11° CONGRESSO NAZIONALE

CAMPUS Cuore

Quello che le Linee Guida Non Dicono

Napoli
5-6 aprile 2024

Full Physiology (FFR, iFR): Le Evidenze Scientifiche

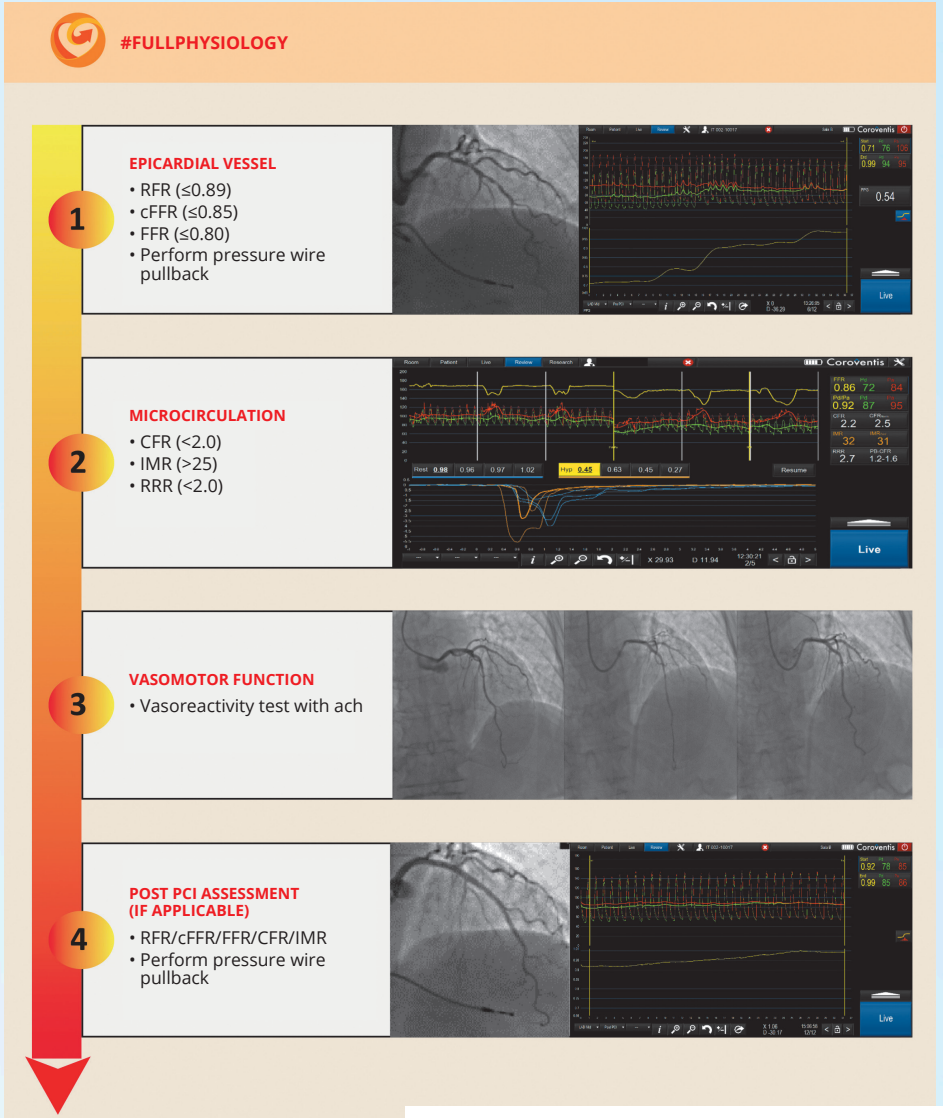
Dott. Luigi Di Serafino

Full Physiology

A modern systematic approach for implementing coronary physiology into daily practice

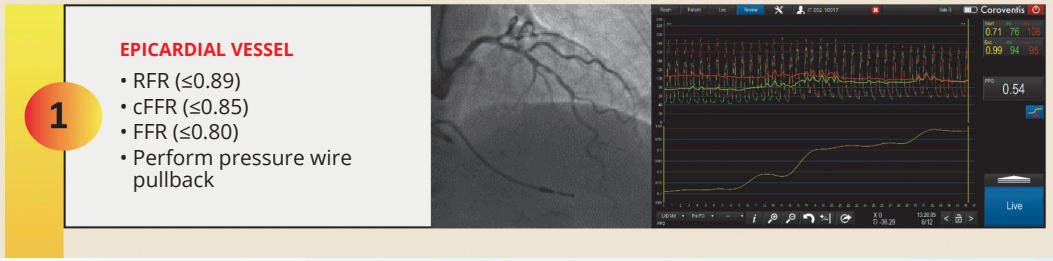
The #FullPhysiology approach consists of a systematic step-by-step assessment of each component of the coronary circulation, including epicardial, microvascular, and vasomotor function.

The approach should be tailored to the patient's clinical presentation and condition.



Scarsini R. et al. Minerva Cardiol Angiol 2023;71:504-14.

#FULLPHYSIOLOGY



Step I: epicardial vessel

The evaluation begins with the measuring the non-hyperemic pressure ratio (NHPR). Following this, fractional flow reserve (FFR) should be assessed.

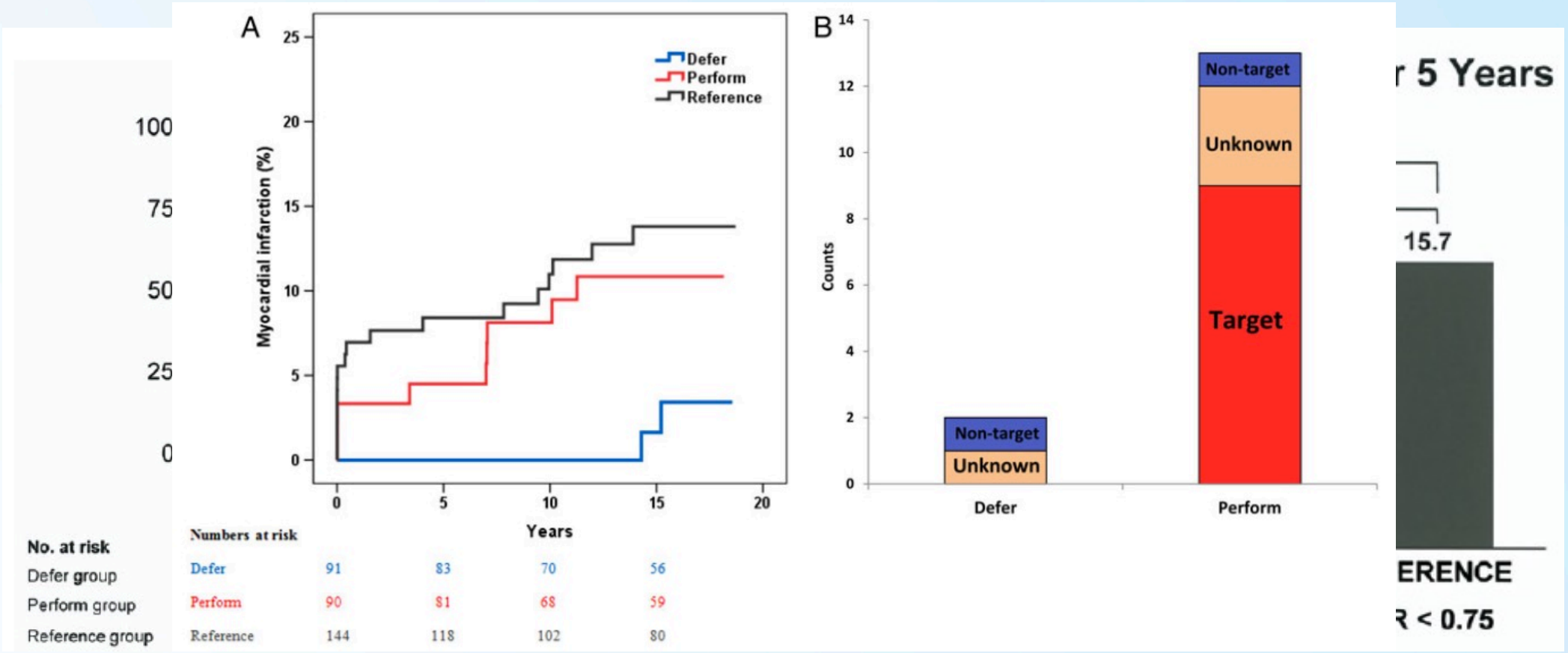
Hyperemic

Farmaco	Somministrazione	Dosaggio	Durata effetto	Plateau
Adenosina	Bolo i.c.	100 µg per la coronaria destra 200 µg per la coronaria sinistra	20 s	No
Adenosina	Infusione continua e.v.	140 µg/kg/min	Entro 60 s dalla fine della somministrazione	Sì
Regadenosone	Bolo e.v.	0.4 mg	60 s	Sì
Nitroprussiato di sodio	Bolo i.c.	0.6 µg/kg	30-60 s	Sì
Papaverina	Bolo i.c.	20 mg	45-60 s	Sì
Nicorandil	Bolo i.c.	2 mg	30-40 s	Sì

≤ 0.80 0.91-0.93 ≤0.89

Kogame N. et al. J Am Coll Cardiol Intv. 2020; 13(14):1617-38

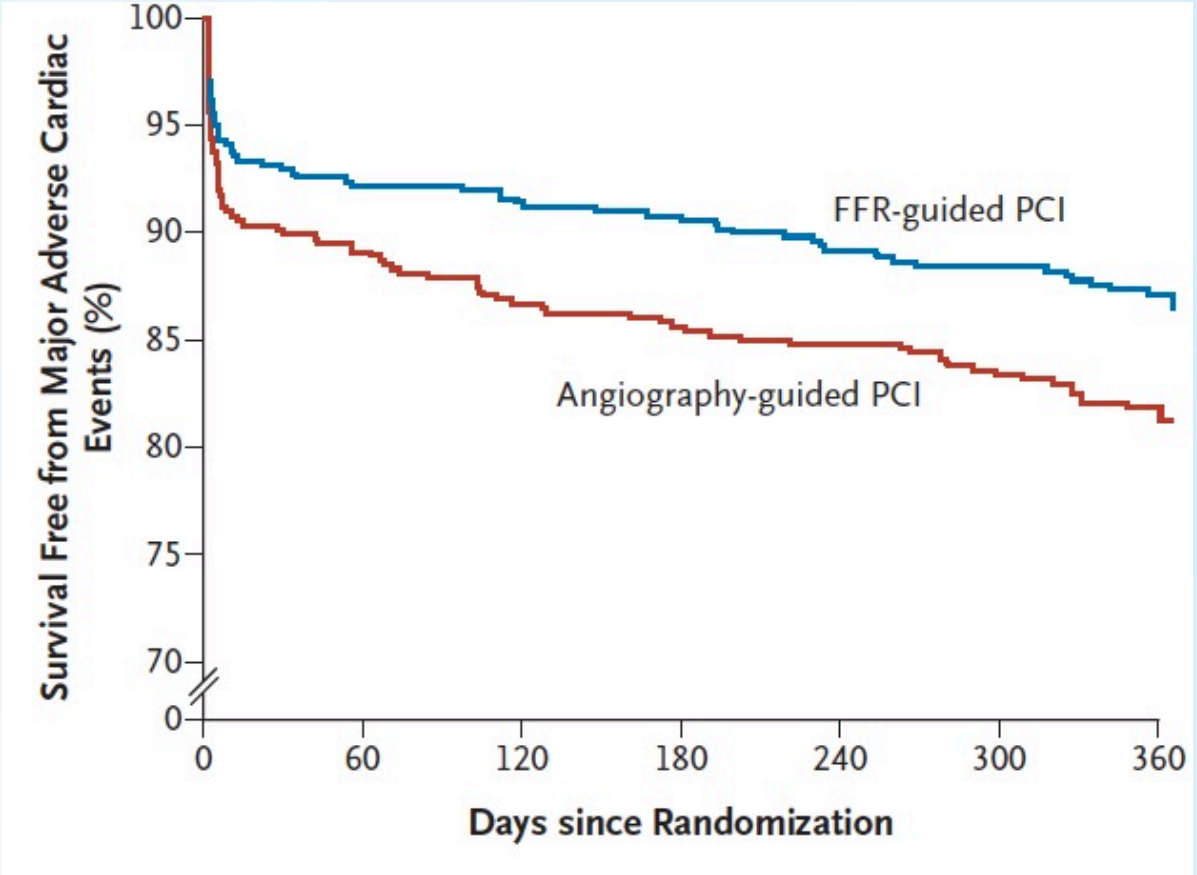
Is it safe to defer PCI for non significant stenoses ?



Pijls N.H.J. et al. J Am Coll Cardiol 2007;49:2105–11
Zimmermann F.M. et al. European Heart Journal (2015) 36, 3182–3188

In MVD patients, is FFR-guided PCI better than Angio-guided PCI?

FFR-guided PCI of MVD patients is associated with a better clinical outcome as compared with angio-guided PCI



Tonino P.A.L. et al. N Engl J Med 2009;360:213-24

DEFINE-FLAIR

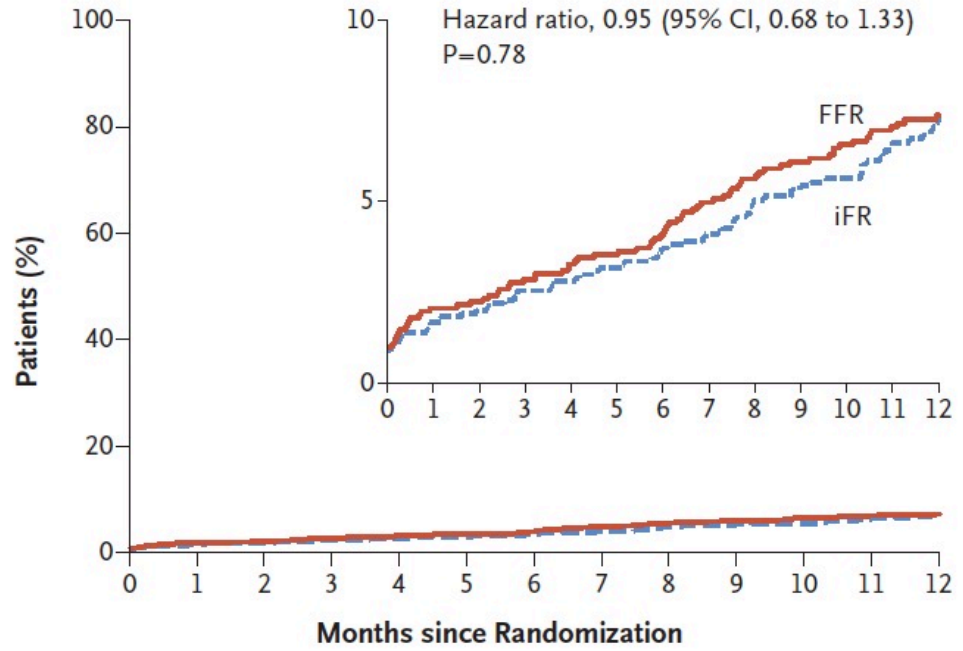


Figure 2. Cumulative Risk of the Primary End Point.

Shown is the cumulative risk of the composite of death from any cause, nonfatal myocardial infarction, or unplanned revascularization at 1 year. The inset shows the same data on an enlarged y axis.

Table 3. Outcomes for Difference in Risk at 1 Year.*

Outcome	iFR Group	FFR Group	Difference in Risk		P Value
	no./total no. (%)		*percentage points (95% CI)*	*percentage points (99% CI)*	
Primary end point: death from any cause, nonfatal myocardial infarction, or unplanned revascularization	78/1148 (6.8)	83/1182 (7.0)	−0.2 (−2.3 to 1.8)†	−0.2 (−2.9 to 2.5)	0.83
Unplanned revascularization	46/1147 (4.0)	63/1181 (5.3)	−1.3 (−3.0 to 0.4)	−1.3 (−3.1 to 1.9)	0.13
Nonfatal myocardial infarction	31/1148 (2.7)	28/1180 (2.4)	0.3 (−1.0 to 1.6)	0.3 (−1.4 to 2.0)	0.62
Death from cardiovascular causes	7/1147 (0.6)	4/1179 (0.3)	0.3 (−0.3 to 0.8)	0.3 (−0.5 to 1.0)	0.34
Death from noncardiovascular causes	15/1147 (1.3)	9/1179 (0.8)	0.5 (−0.3 to 1.4)	0.5 (−0.5 to 1.6)	0.19
Death from any cause	22/1147 (1.9)	13/1179 (1.1)	0.8 (−0.2 to 1.8)	0.8 (−0.5 to 2.1)	0.11

Coronary revascularization guided by iFR was noninferior to revascularization guided by FFR with respect to major adverse cardiac events at 1 year

N Engl J Med 2017;376:1824-34.

iFR SWEDEHEART

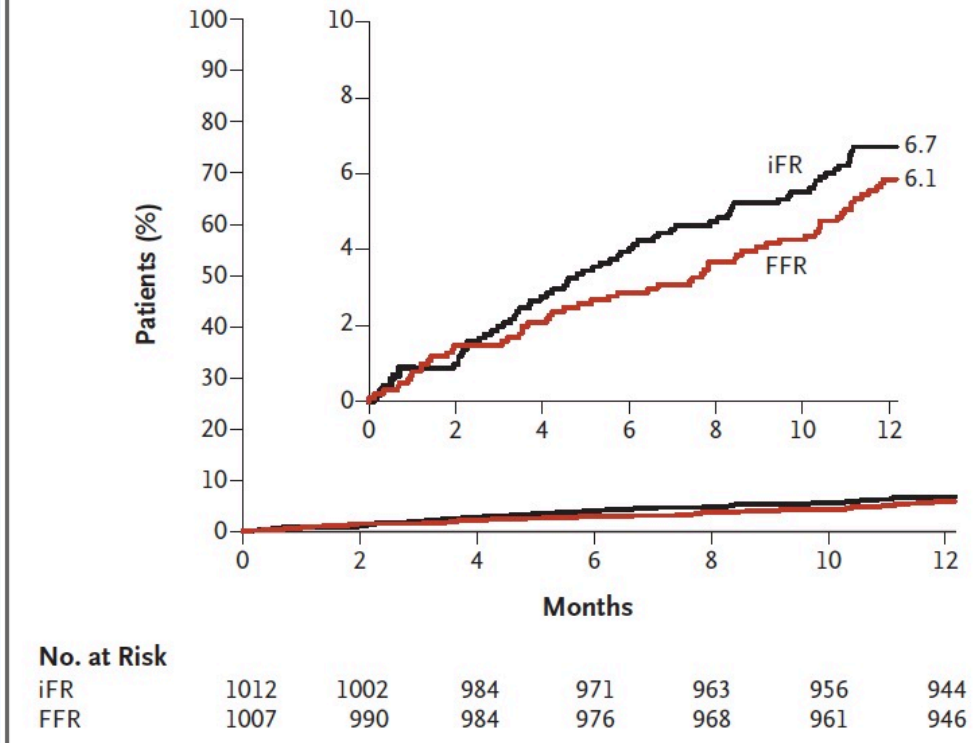


Figure 2. Kaplan–Meier Curves for the Primary End Point.

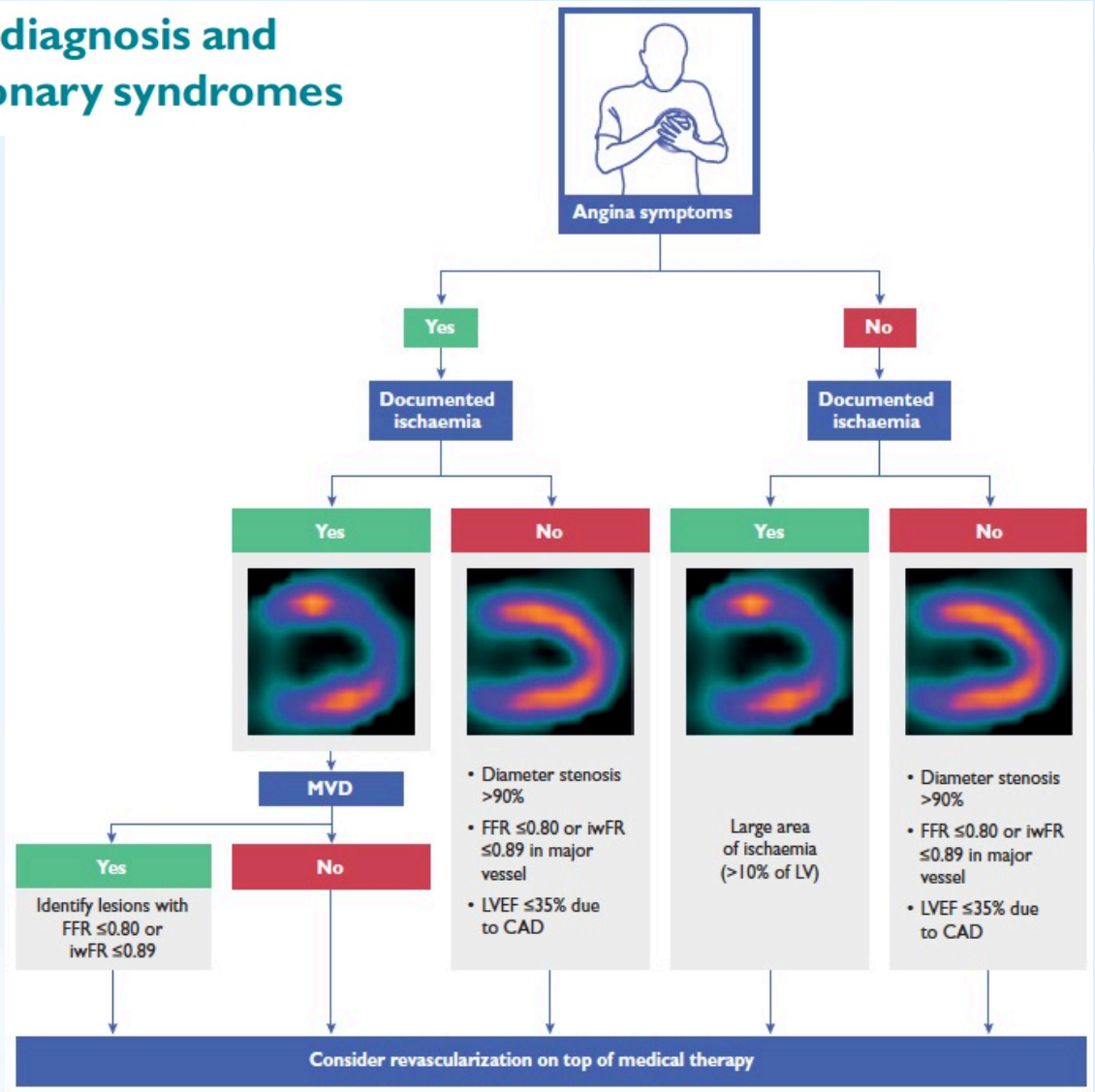
Shown are Kaplan–Meier curves for the cumulative risk of the composite of death from any cause, nonfatal myocardial infarction, or unplanned revascularization within 12 months after the index procedure. The inset shows the same data on an enlarged y axis.

Table 3. End Points at 12 Months in the Per-Protocol Population.

End Point	iFR Group (N=1012)	FFR Group (N=1007)	Hazard Ratio (95% CI)	P Value
	no. (%)			
Primary end point: death from any cause, nonfatal myocardial infarction, or unplanned revascularization	68 (6.7)	61 (6.1)	1.12 (0.79–1.58)	0.53
Death from any cause	15 (1.5)	12 (1.2)	1.25 (0.58–2.66)	0.57
Nonfatal myocardial infarction	22 (2.2)	17 (1.7)	1.29 (0.68–2.44)	0.42
Unplanned revascularization	47 (4.6)	46 (4.6)	1.04 (0.69–1.57)	0.84
Target-lesion revascularization	29 (2.9)	27 (2.7)	1.21 (0.70–2.07)	0.49
Restenosis	19 (1.9)	18 (1.8)	1.05 (0.55–2.01)	0.87
Stent thrombosis*	1 (0.1)	2 (0.2)		
Chest discomfort during procedure				<0.001†
None	982 (97.0)	319 (31.7)		
Mild	26 (2.6)	316 (31.4)		
Moderate	2 (0.2)	285 (28.3)		
Severe	2 (0.2)	87 (8.6)		

N Engl J Med 2017;376:1813-23.

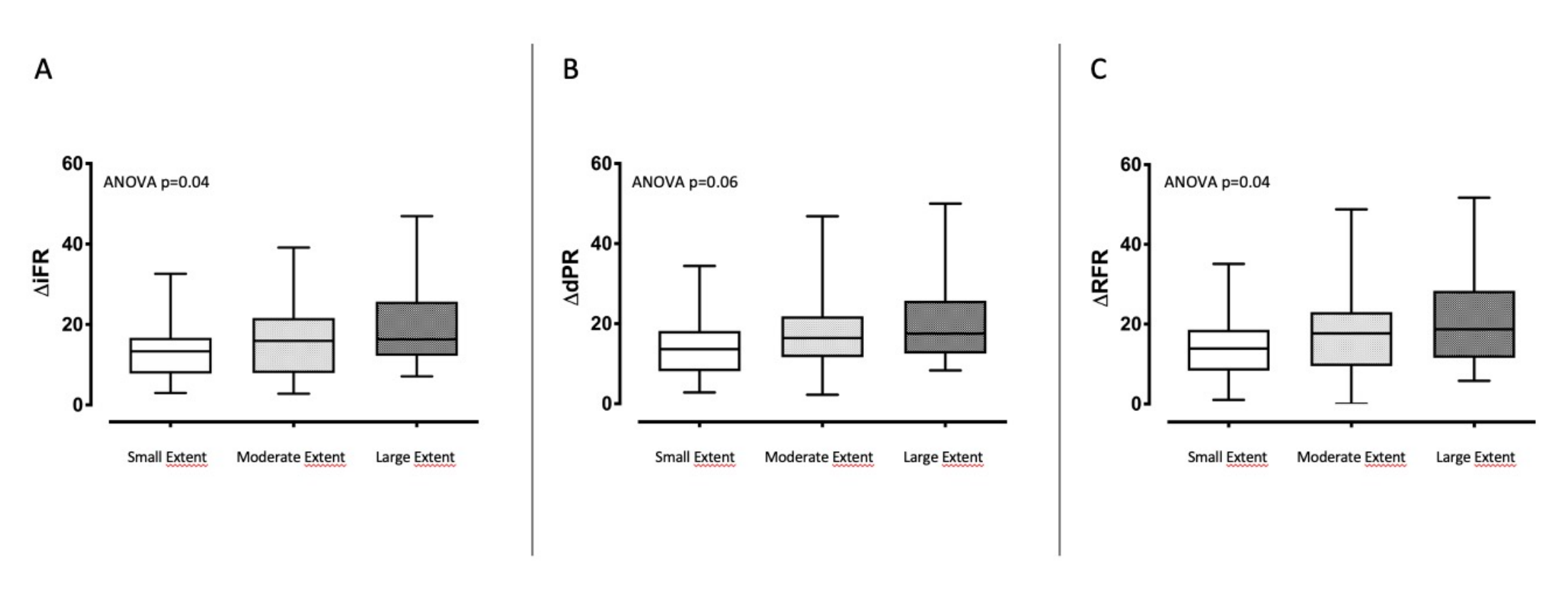
2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes



Knuuti J. et al. European Heart Journal (2019) 00, 1-71

Any advantage in using both FFR and NHPR?

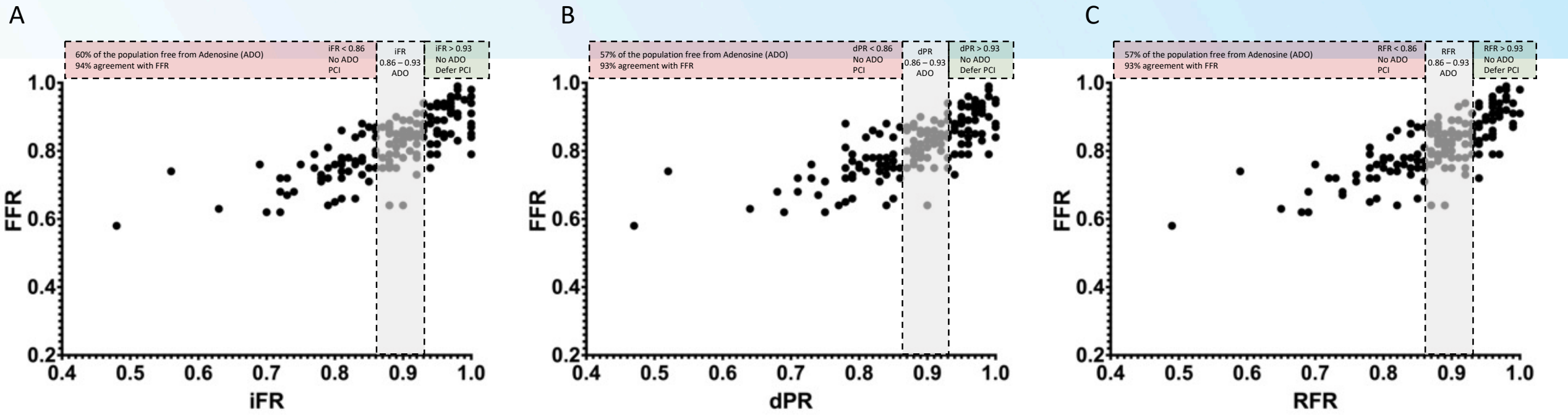
1. Systematically using both non-hyperemic and hyperemic physiology offers the advantage of a comprehensive assessment that includes the vasodilatory response to the hyperemic stimulus.



Di Serafino L. et al. Int J Cardiol. 2023 Jan 1:370:84-89

Any advantage in using both FFR and NHPR?

2. Hybrid approach

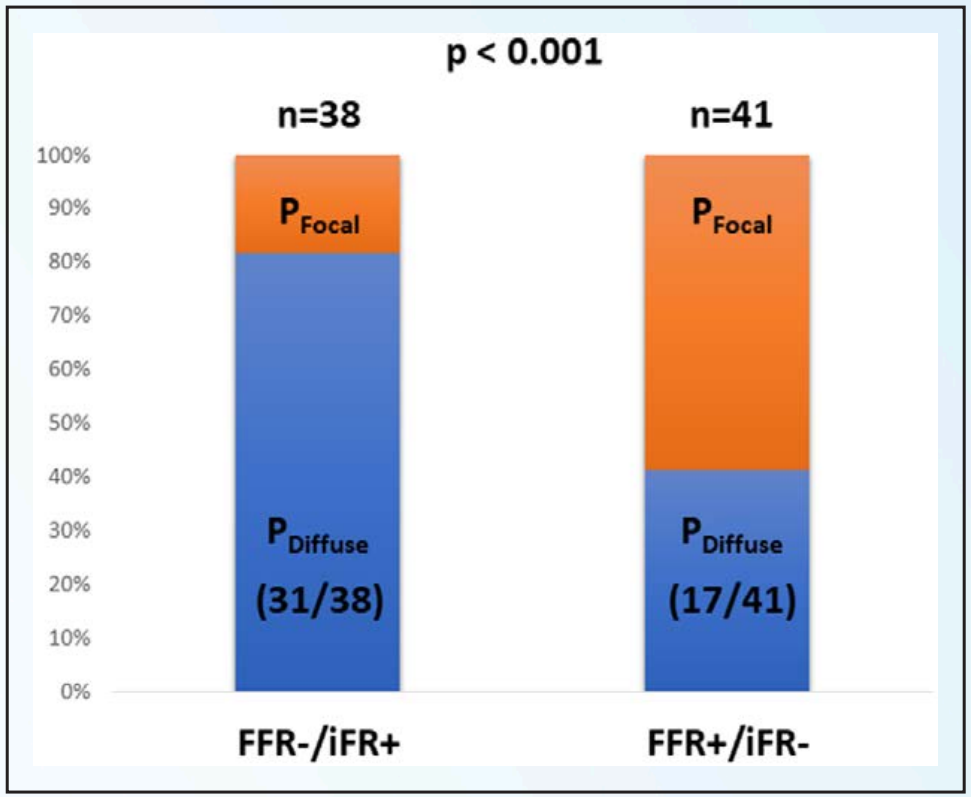


The hybrid NHPR-FFR approach has a 93% classification agreement with an FFR-only strategy.

Di Serafino L. et al. Int J Cardiol. 2023 Jan 1:370:84-89

Any advantage in using both FFR and NHPR?

3. There are clinical scenarios where NHPR/FFR discordance occurs, and measuring both provides a complete picture of the functional status of the coronary vessel.



FFR+/iFR− discordance was significantly more associated with a physiologically focal pattern of disease.

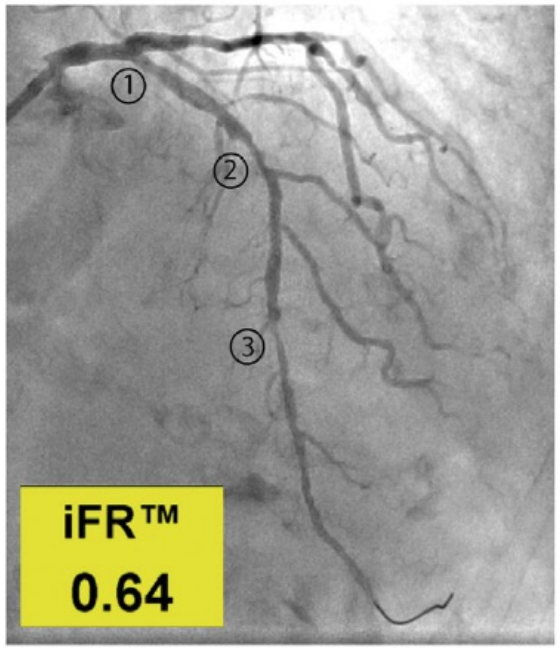
FFR−/iFR+ discordance was significantly more associated with a physiologically diffuse pattern of disease.

Warisawa T. et al. Circ Cardiovasc Interv. 2019;12:e007494

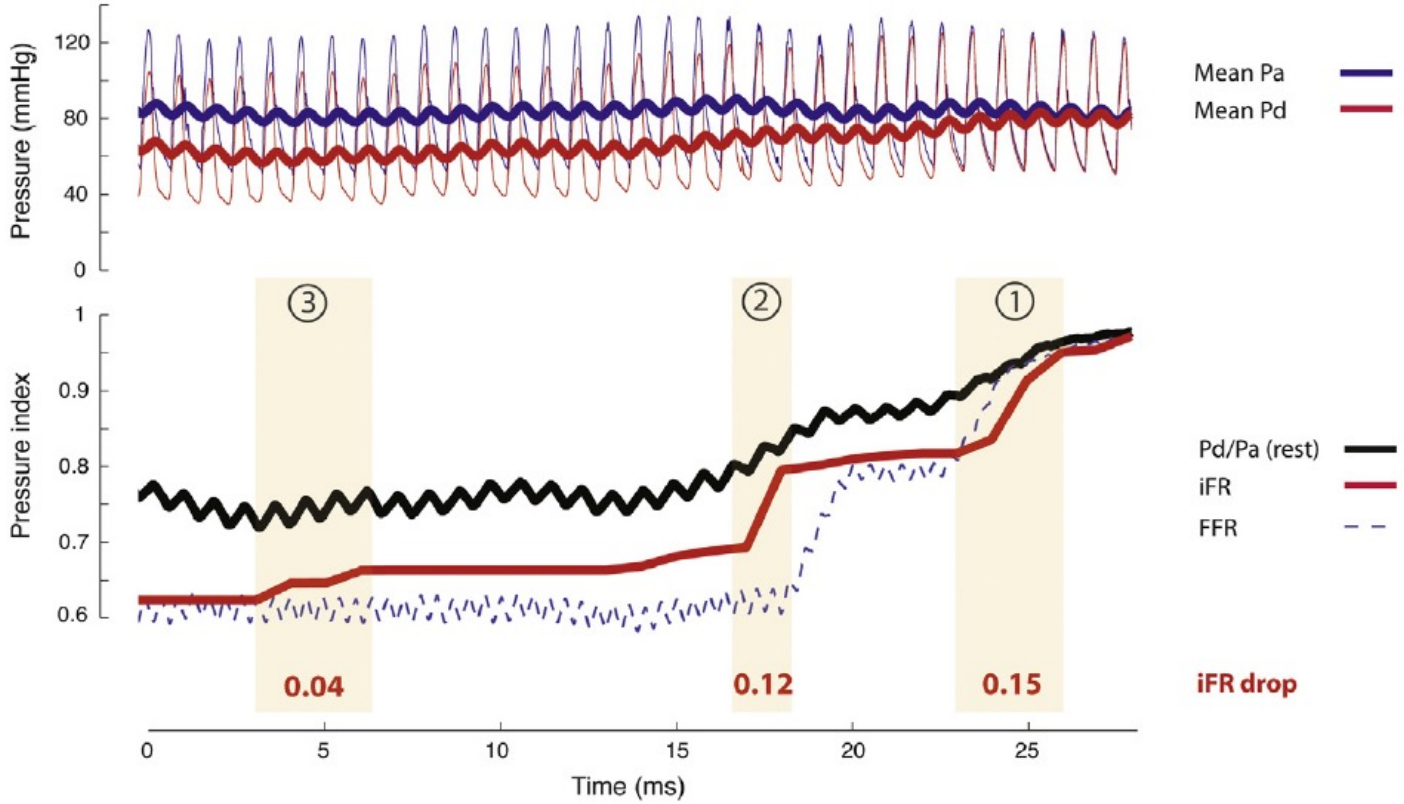
JACC: CARDIOVASCULAR INTERVENTIONS VOL. ■, NO. ■, 2014
© 2014 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jcin.2014.06.015

Pre-Angioplasty Instantaneous Wave-Free Ratio (iFR) Pullback Provides Virtual Intervention and [illegible] Outcome for Se[illegible] Coronary Artery

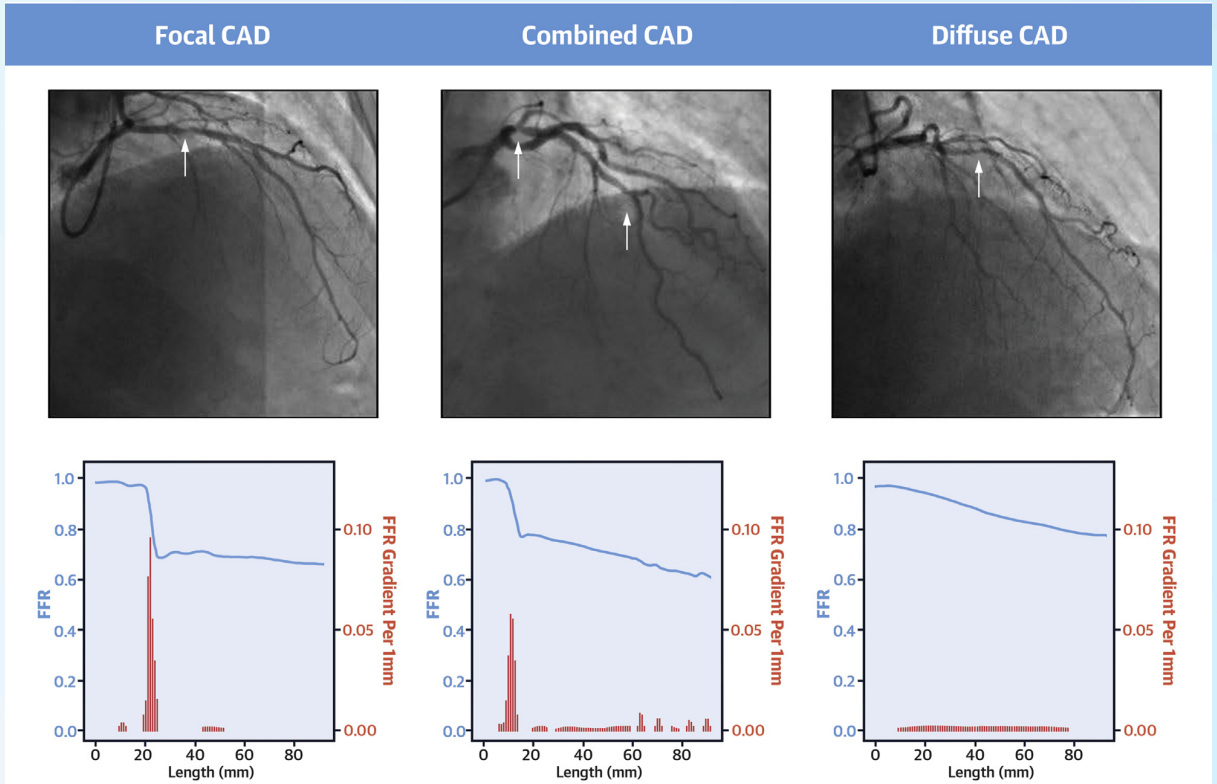
Sukhjinder S. Nijjer, MB ChB,* Sayan Se[illegible]
Mauro Echavarria-Pinto, MD,† Christoph[illegible]
Rodney A. Foale, MD,* Iqbal S. Malik, M[illegible]
Mahmud Al-Bustami, MD,* Raffi R. Kapr[illegible]
Christopher S. Baker, MBBS, PhD,* Mich[illegible]
Jamil Mayet, MB ChB, MD,* Darrel P. Fra[illegible]
Justin E.R. Davies, MBBS, PhD*



Three discrete lesions with diffuse disease; the haemodynamic impact of the lesions can be detected using an iFR manual pullback



Nijjer S.S. et al. J Am Coll Cardiol Intv 2014;



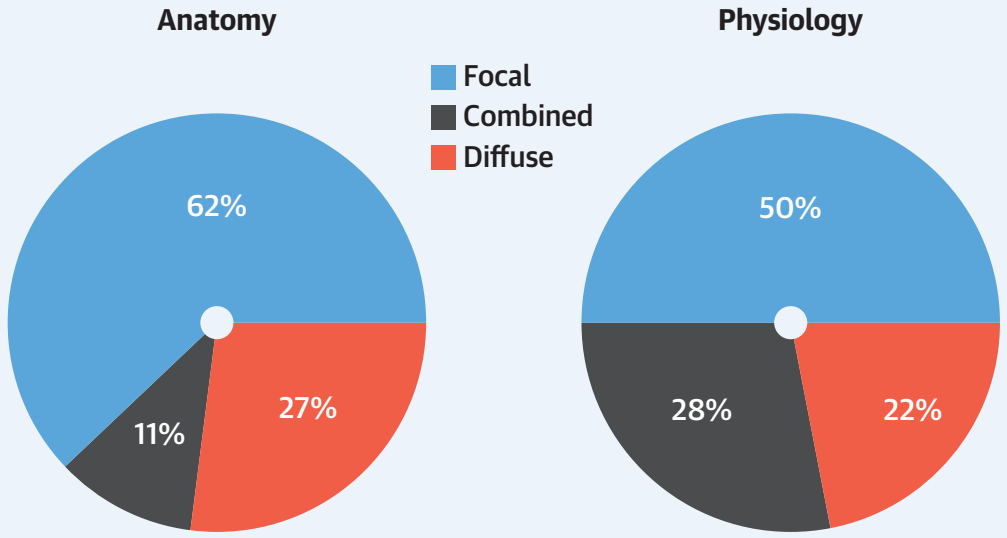
Pullback Pressure Gradients Index

$\{MaxPPG_{20mm}/\Delta FFR_{vessel} + (1\text{-Length with Functional Disease (mm)/Total Vessel Length (mm)})\}/2$

Focal CAD	Combined CAD	Diffuse CAD
$\frac{MaxPPG_{20mm}}{\Delta FFR_{vessel}} = \frac{0.300}{0.325} = 0.923$	$\frac{MaxPPG_{20mm}}{\Delta FFR_{vessel}} = \frac{0.236}{0.387} = 0.610$	$\frac{MaxPPG_{20mm}}{\Delta FFR_{vessel}} = \frac{0.056}{0.193} = 0.290$
Length CAD $= \frac{20}{100} = 0.200$	Length CAD $= \frac{65}{92} = 0.707$	Length CAD $= \frac{74}{101} = 0.733$
PPG Index $= \frac{0.923 + (1\text{-}0.20)}{2} = 0.86$	PPG Index $= \frac{0.610 + (1\text{-}0.707)}{2} = 0.45$	PPG Index $= \frac{0.290 + (1\text{-}0.733)}{2} = 0.28$

Collet C. et al. J Am Coll Cardiol 2019;74:1772–84

Patterns of Coronary Artery Disease

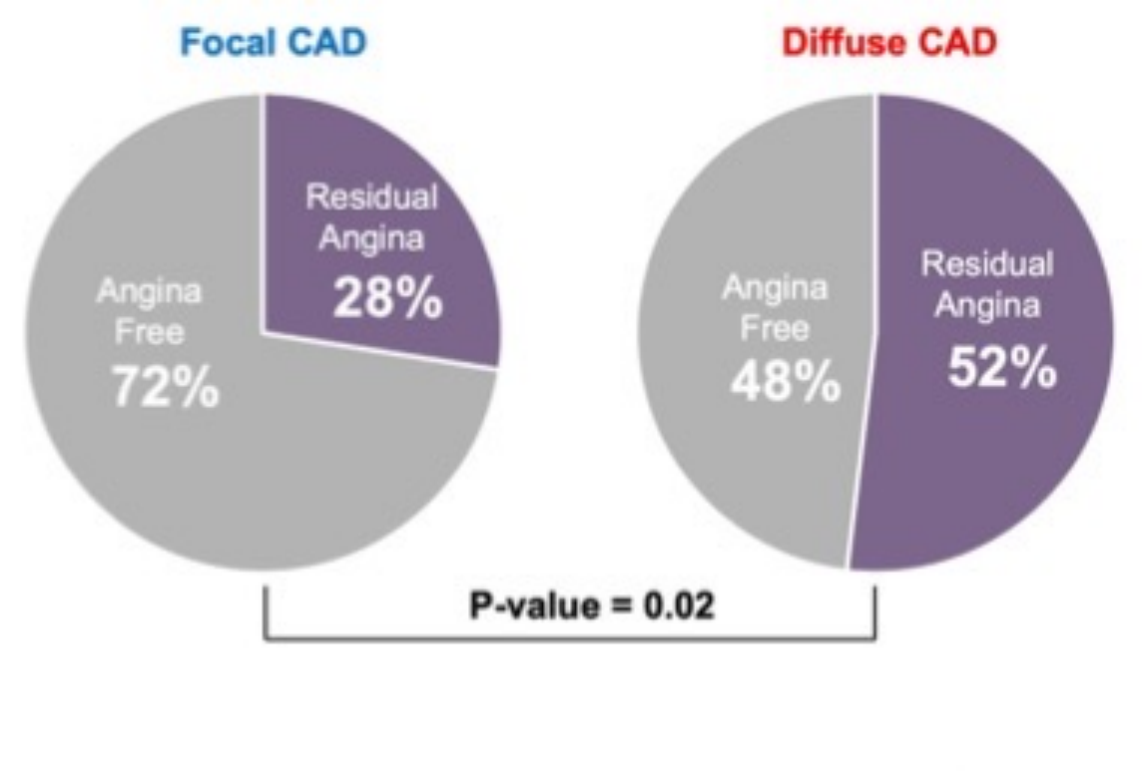


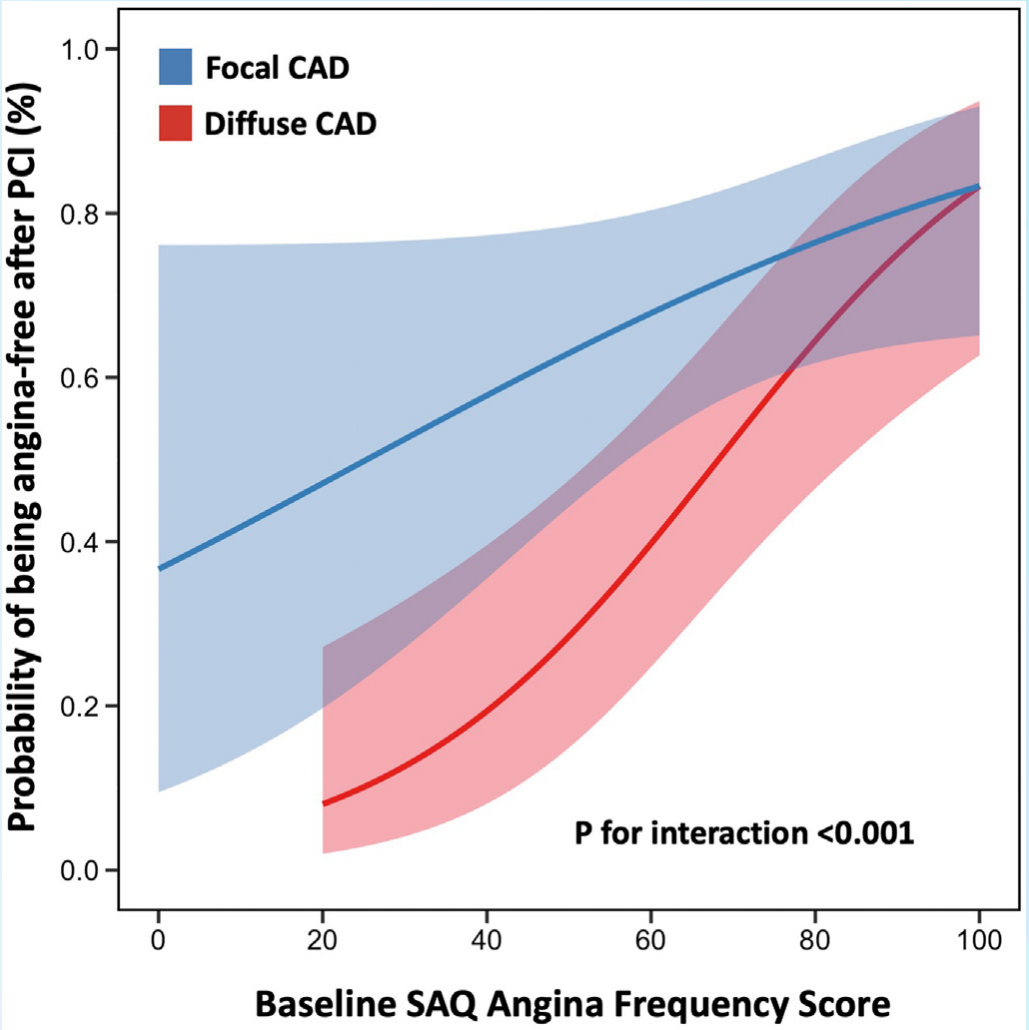
Reclassification of 36% of the cases

Cohen's Kappa 0.42 (95% CI 0.26 to 0.59)

		Anatomy		
		Diffuse	Combined	Focal
Physiology	Diffuse	10	0	9
	Combined	10	7	7
	Focal	3	2	37

Collet C. et al. J Am Coll Cardiol 2019;74:1772–84



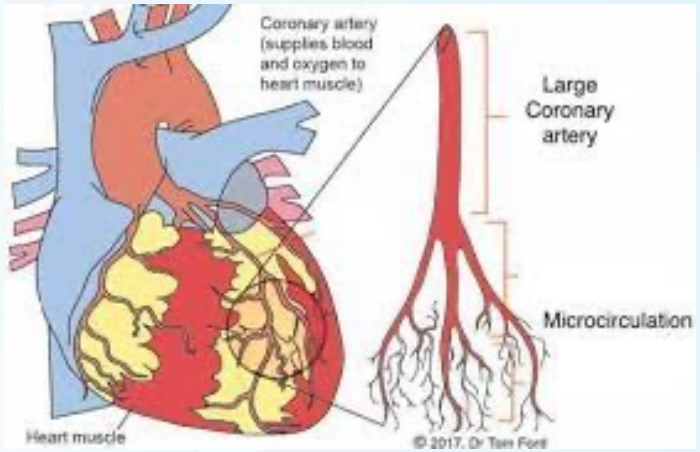


Collet C, et al. J Am Coll Cardiol Intv. 2022;15(24):2506–2518.

#FULLPHYSIOLOGY

Step II: microcirculation

≥ 50% of patients referred for coronary angiogram due to anginal symptoms (and evidence of inducible myocardial ischemia) do not exhibit obstructive CAD (ANOCA/INOCA)

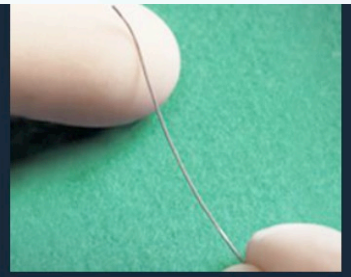


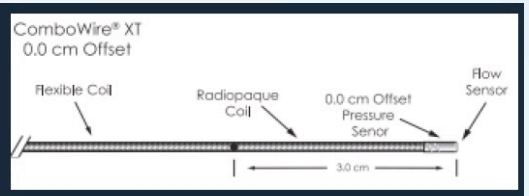
Microvascular angina (MVA) is the clinical manifestation of myocardial ischaemia caused by Coronary Microvascular Dysfunction (CMD).

In this clinical entity, myocardial ischaemia may result from structural remodelling of the microvasculature (leading to fixed reduced conductance) or vasomotor disorders affecting the coronary arterioles (causing dynamic arteriolar obstruction) or both.

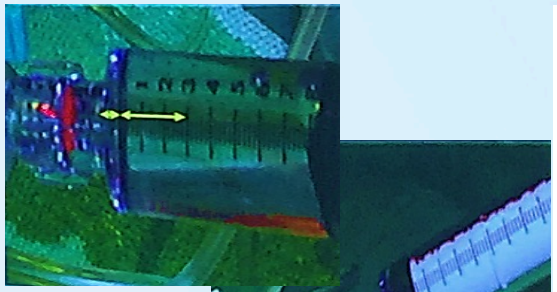
Doppler-based Tools

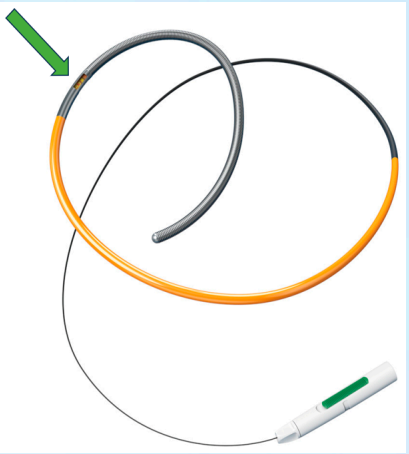
Thermodilution-based Tools



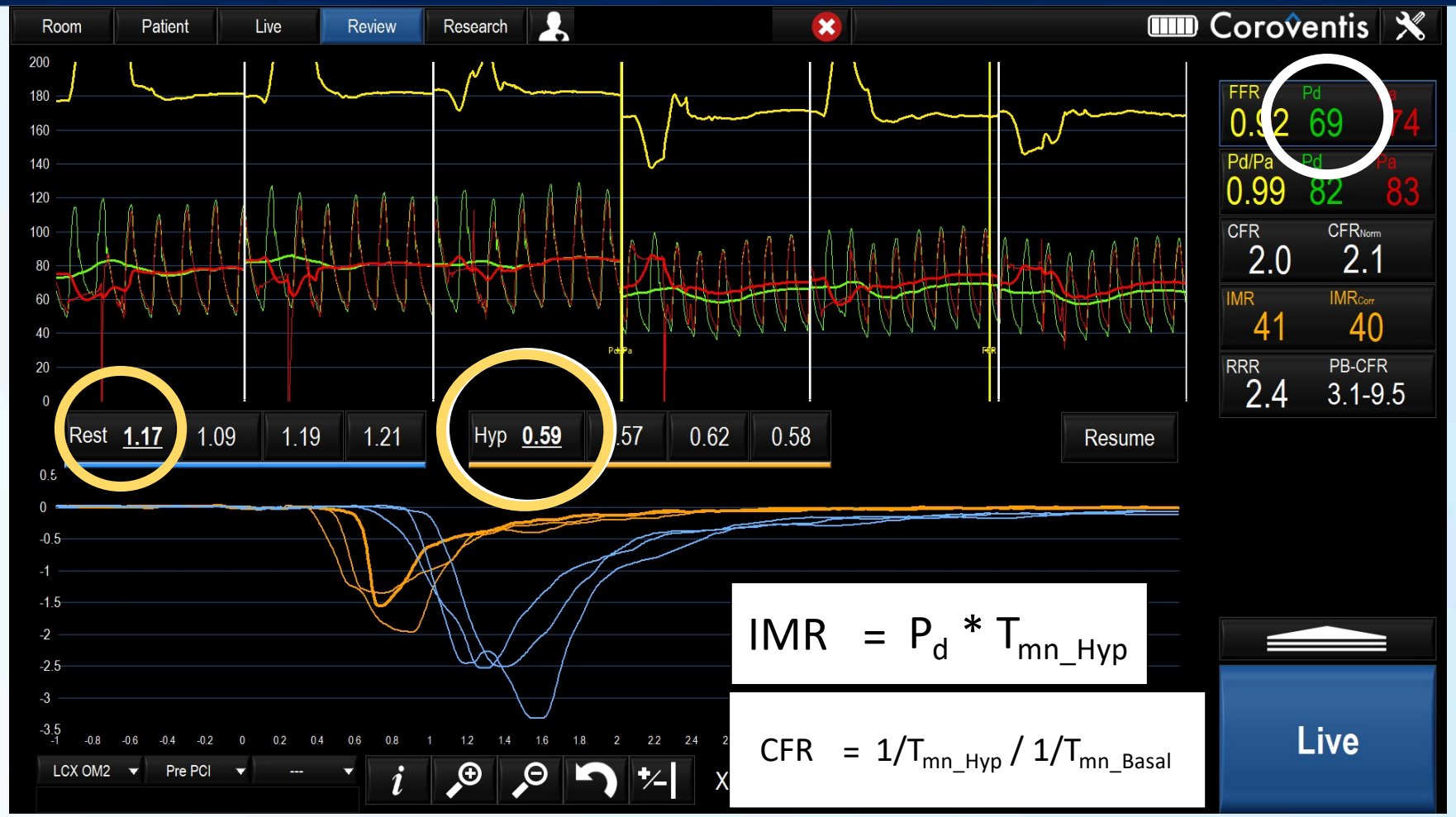


$$HMR\ (mmHg / cm/s) = \frac{P_{distal}\ (mmHg)}{Flow_{velocity}\ (cm/s)}$$





During Adenosine induced maximal hyperemia



A semi-quantitative measure to describe the status of the microcirculation where the mean transit time of a bolus of saline infused into the coronary artery is used as a surrogate for flow

CFR reflects the ability of the entire coronary circulation, encompassing both epicardial and microvascular components, to adapt to increased myocardial oxygen request. Pathological CFR values are considered to be less than 2.0 and serve as a hallmark of CMD in the absence of obstructive CAD.

IMR is a specific index of microcirculatory resistance that exhibits relative independence from hemodynamic conditions. Values equal to or exceeding 25 units are suggestive of CMD.

IMR ≥ 25 **CFR < 2.0**	Structural coronary microvascular dysfunction (CMD)
IMR ≥ 25 **CFR ≥ 2.0**	Compensated (initial) structural CMD
IMR < 25 **CFR < 2.0**	Functional CMD
IMR < 25 **CFR ≥ 2.0**	Preserved coronary microvascular function

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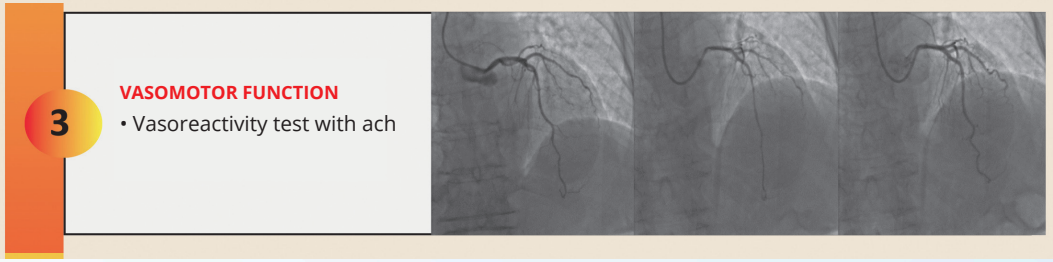
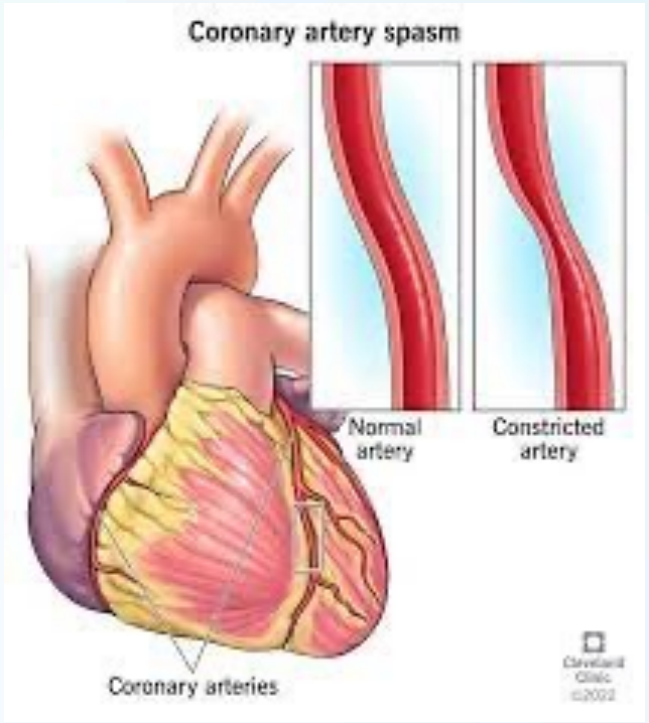


Step III: vasomotor function

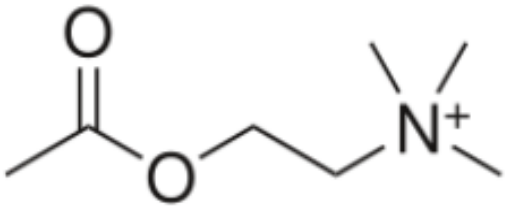
Up to three quarter of ANOCA patients exhibits identifiable disorders of coronary vasomotion, including epicardial or microcirculation vasospasm.



Vasospastic angina (VSA) is the clinical manifestation of myocardial ischaemia caused by dynamic epicardial coronary obstruction caused by a vasomotor disorder.

Intracoronary acetylcholine to evaluate epicardial spasm and/or microcirculatory spasm

Acetylcholine (Ach) causes:

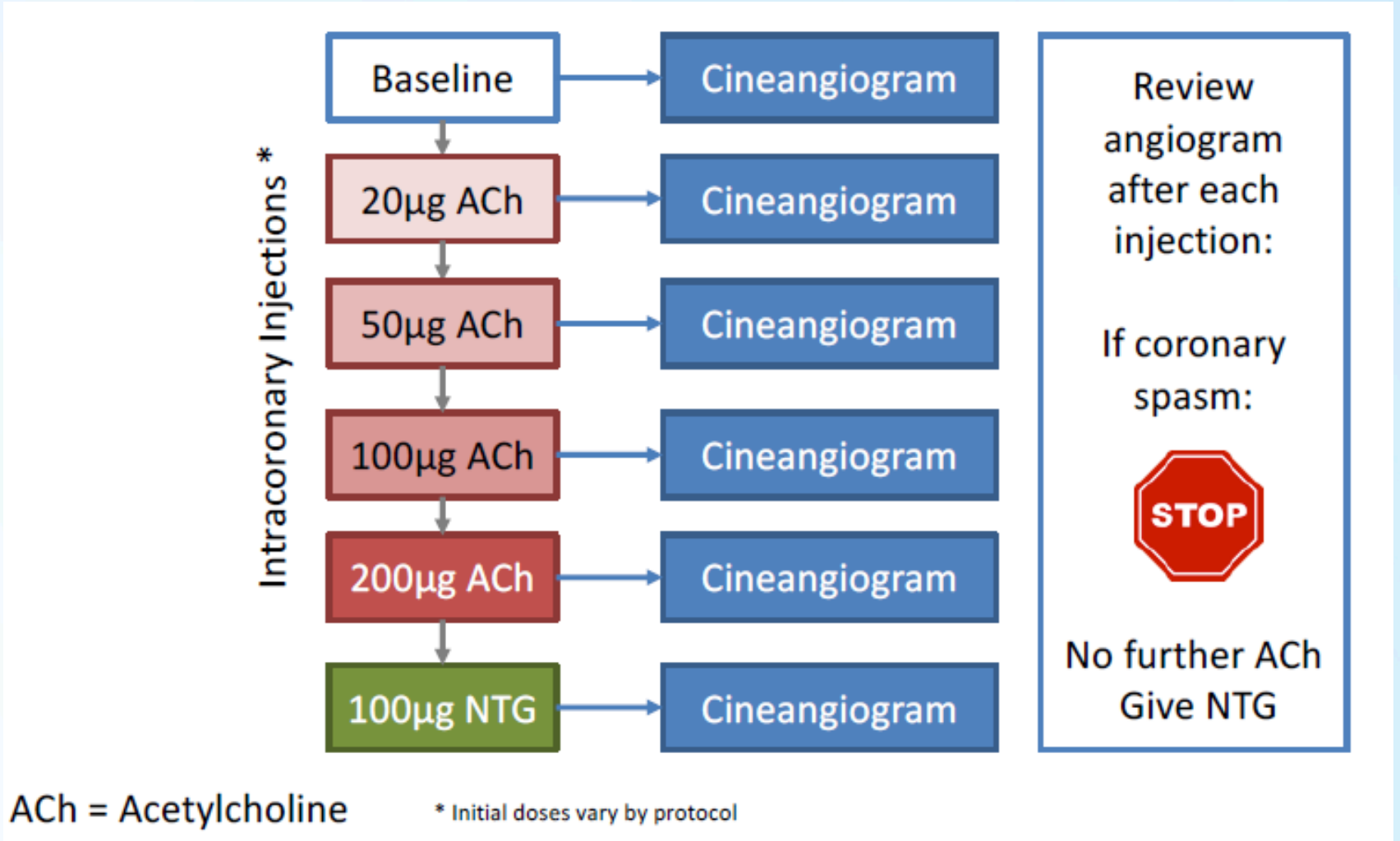


- Endothelial ***nitric oxide-mediated vasodilatation***
- Vascular smooth muscle ***vasoconstriction***

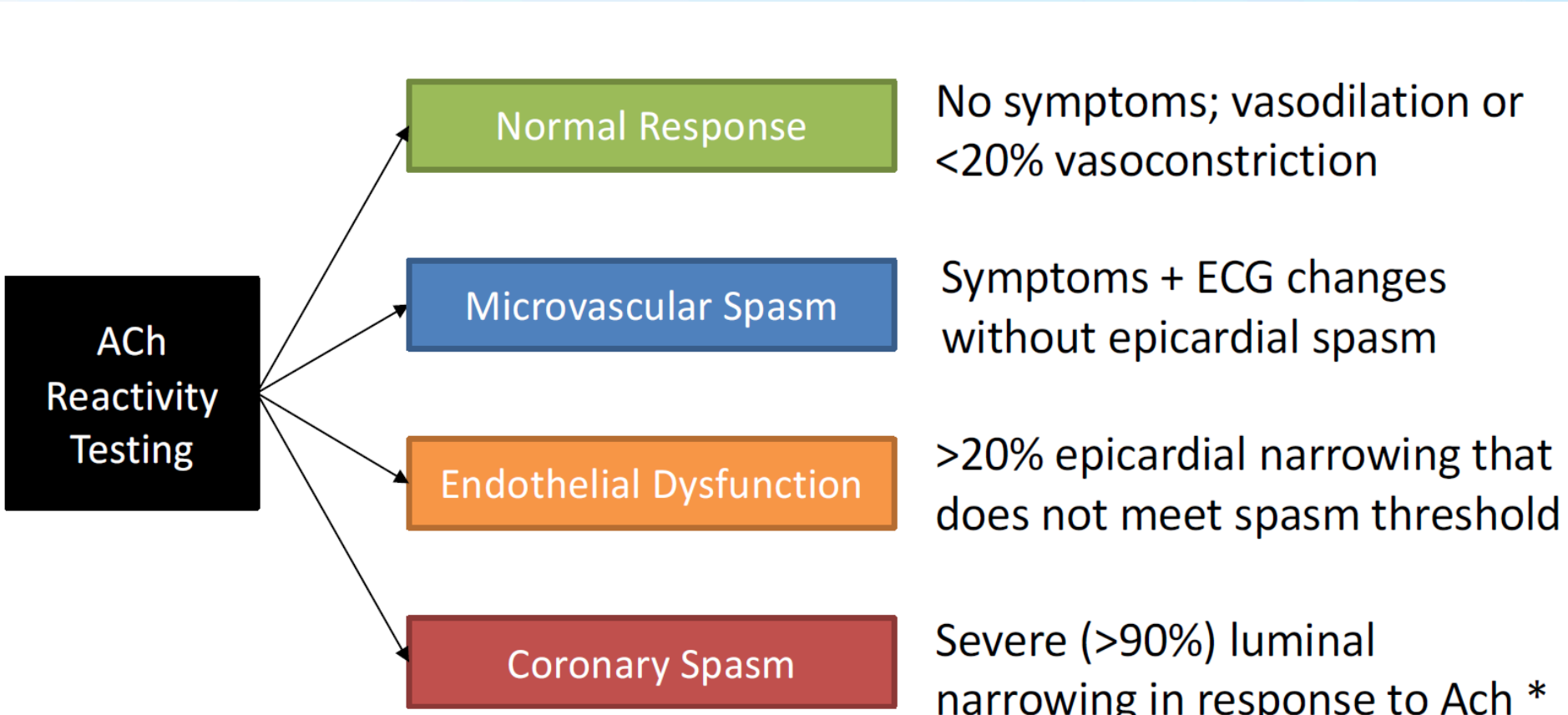
Response depends on integrity of the endothelium:

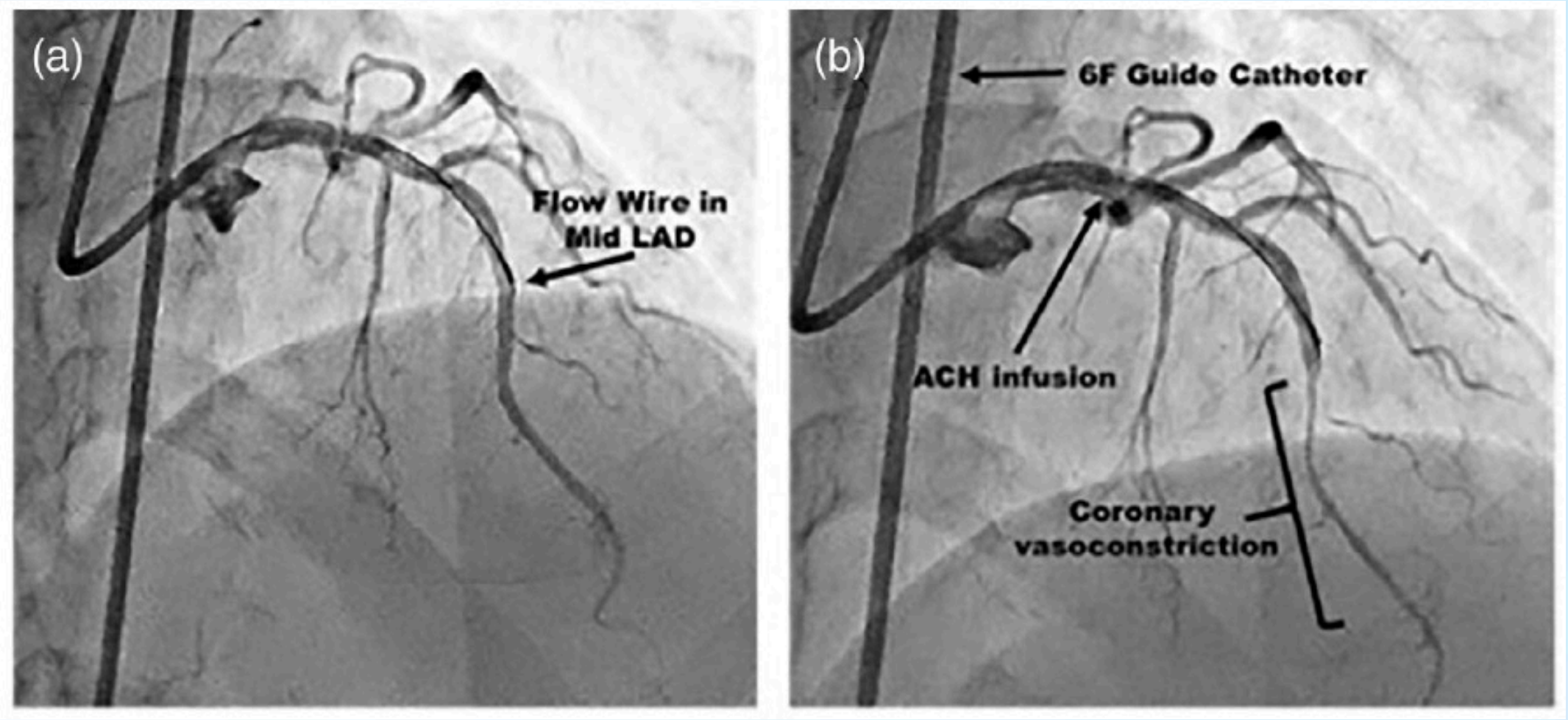
Normal response is either vasodilatation or mild vasoconstriction (≤ 20% diameter narrowing)

Coronary reactivity testing: escalating acetylcholine doses



Interpretation of intracoronary acetylcholine




(a)
Flow Wire in
Mid LAD
(b)
6F Guide Catheter
ACH infusion
Coronary
vasoconstriction

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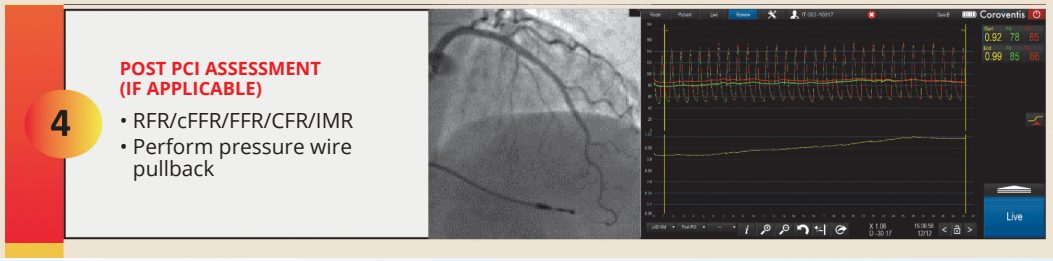
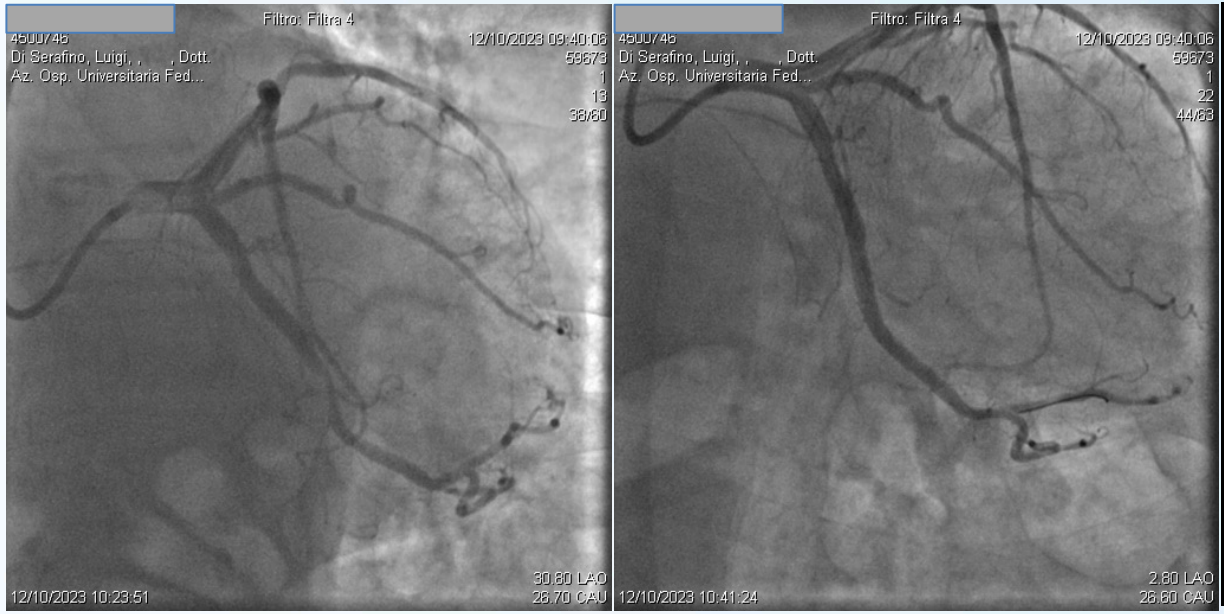
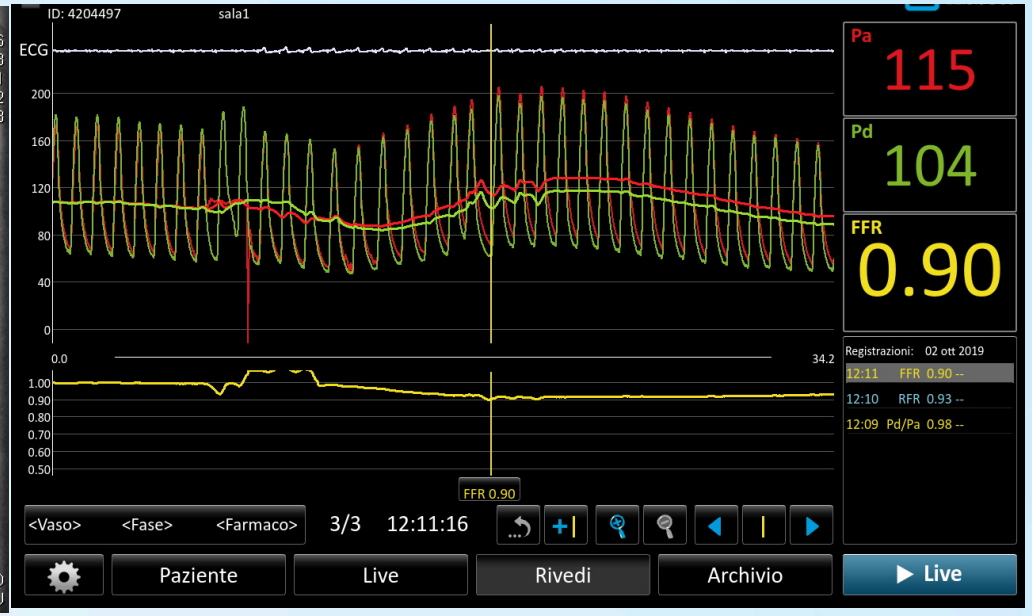


Step IV: Post PCI Assessment

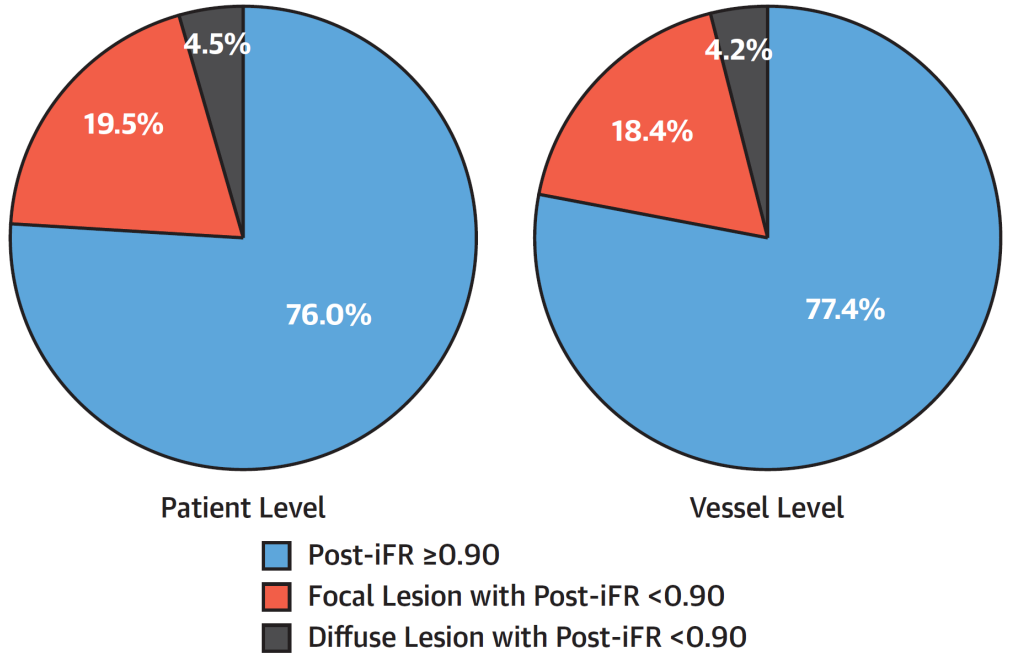
In vessels treated with PCI, it is important to repeat the functional assessment. Pressure wire pullback may highlight residual focal drop inside and/or outside the stent.





Over the last decade, criticism concerning the use of angiography alone to guide revascularisation decisions has been extended to the decision of when an optimal functional result of the intervention has been achieved.

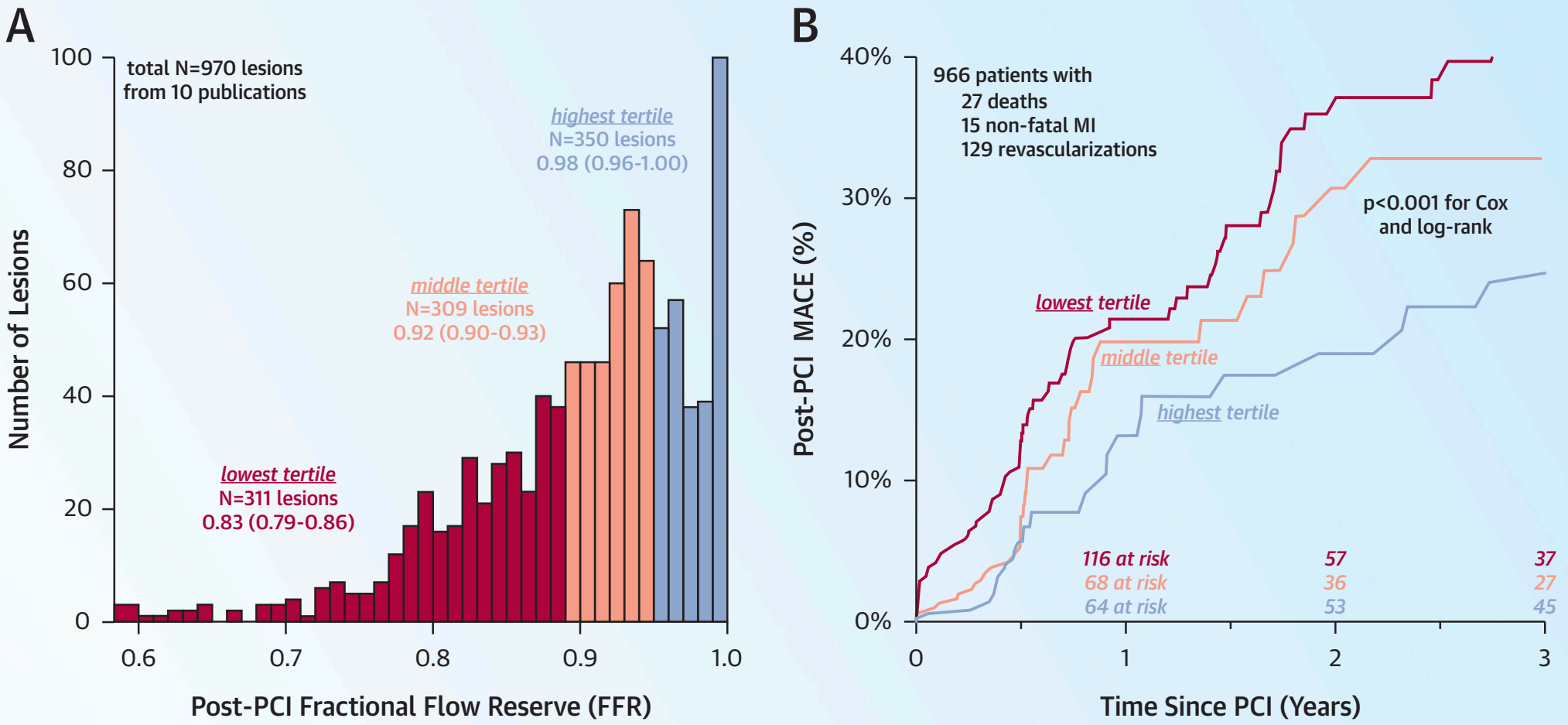
CENTRAL ILLUSTRATION Post-Percutaneous Coronary Intervention Coronary Physiology



Jeremias, A. et al. J Am Coll Cardiol Intv. 2019;12(20):1991-2001.

Percentage of vessels with post-percutaneous coronary intervention (PCI) ischemia, defined as an instantaneous wave-free ratio (iFR) of <0.90 on patient level **(left)** and vessel level **(right)** after angiographically successful procedure. A total of 24% of patients and 22.6% of vessels had residual ischemia. The majority of vessels with iFR <0.90 contained focal lesions versus diffuse disease, potentially amendable to further optimization with additional PCI.

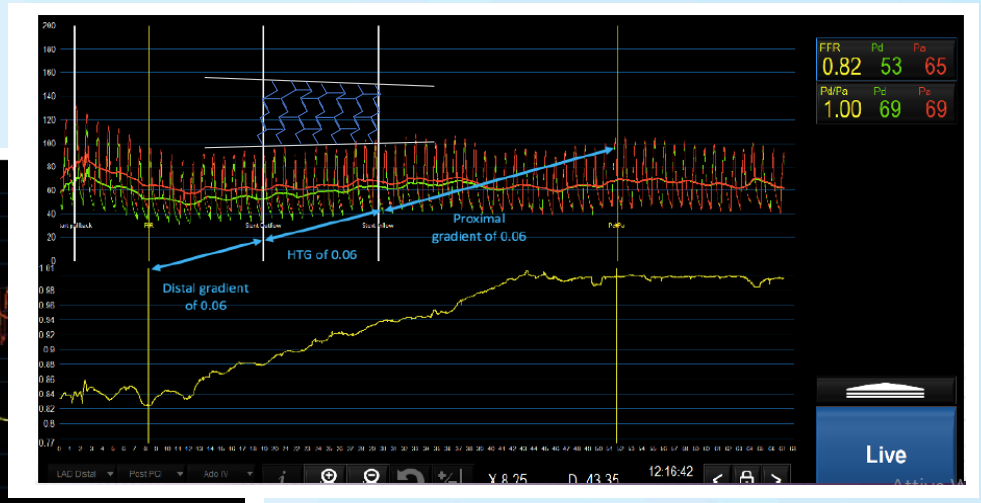
The DEFINE PCI Study Jeremias A. et al. J Am Coll Cardiol Intv 2019;12:1991–2001



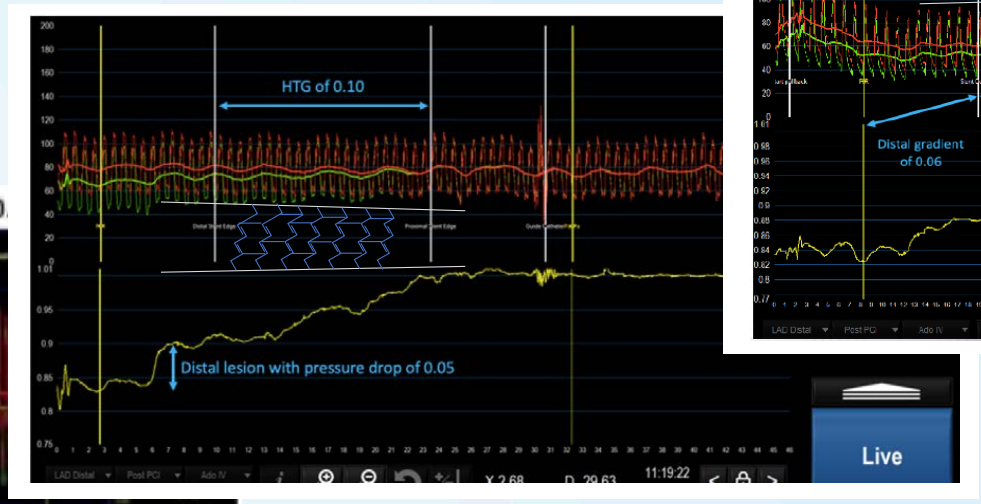
Johnson N.P. et al. J Am Coll Cardiol. 2014 Oct 21;64(16):1641-54.

Reasons for a suboptimal post-PCI FFR

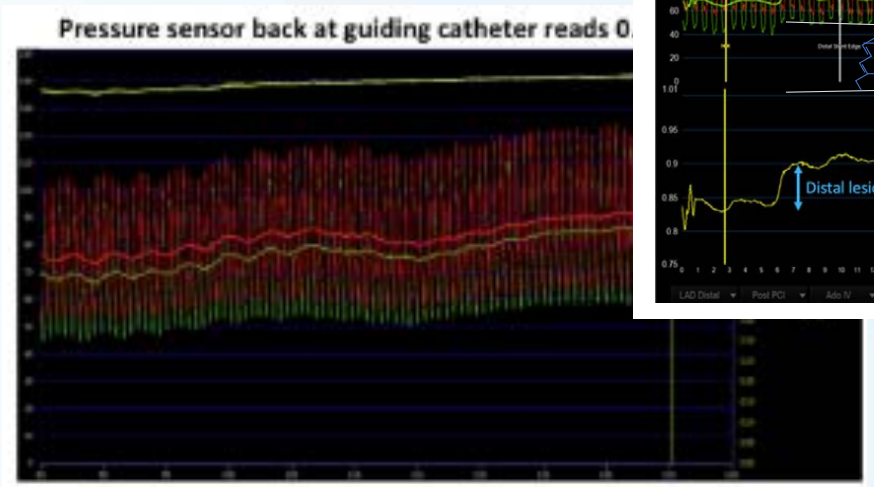
Diffuse Disease



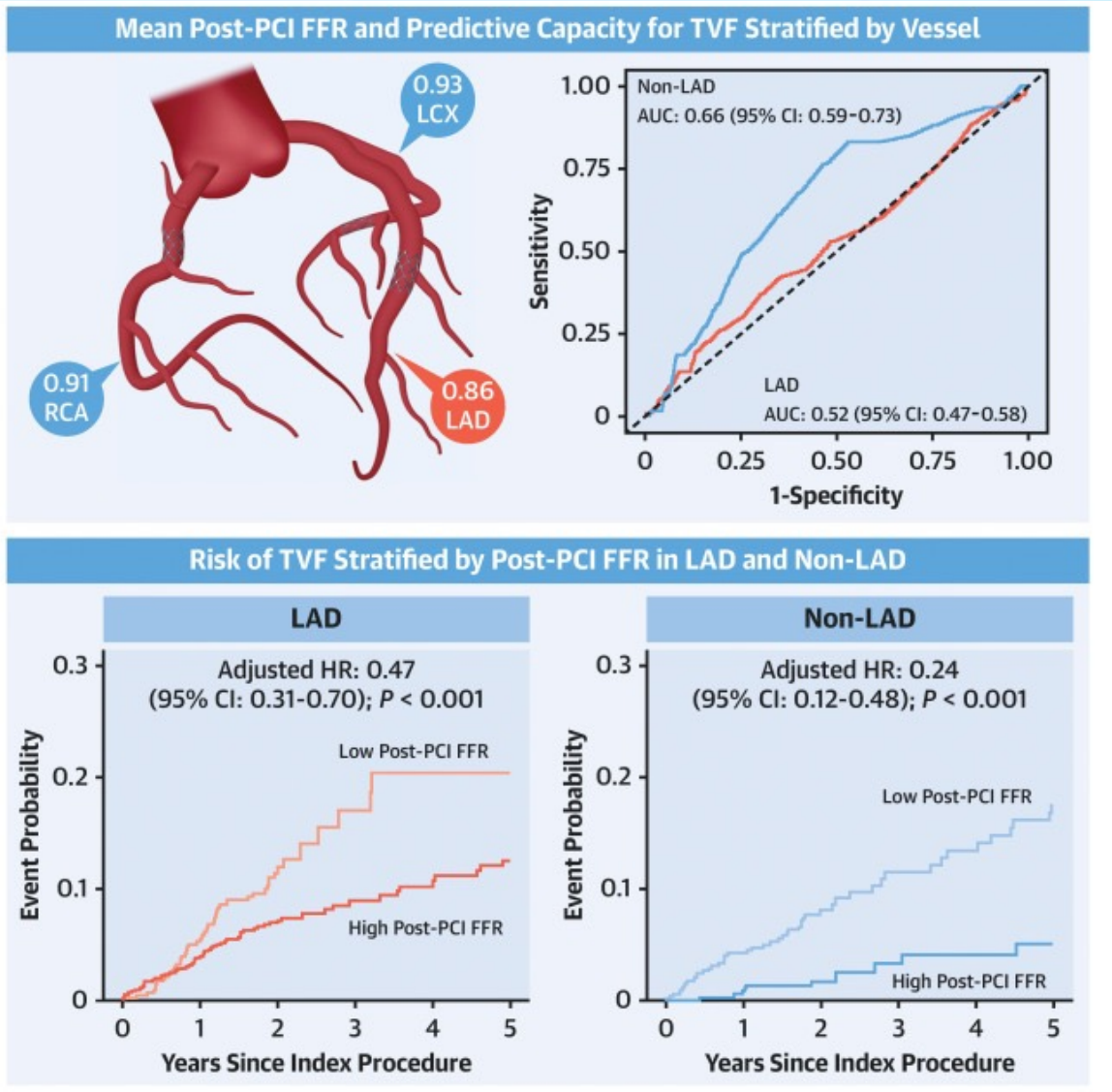
In-Stent +/- Focal Distal Stenosis



Pressure Drift



The LAD is associated with a lower post-PCI FFR than non-LAD arteries, emphasizing the importance of interpreting post-PCI FFR on a vessel-specific basis.



Collet C, et al. ACC Cardiovasc Interv. 2023 Oct 9;16(19):2396-2408.

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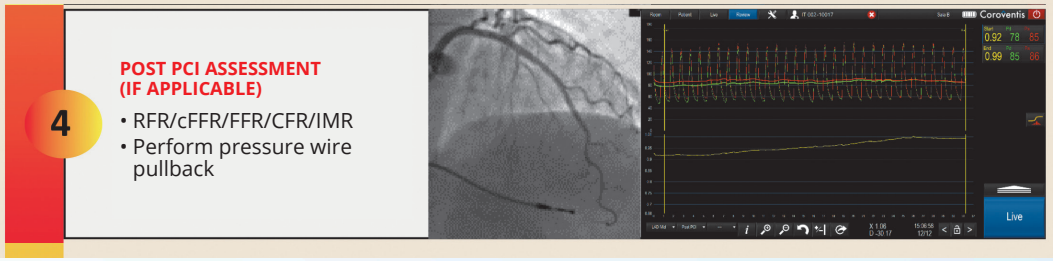
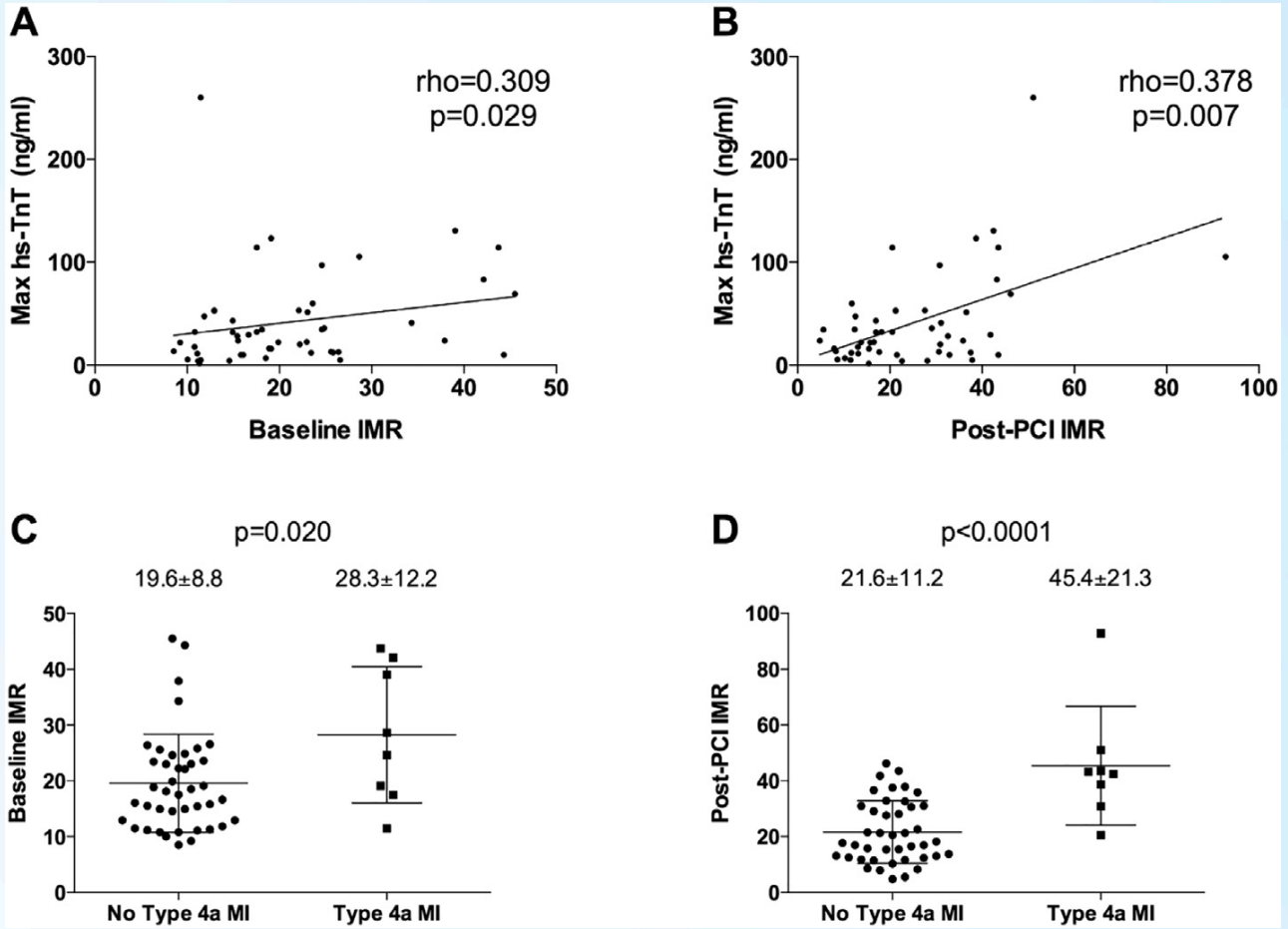


Step IV: Post PCI Assessment

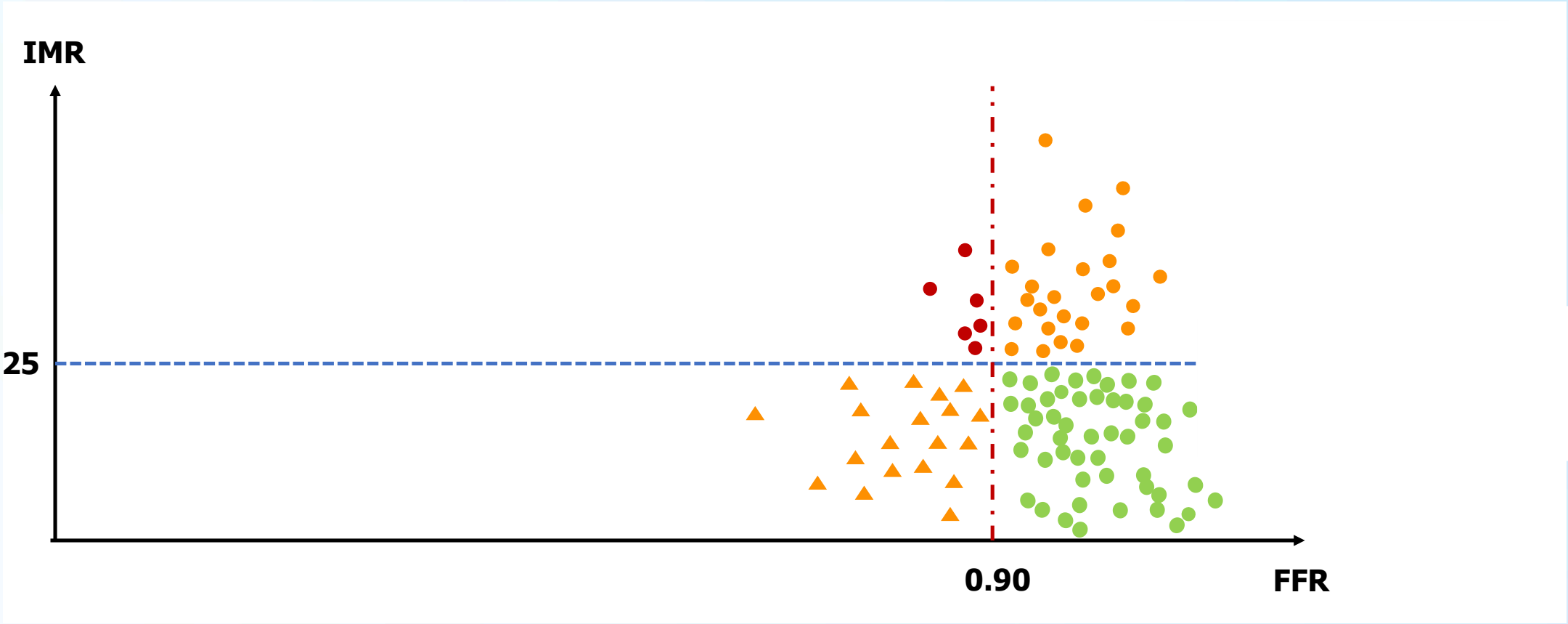
Patients with positive post-PCI FFR values are at higher risk of target vessel failure, whereas those with positive post-PCI IMR values may experience residual angina.

Pre- and post-PCI microcirculation assessment could provide a more complete picture of the physiological findings and contribute to better risk stratification for cardiovascular events of patients undergoing revascularization



Dynamic changes of microvascular resistance are strongly associated with the PCI-related myocardial injury and post-PCI IMR is a strong predictor of type 4a MI in patients with stable CAD undergoing elective PCI.

Mangiacapra F. et al. International Journal of Cardiology 306 (2020) 42–46



Adapted from Serruys PW, JACC Cardiovasc Interv. 2022;15:2519-2522

The optimal treatment of patients requires a complete diagnostic workflow in the cath-lab

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Thank You

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