

William Fulton, MD thesis, University of Glasgow 1963

# The #FullPhysiology journey: Past, Present and Future

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Roma*



# Potential conflicts of interest

**Speaker's name: Antonio Maria Leone**

**I have the following potential conflicts of interest to report:**

Dr. A.M. Leone is an advisor for Abbott Vascular and received speaking honoraria from Abbott Vascular, Medtronic, Menarini, Bayer, Daichii Sankyo and Bruno Farmaceutici.

All contents provided by Dr. Leone unless otherwise noted



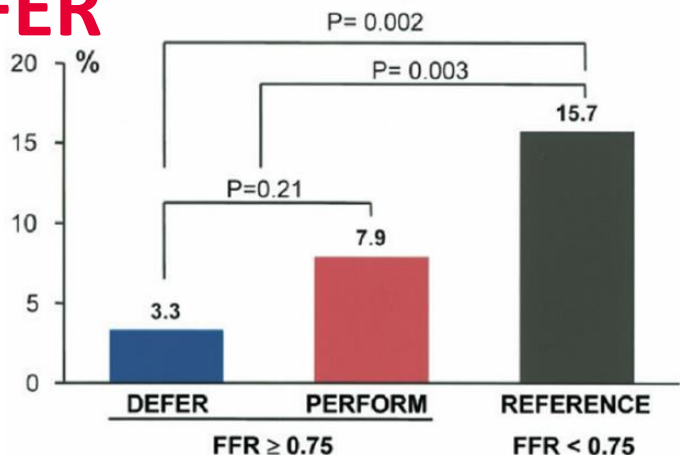
# Past



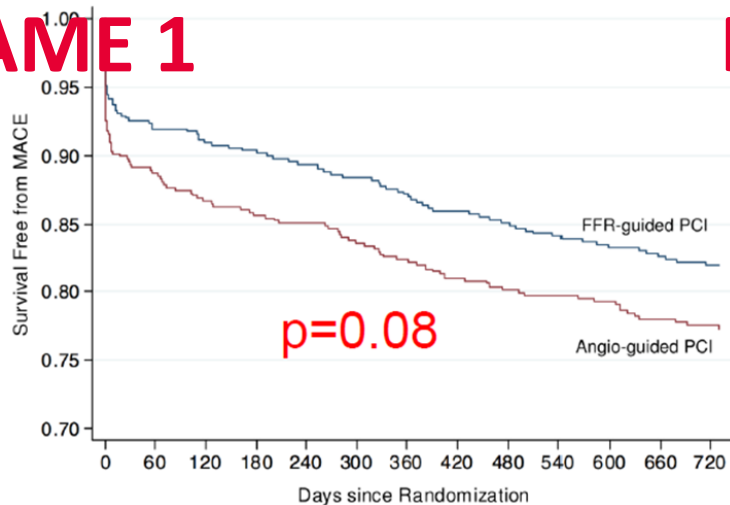
# What ICs know about invasive physiology

**DEFER**

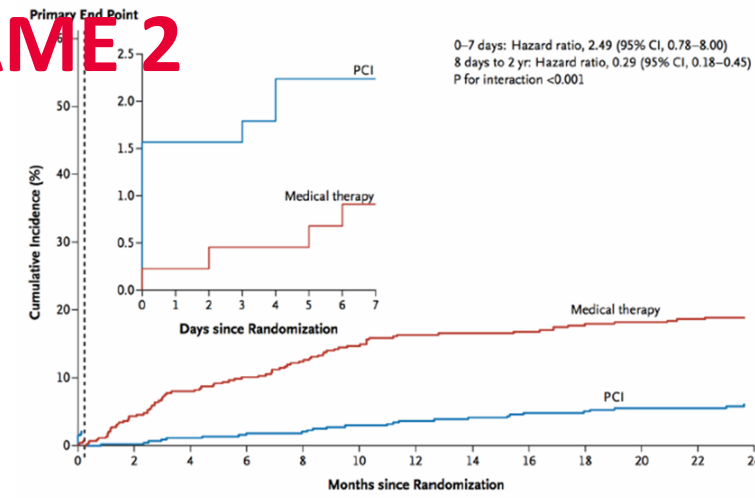
Cardiac Death and Acute MI after 5 Years



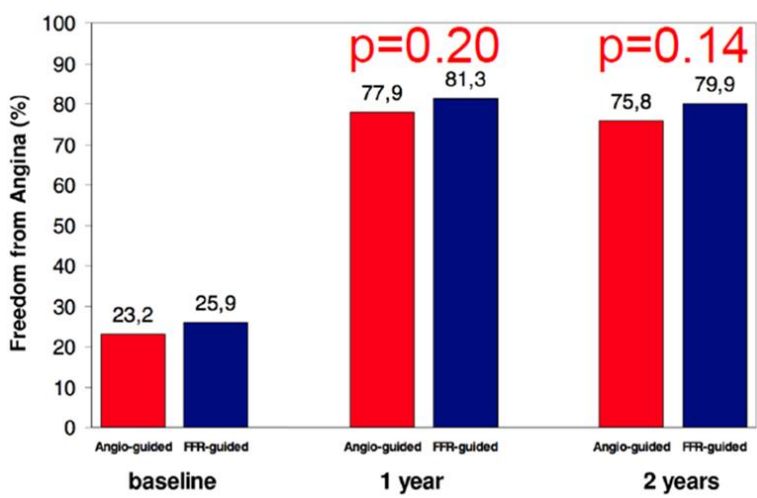
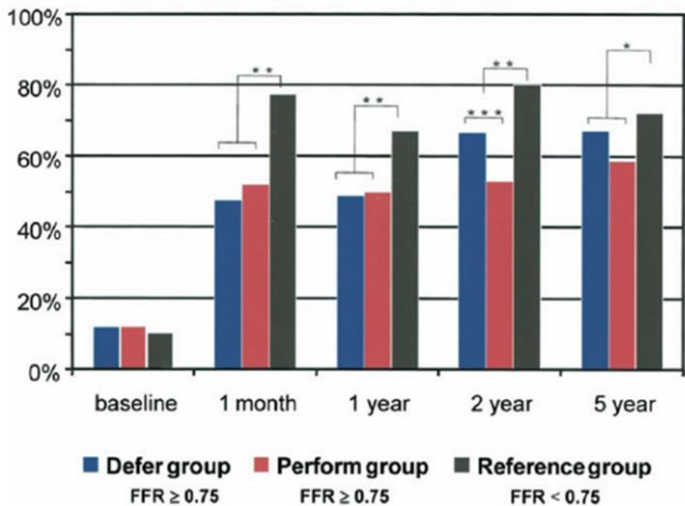
**FAME 1**



**FAME 2**



% Patients Free from Chest Pain

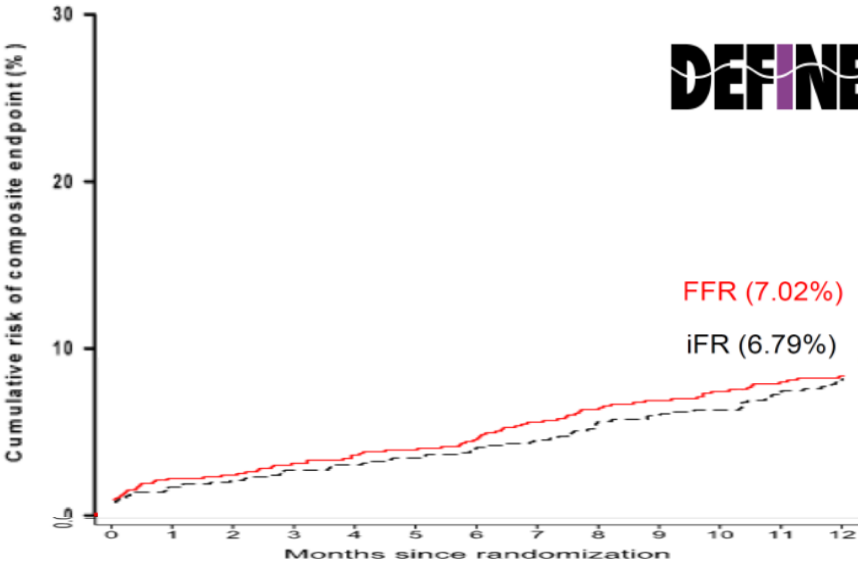


Time Point	Treatment	No CCS I-IV / No total	Randomised trial		Randomised trial compared to registry	
			RR (95% CI)	P value	RR (95% CI)	P value
Baseline	PCI+MT	314/447	1.04 (0.95-1.13)	0.42	1.09 (0.96-1.24)	0.17
	MT alone	298/440	1.00 (reference)		1.05 (0.92-1.20)	0.45
	Registry	107/166			1.00 (reference)	
30 Days	PCI+MT	45/441	0.36 (0.26-0.49)	<0.001	0.66 (0.42-1.04)	0.08
	MT alone	123/431	1.00 (reference)		1.85 (1.25-2.73)	0.001
	Registry	25/162			1.00 (reference)	
6 Months	PCI+MT	33/440	0.41 (0.28-0.60)	<0.001	0.47 (0.29-0.76)	0.002
	MT alone	80/434	1.00 (reference)		1.16 (0.77-1.73)	0.48
	Registry	26/183			1.00 (reference)	
12 Months	PCI+MT	26/437	0.39 (0.25-0.61)	<0.001	0.38 (0.23-0.64)	<0.001
	MT alone	65/429	1.00 (reference)		0.96 (0.63-1.47)	0.86
	Registry	25/159			1.00 (reference)	
24 Months	PCI+MT	25/425	0.49 (0.31-0.77)	0.002	0.40 (0.23-0.69)	0.001
	MT alone	51/424	1.00 (reference)		0.82 (0.52-1.30)	0.40
	Registry	23/157			1.00 (reference)	

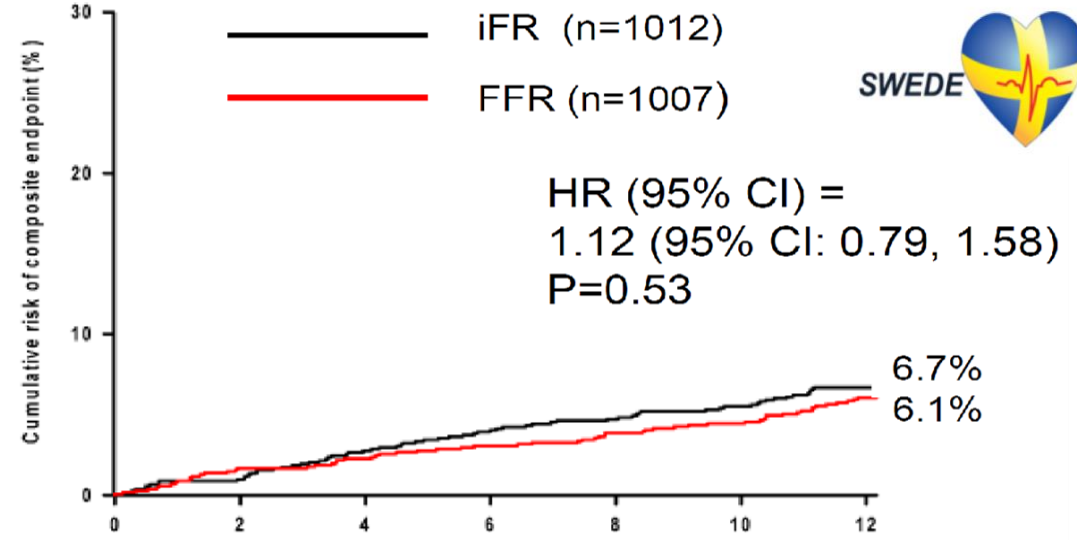


# What ICs know about invasive physiology

**DEFINE FLAIR**



Variable	iFR Group (N=1242)	FFR Group (N=1250)	P Value†
Radial-artery approach — no. of patients (%)	896 (72.1)	888 (71.0)	0.54
Procedure time — min			
Median	40.5	45.0	0.001
Functionally significant lesions — no. (% of total vessels evaluated)‡	451 (28.6)	557 (34.6)	0.004
≥1 Functionally significant lesions present — no. of patients (%)§	426 (34.3)	486 (38.9)	0.02
Mean iFR	0.91±0.09	NA	
Mean FFR	NA	0.83±0.09	
Percent of lesions within the FFR range			
<0.60	NA	1.96	
0.60–0.90	NA	75.08	
>0.90	NA	22.96	
Revascularization performed — no. of patients (%)			
Total	590 (47.5)	667 (53.4)	0.003
CABG	25 (2.0)	42 (3.4)	0.04
PCI	565 (45.5)	625 (50.0)	0.02
Stents placed — no. (% of total stents placed)			
Total	822 (100)	906 (100)	0.86
Drug-eluting stent	811 (98.7)	893 (98.6)	
Bioresorbable vascular scaffold	11 (1.3)	13 (1.4)	
No. of stents placed per patient	0.66±0.92	0.72±0.96	0.09

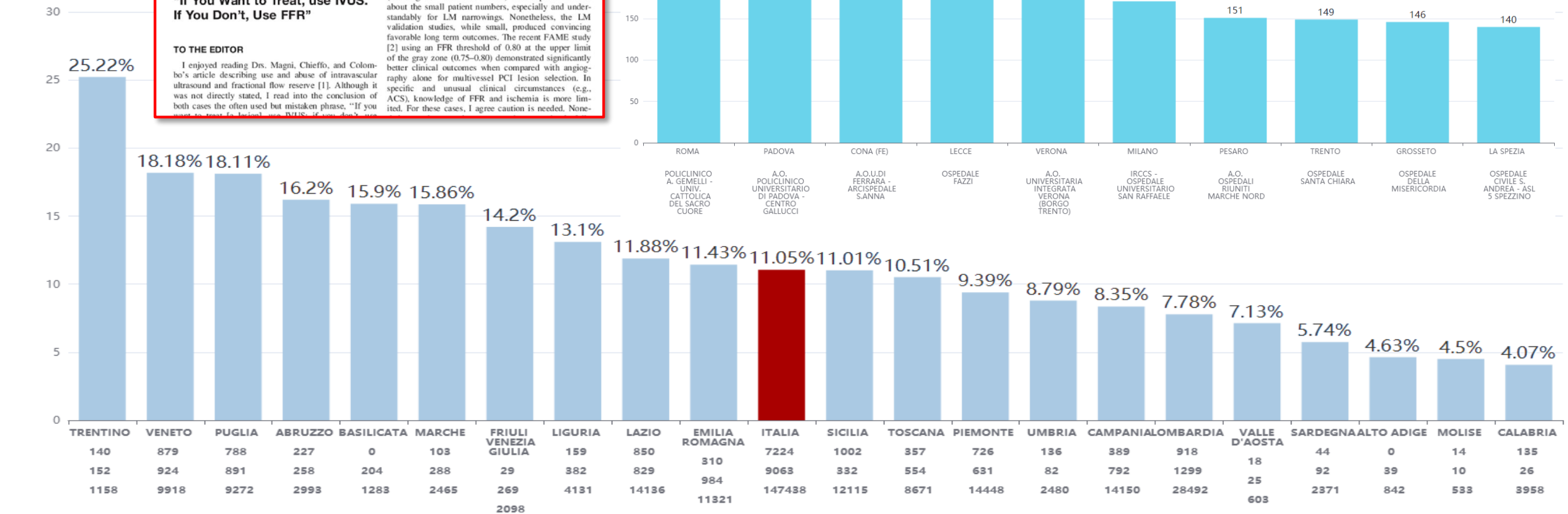


Characteristic	iFR Group (N=1012)	FFR Group (N=1007)	P Value
Procedure time — min†			0.09
Median	50.8	53.1	
Interquartile range	13.8–87.8	18.1–88.1	
Fluoroscopy time — min			0.57
Median	10.5	10.2	
Interquartile range	6.3–16.8	6.5–16.0	
Intravenous adenosine administered — no. of patients (%)	NA	695 (69.0)	
Total no. of lesions evaluated	1568	1436	
No. of lesions evaluated per patient	1.55±0.86	1.43±0.70	0.002
Hemodynamically important lesions — no. (% of total lesions evaluated)‡	457 (29.1)	528 (36.8)	<0.001
No. of hemodynamically important lesions per patient‡	0.45±0.71	0.52±0.68	0.05
Mean iFR	0.91±0.10	NA	
Mean iFR in hemodynamically important lesions‡	0.80±0.13	NA	
Mean FFR	NA	0.82±0.10	
Mean FFR in hemodynamically important lesions‡	NA	0.72±0.08	
Total no. of stents placed	698	787	
No. of stents placed per patient undergoing PCI	1.58±1.08	1.73±1.19	0.05
CABG as primary revascularization procedure — no. of patients (%)	93 (9.2)	113 (11.2)	0.13
Revascularization performed — no. of patients (%)	536 (53.0)	569 (56.5)	0.11



# How ICs translate invasive physiology in practice

2021



**Catheterization and Cardiovascular Interventions 74:811-813 (2009)**

**Letter to the Editor**

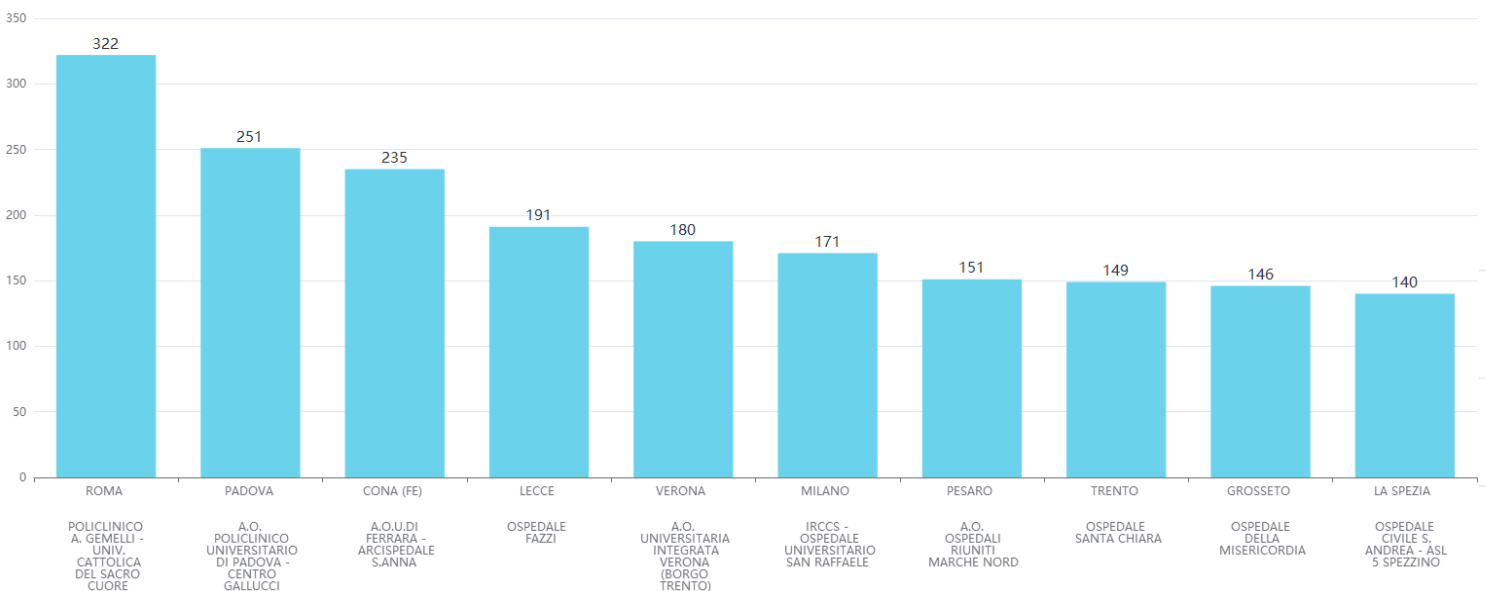
**Use and Abuse of IVUS and FFR by Magni V et al. or Why You Shouldn't Believe The Saying, "If You Want to Treat, use IVUS. If You Don't, Use FFR"**

**TO THE EDITOR**

I enjoyed reading Drs. Magni, Chieffo, and Colombo's article describing use and abuse of intravascular ultrasound and fractional flow reserve [1]. Although it was not directly stated, I read into the conclusion of both cases the often used but mistaken phrase, "If you want to treat, use IVUS; if you don't use IVUS, use FFR."

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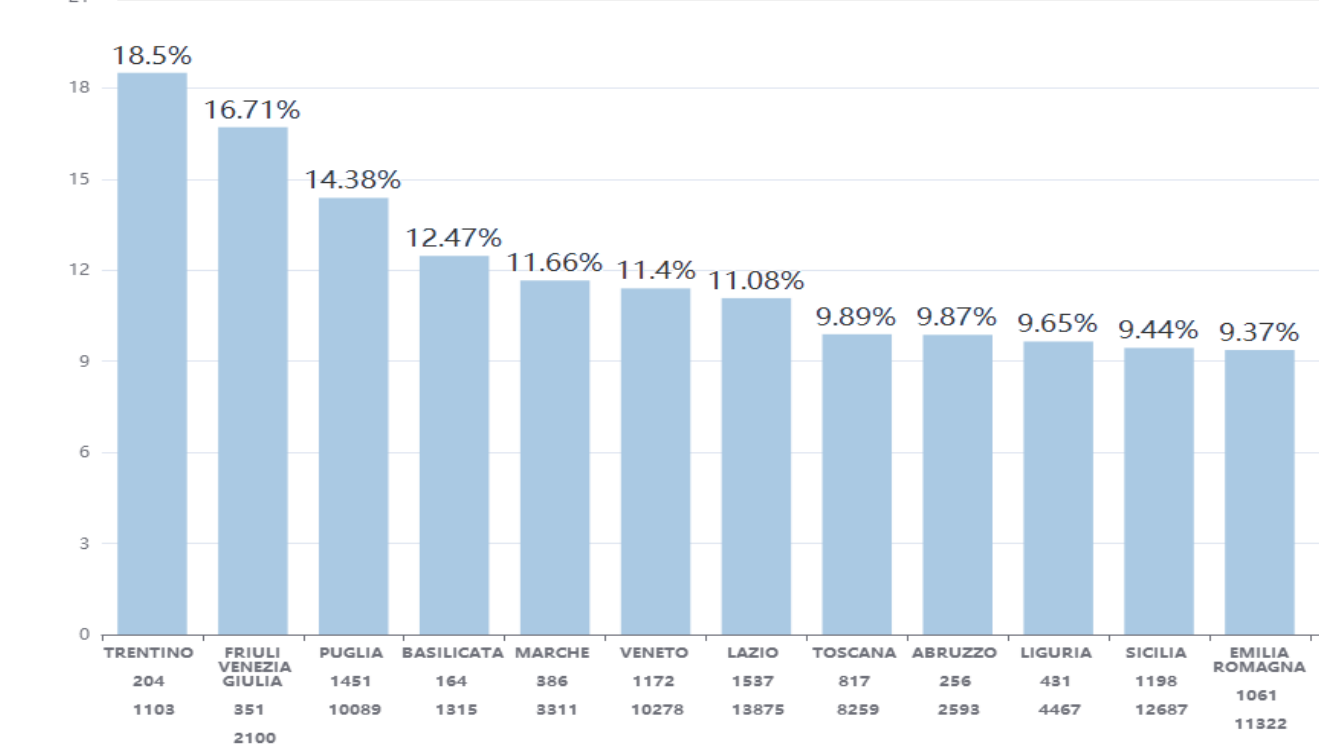
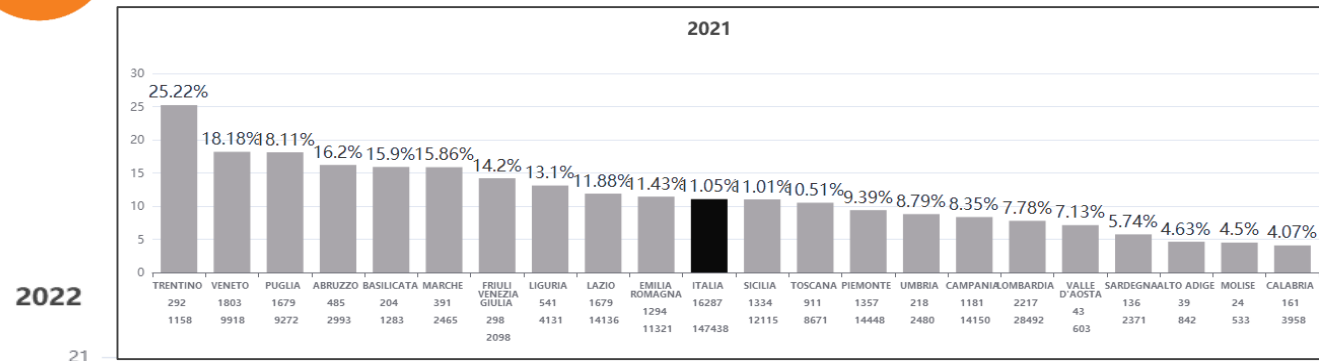
On review of the FFR and IVUS ischemic thresholds, Magni et al. summarize five selected FFR studies (omitting 15 additional studies) and express concern about the small patient numbers, especially and understandably for LM narrowings. Nonetheless, the LM validation studies, while small, produced convincing favorable long term outcomes. The recent FAME study [2] using an FFR threshold of 0.80 at the upper limit of the gray zone (0.75-0.80) demonstrated significantly better clinical outcomes when compared with angiography alone for multivessel PCI lesion selection. In specific and unusual clinical circumstances (e.g., ACS), knowledge of FFR and ischemia is more limited. For these cases, I agree caution is needed. None-



$$\frac{\text{Invasive Assessment}}{\text{Coronary Angiograms}} = \frac{16.287}{280.604} = 5.8\%$$



# How ICs translate invasive physiology in practice



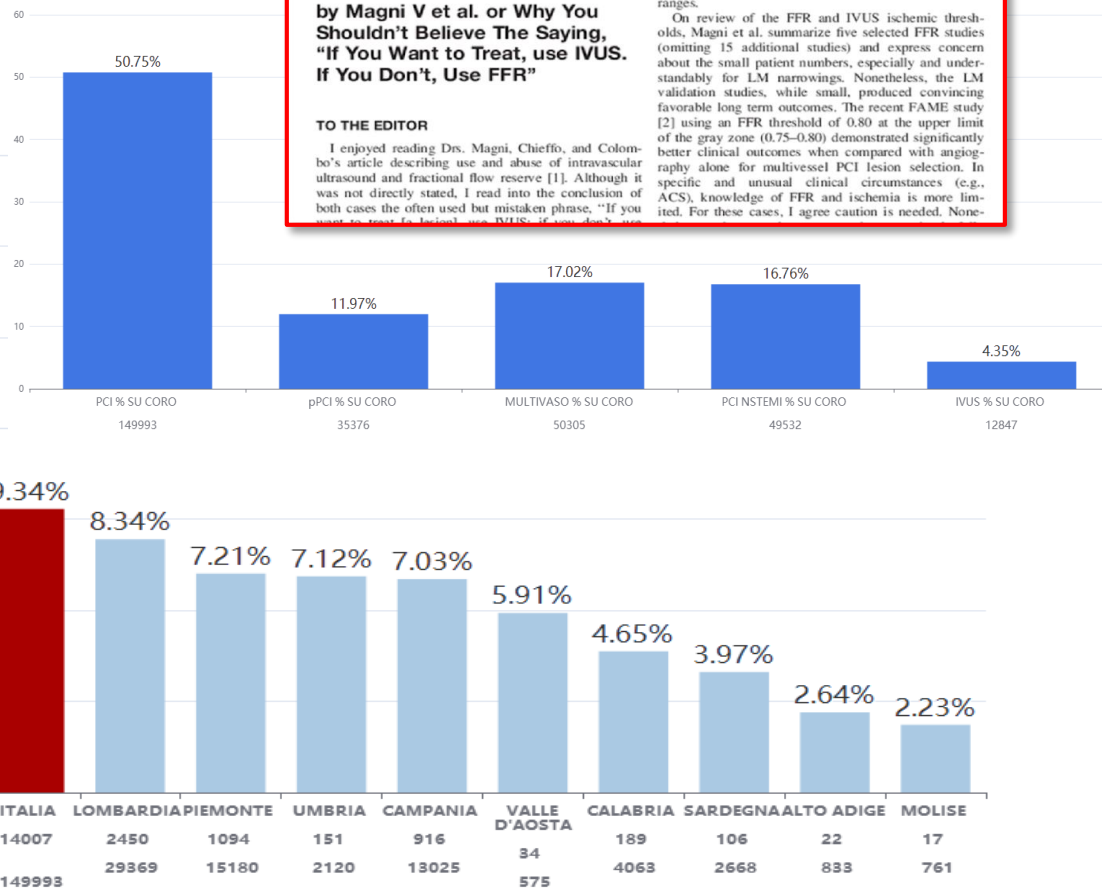
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$$\frac{\text{Invasive Assessment}}{\text{Coronary angiograms}} = \frac{14007}{295576} = 4.7\%$$



# The #FullPhysiology group



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- No Club / «niche»
- Sharing a common language
- Expressing the full potential of physiology in daily practice (case-based approach)



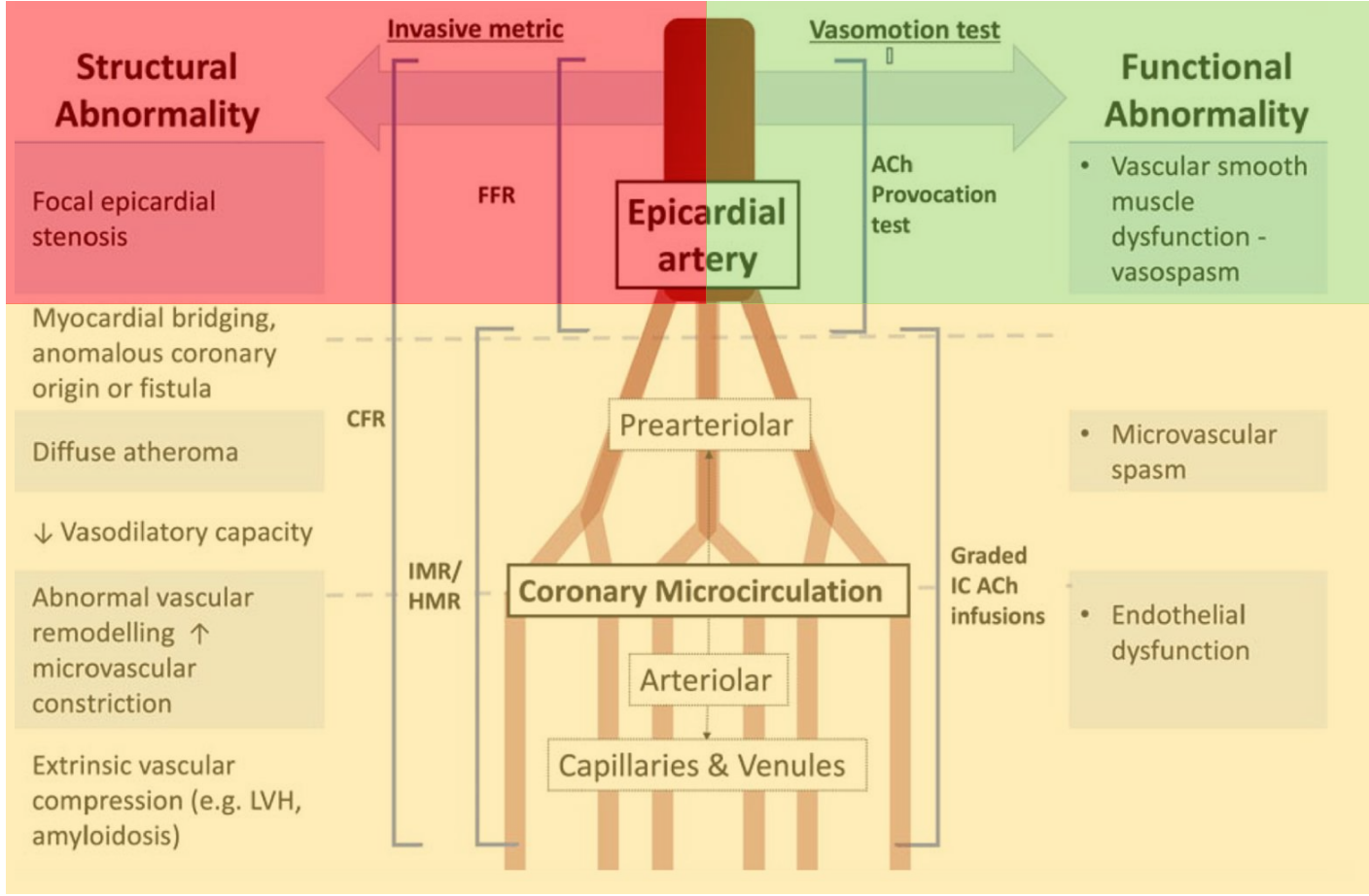
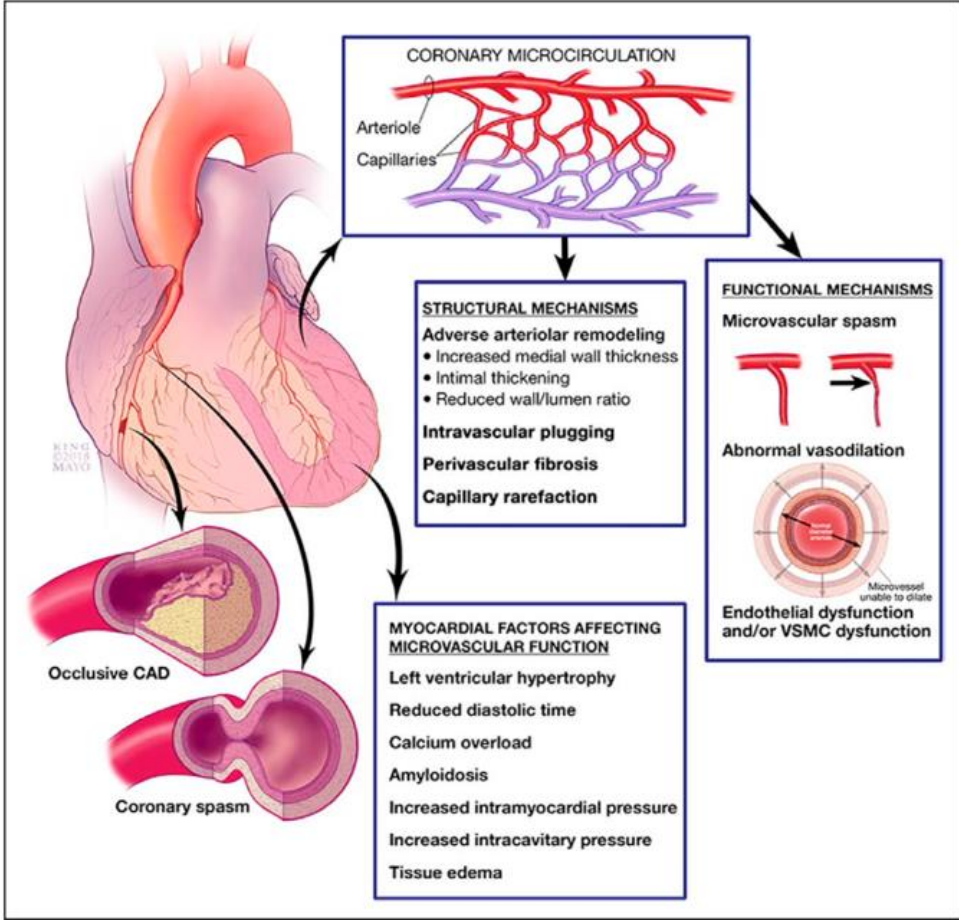


# Coronary circulation as a continuum





# F. Ph. For Structural and Functional abn.



Crea F, et al. *Eur Heart J* 2016;37:1514-6

Courtesy from T. Engstroem



# ESC guidelines for CCS

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<u>Guidewire-based CFR and/or microcirculatory resistance measurements should be considered in patients with persistent symptoms, but coronary arteries that are either angiographically normal or have moderate stenoses with preserved iwFR/FFR.</u> <a href="#">412,413</a>	<b>IIa</b>	<b>B</b>
<u>Intracoronary acetylcholine with ECG monitoring may be considered during angiography, if coronary arteries are either angiographically normal or have moderate stenoses with preserved iwFR/FFR, to assess microvascular vasospasm.</u> <a href="#">412,438–440</a>	<b>IIb</b>	<b>B</b>
Transthoracic Doppler of the LAD, CMR, and PET may be considered for non-invasive assessment of CFR. <a href="#">430–432,441</a>	<b>IIb</b>	<b>B</b>

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
An ECG is recommended during angina if possible.	<b>I</b>	<b>C</b>
Invasive angiography or coronary CTA is recommended in patients with characteristic episodic resting angina and ST-segment changes, which resolve with nitrates and/or calcium antagonists, to determine the extent of underlying coronary disease.	<b>I</b>	<b>C</b>
Ambulatory ST-segment monitoring should be considered to identify ST-segment deviation in the absence of increased heart rate.	<b>IIa</b>	<b>C</b>
<u>An intracoronary provocation test should be considered to identify coronary spasm in patients with normal findings or non-obstructive lesions on coronary arteriography and a clinical picture of coronary spasm, to diagnose the site and mode of spasm.</u> <a href="#">412,414,438–440</a>	<b>IIa</b>	<b>B</b>



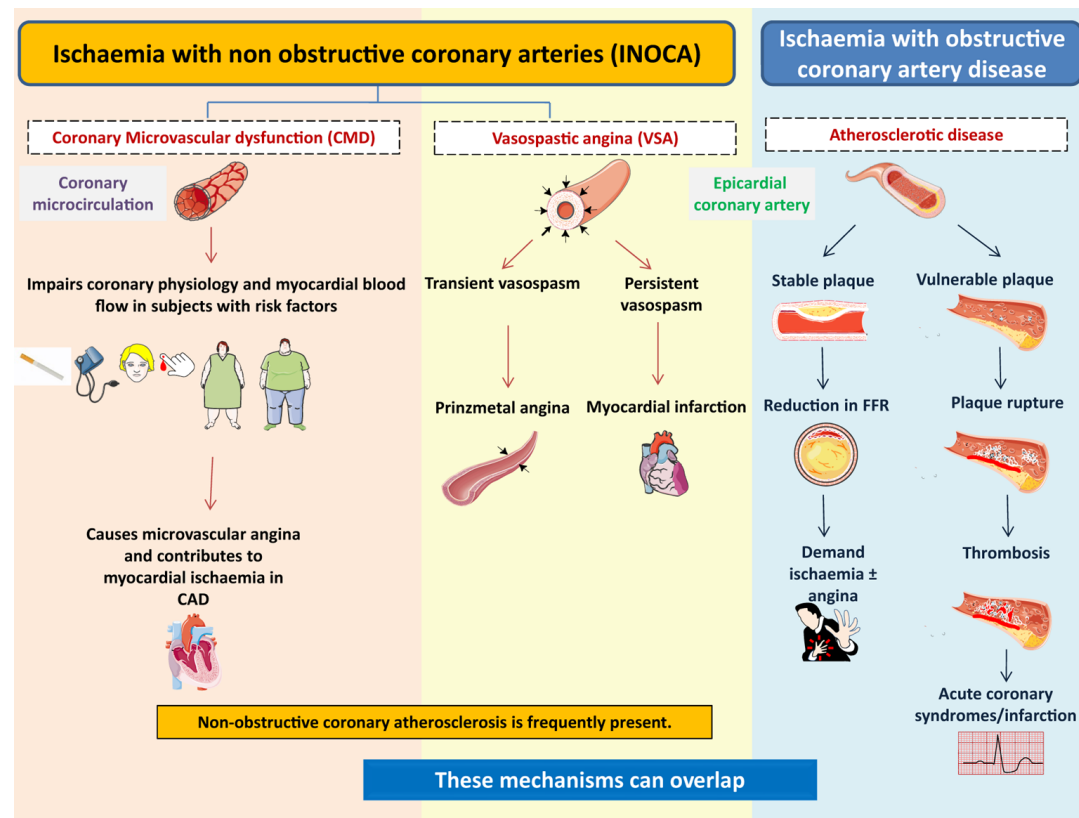
# Terminology: A continuum of Angina Endotypes on CCS

- 1 Obstructive Epicardial CAD**
  - NHPR  $\leq 0.89$  and/or cFFR  $\leq 0.83$  and/or FFR  $\leq 0.80$
- 2 Microvascular angina**
  - Structural: IMR >25**
  - Functional\*: CFR < 2.0 (+ FFR > 0.80 and IMR  $\leq 25$ )**
- 3 Vasospastic angina**

angina + ST changes and >90% epicardial spasm
- 4 Mixed Angina**

combination of 1, 2 and 3
- 5 Non cardiac pain**

exclusion of 1-2-3

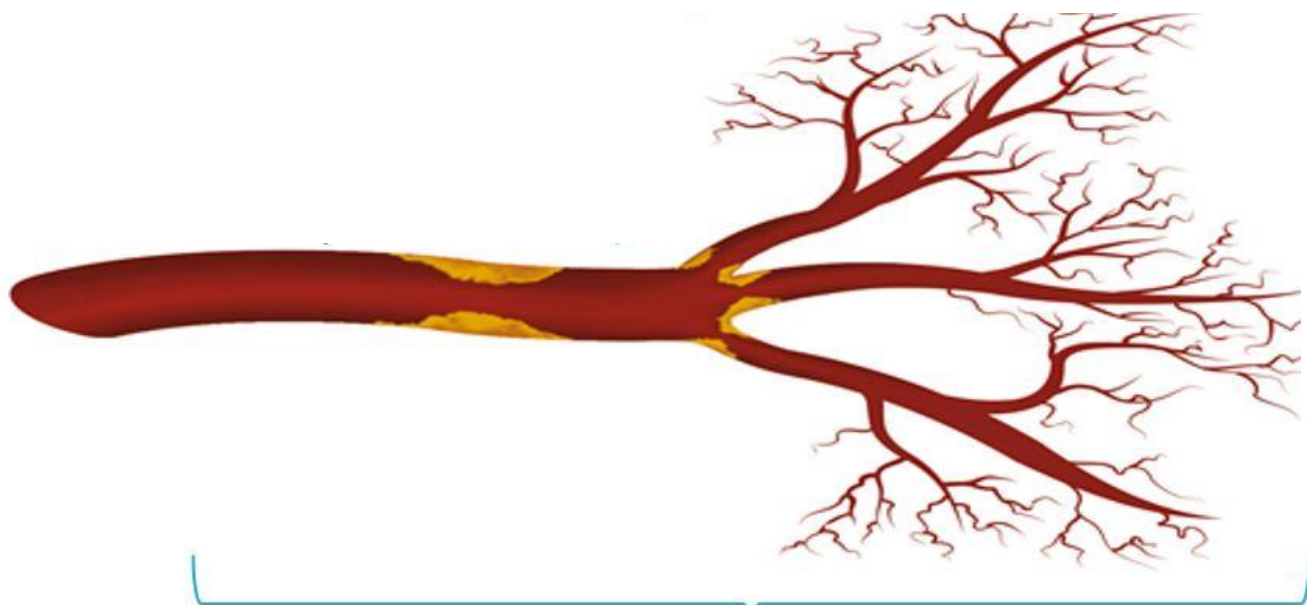


Kunadian EHJ 2020 (mod)

\*+MV spasm: angina + ST changes and no epicardial spasm (+  $\uparrow T_{mn}$ ) by COVADIS definition

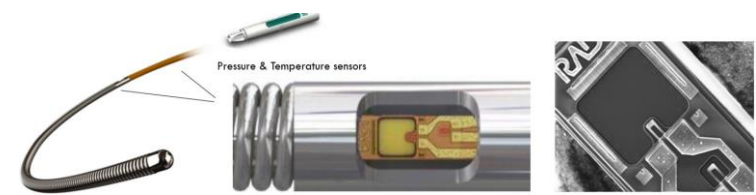
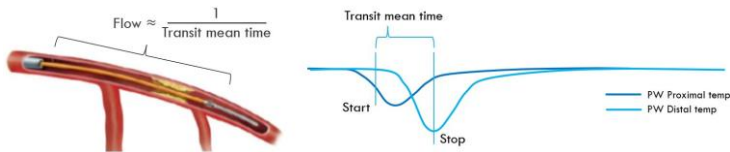


# Different indexes for different compartments?



**CFR** = Flow at rest vs Flow at Hyperemia (au)

Affected by epicardial AND micro-circulatory disease



$$CFR = \frac{\text{Hyperemic Flow}}{\text{basal flow}}$$

$$\text{Flow} \approx 1 / T_{mn} \text{ (mean transit time)}$$

$$CFR = \frac{1 / hT_{mn}}{1 / rT_{mn}}$$

$$CFR = \frac{rT_{mn}}{hT_{mn}}$$

Pathological value < 2.0

Nico H.J. Pijls, *Circulation*. 2001;104:2003-2006  
Fearon et al. *Circulation*. 2003;107:3129-3132



# Our Ado and Ach protocols

## Adenosine 140 mcg/Kg/min

X vials (see below) of Adenosine diluted in 60 ml di NaCl 0.9% and infused in 2'

Weight	Adenosine vials
60 Kg	2.8 vials
70 Kg	3.3 vials
80 Kg	3.7 vials
90 Kg	4.2 vials
100 Kg	4.7 vials

## Acetilcholine

- 1 vial of Miovisin 20mg/2ml diluted in 100 ml of NaCl 0.9%
- 1 ml of this solution (200 mcg/ml) diluted with 19 ml of 0.9% NaCl = 20 ml of 10 mcg/ml Ach (Master solution)
- Take from the Master solution:
  - 2 ml + 18 ml of 0.9% NaCl % (20 mcg)
  - 5ml + 15 ml of 0.9% NaCl % (50 mcg)
  - 10 ml + 10 ml of 0.9% NaCl % (100 mcg)
  - 20 ml (200 mcg)
- infuse manually in the LCA incremental doses oh Ach (20-50-100-200 mg) in 2 minutes (rarely we infuse incremental doses of Ach 20-50-80 mg in the RCA)



GAZZETTA UFFICIALE DELLA REPUBBLICA ITALIANA

AGENZIA ITALIANA DEL FARMACO

DETERMINA 28 luglio 2022

Inserimento del medicinale Acetilcolina cloruro nell'elenco dei medicinali erogabili a totale carico del Servizio sanitario nazionale, ai sensi della legge 23 dicembre 1996, n. 648, come test farmacologico per la valutazione della funzione vascolare coronarica limitatamente all'uso durante le procedure di cateterismo/coronarografia (Allegato 6). (Determina n. 90282). (22A04477) (GU Serie Generale n.182 del 05-08-2022)

di AIFA del 14 luglio 2022 n. 30 - punto n. 1;

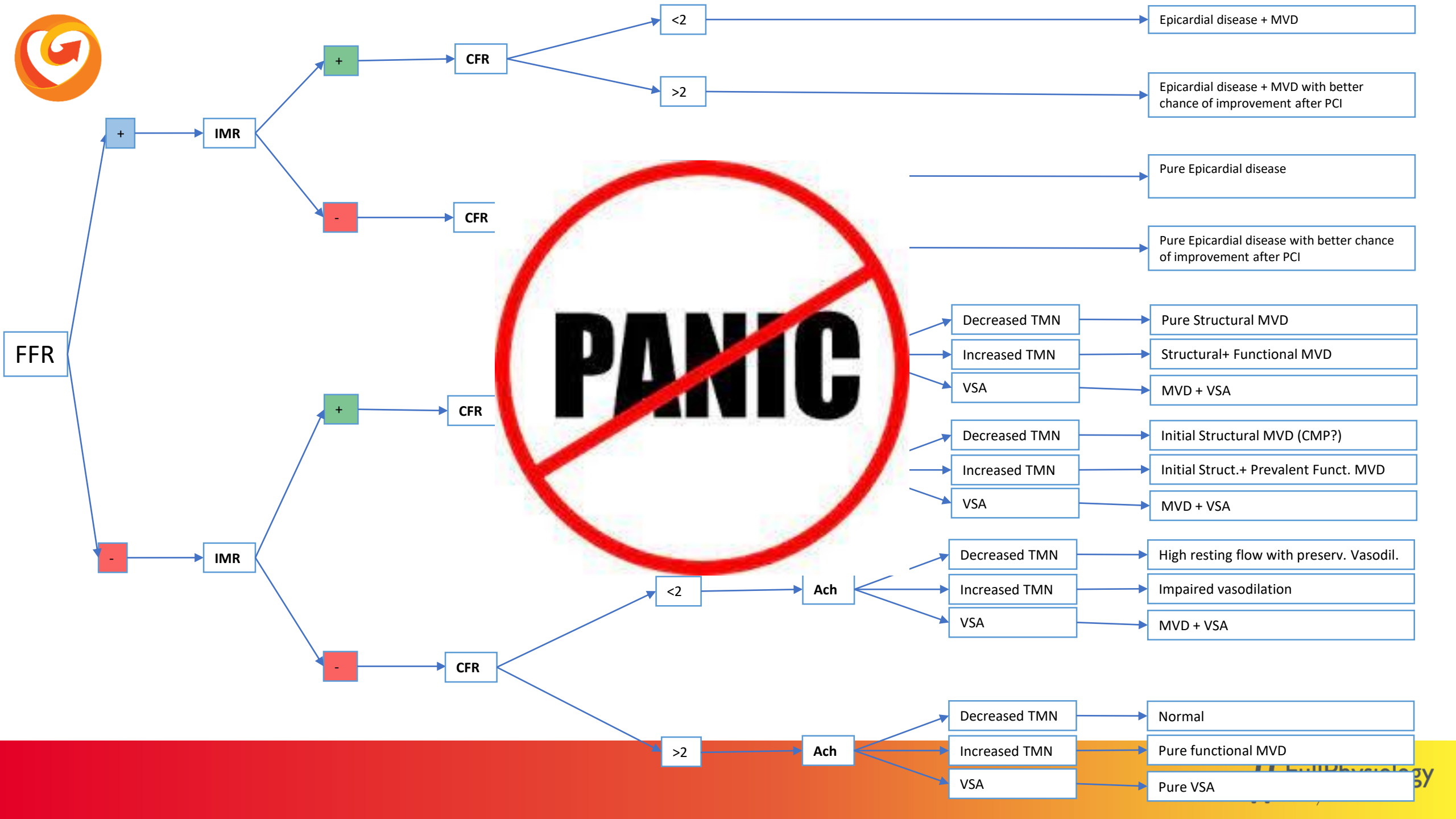
Ritenuto, pertanto, di includere il medicinale Acetilcolina cloruro nell'elenco dei medicinali erogabili a totale carico del Servizio sanitario nazionale, ai sensi della legge 23 dicembre 1996, n. 648, come test farmacologico per la valutazione della funzione vascolare coronarica limitatamente all'uso durante le procedure di cateterismo/coronarografia;

Determina:

Art. 1

Nell'elenco dei medicinali erogabili a totale carico del Servizio sanitario nazionale, ai sensi della legge 23 dicembre 1996, n. 648,

Approved!





# Present



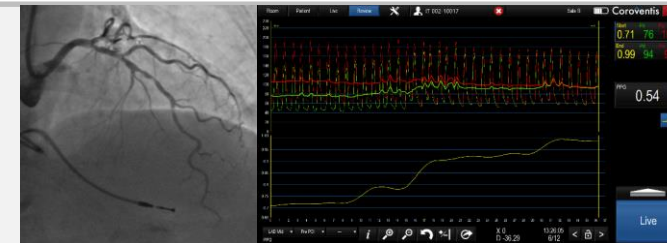


# What is #FullPhysiology assessment

1

## Epicardial disease assessment

- NHPR ( $\leq 0.89$ )
- cFFR ( $\leq 0.83$ )
- FFR ( $\leq 0.80$ ) -> perform pullback



2

## Microvascular disease assessment

- IMR ( $> 25$ )
- CFR ( $< 2.0$ )
- RRR ( $< 2.0$ )\*

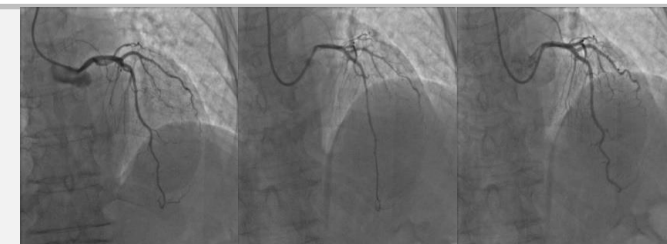
$$*Resistive\ resistance\ ratio = \frac{T_{rm} * P_{dr}}{T_{hm} * P_{dh}}$$



3

## Vasomotor testing

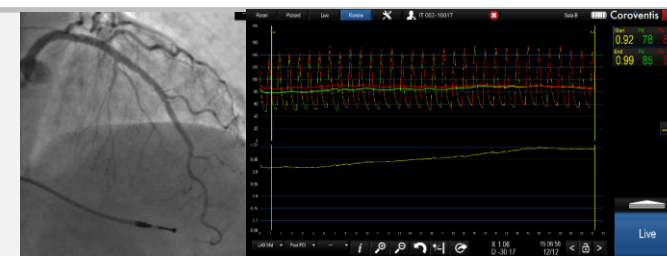
- Ach



4

## Post PCI Full Physiology assessment if applicable

- NHPR/cFFR/IMR/CFR/FFR -> perform pullback





# The #FullPhysiology Approach

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Online version at <https://www.minervamedica.it>

Minerva Cardiology and Angiology 2023 October;71(5):504-14  
DOI: 10.23736/S2724-5683.23.06414-1

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## REVIEW

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### #FullPhysiology: a systematic step-by-step guide to implement intracoronary physiology in daily practice

Roberto SCARSINI <sup>1\*</sup>, Gianluca CAMPO <sup>2</sup>, Luigi DI SERAFINO <sup>3</sup>,  
Sofia ZANON <sup>1</sup>, Francesca RUBINO <sup>1</sup>, Giovanni MONIZZI <sup>4</sup>,  
Simone BISCAGLIA <sup>2</sup>, Marco ANCONA <sup>5</sup>, Alberto POLIMENI <sup>6</sup>, Giampaolo NICCOLI <sup>7</sup>,  
Massimo FINESCHI <sup>8</sup>, Italo PORTO <sup>9</sup>, Antonio M. LEONE <sup>10</sup>



DOI: [10.23736/S2724-5683.23.06414-1](https://doi.org/10.23736/S2724-5683.23.06414-1)



# What is #FullPhysiology assessment

## ABSTRACT

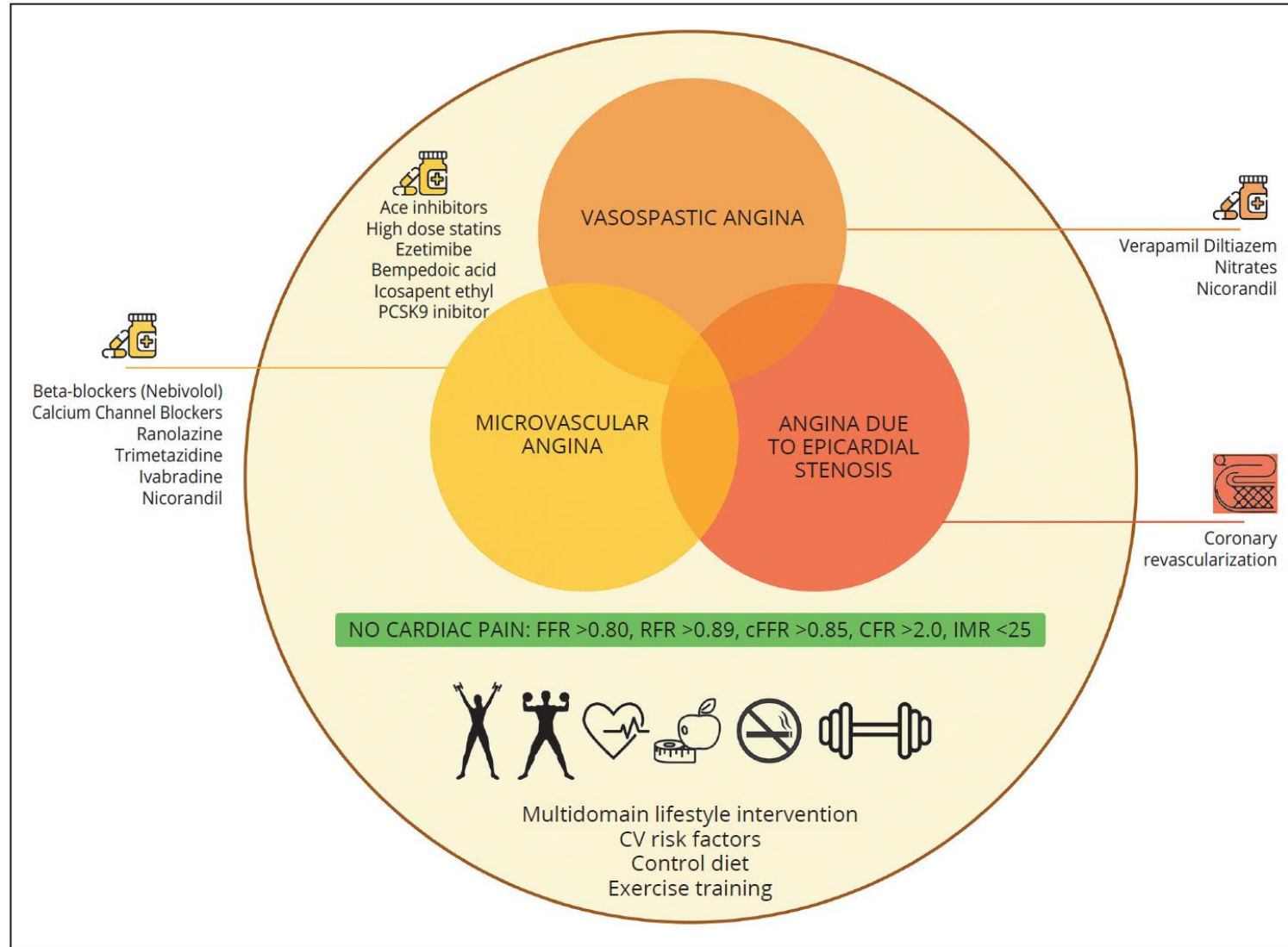
#FullPhysiology is a comprehensive and systematic approach to evaluate patients with suspected coronary disease using PressureWire technology (Abbott Vascular, Santa Clara, CA, USA). This advancement in technology enables the investigation of each component of the coronary circulation, including epicardial, microvascular, and vasomotor function, without significantly increasing procedural time or technical complexity. By identifying the predominant physiopathology responsible for myocardial ischemia, #FullPhysiology enhances precision medicine by providing accurate diagnosis and facilitating tailored interventional or medical treatments. This overview aims to provide insights into modern coronary physiology and describe a systematic approach to assess epicardial flow-limiting disease, longitudinal physiological vessel analysis, microvascular and vasomotor dysfunction, as well as post- percutaneous coronary intervention (PCI) physiological results.

(Cite this article as: Scarsini R, Campo G, Di Serafino L, Zanon S, Rubino F, Monizzi G, *et al.* #FullPhysiology: a systematic step-by-step guide to implement intracoronary physiology in daily practice. *Minerva Cardiol Angiol* 2023;71:504-14. DOI: 10.23736/S2724-5683.23.06414-1)

KEY WORDS: Myocardial ischemia; Physiopathology; Technology.



# #FullPhysiology-based therapy



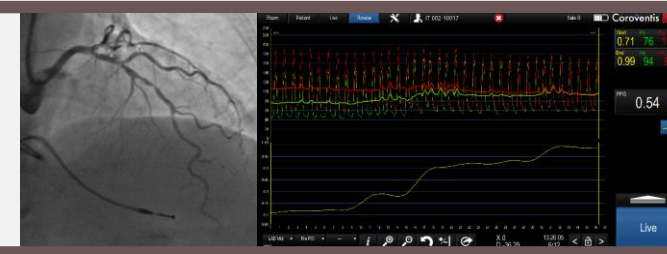


# What is #FullPhysiology assessment

1

## Epicardial disease assessment

- NHPR ( $\leq 0.89$ )
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- FFR ( $\leq 0.80$ ) -> perform pullback



2

## Microvascular disease assessment

- IMR ( $> 25$ )
- CFR ( $< 2.0$ )
- RRR ( $< 2.0$ )\*

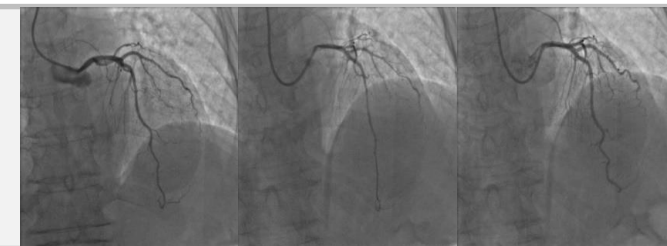
$$*Resistive\ resistance\ ratio = \frac{T_{rm} * P_{dr}}{T_{hm} * P_{dh}}$$



3

## Vasomotor testing

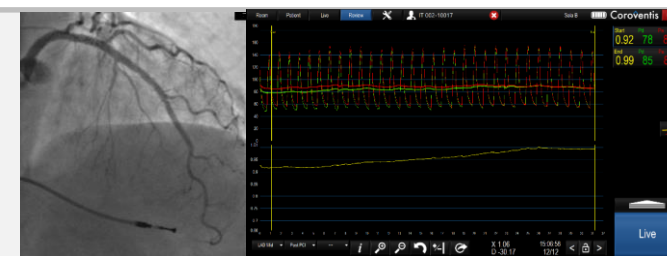
- Ach



4

## Post PCI Full Physiology assessment if applicable

- NHPR/cFFR/IMR/CFR/FFR -> perform pullback



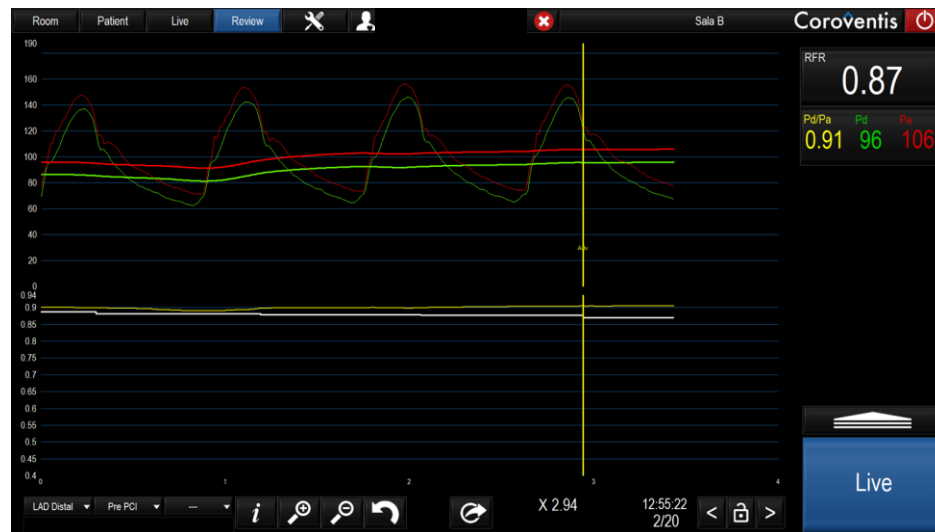


# Epicardial disease assessment

*Pd/Pa*



*RFR*



*cFFR*



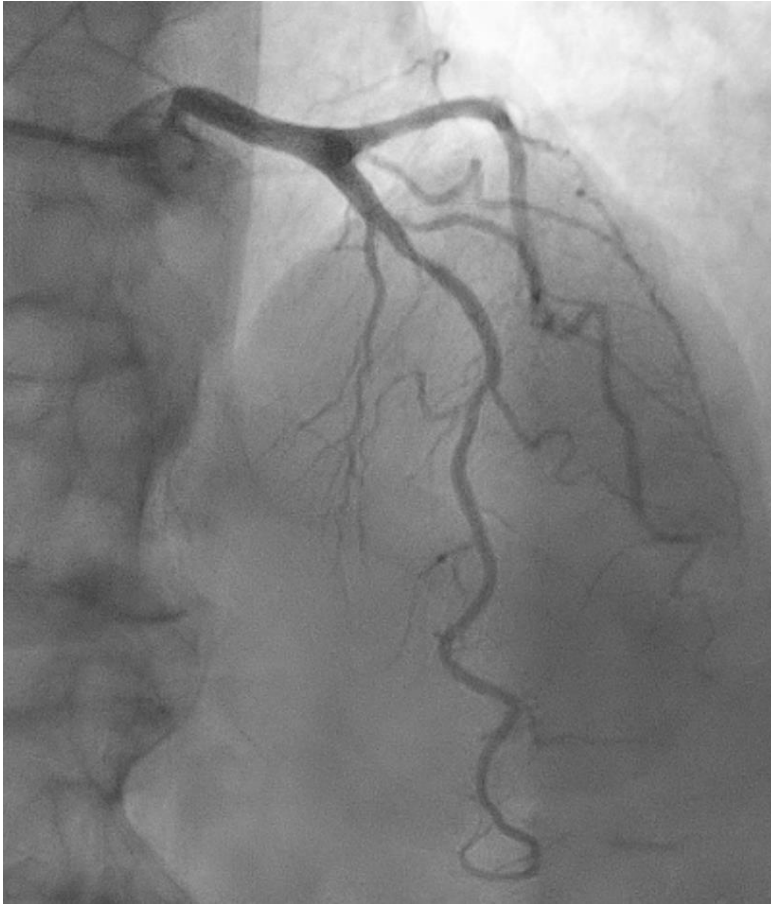
*FFR*





# Epicardial disease assessment

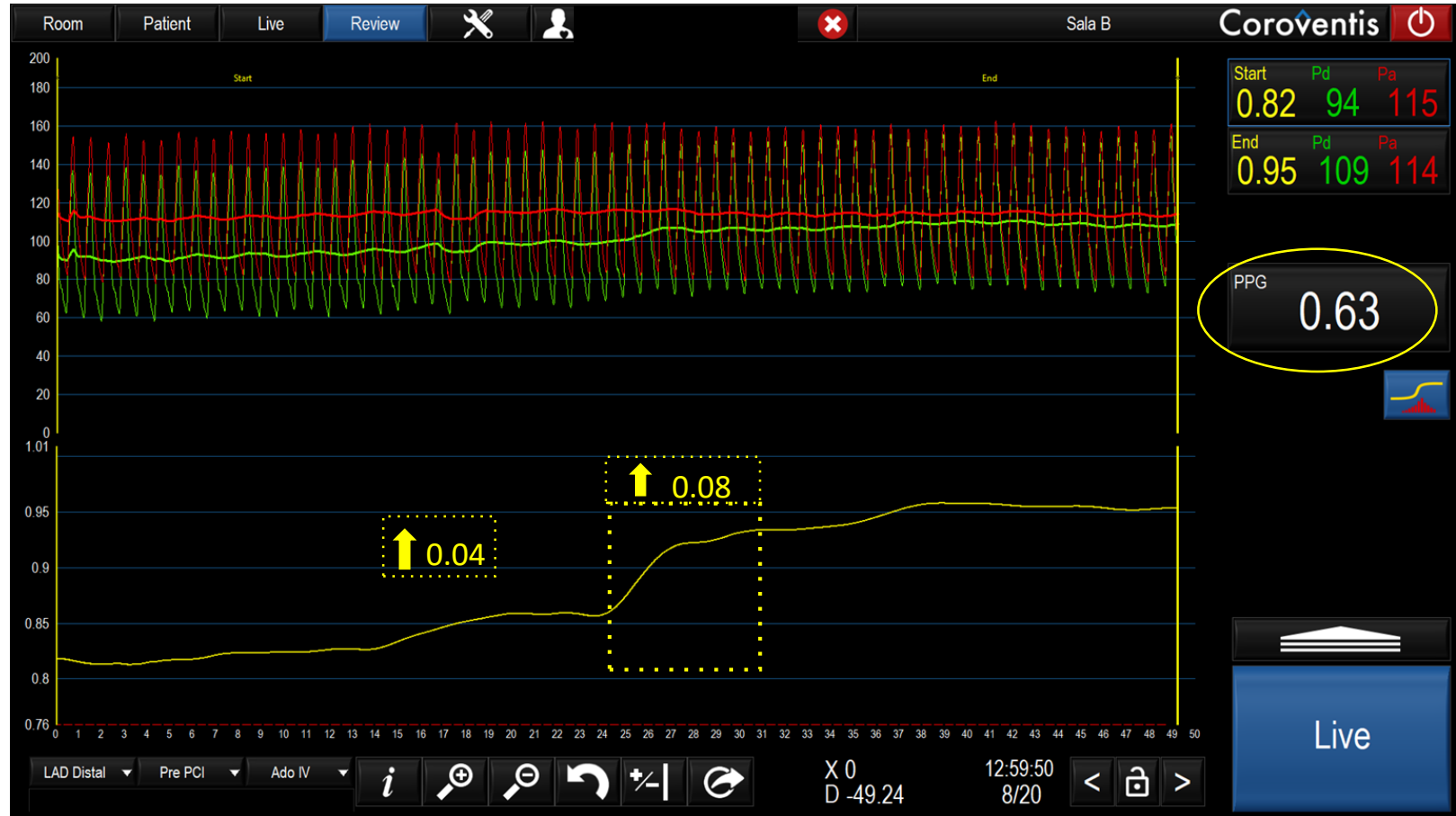
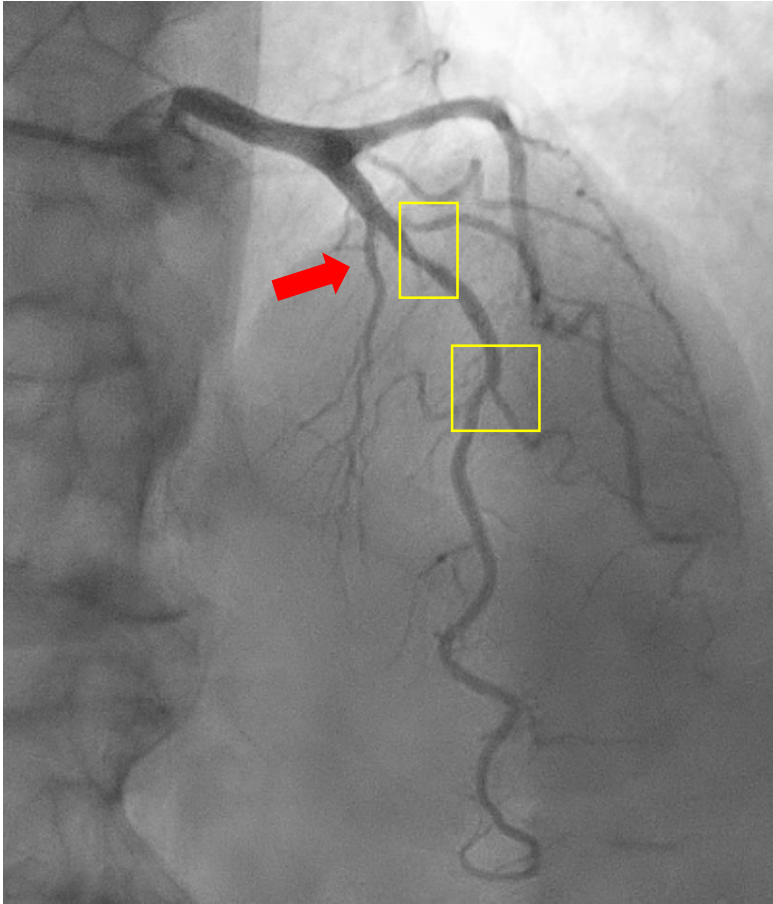
*The importance of pullback*





# Epicardial disease assessment

*The importance of pullback*





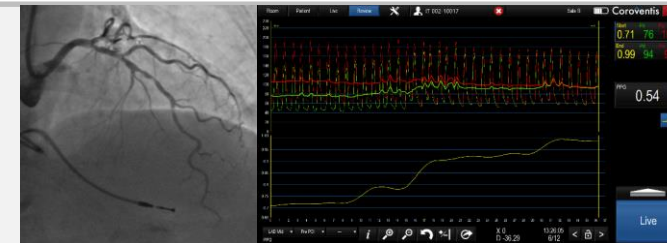


# What is #FullPhysiology assessment

1

## Epicardial disease assessment

- NHPR ( $\leq 0.89$ )
- cFFR ( $\leq 0.83$ )
- FFR ( $\leq 0.80$ ) -> perform pullback



2

## Microvascular disease assessment

- IMR ( $> 25$ )
- CFR ( $< 2.0$ )
- RRR ( $< 2.0$ )\*

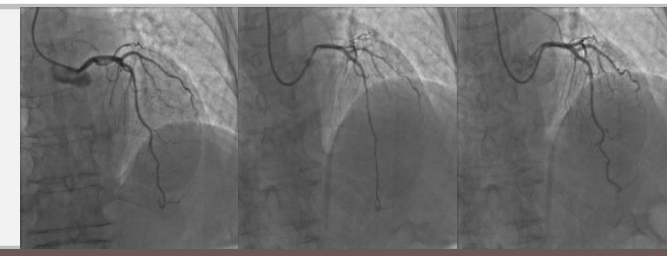
$$*Resistive\ resistance\ ratio = \frac{T_{rm} * P_{dr}}{T_{hm} * P_{dh}}$$



3

## Vasomotor testing

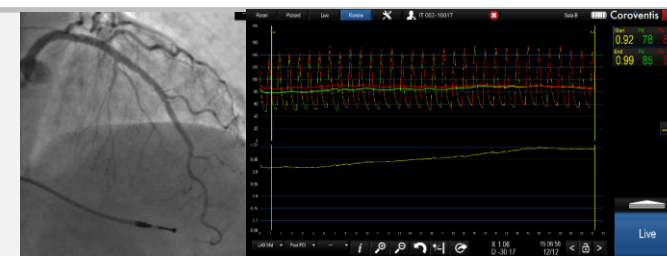
- Ach



4

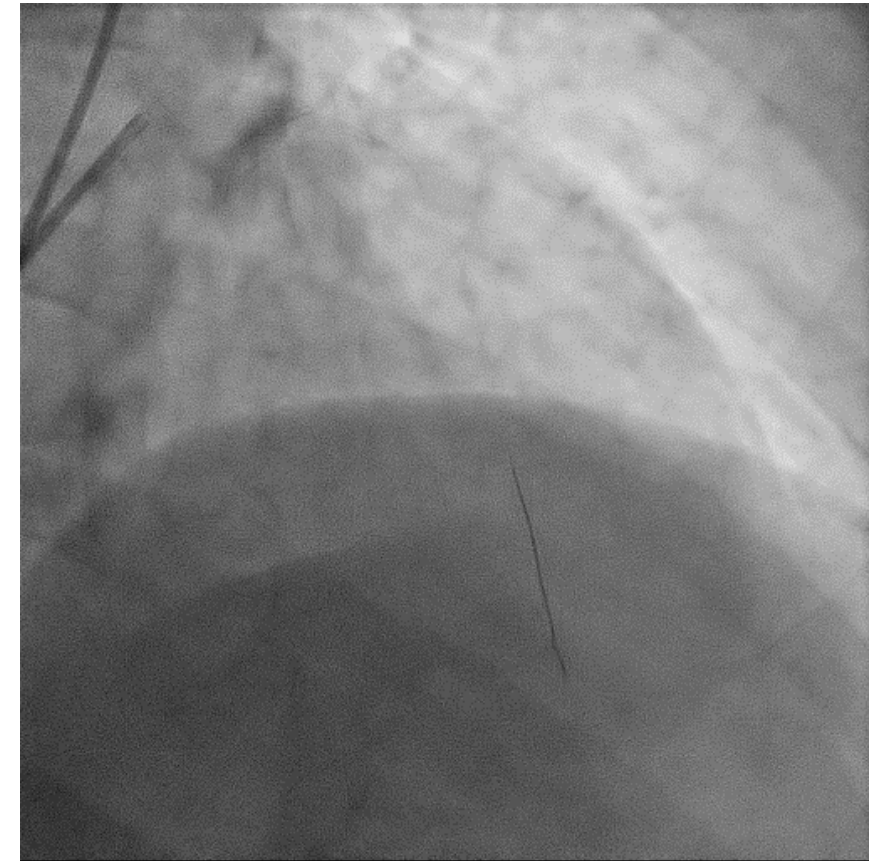
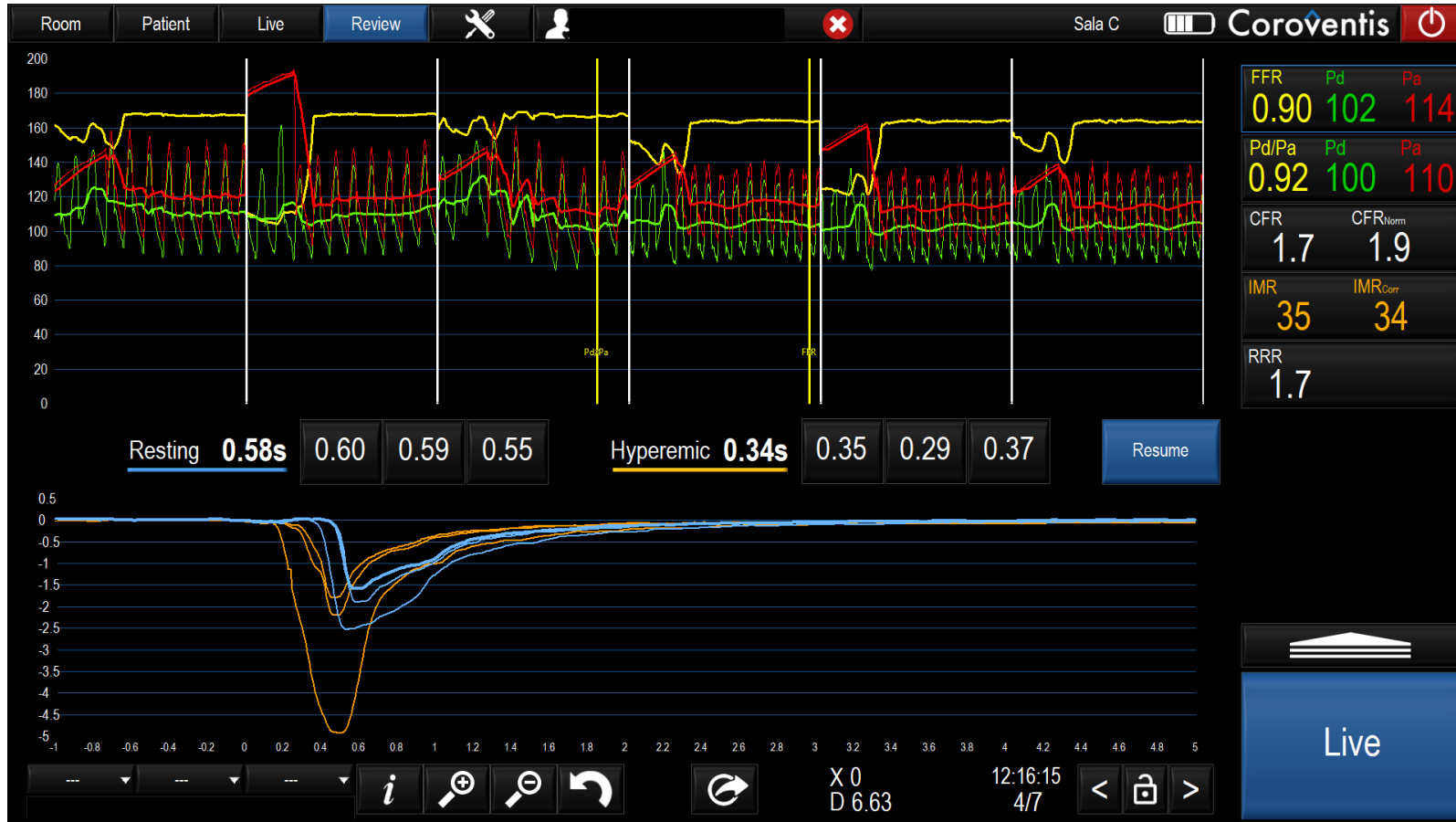
## Post PCI Full Physiology assessment if applicable

- NHPR/cFFR/IMR/CFR/FFR -> perform pullback



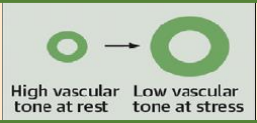


# Microvascular disease assessment / Vasomotor testing



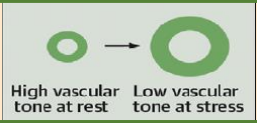
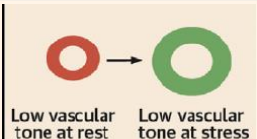
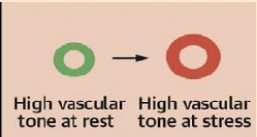
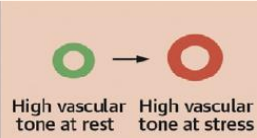


# Different endotypes of INOCA

	Mechanism	Invasive Physiology	Therapy
<b>Normal</b>	Normal 	CFR>2 AND IMR<25	Primary prevention Lifestyle change

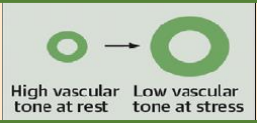
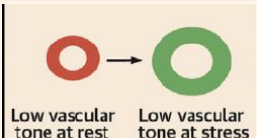






# Different endotypes of INOCA

	Mechanism	Invasive Physiology	Therapy
<b>Normal</b>	Normal 	CFR>2 AND IMR<25	Primary prevention Lifestyle change
<b>Functional CMD</b>	Impaired Vasodilation 	CFR<2 (2.5) AND IMR<25	Treat non cardiac disease ARBs β-Blockers (nebivolol) Ranolazine
<b>Compensated Structural CMD</b>	Early abnormal MV resistance 	CFR>2 AND IMR≥25	Lifestyle (rehabilitation?) ARBs β-Blockers (nebivolol) Ranolazine
<b>Structural CMD</b>	Abnormal MV resistance 	CFR<2 (2.5) AND IMR≥25	Lifestyle (rehabilitation?) ARBs β-Blockers (nebivolol) Ranolazine



# Different endotypes of INOCA

	Mechanism		Invasive Physiology	Therapy
<b>Normal</b>	Normal		CFR>2 AND IMR<25	Primary prevention
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<b>Structural CMD</b>	Abnormal MV resistance		CFR<2 (2.5) AND IMR≥25	Lifestyle (rehabilitation?) ARBs β-Blockers (nebivolol) Ranolazine
<b>Vasospastic Angina</b>	Epicardial spasm		Angina + ST deviation with epicardial spasm	CCB Nitrates
<b>Microvascular Spasm</b> ?	Impaired ED vasodilatation / MV spasm		Angina + ST deviation w/o epicardial spasm	CCB Nitrates

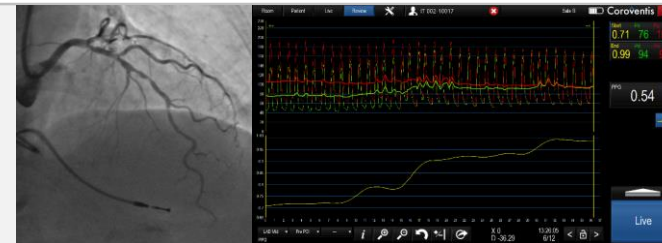


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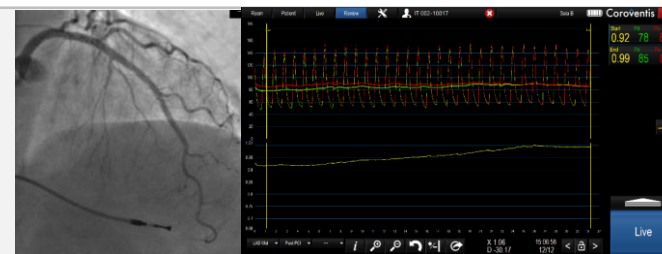
- Ach



4

## Post PCI Full Physiology assessment if applicable

- NHPR/cFFR/IMR/CFR/FFR -> perform pullback



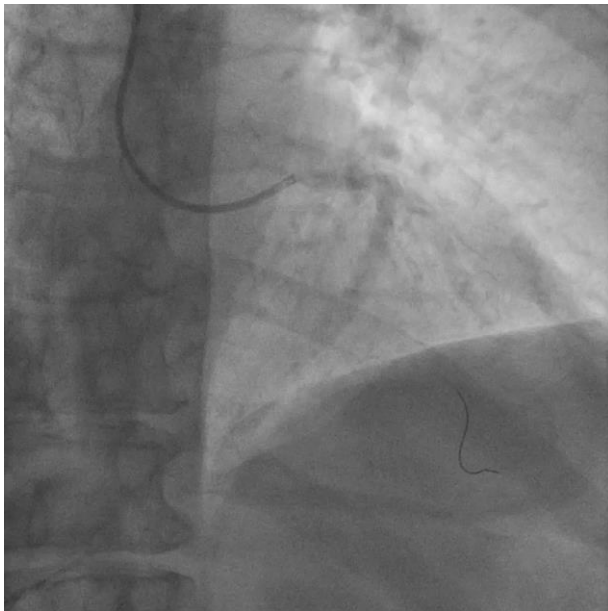
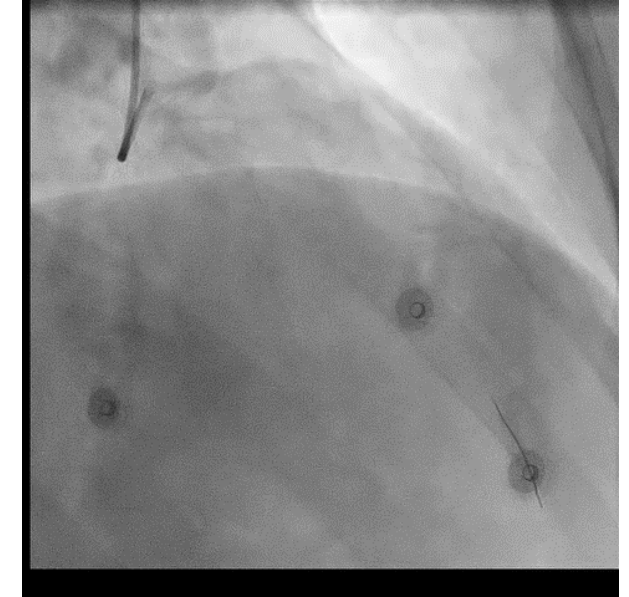


# Diagnosis according to COVADIS definitions

## Vasospastic angina

J. F. Beltrame et al., Eur Heart J 38, 2565 (2017)

Vasospastic angina	Epicardial spasm	Angina symptoms during ACh bolus (e.g. 100 µg acetylcholine over 20 seconds) AND: <ul style="list-style-type: none"> <li>• ST-segment deviation on ECG</li> <li>• &gt;90% epicardial coronary constriction during ACh reduction[34]</li> </ul>
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## Coronary Microvascular Dysfunction

P. Ong et al., Int J Cardiol 250, 16 (2018)

Disorder	Symptoms	Clinical measurement
Microvascular angina	Abnormal microvascular resistance	<ul style="list-style-type: none"> <li>• IMR <math>\geq 25</math>[27]</li> <li>• Hyperaemic microvascular resistance <math>\geq 2.5</math> mmHg/cm/s[28]</li> </ul>
	Impaired coronary vasorelaxation	<ul style="list-style-type: none"> <li>• CFR by thermodilution <math>&lt; 2.0</math>[25]</li> </ul>
Microvascular spasm	Angina symptoms with ACh infusion AND:	<ul style="list-style-type: none"> <li>• ST-segment deviation on ECG</li> <li>• No significant epicardial coronary spasm (<math>&lt; 90\%</math> diameter reduction)</li> </ul>

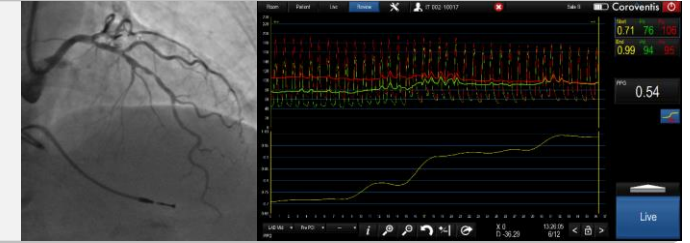


# What is #FullPhysiology assessment

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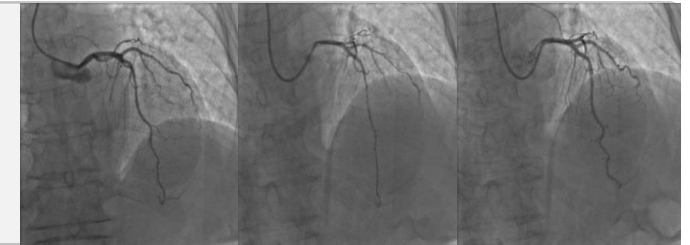
$$*Resistive\ resistance\ ratio = \frac{T_{rm} * P_{dr}}{T_{hm} * P_{dh}}$$



3

## Vasomotor testing

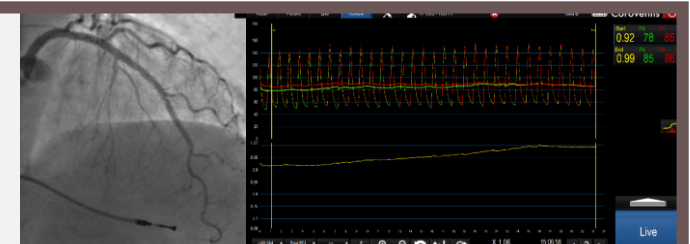
- Ach



4

## Post PCI Full Physiology assessment if applicable

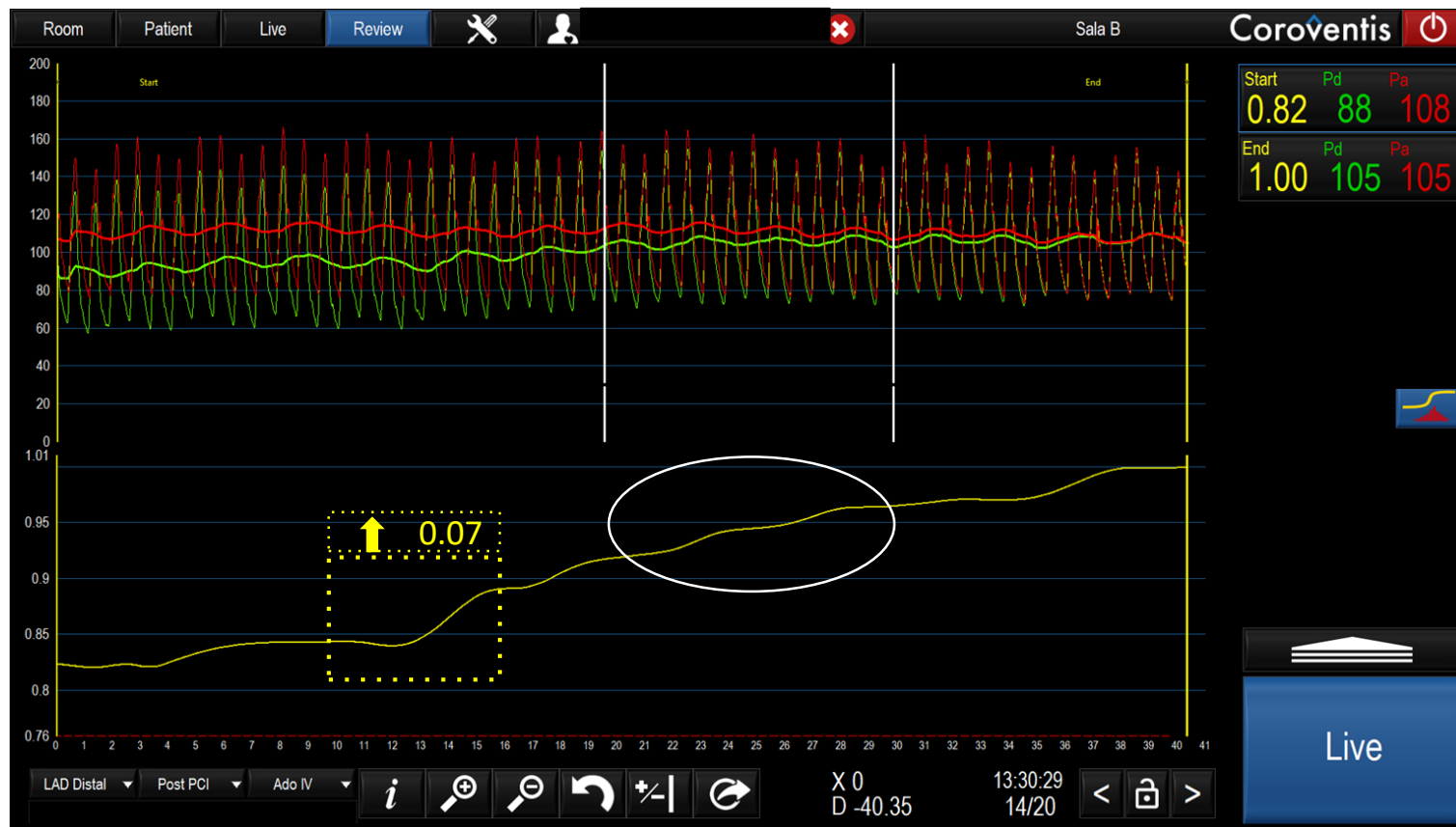
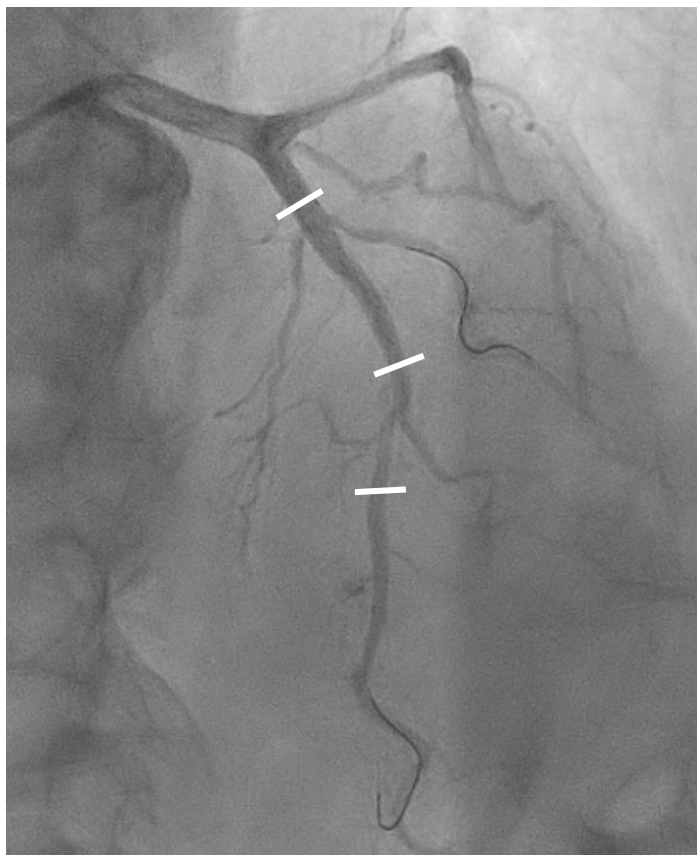
- NHPR/cFFR/IMR/CFR/FFR -> perform pullback





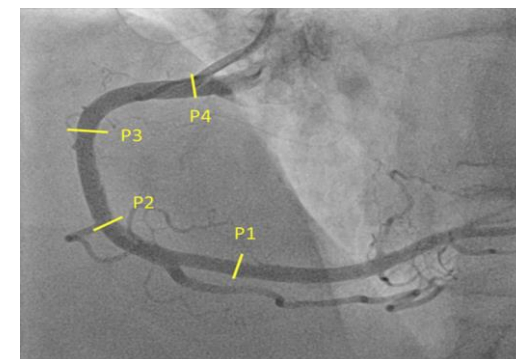
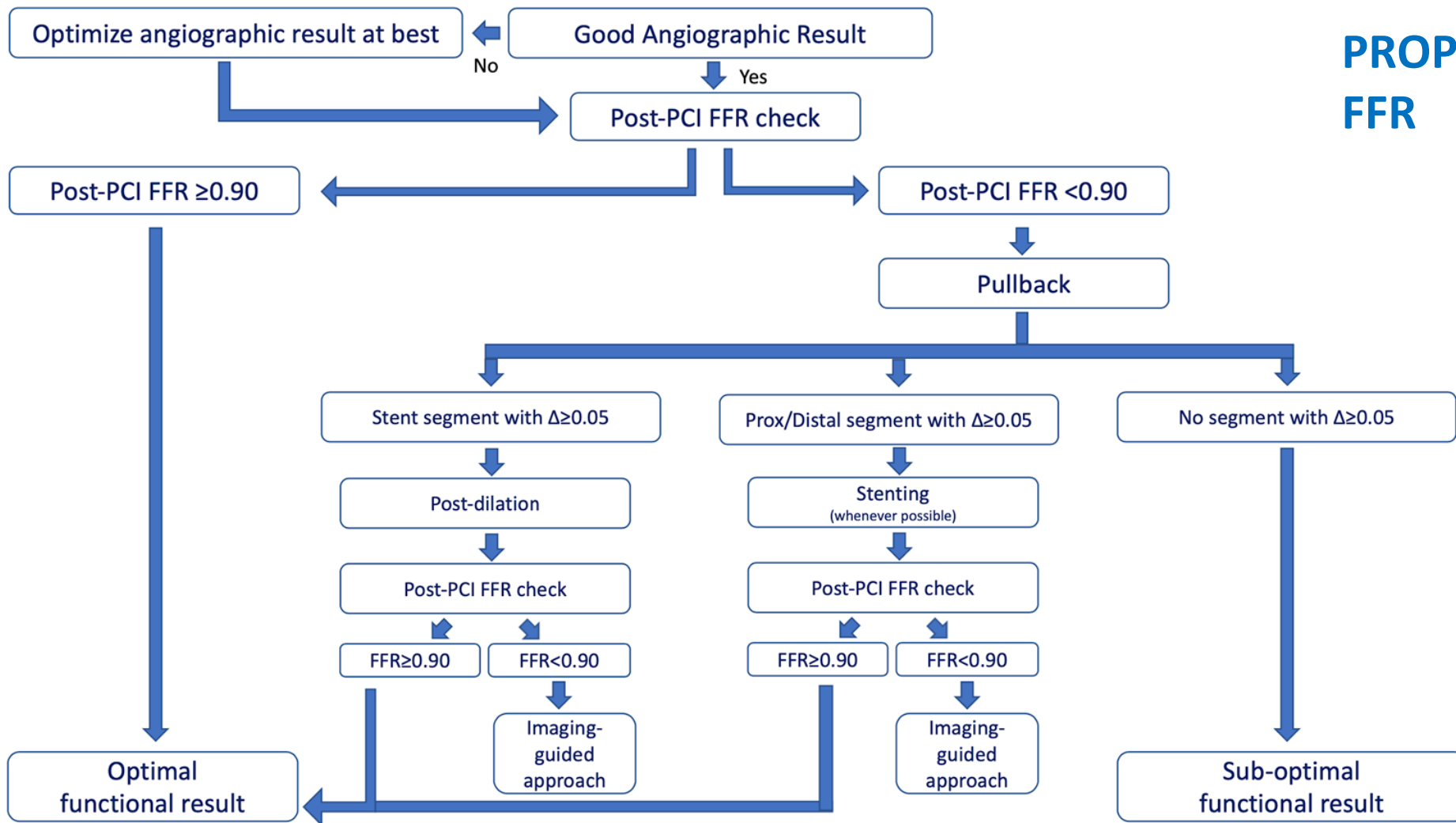


# Pullback assessment in hyperemia post PCI





# How to manage an unsatisfactory post-PCI FFR

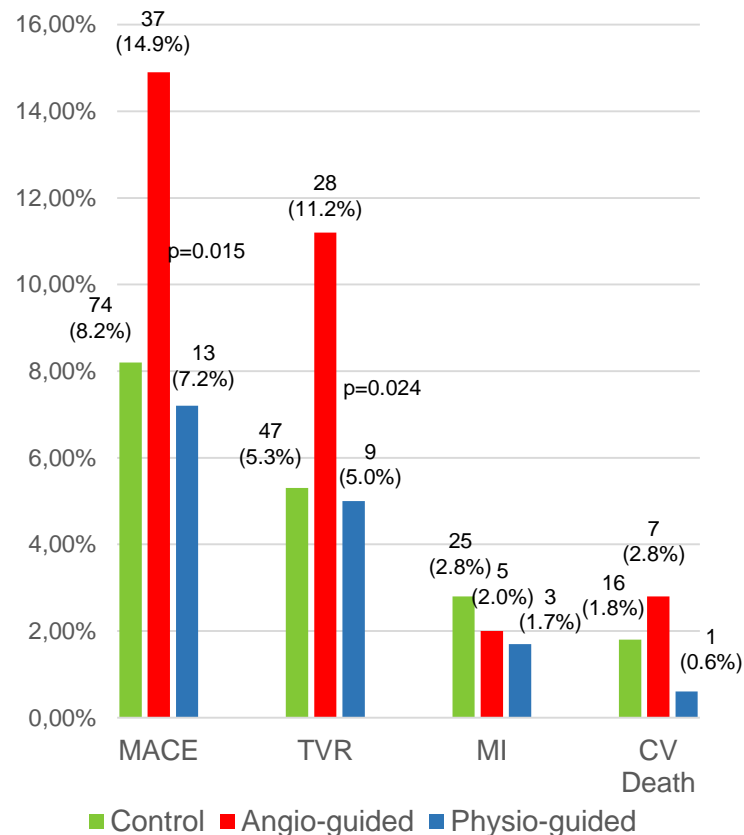


- P1: 20mm distal of stent
- P2: distal stent edge
- P3: proximal stent edge
- P4: ostium (drift)

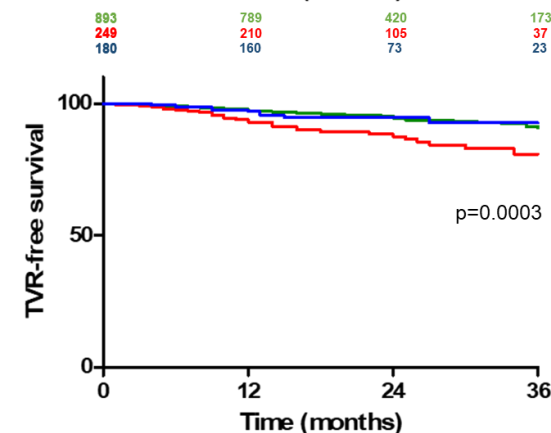
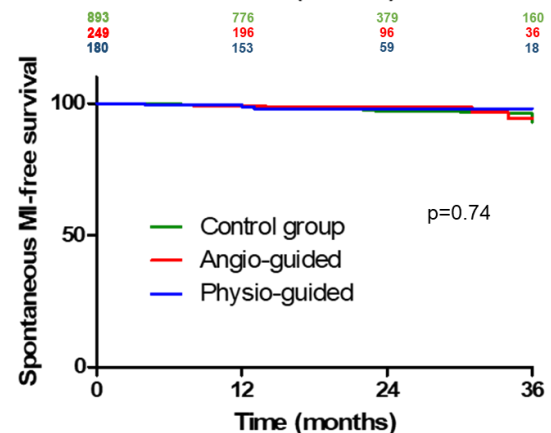
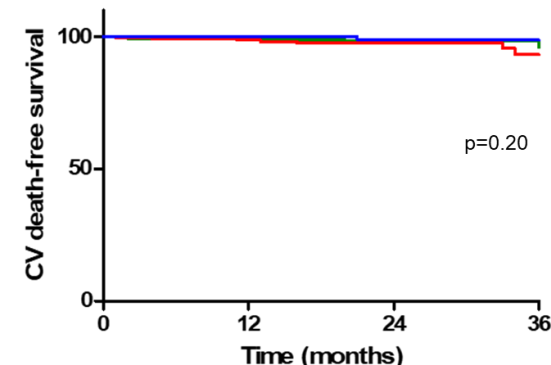
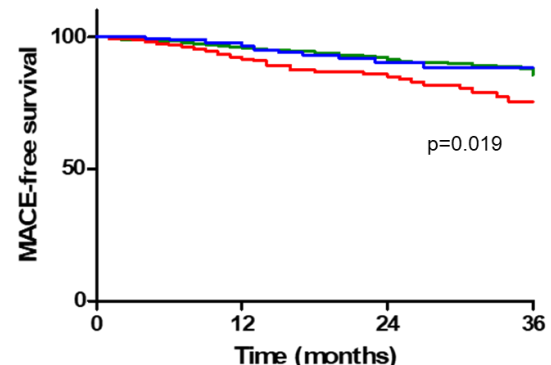


# Importance of post PCI physiology

## PROPHET-FFR Study



21 months (IQR 14-32)



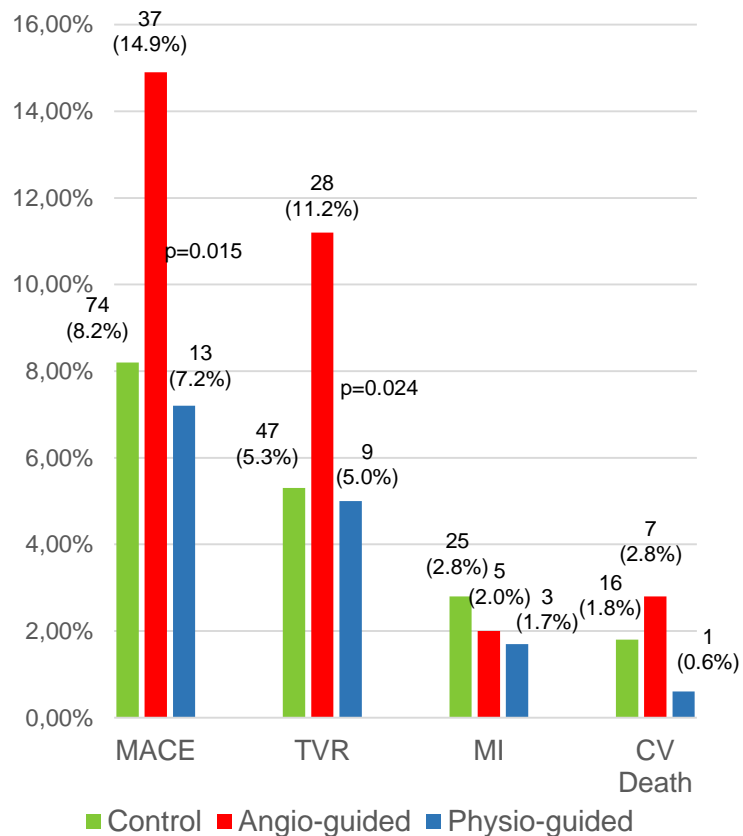
Leone LBT EuroPCR 2022

Leone Frontiers Cardiovasc Med 2022

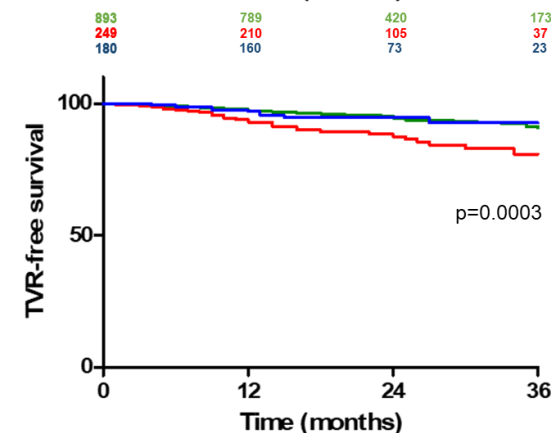
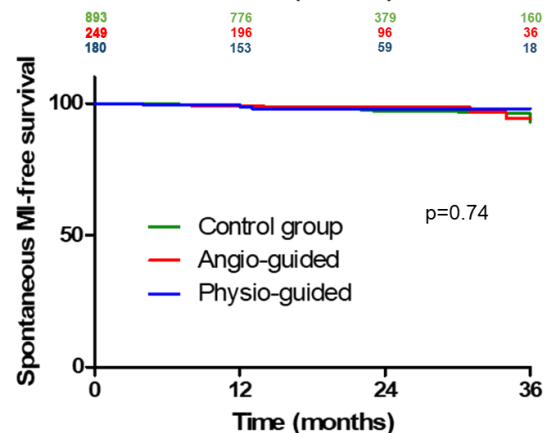
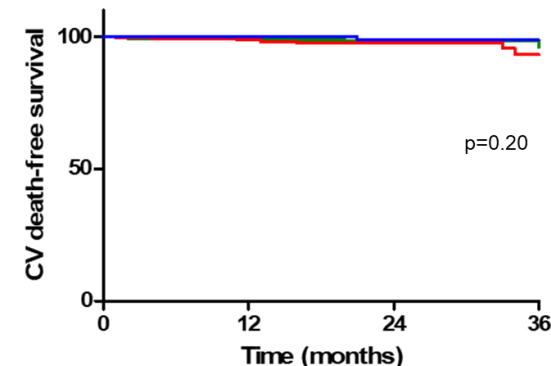
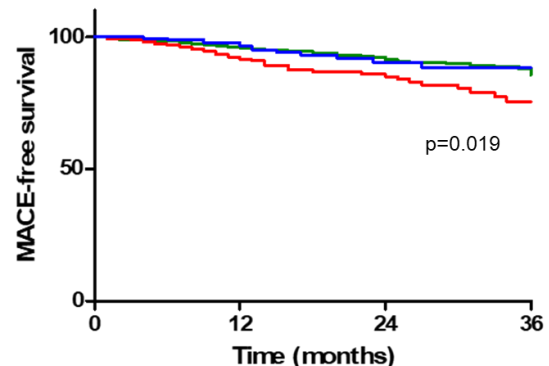


# Importance of post PCI physiology

## PROPHET-FFR Study



21 months (IQR 14-32)



Leone LBT EuroPCR 2022

Leone Frontiers Cardiovasc Med 2022



# Collaborations

Brief report

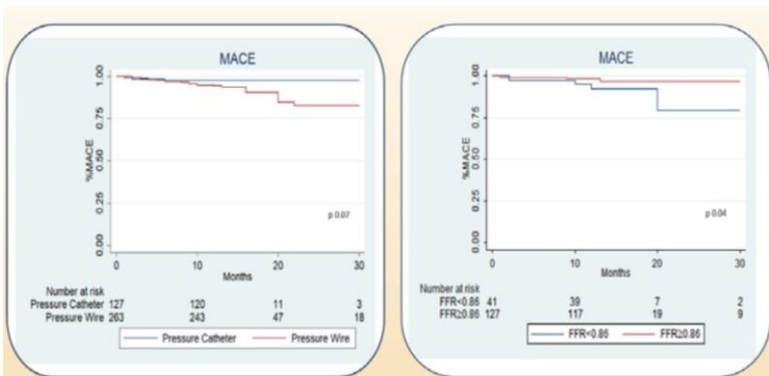
## Efficacy of "Physiology-Guided PCI" Using Pressure Catheter in Comparison to Conventional Pressure Wires: A Multicenter Analysis



G. Anastasia, MD<sup>a,b</sup>, D. Galante, MD<sup>c,d</sup>, S. Biscaglia, MD<sup>e</sup>, R. Vergallo, MD, PhD<sup>a,b</sup>, F. Di Giusto, MD<sup>d</sup>, S. Migliaro, MD<sup>f</sup>, E. Petrolati, MD<sup>g</sup>, A. Vicerè, MD<sup>h</sup>, D. Scancarello, MD<sup>f</sup>, A. Marrone, MD<sup>f</sup>, F.M. Verardi, MD<sup>g</sup>, G. Campaniello, MD<sup>g</sup>, C. Giuliana, MD<sup>g</sup>, C. Pollio Benvenuto, MD<sup>g</sup>, V. Viccaro, MD<sup>g</sup>, S. Todisco, MD<sup>g</sup>, F. Burzotta, MD<sup>h,i</sup>, C. Aurigemma, MD<sup>g</sup>, E. Romagnoli, MD<sup>g</sup>, C. Trani, MD<sup>h,g</sup>, F. Crea, MD<sup>g</sup>, I. Porto, MD<sup>a,b</sup>, G. Campo, MD<sup>g</sup>, and A.M. Leone, MD<sup>c,d,g,h</sup>

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https://doi.org/10.1016/j.amjcard.2024.01.020

www.ajconline.org



## L'ischemia miocardica in assenza di coronaropatia ostruttiva: stato dell'arte

Giulia Ghizzoni<sup>1,2</sup>, Luigi Di Serafino<sup>3</sup>, Giulia Botti<sup>1,2</sup>, Domenico Galante<sup>4,5</sup>, Domenico D'Amario<sup>6</sup>, Stefano Benenati<sup>7,8</sup>, Filippo Luca Gurgoglione<sup>9</sup>, Renzo Laborante<sup>10</sup>, Graziella Pompei<sup>11</sup>, Italo Porto<sup>7,12</sup>, Gianluca Calogero Campo<sup>11</sup>, Giampaolo Niccoli<sup>9</sup>, Giovanni Esposito<sup>3</sup>, Antonio Maria Leone<sup>4,5</sup>, Alaide Chieffo<sup>1,2</sup>

G Ital Cardiol 2023;24(10 Suppl 2):5S-20S

The American Journal of Cardiology

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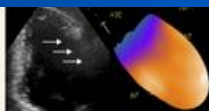
RESEARCH ARTICLE | ARTICLES IN PRESS

## Comprehensive Angiography-Derived Functional Assessment of Epicardial and Microvascular Coronary Disease, Correlation With Noninvasive Myocardial Stress Imaging

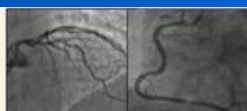
Francesco Della Mora, MD • Leonardo Portolan, MD • Dimitrios Terentes-Printzios, MD PhD • Andrea Vicerè, MD • Stefano Andreaggi, MD • Marco Biasin, MD • Gabriele Pesarini, MD PhD • Domenico Tavella, MD • Caterina Maffei, MD • Elvin Tafciu, MD • Giovanni Benfari, MD PhD • Dimitrios Oikonomou, MD • Konstantia-Paraskevi Gkini, MD • Domenico Galante, MD • Konstantinos Tsioufis, MD PhD • Charalambos Vlachopoulos, MD PhD • Antonio Maria Leone, MD • Flavio Ribichini, MD • Roberto Scarsini, MD PhD

Published: February 29, 2024 • DOI: https://doi.org/10.1016/j.amjcard.2024.01.037

319 patients with myocardial stress imaging and coronary angiographic assessment

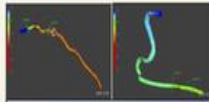


Inducible myocardial ischemia

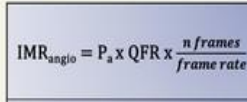


Intermediate coronary artery stenosis

917 vessels with combined epicardial and microvascular coronary assessment

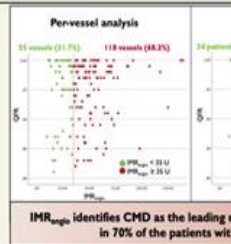
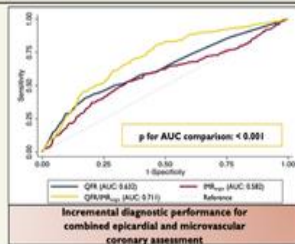


Epicardial assessment (QFR)



Microvascular assessment (IMR<sub>angio</sub>)

$$IMR_{angio} = P_a \times QFR \times \frac{n \text{ frames}}{\text{frame rate}}$$



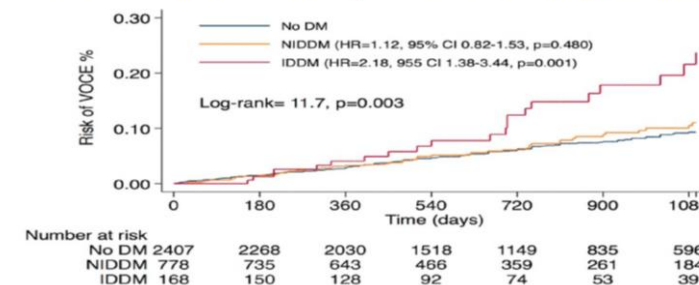
Clinical Research in Cardiology (2023) 112:1331–1342  
https://doi.org/10.1007/s00392-023-02243-y

ORIGINAL PAPER



## Intracoronary physiology-guided percutaneous coronary intervention in patients with diabetes

Roberto Scarsini<sup>1,8</sup> • Matteo Tebaldi<sup>2</sup> • Francesca Rubino<sup>1,8</sup> • Sara Sgreva<sup>1,8</sup> • Giovanni Vescovo<sup>3</sup> • Marco Barbierato<sup>3</sup> • Andrea Vicerè<sup>4</sup> • Domenico Galante<sup>5</sup> • Concetta Mammine<sup>1</sup> • Mattia Lunardi<sup>1</sup> • Domenico Tavella<sup>1</sup> • Gabriele Pesarini<sup>1</sup> • Gianluca Campo<sup>7</sup> • Antonio Maria Leone<sup>5,6</sup> • Flavio Luciano Ribichini<sup>1,8</sup>



JACC: Cardiovascular Interventions  
Volume 17, Issue 2, 22 January 2024, Pages 277-287

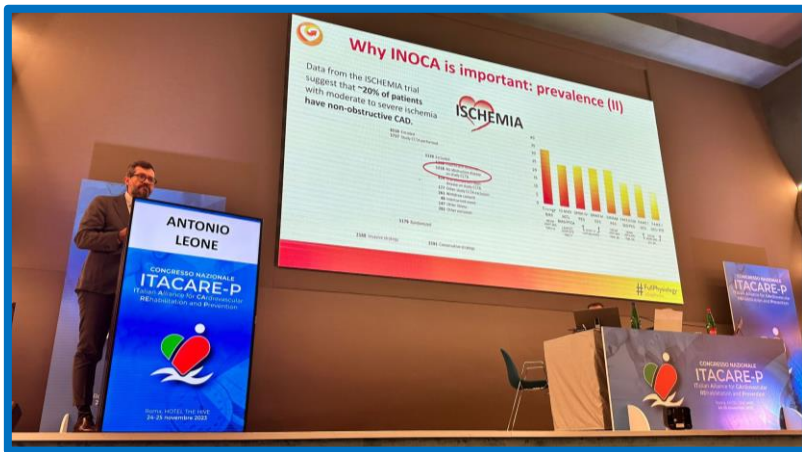
Original Research  
Coronary

## Coronary Physiology Guidance vs Conventional Angiography for Optimization of Percutaneous Coronary Intervention: The AQVA-II Trial

Simone Biscaglia MD<sup>a</sup> • Filippo Maria Verardi MD<sup>a</sup> • Andrea Erriquez MD<sup>a</sup> • Iginio Colaiori MD<sup>b</sup> • Marta Cocco MD<sup>a</sup> • Anna Cantone MD<sup>a</sup> • Graziella Pompei MD<sup>a</sup> • Andrea Marrone MD<sup>a</sup> • Serena Caglioni MD<sup>a</sup> • Carlo Tumscitz MD<sup>a</sup> • Carlo Penzo MD<sup>a</sup> • Marco Manfrini PhD<sup>c</sup> • Antonio Maria Leone MD<sup>d</sup> • Francesco Versaci MD<sup>b</sup> • Gianluca Campo MD<sup>a</sup>



# Disseminations





# Future



# Italian registries



## INOCA-IT Registry



- IRCCS San Raffaele Hospital, Milano
- Policlinico Universitario A. Gemelli IRCCS/ Ospedale Fatebenefratelli Gemelli Isola, Roma
- Azienda Ospedaliera Universitaria Federico II, Napoli



Università degli Studi di Napoli FEDERICO II  
AZIENDA OSPEDALIERA UNIVERSITARIA

Dipartimento ad Attività Integrate di Emergenze Cardiovascolari,  
Medicina Clinica e dell'Invecchiamento

**UOC Cardiologia Emodinamica e UTIC**  
Direttore: Prof. Giovanni Esposito

### PROTOCOLLO DI STUDIO CLINICO

**Caratterizzazione di diversi fenotipi di disfunzione microvascolare e il loro impatto sulla severità dell'angina nei pazienti con angina cronica in assenza di malattia coronarica ostruttiva.**

Versione 1.1 del 12/05/2023

**Titolo breve:** Studio MiVa: uno studio di registro multicentrico in pazienti con angina microvascolare

#### Sponsor

Dipartimento di Scienze Biomediche Avanzate dell'università Federico II di Napoli

P.I. Prof. Giovanni Esposito-Prof. Ciro Indolfi

Co-P.I. Prof. Luigi Di Serafino; Prof. Alberto Polimeni

Indirizzo Via Sergio pansini,5 Napoli

Telefono/Fax: 0817463075

e-Mail [espogiov@unina.it](mailto:espogiov@unina.it)

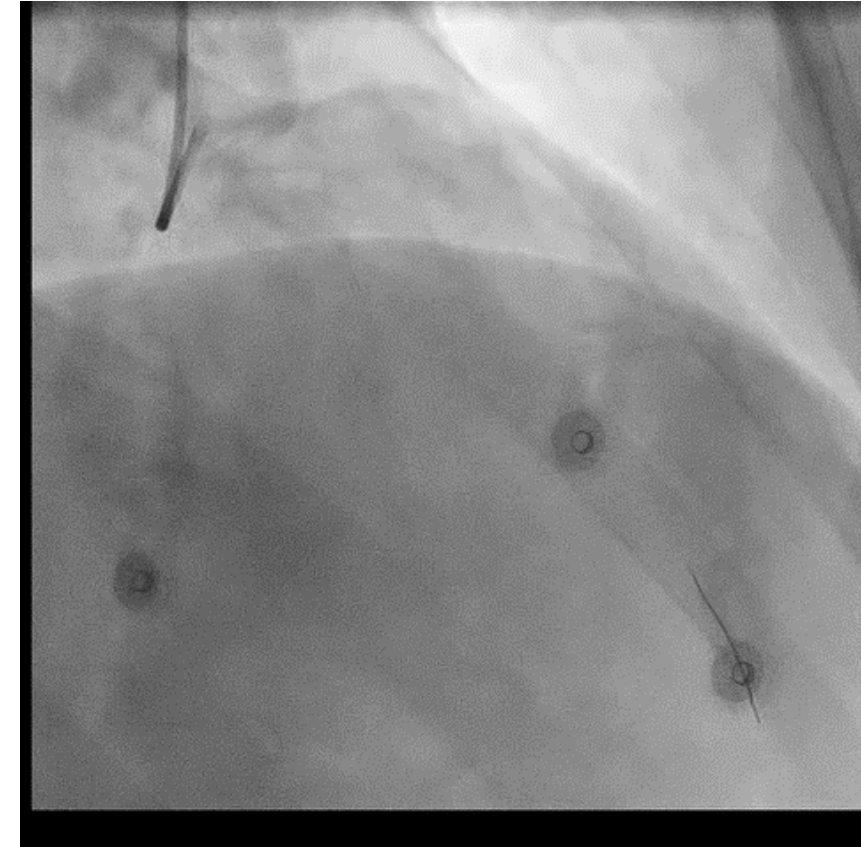
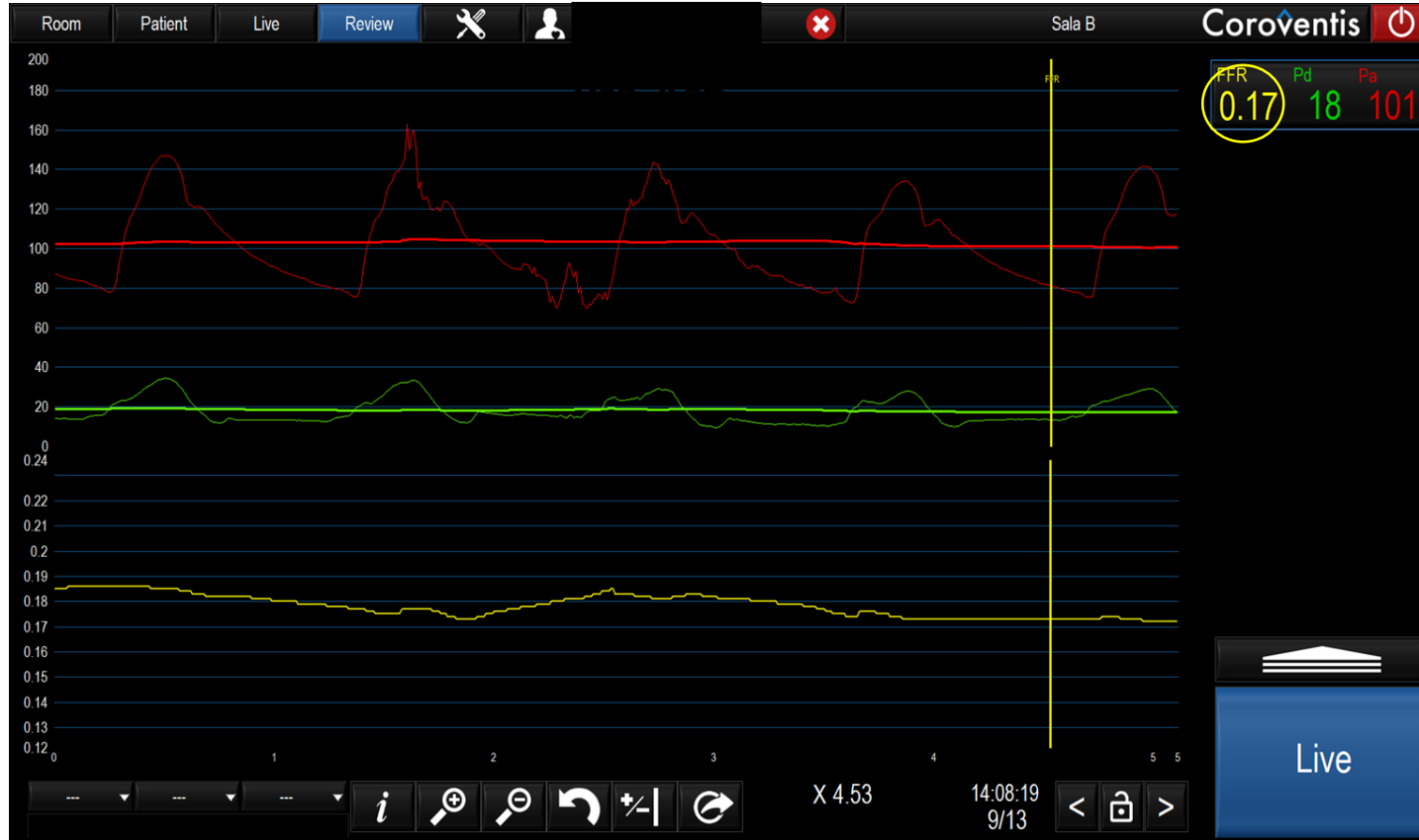




# #FullPhysiology 2.0

## Invasive Functional demonstration of Epicardial Spasm

- Typical chest pain
- ECG changes: ST segment elevation
- Epicardial spasm (>90%) with distal occlusion of LAD

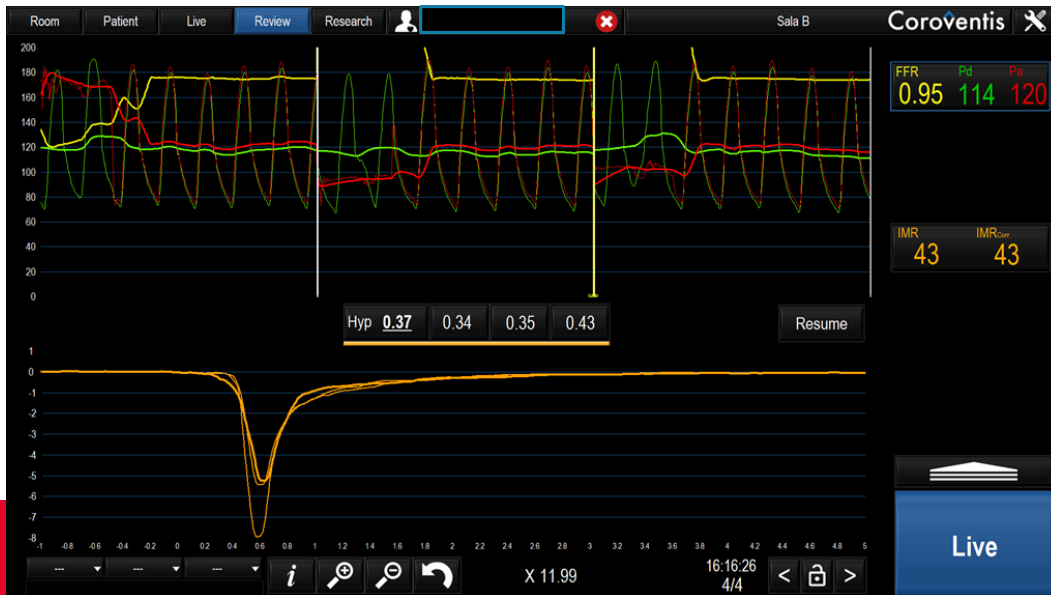
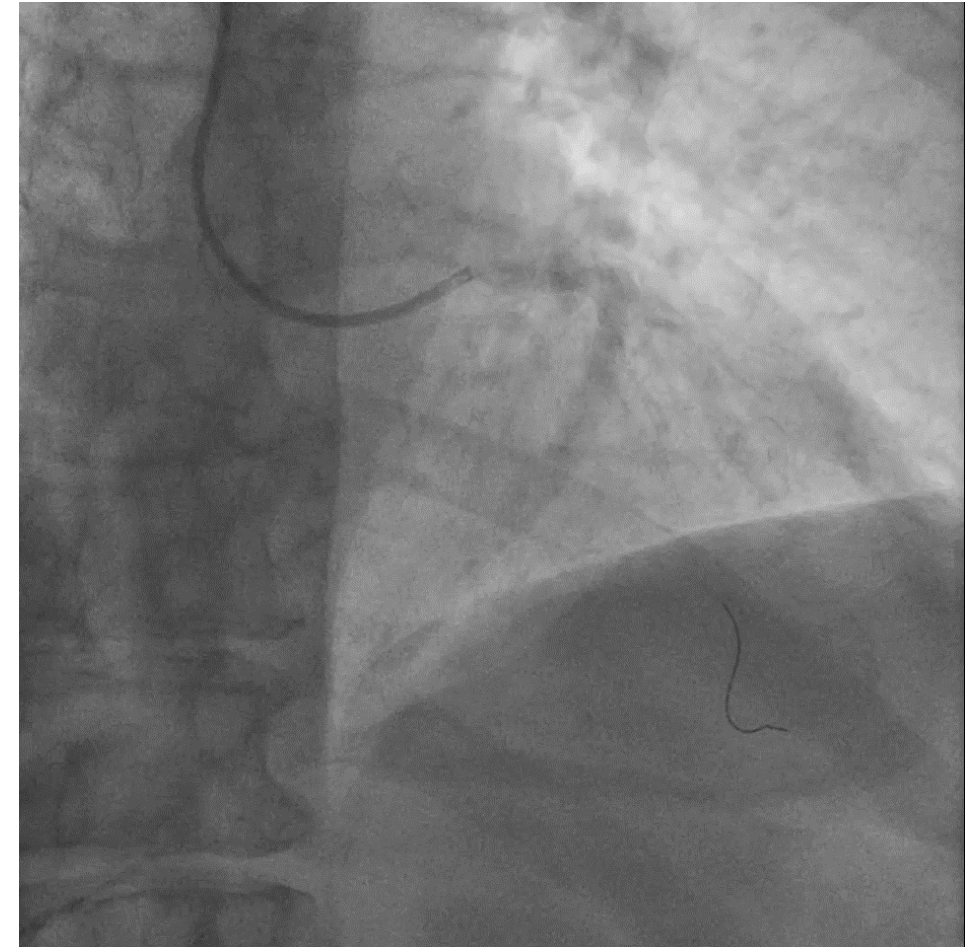
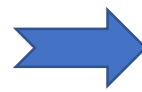
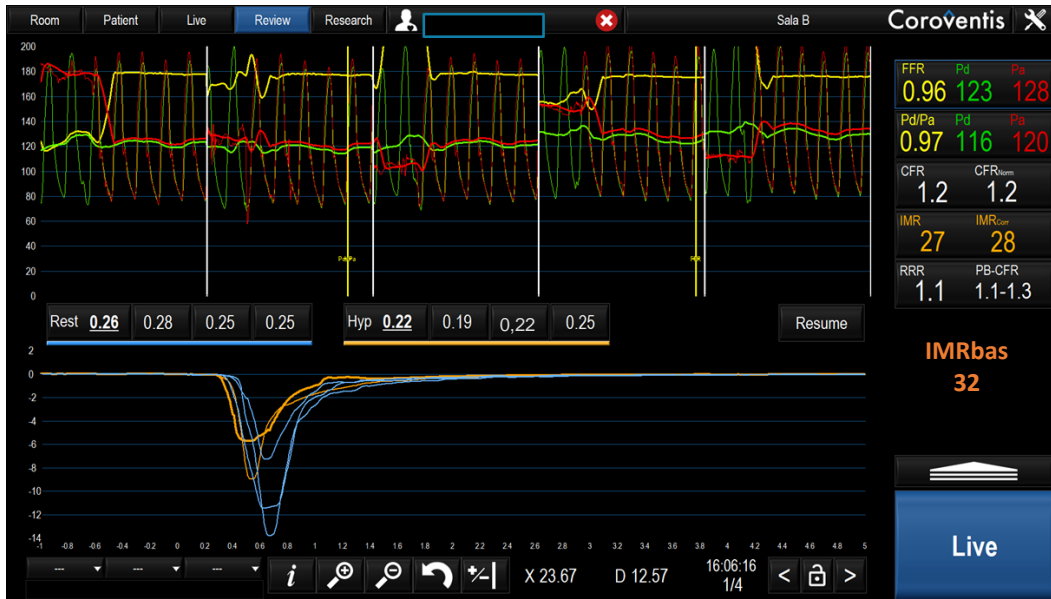




# #FullPhysiology 2.0

## Invasive Functional demonstration of Microvascular Spasm

- Typical chest pain
- ECG changes
- NO epicardial spasm



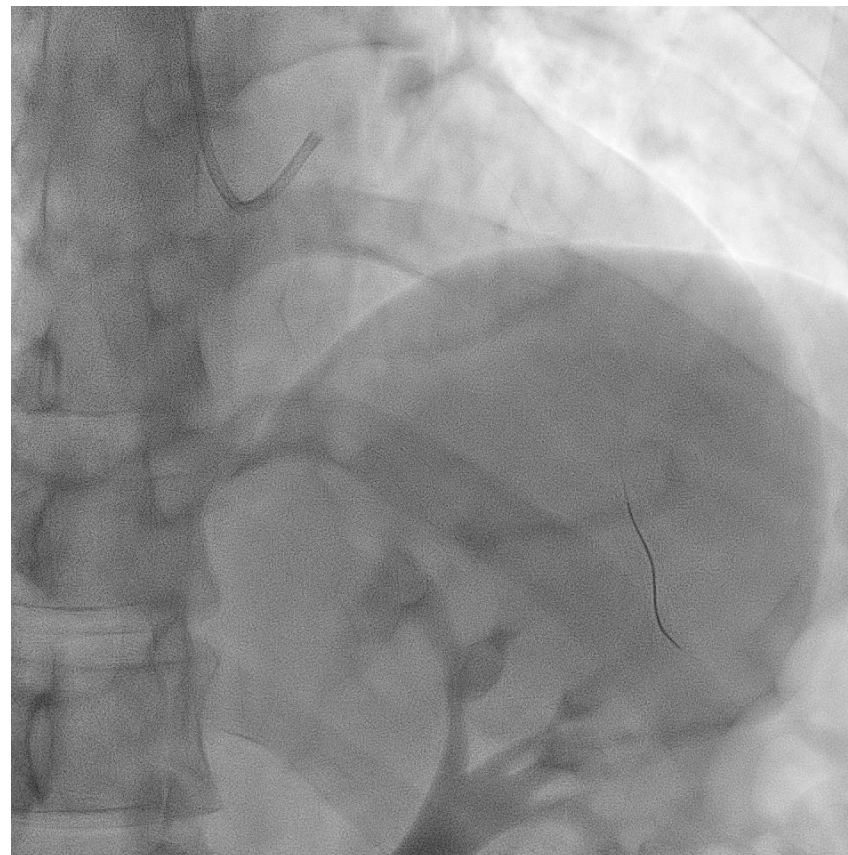
Real Microvascular Spasm



# #FullPhysiology 2.0

## Invasive Functional demonstration of Microvascular Spasm

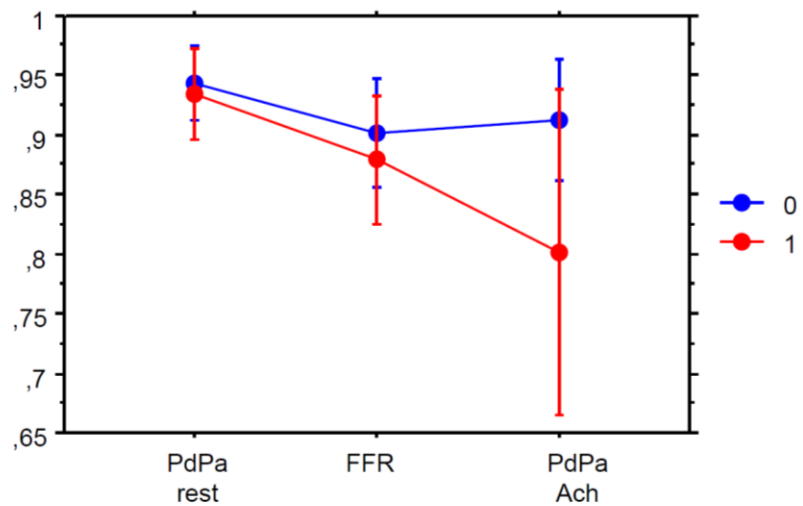
- Typical chest pain
- ECG changes
- NO epicardial spasm



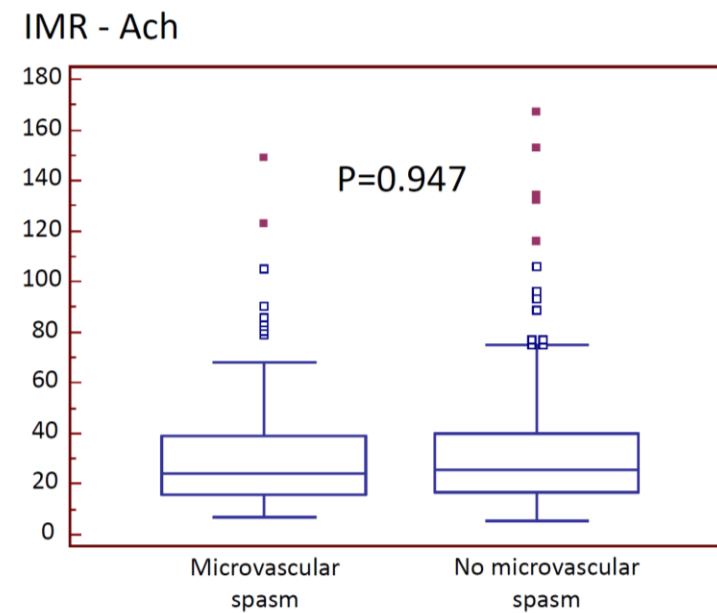
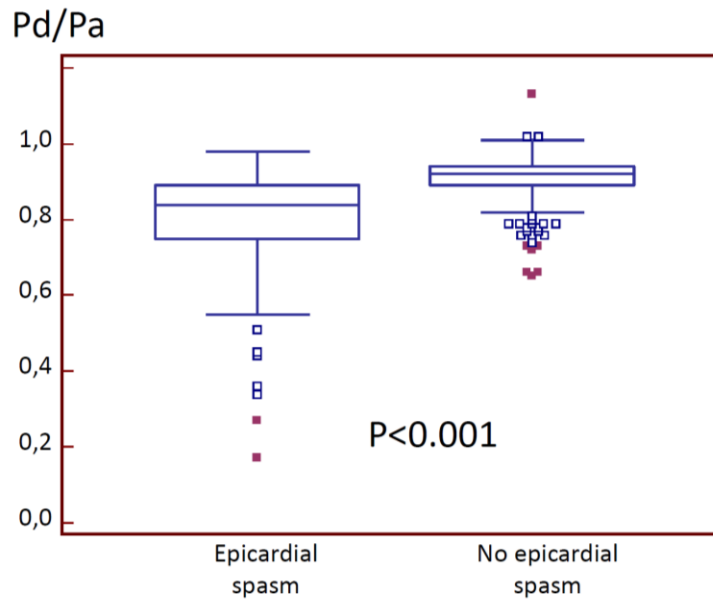
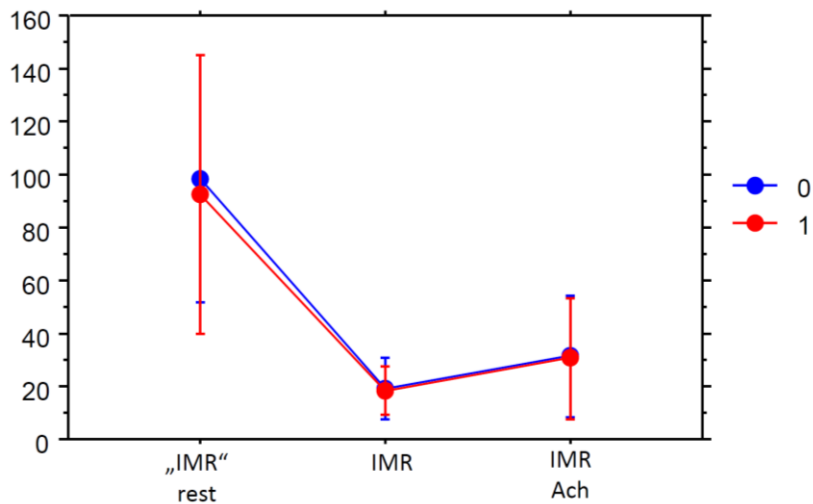
**False Microvascular Spasm**



# #FullPhysiology 2.0



- Hemodynamic definition of spasm
- New entity?



Quantification of acetylcholine responses using guidewire thermodilution: a multicentre study

H. Renteria, S. Miner, A.M. Leone, D. Ang, C. Berry, E-Z Celepli, G Gagno, G. Esposito, D. Nachoski, D. Galante, G. Campo, J. Escaned, T. Gori

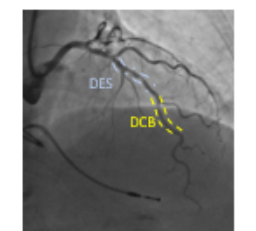
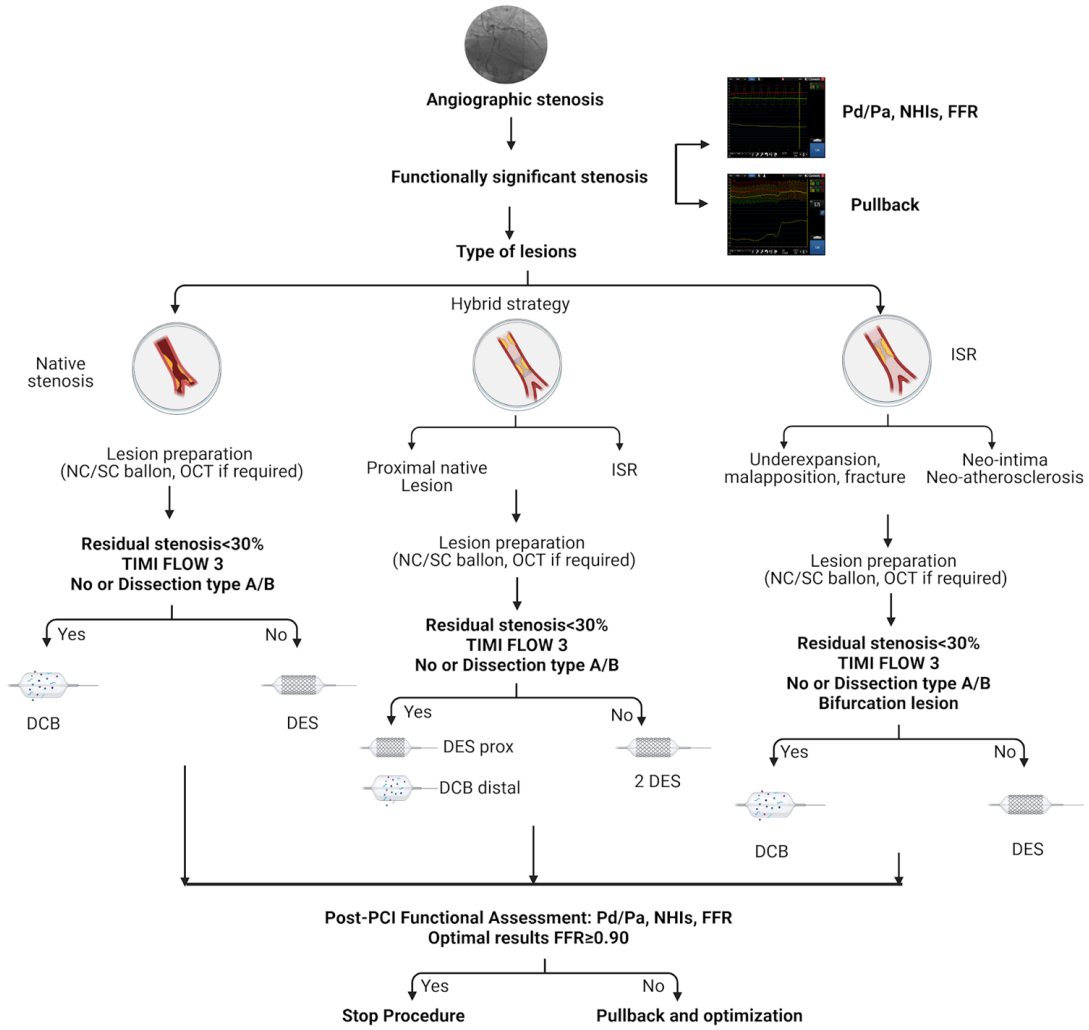


# Integration of #FullPhysiology in DCB PCI

Fondazione Policlinico Universitario A. Gemelli IRCCS/ Gemelli Isola - Rome (Italy)

- Data collection period: 2018-2024
- Total DCB-PCI (2018-2024): 668
- Physiology guided DCB-PCI: 31 (4.6%).

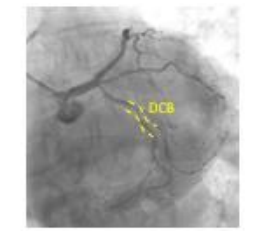
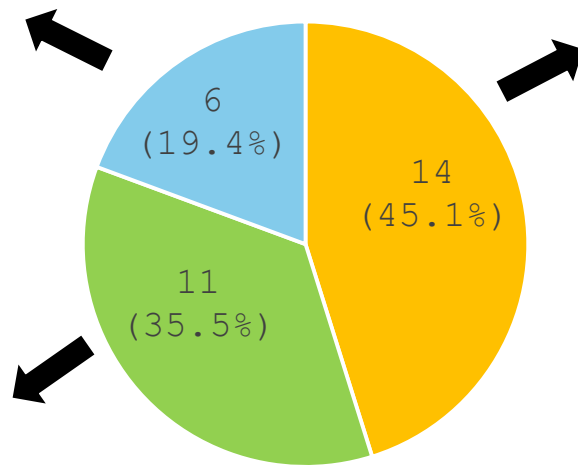
«...utilization of Physiology to optimize an angiographically acceptable DCB-PCI»



Proximal DES+ Distal DCB



ISR DCB



De novo lesions DCB

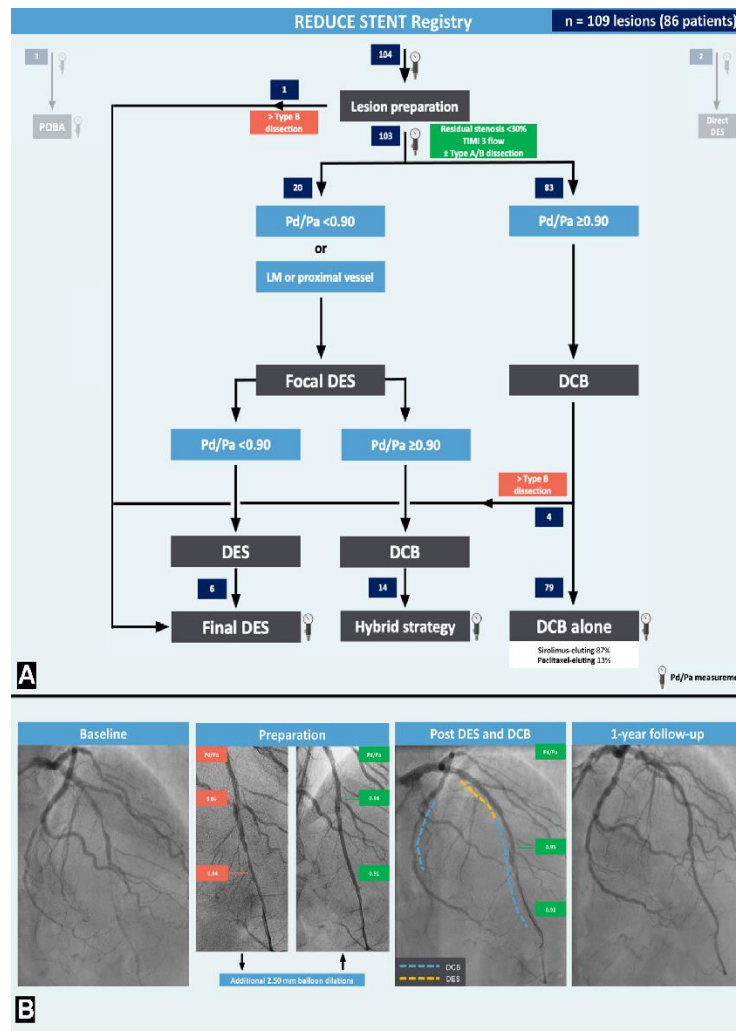


# Integration of @Fullphysiology in DCB PCI

## Drug-Coated Balloon Angioplasty Guided by Post-Percutaneous Coronary Intervention Pressure Gradient

The REDUCE-STENT Retrospective Registry

«...utilization of the distal coronary-to-aortic pressure ratio (Pd/Pa) post-lesion preparation to safely limit stenting when the result is considered angiographically imperfect...»



## TVF

	Definite	Probable
Acute	0	0
Subacute	0	1
Late	1	0
Very late	0	1

Target vessel MI	1 (0.01%)
TLF	11 (13.2%)
TVR	8 (8.7%)

Median follow-up 246 days (interquartile range 136-400 days)



# The future of #FullPhysiology starts today



From INROAD to SAMCRO  
S. Biscaglia



MiVa  
L. Di Serafino



MICROREV-DCM  
R. Scarsini



REDUCE CMD  
F. D'Ascenzo



RIALTO PRO  
D. D'Amario



PROMISE  
R. Montone



# Conclusions

1

We have relatively **simple tools** to comprehensively assess coronary circulation in a short time\*

2

A **correct diagnosis** can have important therapeutic and prognostic implications

3

INOCA has an important **socio-economic impact** and now can be **treated appropriately** only using an invasive guide using a pressure/thermodilution wire

4

INOCA is a useful model for a variety of clinical settings in which **#FullPhysiology** can make the difference including PCI

\*Mean procedural time  $20 \pm 7$  minutes from the first NHPR to the end of the test



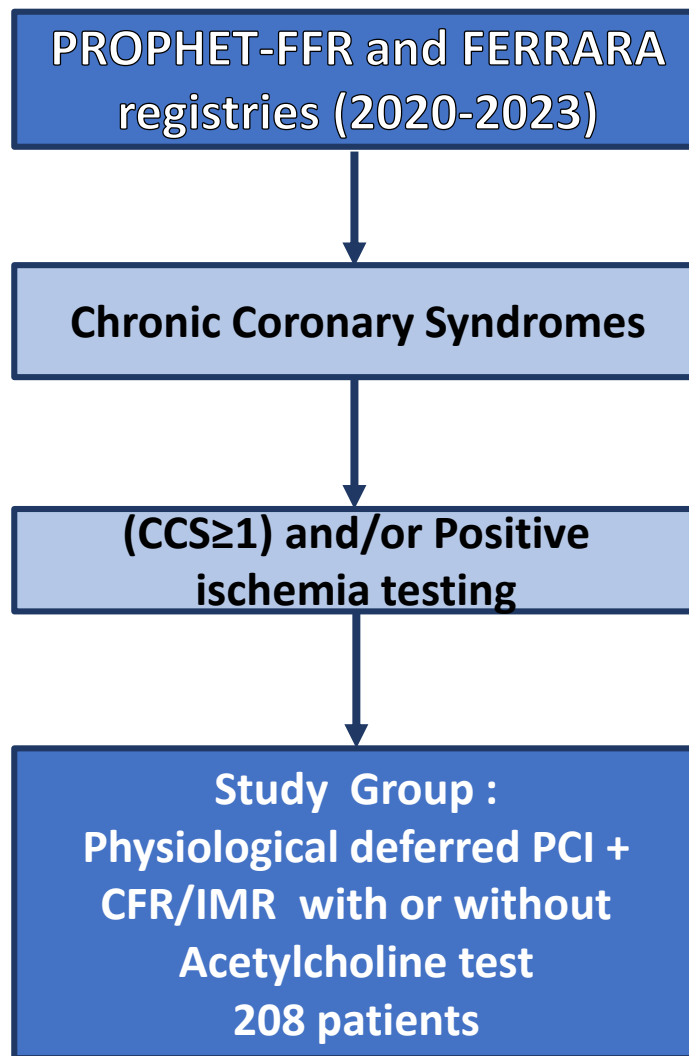
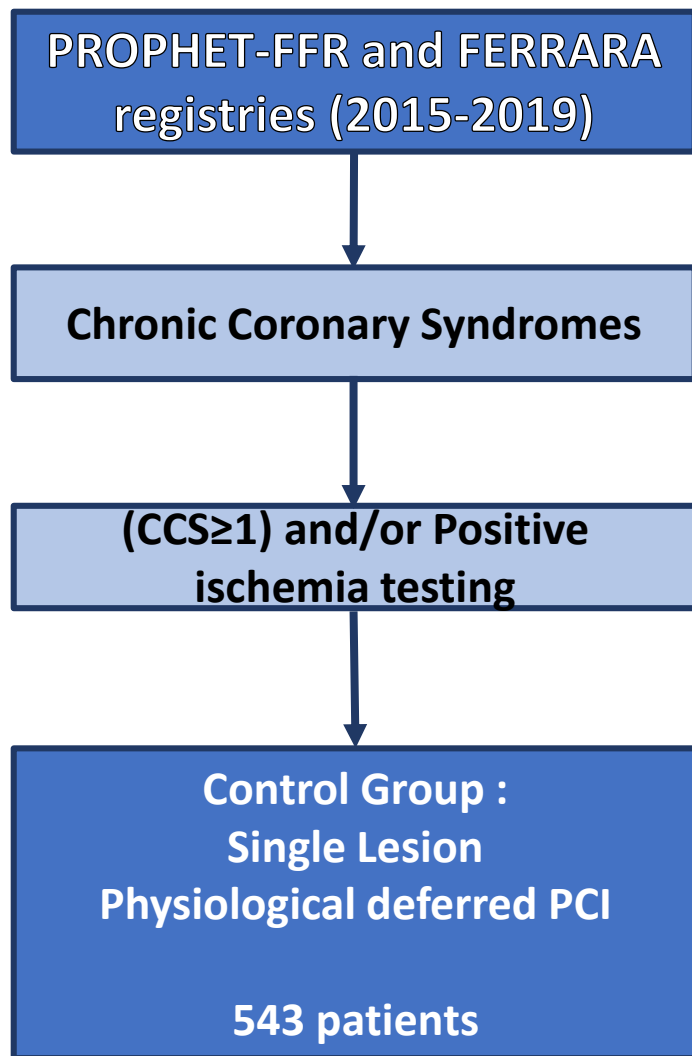


# Conclusions...

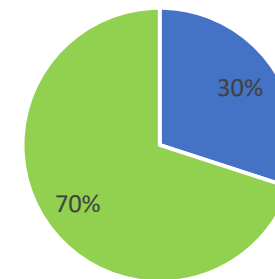




# Usefulness of #FullPhysiology in daily practice

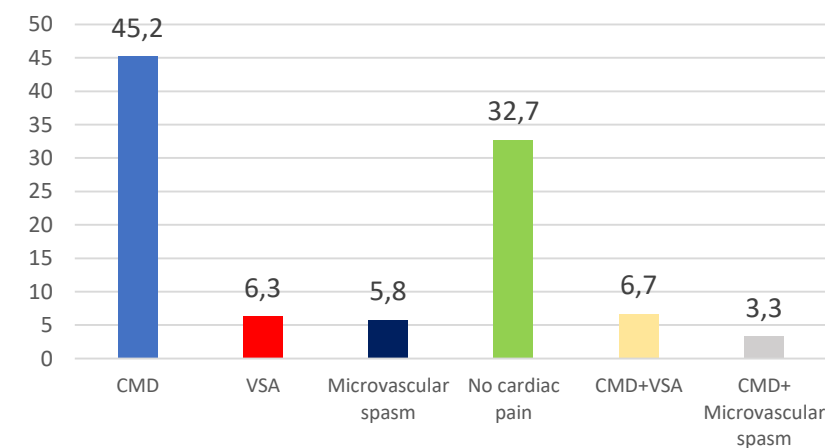


Modality of Physiological assessment



■ CFR/IMR ■ CFR/IMR plus Ach

Diagnosis %





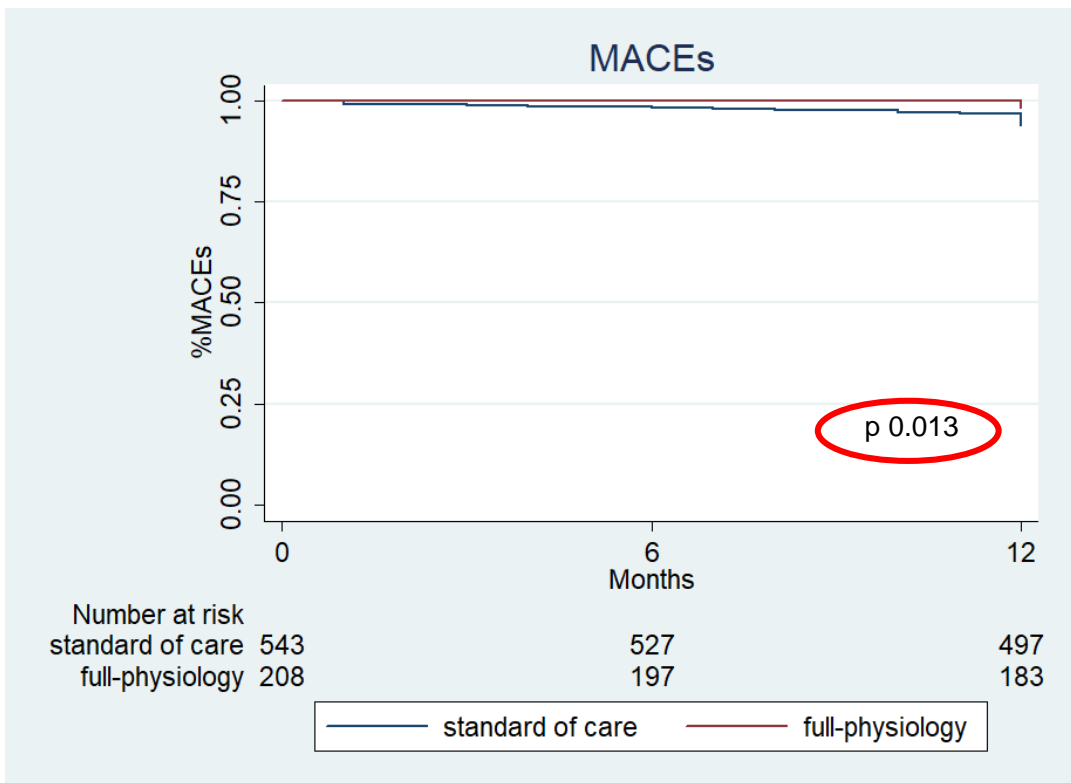
# Usefulness of #FullPhysiology in daily practice

Patients (n=751)	Global	Standard of care (n= 543)	#FullPhysiology (n=208)	p value
Age (mean ± SD)	68.1±10.9	68.8±10.2	66.1±12.3	<0.01
Male sex (%)	62	65.2	53.6	<0.01
Hypertension (%)	77.2	80.5	68.6	<0.01
Smoking (%)	44.9	45.0	44.7	0.945
Dyslipidemia (%)	66	65.9	66.3	0.918
Diabetes (%)	26.2	26.9	24.3	0.488
CKD (%)	14.4	15.1	12.5	0.37
History of CAD	33.2	34	32	0.637
EF (mean ± SD)	55.8±10.4	56.5±9.5	53.8±12.3	<0.01
BMI (mean ± SD)	28.2±16.8	27.2±4.6	29.9±6.8	0.08
CCS 3-4 (%)	-	-	-	-
Previous MI (%)	21.3	18.6	28.5	<0.01
Previous PCI (%)	33.5	32.17	39.4	0.09
Vessel (n=751)	Global	Standard of care (n= 543)	#FullPhysiology (n=208)	p value
FFR (mean ± SD)	0.89±0.04	0.89±0.04	0.89±0.04	0.239
LAD (%)	78.4	75.3	86.5	<0.01
LCX (%)	9.1	9.9	6.7	0.170
RCA (%)	12.5	14.8	6.8	<0.01



# Usefulness of #FullPhysiology in daily practice

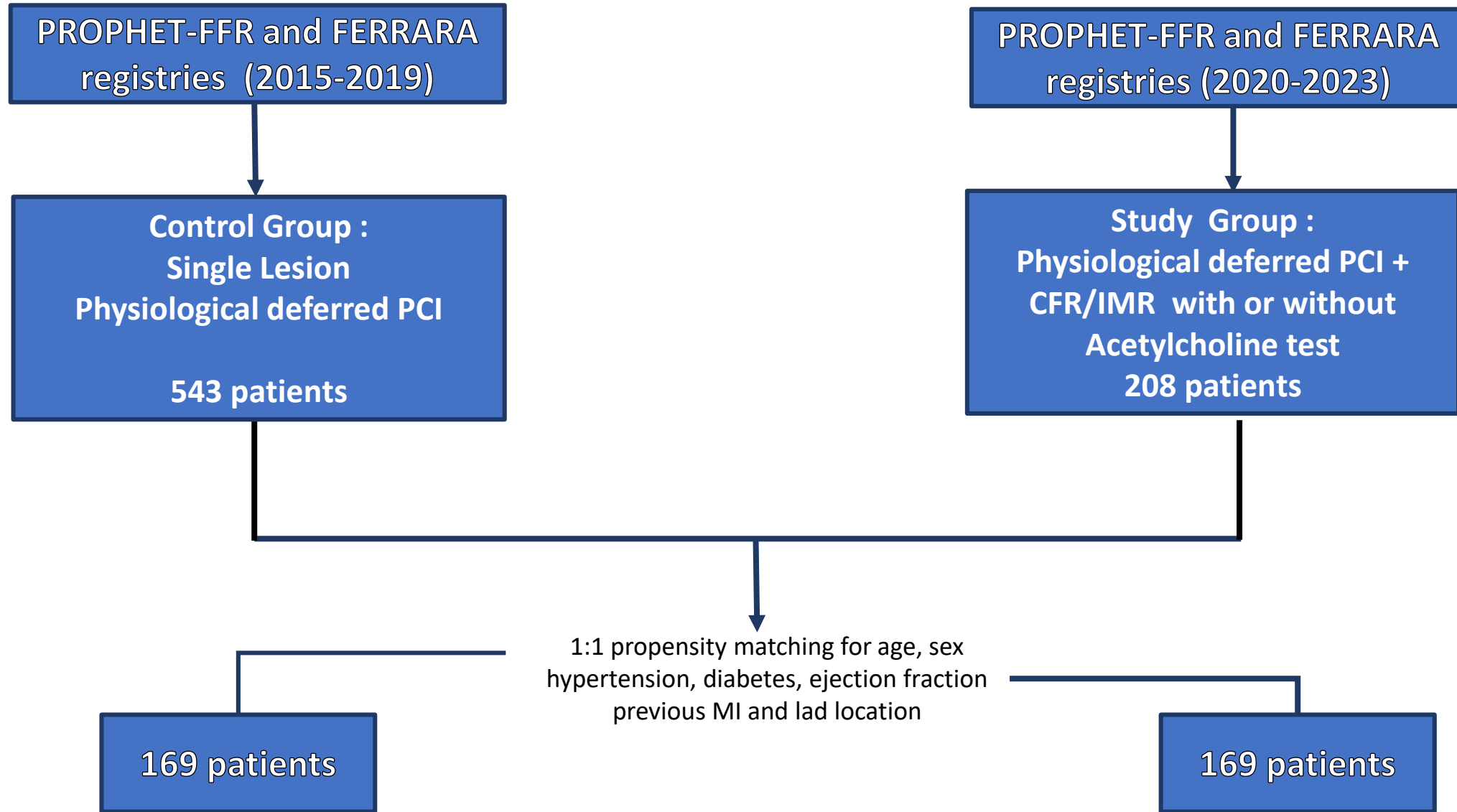
Follow up 12 months



	Standard of care (n=543)	#FullPhysiology (n=208)	p value (chi2)
Follow up (mean± DS)	11.5±1.8	11.3±2.1	0.132
MACEs (%)	5.9	1.4	0.009
TVR (%)	2.6	0	0.02
MI (%)	0.7	0.4	0.7
Cardiac Hospitalization (%)	5.7	1.4	0.011
Cardiac Death (%)	0.4	0	0.381



# Usefulness of #FullPhysiology in daily practice





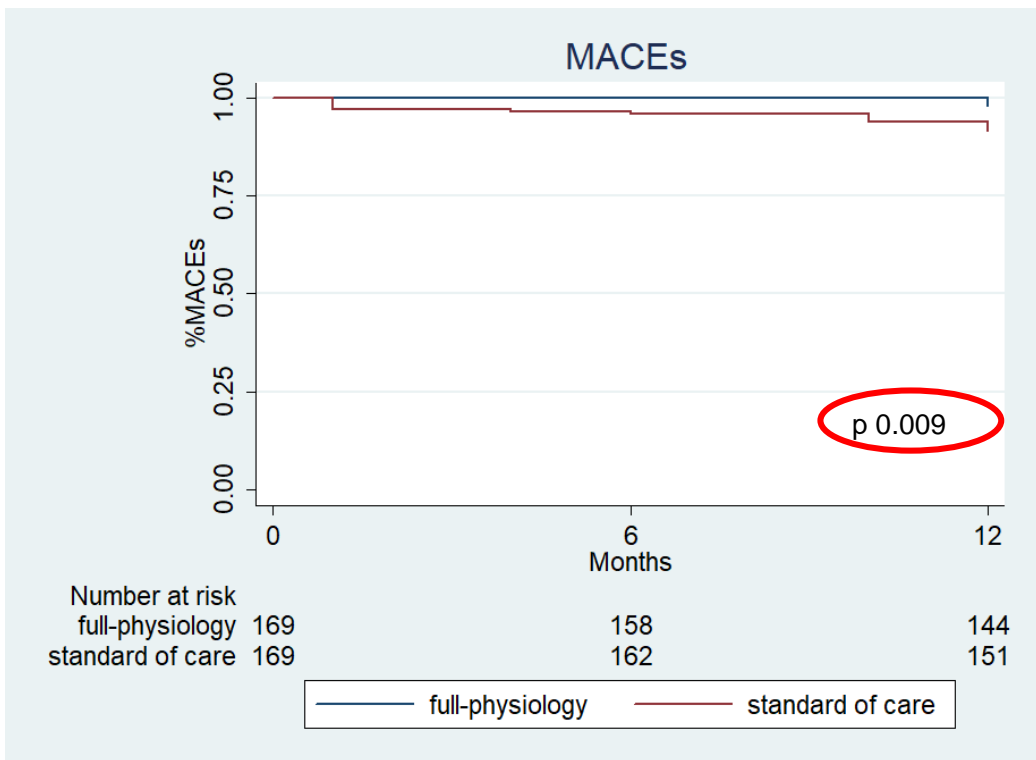
# Usefulness of #FullPhysiology in daily practice

Patients (n=338)	Standard of care (n= 169)	#FullPhysiology (n=169)	p value
Age (mean ± SD)	66.5±11.6	66.6±12.1	0.952
Male sex (%)	48	49.7	0.744
Hypertension (%)	70.4	68	0.637
Smoking (%)	41.3	47.3	0.266
Dyslipidemia (%)	60.7	67.4	0.197
Diabetes (%)	27.8	24.8	0.536
CKD (%)	17.7	13.1	0.236
EF (mean ± SD)	53.0±11.9	53.7±12.5	0.601
BMI (mean ± SD)	27.0±5.7	30.3±8.7	0.257
Previous MI (%)	27.2	28.9	0.716
Previous PCI (%)	38.4	36.7	0.736
Vessel (n=338)	Standard of care (n= 169)	#FullPhysiology (n=169)	p value
FFR (mean ± SD)	0.88±0.04	0.89±0.04	0.158
LAD (%)	86.4	87.6	0.746



# Usefulness of #FullPhysiology in daily practice

Follow up 12 months



	Standard of care (n=169)	#FullPhysiology (n=169)	p value (chi2)
Follow up (mean± DS)	11.4±2.2	11.2±2.3	0.312
MACEs (%)	8.2	1.8	0.006
TVR (%)	4.7	0	0.004
MI (%)	0.6	0.6	1
Cardiac Hospitalization (%)	8.2	1.8	0.006
Cardiac Death (%)	0.6	0	0.316



#Grazie

