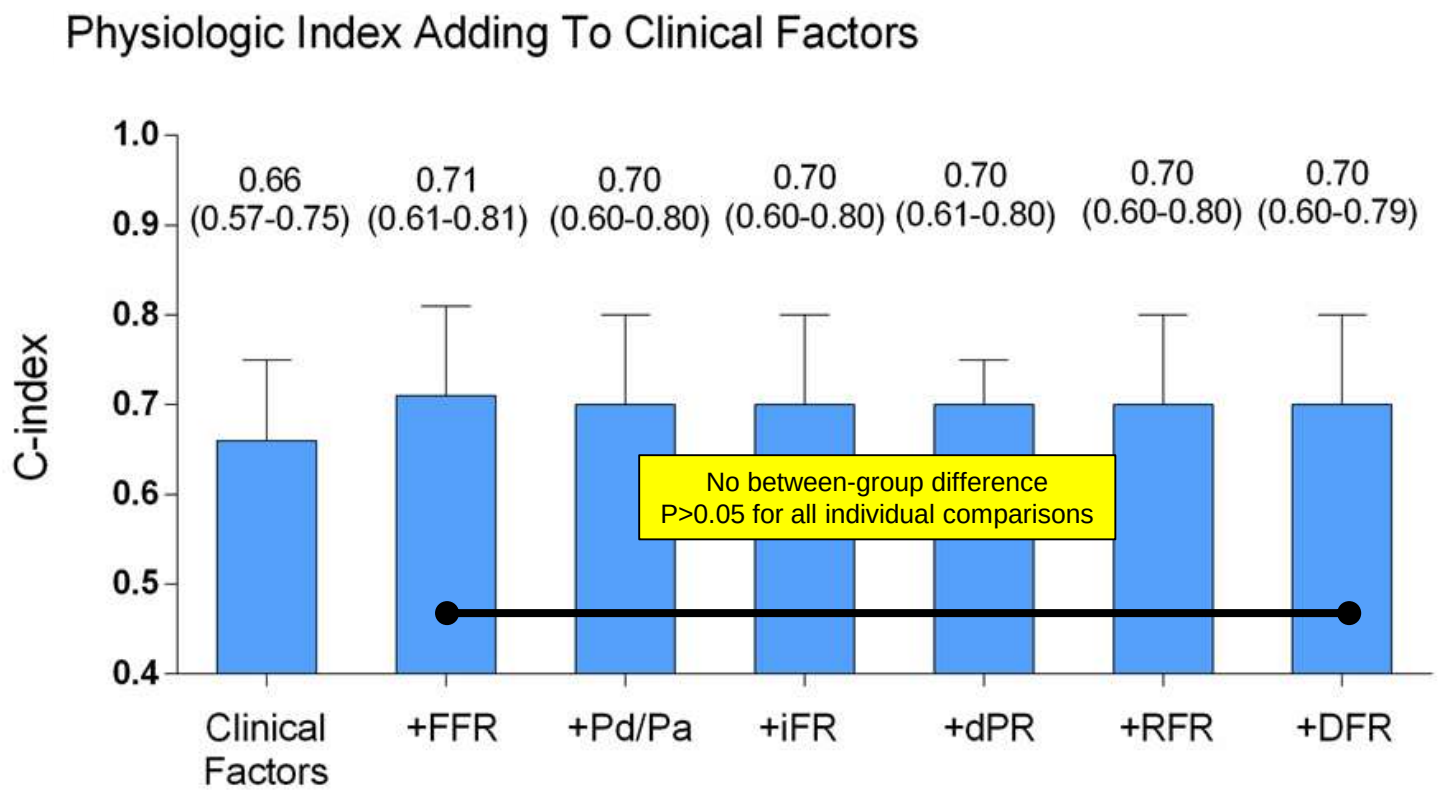


Independent Predictive Value

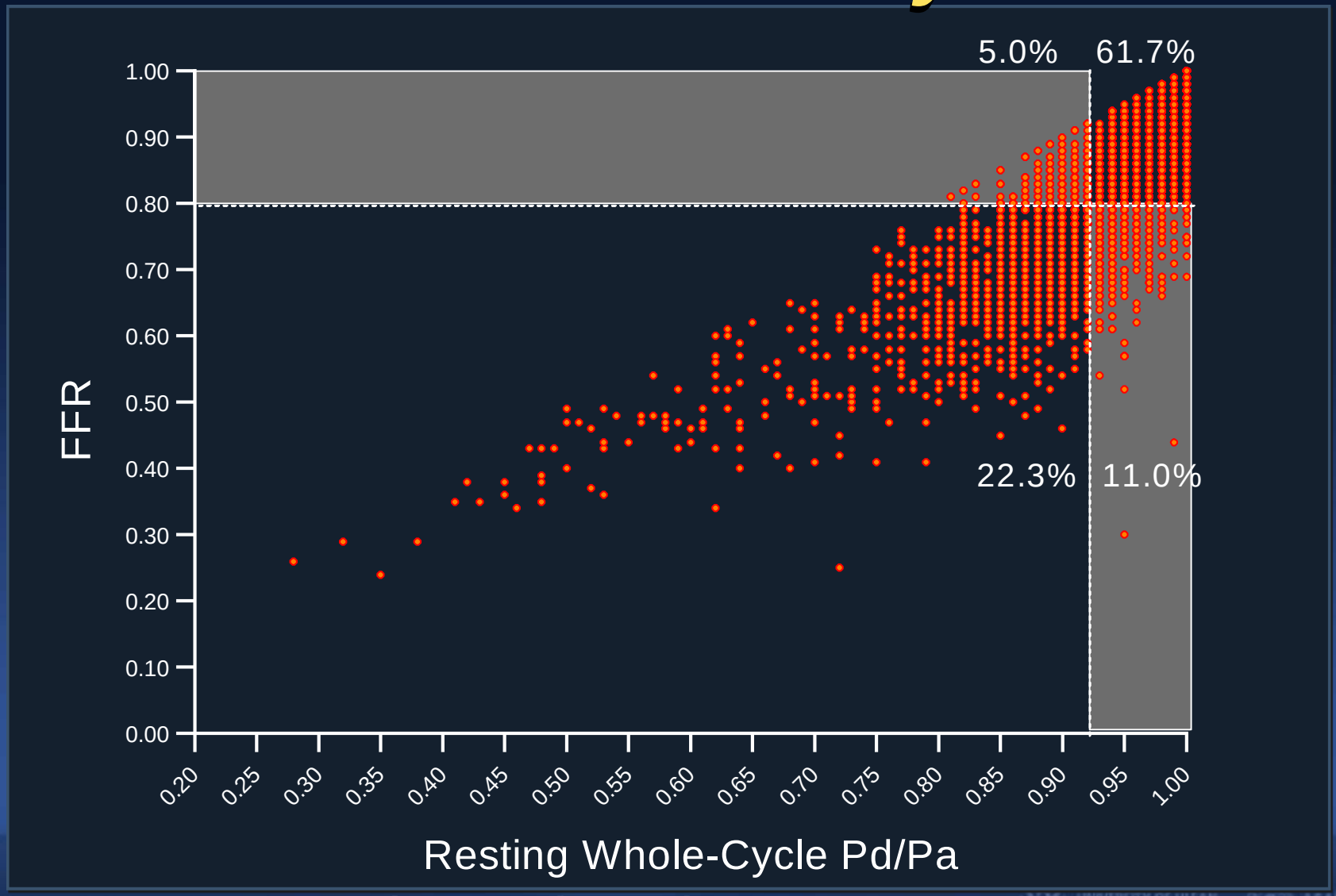
	Adjusted HR*	95% CI	P Value
FFR (≤0.80 vs. >0.80)	2.16	1.19-3.92	0.011
Resting Pd/Pa (≤0.92 vs. >0.92)	2.17	1.17-4.03	0.015
iFR (≤0.89 vs. >0.89)	2.24	1.22-4.11	0.010
dPR (≤0.89 vs. >0.89)	2.64	1.43-4.86	0.002
RFR (≤0.89 vs. >0.89)	2.45	1.35-4.45	0.003
DFR (≤0.89 vs. >0.89)	2.44	1.32-4.50	0.004

* Adjusted for clinical presentation, previous heart failure, lesion location, and diameter stenosis

Prognostic Performance



Resting Pd/Pa and FFR:
84% Accuracy



Predictors of Resting Pd/Pa and FFR Discordance

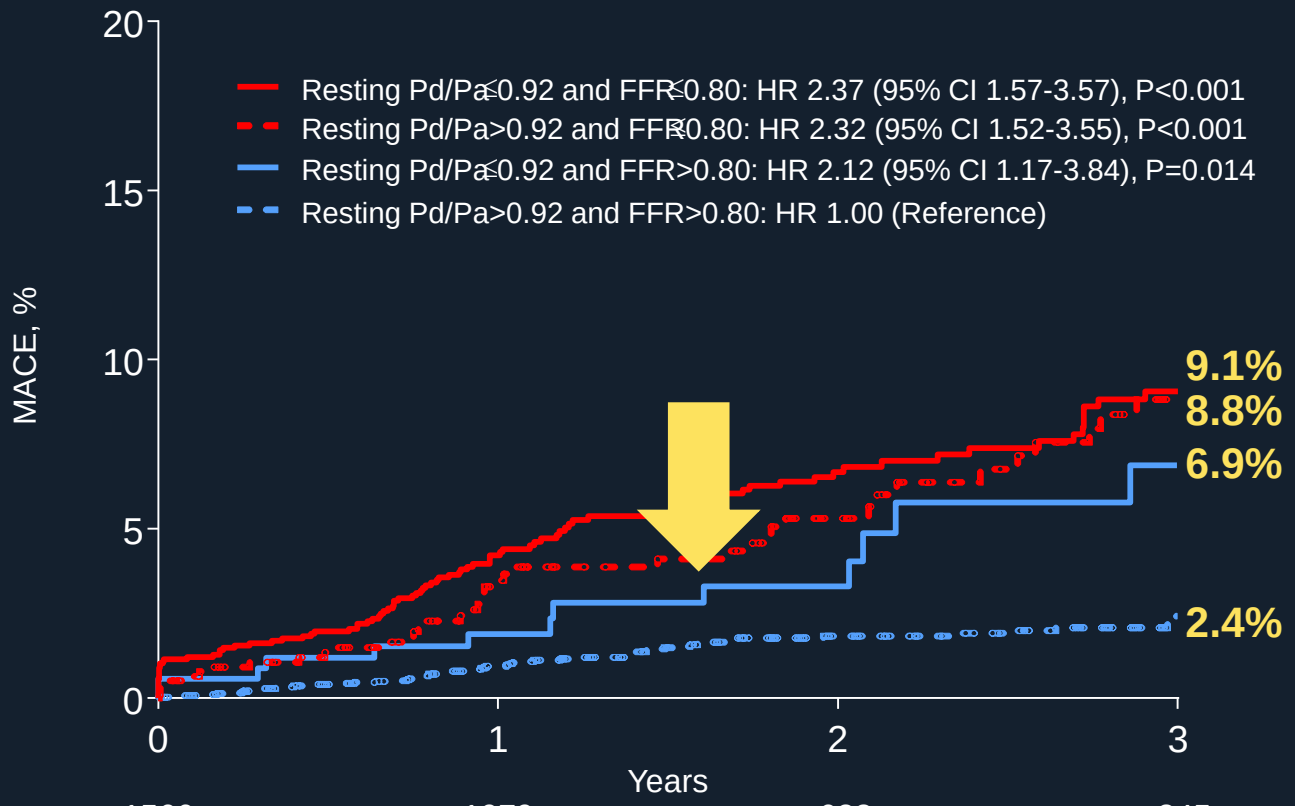
	Odds Ratio	95% CI	P Value
Resting Pd/Pa≤0.92 and FFR>0.80 Very Small Hyperemic Pressure Drop			
Age	1.02	1.01-1.03	0.004
Gender (Male)	0.74	0.59-0.94	0.012
Diabetes	1.50	1.19-1.89	0.001
Hyperlipidemia	0.72	0.57-0.91	0.005
Left main and LAD (vs. others)	4.38	3.28-5.85	<0.001
Proximal location (vs. mid 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)		1.45-2.22	<0.001
Diabetes	0.80	0.66-0.96	0.016
Family history	0.65	0.50-0.87	0.003
Chronic renal failure	0.32	0.14-0.75	0.008
Left main and LAD (vs. others)	1.36	1.14-1.62	0.001
Diameter stenosis (≥50%)	4.06	3.16-5.21	<0.001
AHA/ACC lesion B2C lesion	1.44	1.20-1.71	<0.001

Low CFR phenotype

Super normal CFR phenotype

Without hyperemia, clinically important subsets with moderately but significantly increased risk of cardiac events could not be identified

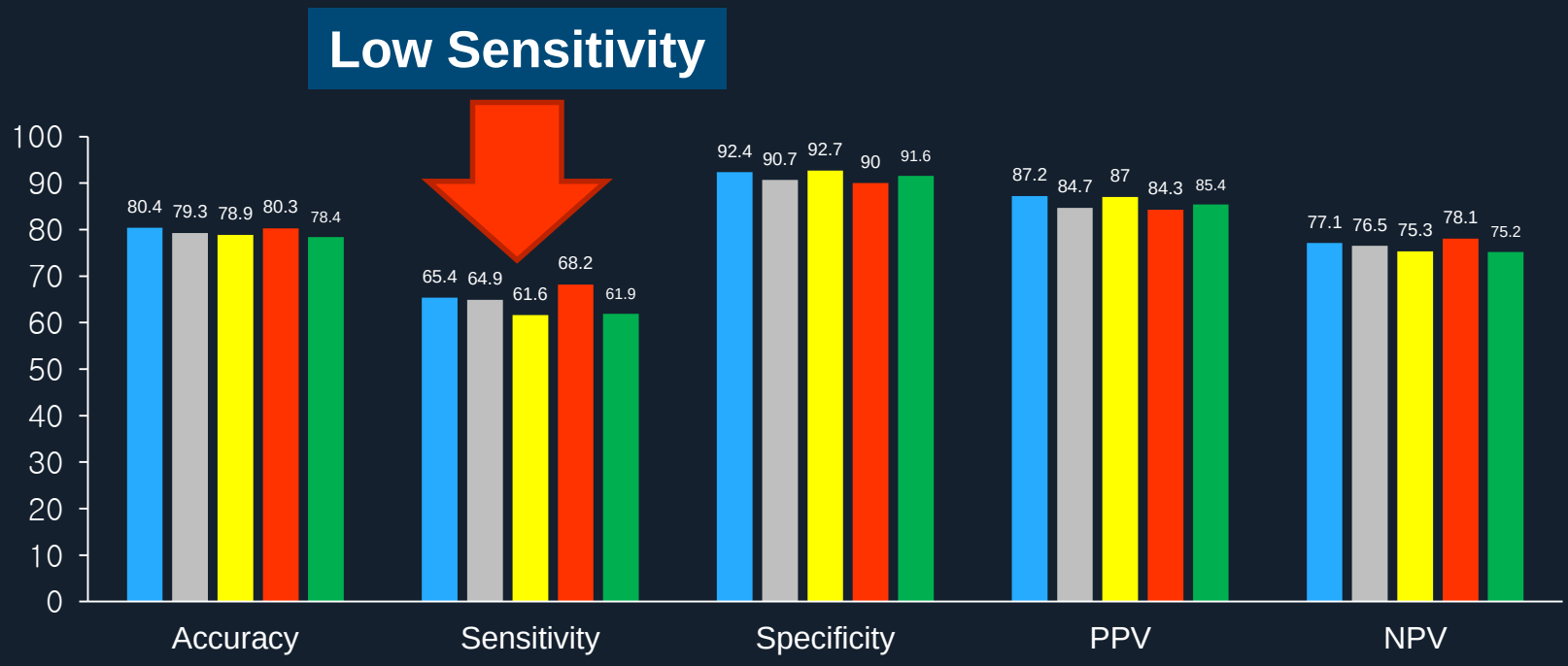
For Cardiac Death, MI, RR



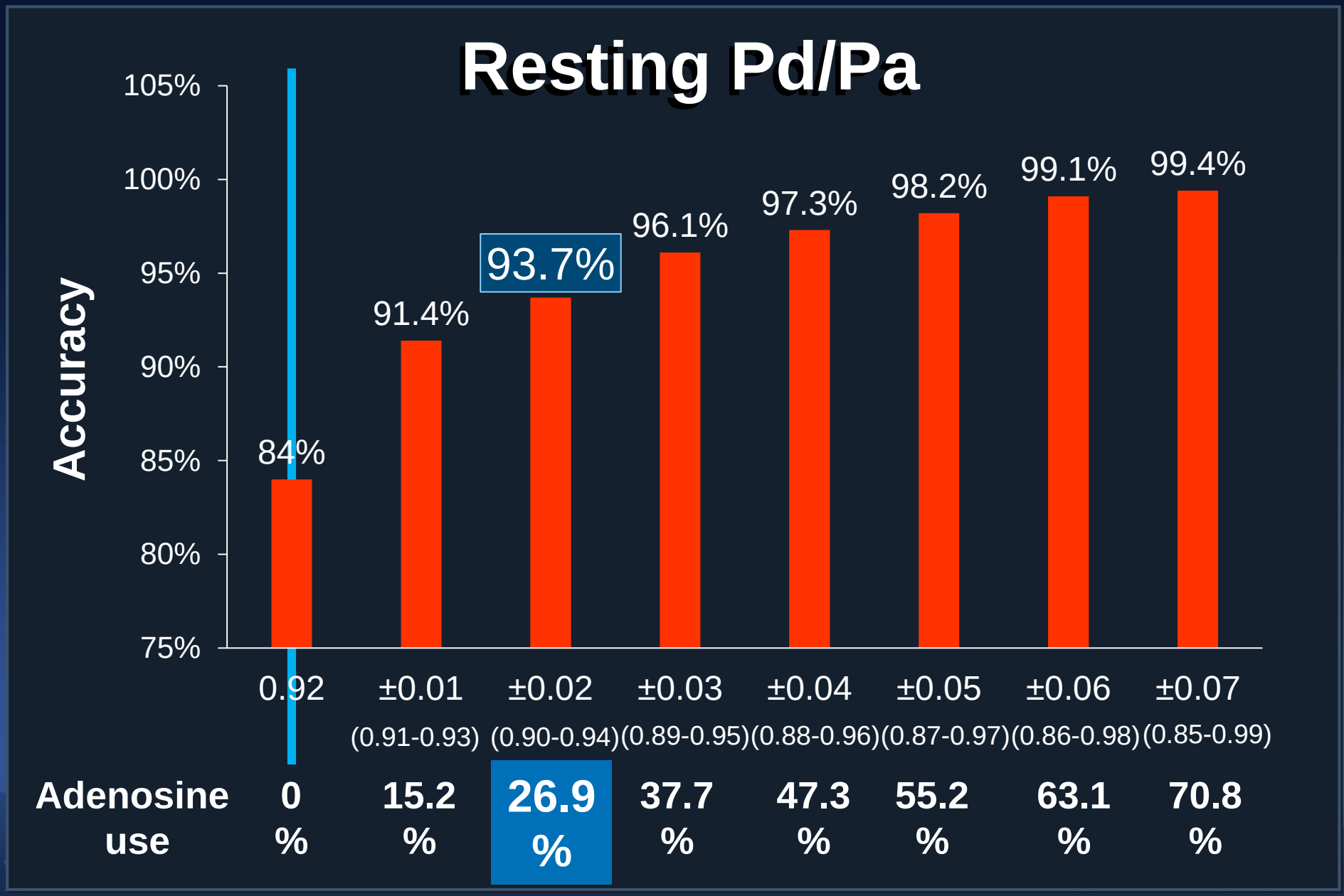
Lesion at risk				
Pd/Pa ≤0.92 and FFR≤0.80	1566	1079	623	345
Pd/Pa>0.92 and FFR ≤0.80	772	527	324	183
Pd/Pa ≤0.92 and FFR>0.80	351	244	151	71
Pd/Pa>0.92 and FFR>0.80	4325	3099	1730	864

Prediction of FFR 0.80

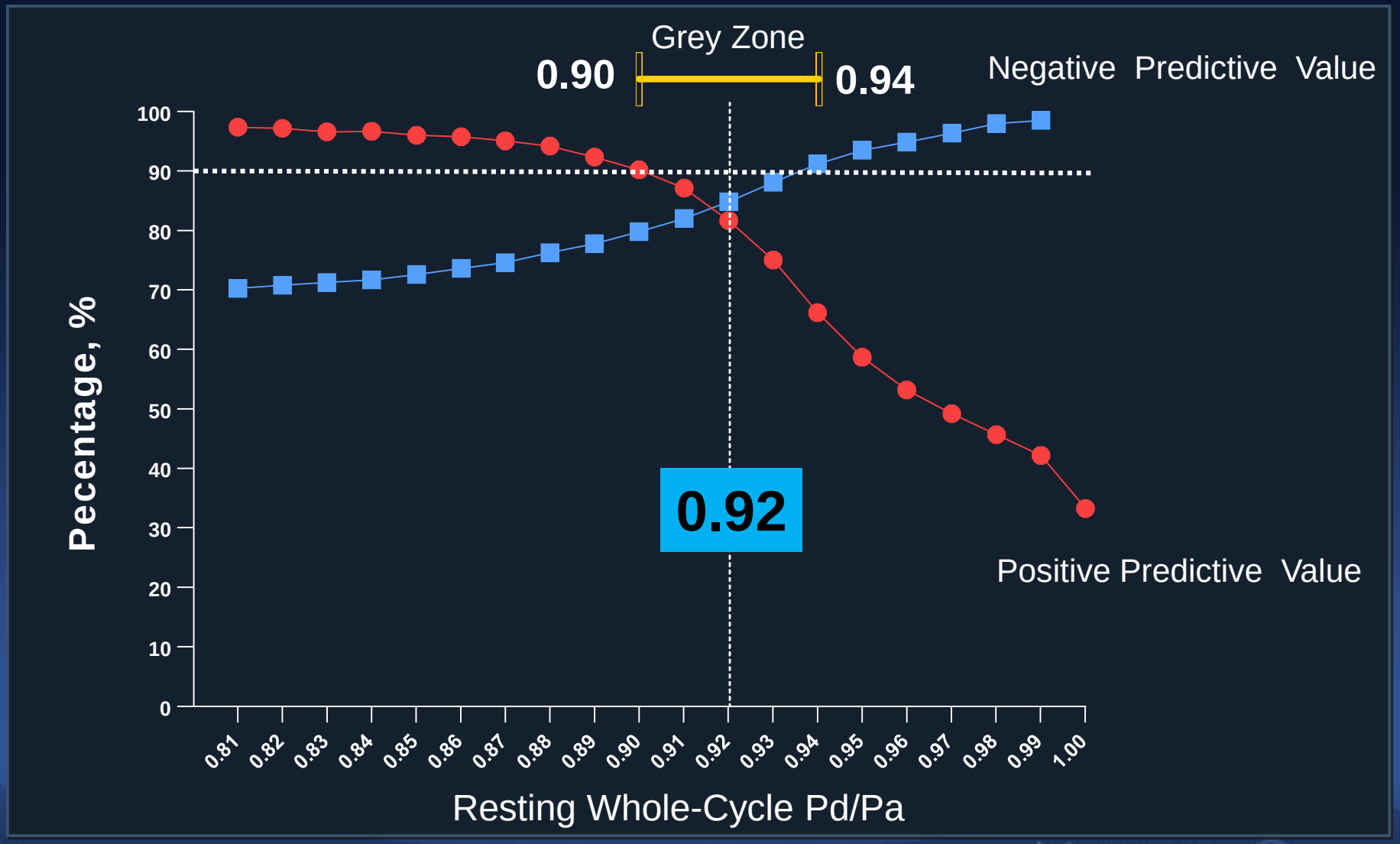
	AUC	Conventional Cut-off
Resting Pd/Pa	0.882 (0.868 - 0.896)	≤0.92
iFR	0.881 (0.868 - 0.895)	≤0.89
dPR	0.884 (0.870 - 0.897)	≤0.89
RFR	0.888 (0.875 - 0.901)	≤0.89
DFR	0.875 (0.861 - 0.889)	≤0.89



Accuracy and Selective Adenosine Use



Positive/Negative Predictive Value



Summary

- NHPRs do not represent resting flow but is a surrogate of FFR
- All NHPR (resting Pd/Pa, iFR, dPR, RFR, DFR) showed equivalent diagnostic and prognostic performance.
- Overall concordance rate between NHPR and FFR was about 80-85%%.
- Use of a hybrid strategy with selective adenosine use improve agreement rate between FFR and NHPR by > 90%
- That integration of NHPR and FFR identified unique clinical, physiologic, and prognostic phenotype of patients.
- However, for NHPRs to be clinically relevant physiologic indexes, further study should evaluate their own physiologic meanings.
- New Data: discordant lesion prognosis will be presented at 5:16 PM on Monday, 29th April.