Coronary Microvascular Dysfunction

Are you confused?

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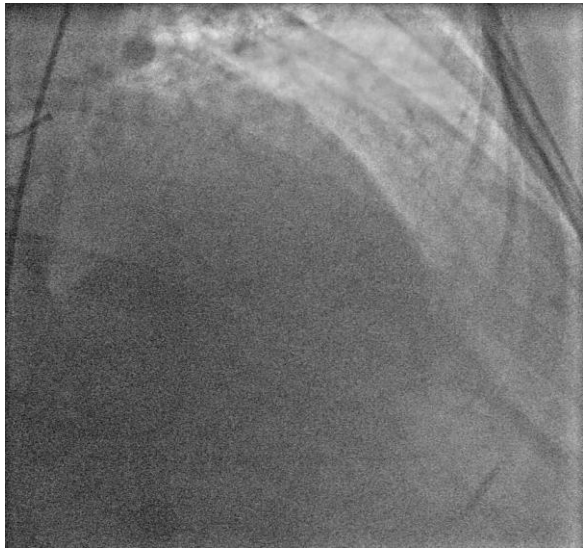
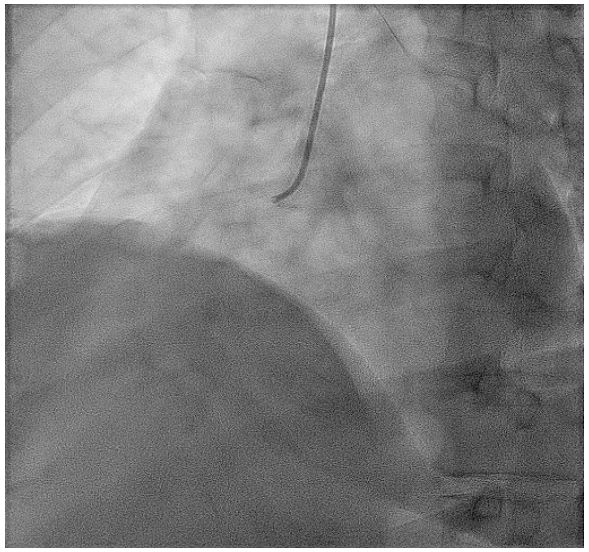
SYMPTOMATIC PATIENT





POSSIBLE DIAGNOSES

- Palpitations
- Musculoskeletal
- Pulmonary
- Gastrointestinal
- Anxiety

DETERMINATION

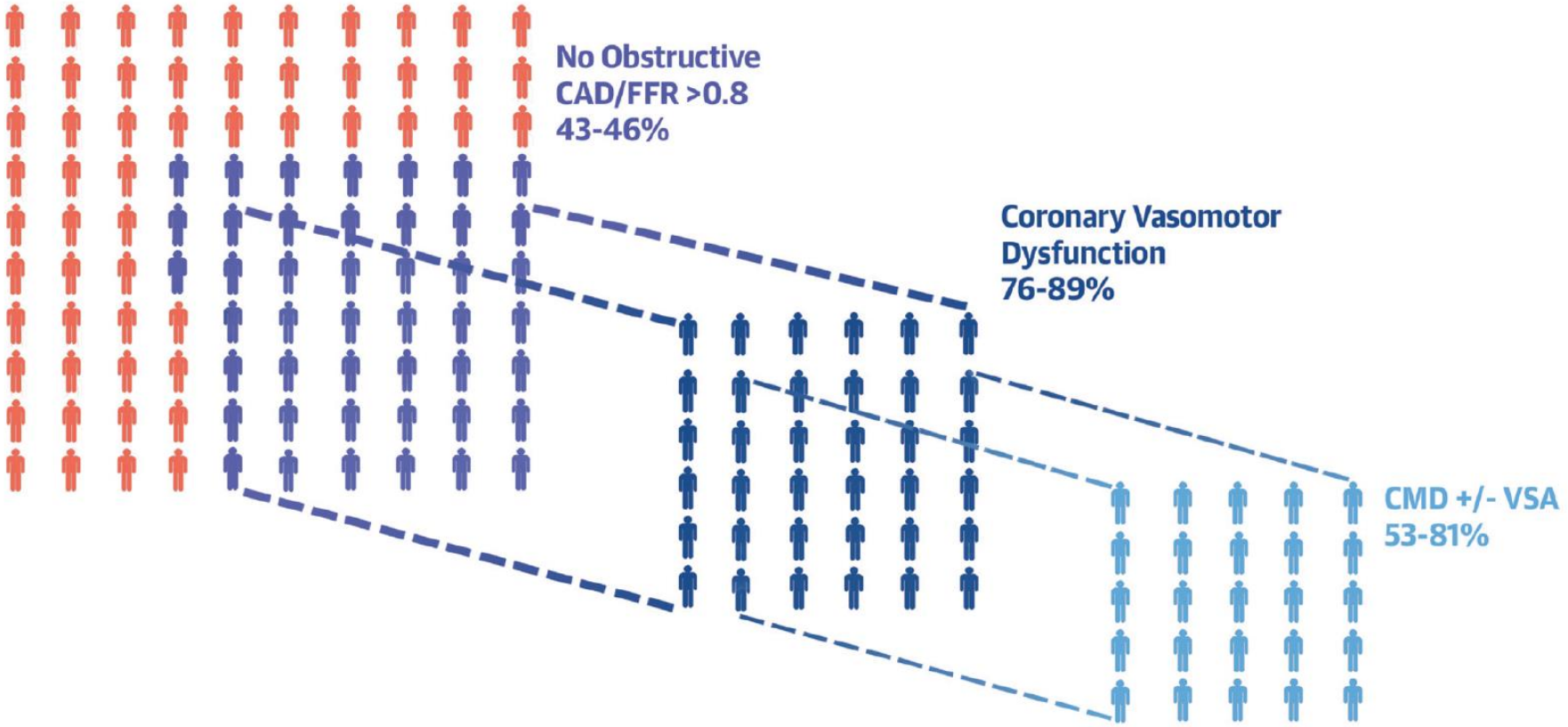
- Negative ILR/ 30-day monitor
- Non-palpable
- Negative CT/PFT
- Negative EGD
- Low clinical probability

?

Prevalence and Importance of CMD

CMD is Prevalent

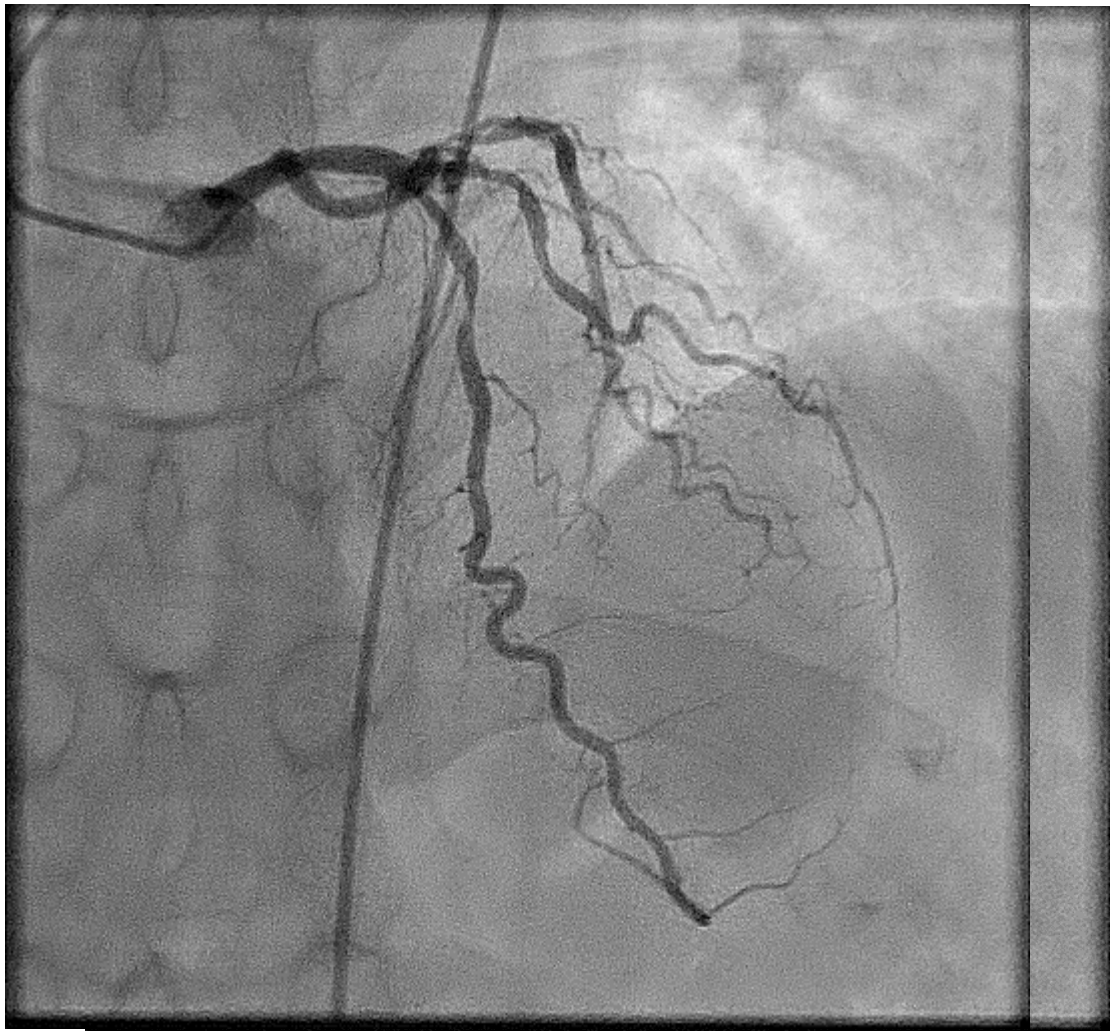
- **STABLE CAD REFERRED FOR INVASIVE CORONARY EVALUATION:**



Ford TJ et al. J Am Coll Cardiol 2018; 72:2841–55;
Suda A et al. J Am Coll Cardiol 2019; 74:2350-60;
Taqueti VR J Am Coll Cardiol 2019 Nov 12;74(19):2361-64

Could it be cardiac? Could it be the microcirculation?

Epicardial



Microcirculation

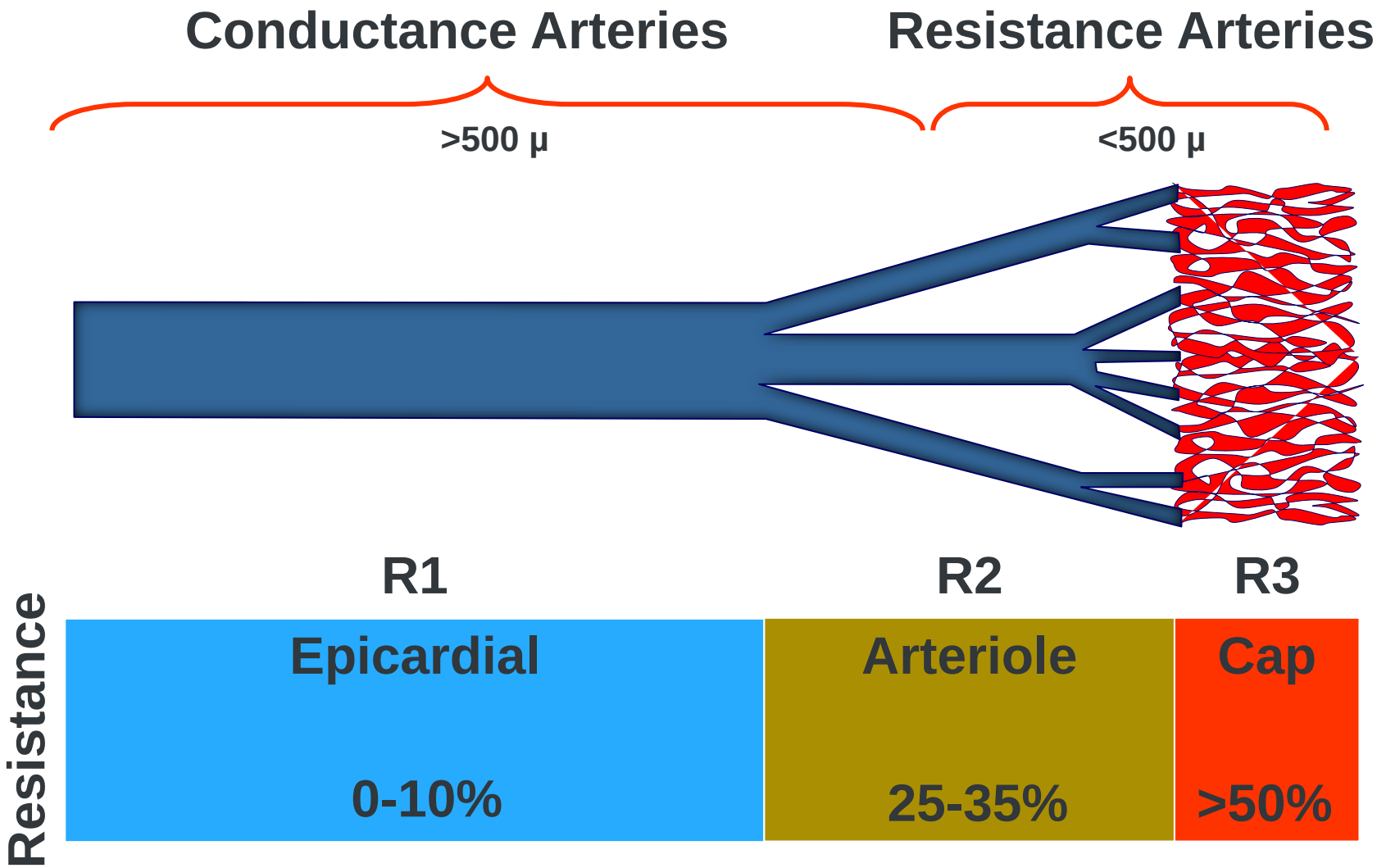
Methods of assessing the coronary microcirculation

Non-invasive	Invasive
PET (Positron Emission Tomography) *Passive diagnosis of exclusion*	**IMR** (Index for Microcirculatory Resistance) Bolus thermo-dilution
CMR (Cardiac Magnetic Resonance Imaging) *Poorly validated*	**CFR** (Coronary Flow Reserve) Doppler or Bolus thermo-dilution
MBG (Myocardial Blush Grade) *Poor reproducibility*	**Absolute Flow and Resistance** Continuous thermo-dilution
TIMI Score (Thrombolysis In Myocardial Infarction) *Validated for ACS*	

Pressure & Flow

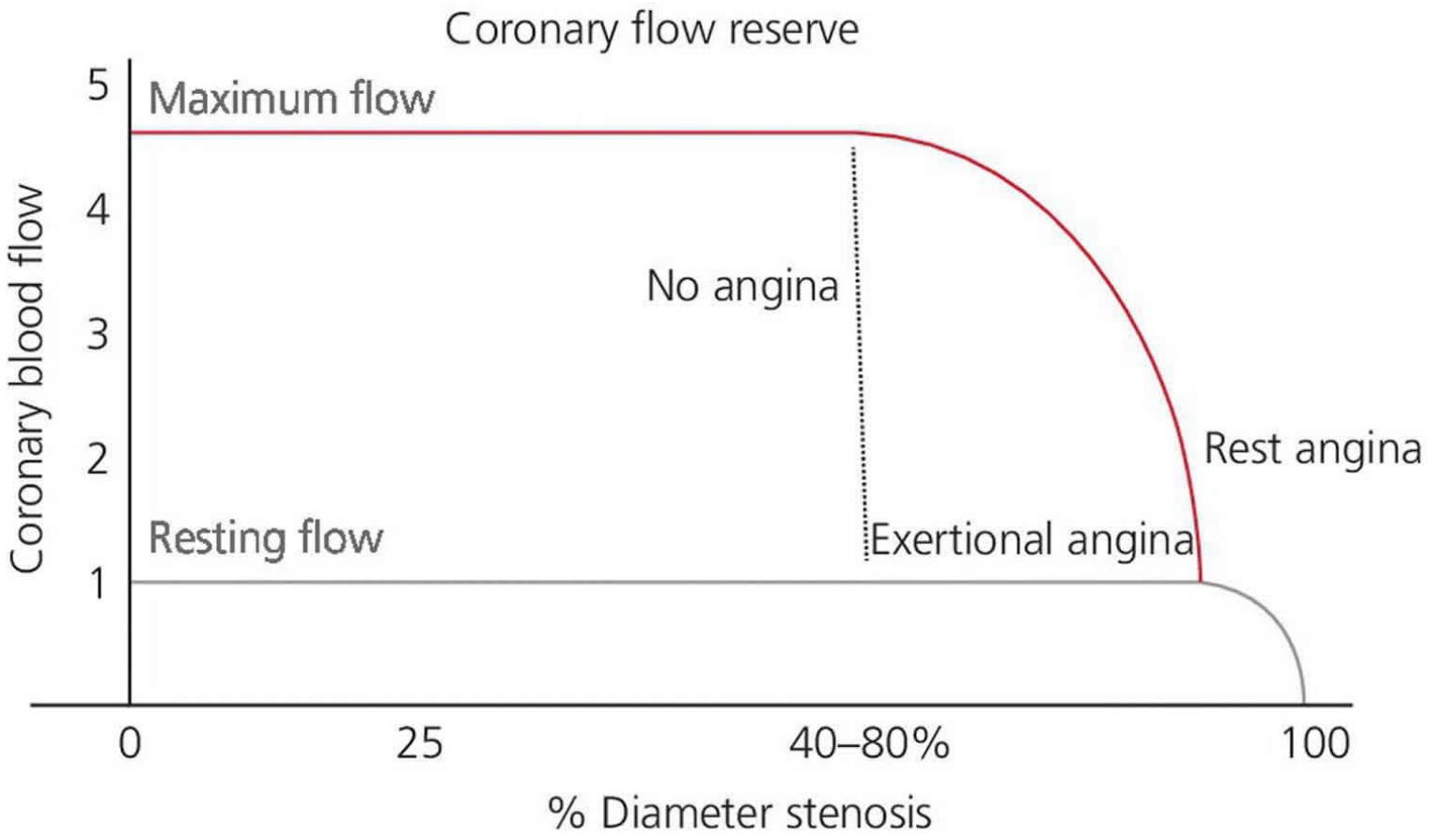
Let’s learn the language

Basic Coronary Physiology



Coronary Flow Reserve

Coronary Flow Reserve

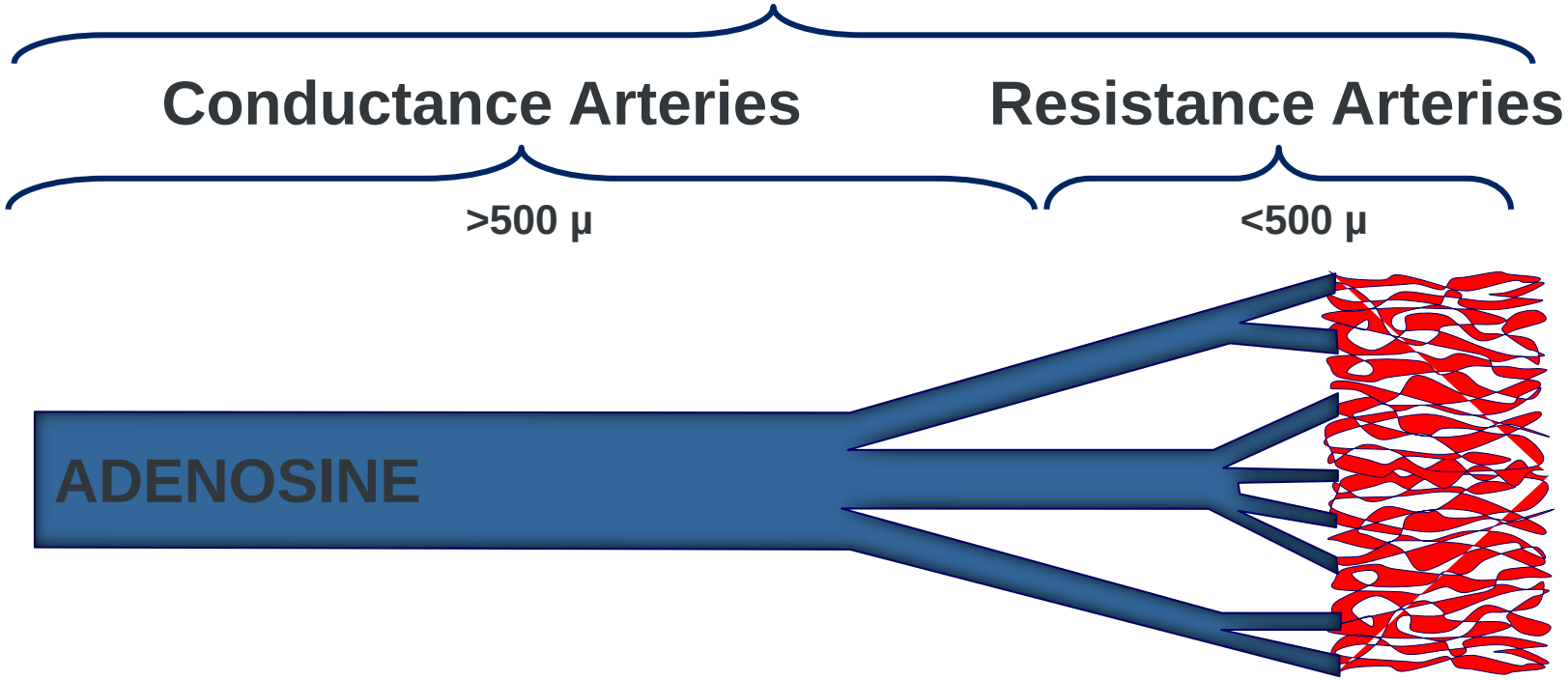


Maximal flow/Basal flow

- Decreases with increasing stenosis
- Culprit can be at R1, R2, R3

- ***Not microvascular specific***
- ***Normal values unclear***
- ***Perturbed by resting HD***

Coronary Flow Reserve



A ---------- B

Time (sec) = Basal Flow (Rest flow)

A ---------- B

Time (sec) = Flow at hyperemia (Maximal Flow)

Coronary Flow Reserve

In English: CFR is your ability to increase flow to your heart, when you need it.

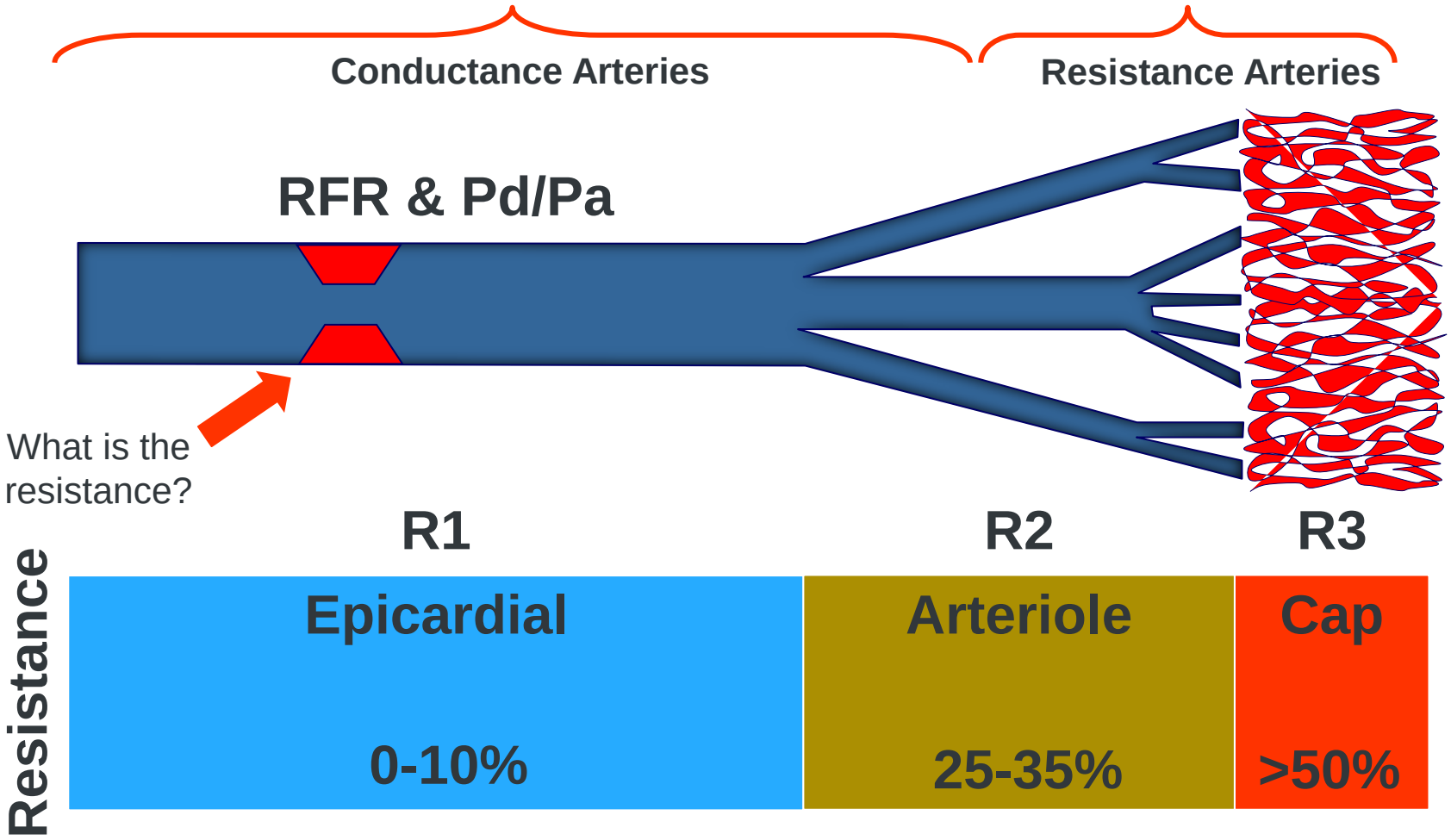
You see a bear in the woods, and need to run, your CFR is important to that response.

Major limitations for CFR assessment for the heart are

- Its very dynamic
- If the CFR is abnormal you don’t know why
- A low CFR certainly does not have to be caused by heart disease

Resting Full-Cycle Ratio and Pd/Pa

Resting Full-Cycle Ratio and Pd/Pa



Resting Full-Cycle Ratio and Pd/Pa

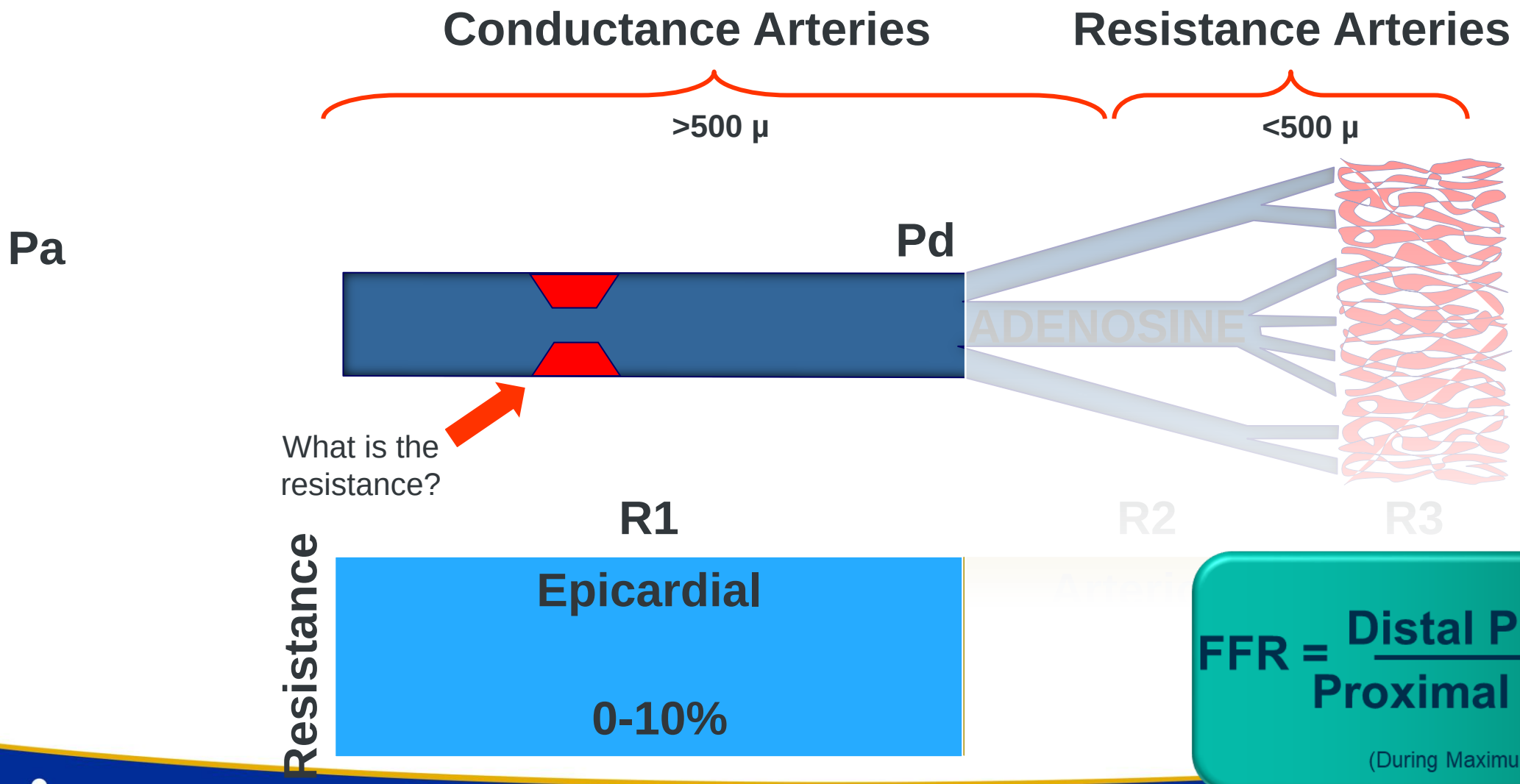
In English:

RFR and Pd/Pa determine the resistance across a coronary stenosis, ignoring the microcirculation (assuming a basal level of resistance when the distal coronary pressure is the lowest and the aortic pressure is the highest).

They are epicardial stenosis specific

Fractional Flow Reserve

Fractional Flow Reserve



$$FFR = \frac{\text{Distal Pressure } (P_d)}{\text{Proximal Pressure } (P_a)}$$

(During Maximum Hyperemia)

Fractional Flow Reserve

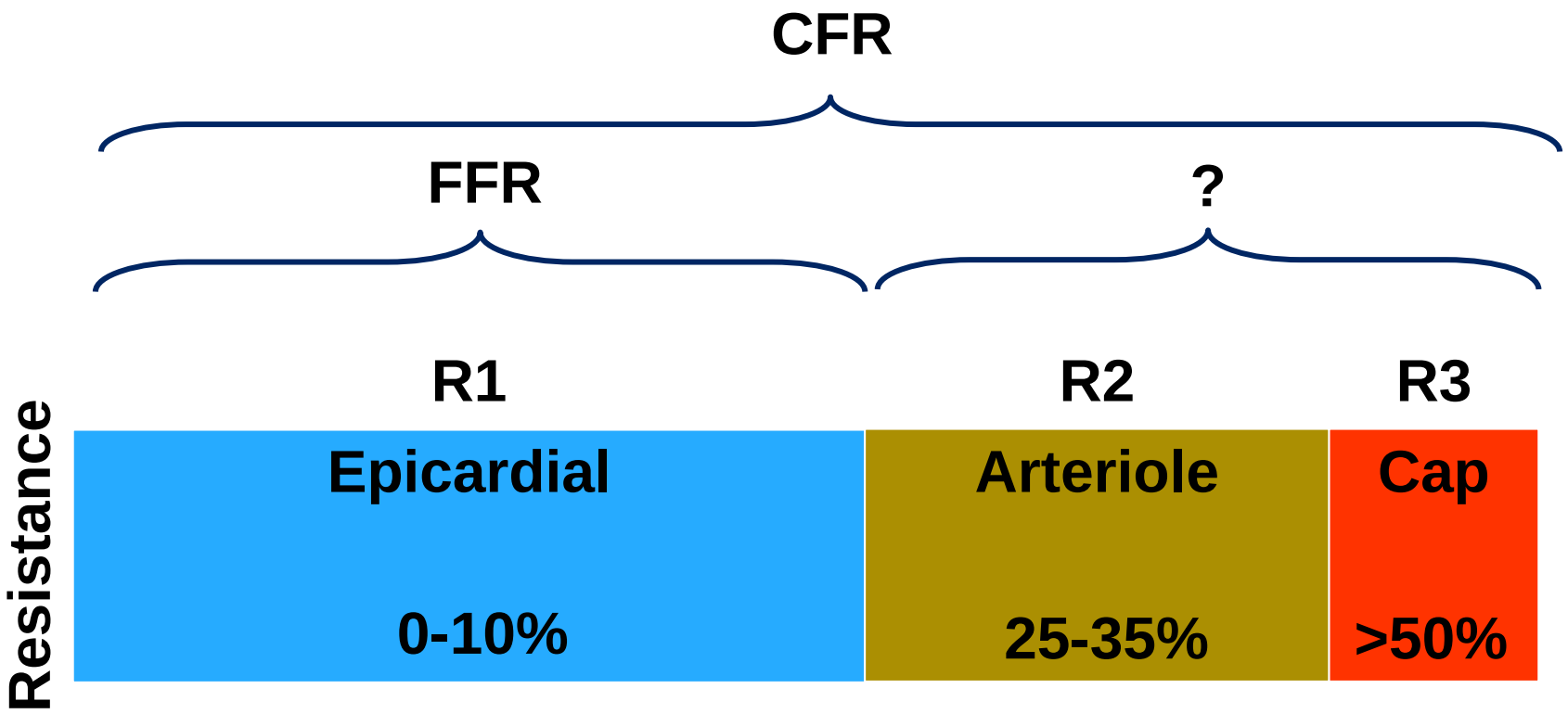
In English:

FFR determines the resistance across a coronary stenosis, including the microcirculation.

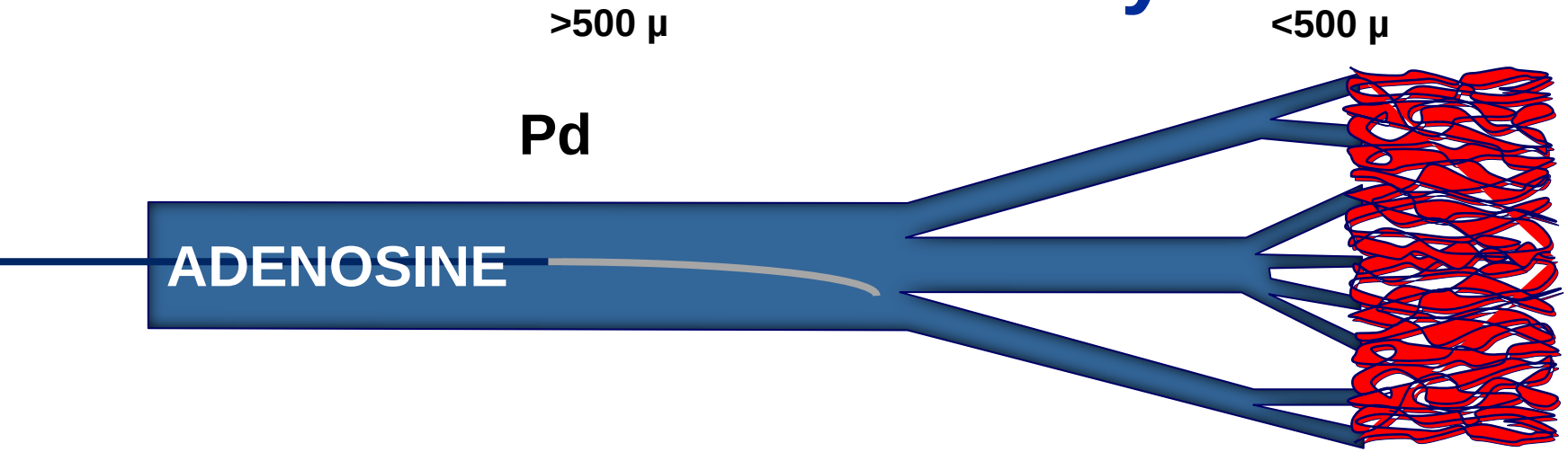
They are epicardial stenosis specific

The Microcirculation

The Microcirculation



Index of Microcirculatory Resistance



In english - a surrogate for the fastest flow
i.e. when the IMR is high, the flow is reduced at the microcirculatory level as all other coronary resistance has been removed)

A ---------- B

Time (sec) = Flow at hyperemia

Lowest diastolic pressure (Pd) * mean transit time at hyperemia = Index of Microcirculatory Resistance

Index of Microcirculatory Resistance

In English:

IMR is a snap-shot of the resistance in your microcirculation

Major limitations for IMR assessment

- MC function is dynamic
- IMR is snapshot

Four Criteria for Diagnosing Microvascular Angina

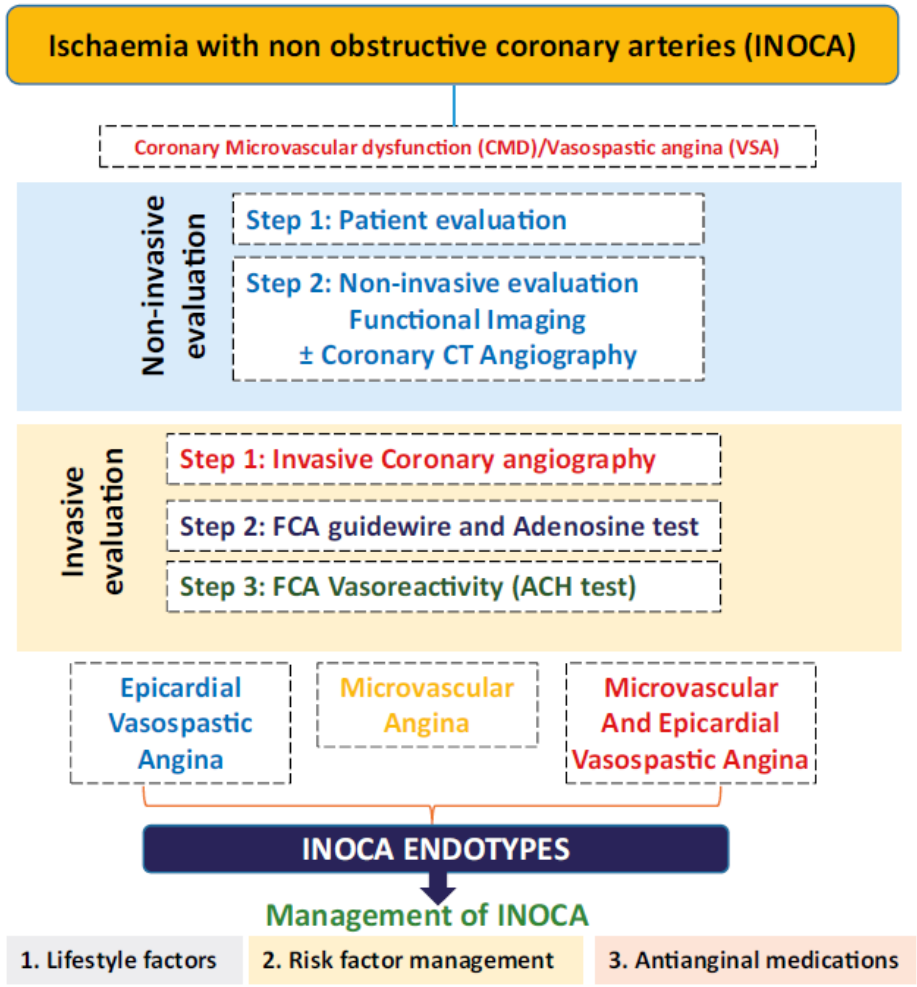
Presence of symptoms suggestive of myocardial ischemia	**ANGINA**
Objective documentation of ischemia	**ISCHEMIA**
Absence of obstructive CAD (< 50% stenosis on coronary angiography or FFR > 0.8)	**NOCAD**
Confirmation of a reduced coronary flow reserve / IMR or spasm (CFR < 2.0, IMR > 25, or positive acetylcholine test)[2]	**IMR/CFR/SPASM**

1. P. Ong et al. International Journal of Cardiology 250 (2018) 16–20
2. Ford TJ, et al. Heart 2018;**104**:284–292. doi:10.1136/heartjnl-2017-311446

EAPCI Consensus Document 2020

- **Recommendations**

1. INOCA should be recognized as a clinically important entity in daily clinical practice.
2. A systematic approach to diagnose and treat these patients should be implemented by clinicians and interventional cardiologists dealing with these patients.
3. National and international scientific societies, as well as the pharmaceutical and biomedical industries to support future research to address the incomplete understanding of the pathophysiology, the lack of targeted pharmacological treatment, and the evidence-based management of patients with INOCA.
4. Creating awareness of this condition through campaigns and media to ensure timely provision of care to these patients.

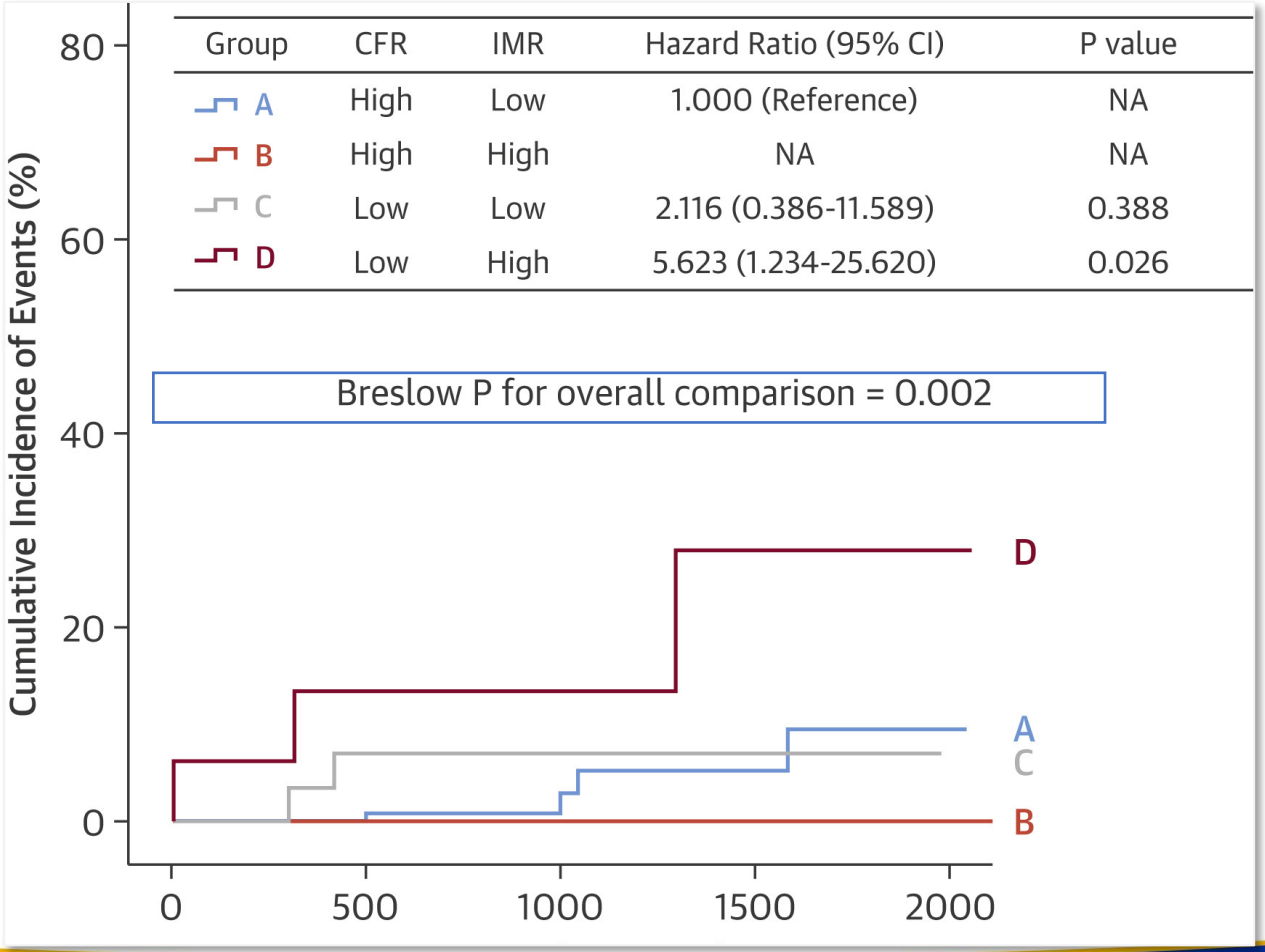


1. Kunadian, Vijay; EAPCI Expert Consensus Document *EHJ & Eurointervention* 2020: ehaa503

Clinical Relevance

Low CFR with High IMR has been Associated with Poor Prognosis

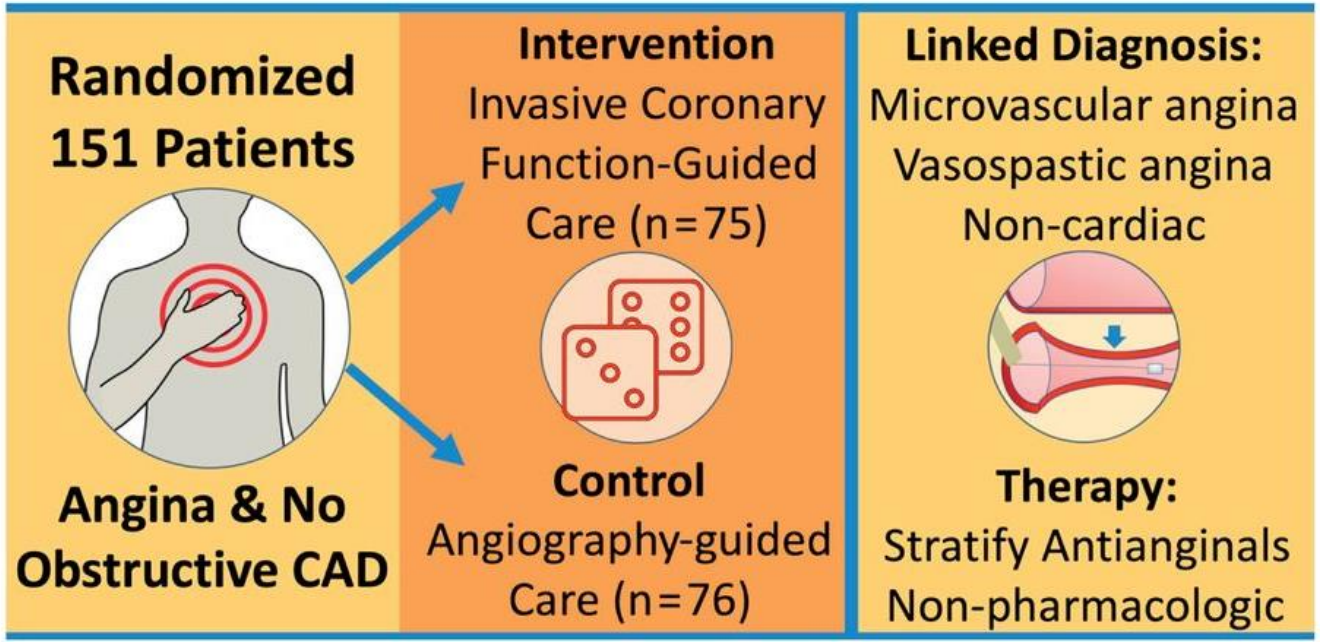
313 patients (FFR > 0.8): Low CFR and high IMR had a significantly higher rate of death, MI or Revascularisation



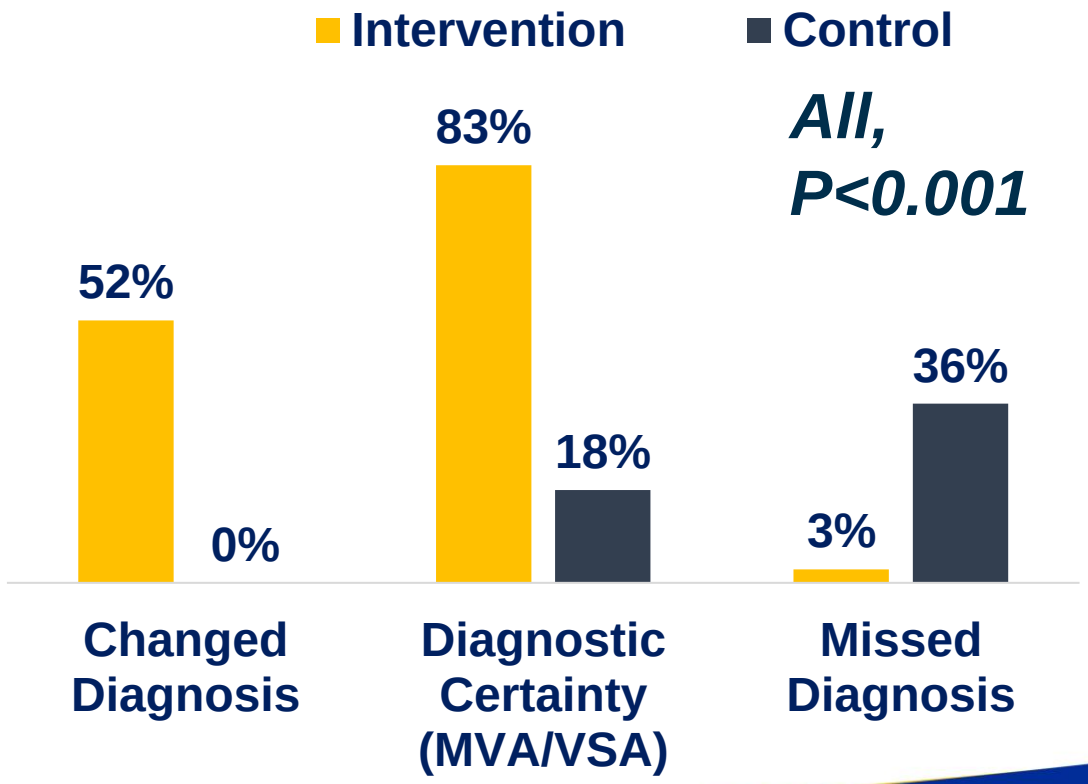
1. Lee JM, et al. *JACC*.2016;67:1158-1169

Diagnostic Utility - CorMicA

Study Overview



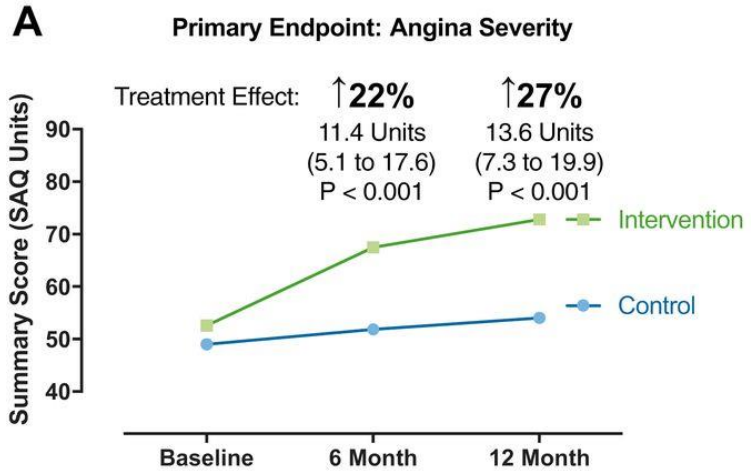
Diagnostic Utility

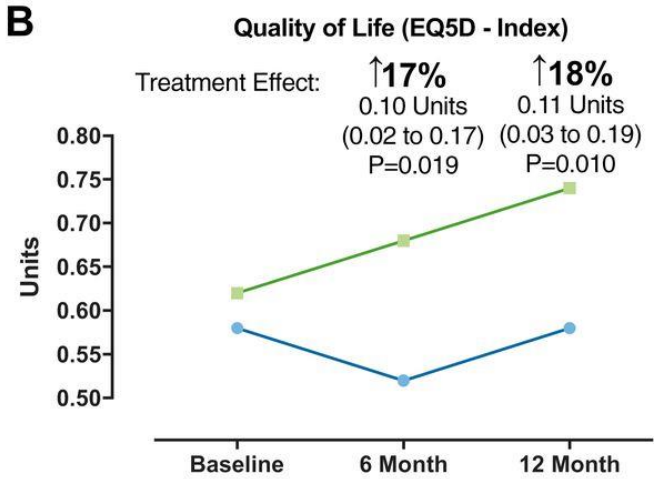


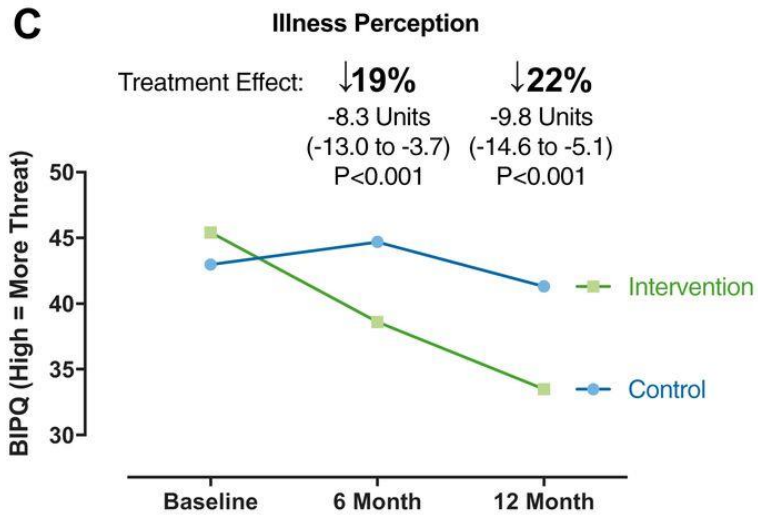
Ford et al. JACC 2018 Dec;72(23)

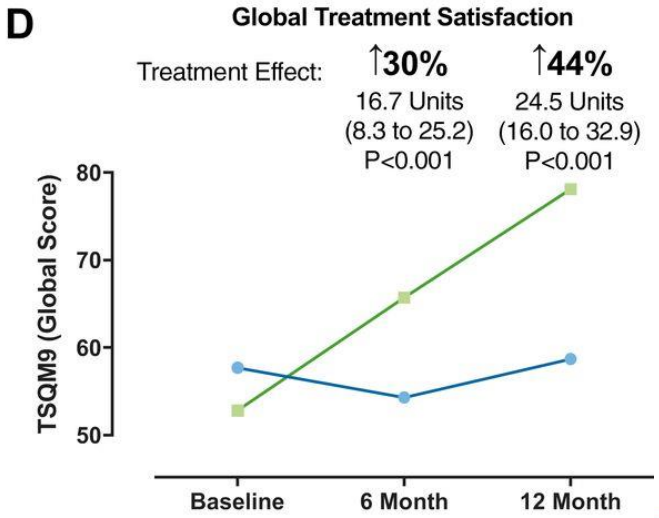
Primary Efficacy Endpoint:

Significant Decrease in Angina and Increase in Quality of Life







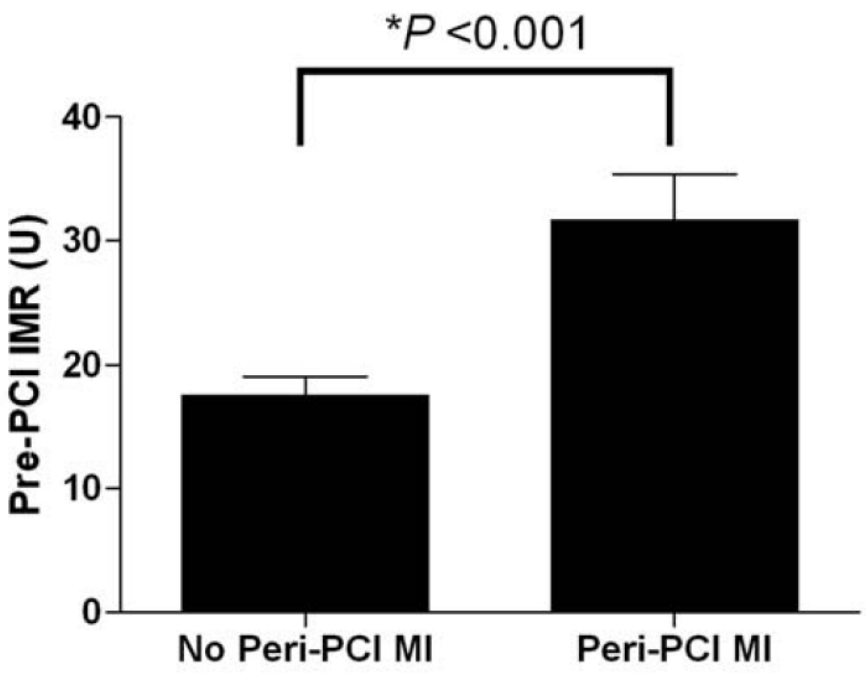


Ford et al. J Am Coll Cardiol Intv 2020;13:33-45

Ford et al. JACC 2018 Dec;72(23).

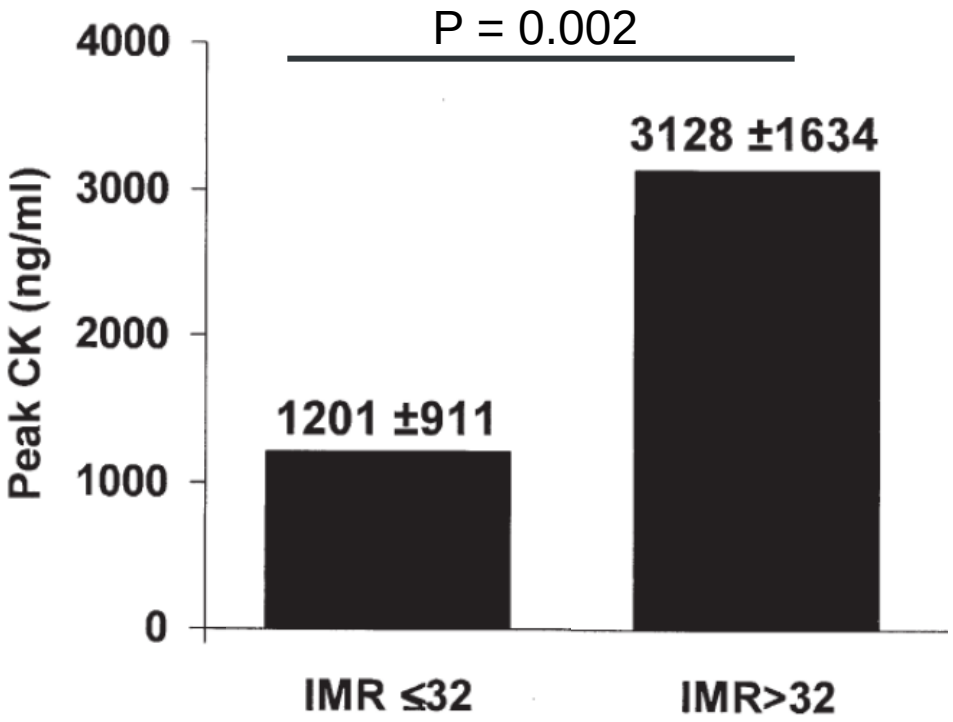
IMR Predicts Peri-PCI MI in Stable Angina and ACS

IMR measured before PCI in 50 stable patients undergoing LAD PCI



Ng, et al. Circ Cardiovasc Interv 2012;5:515-22.

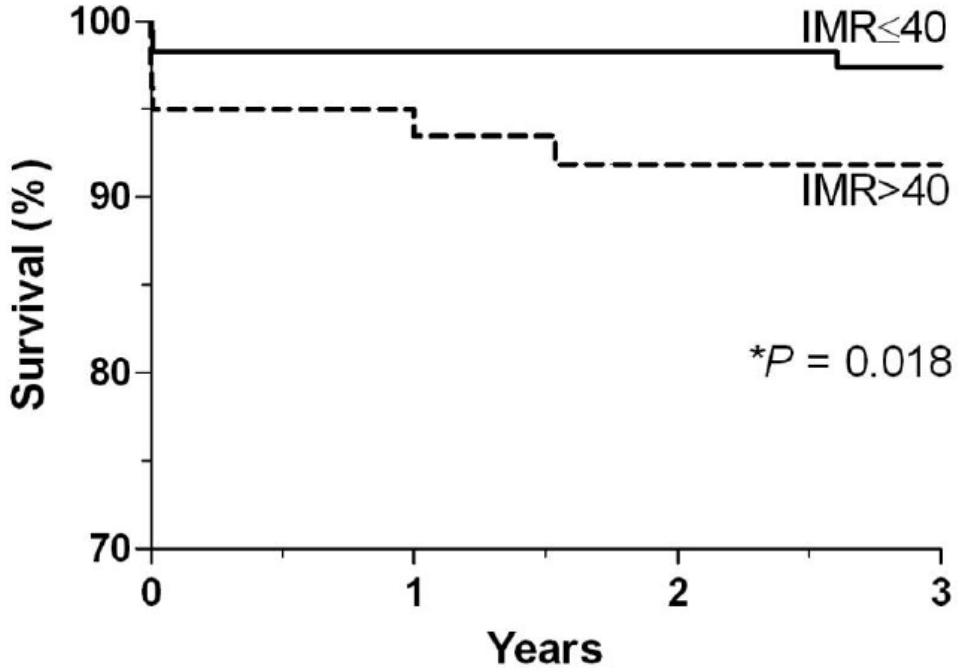
IMR predicts peak CK in patients with STEMI



J Am Coll Cardiol 2008;51:560-5

IMR Predicts Outcomes in STEMI

Multicenter study evaluating relationship between IMR and longer-term outcomes in 253 STEMI patients

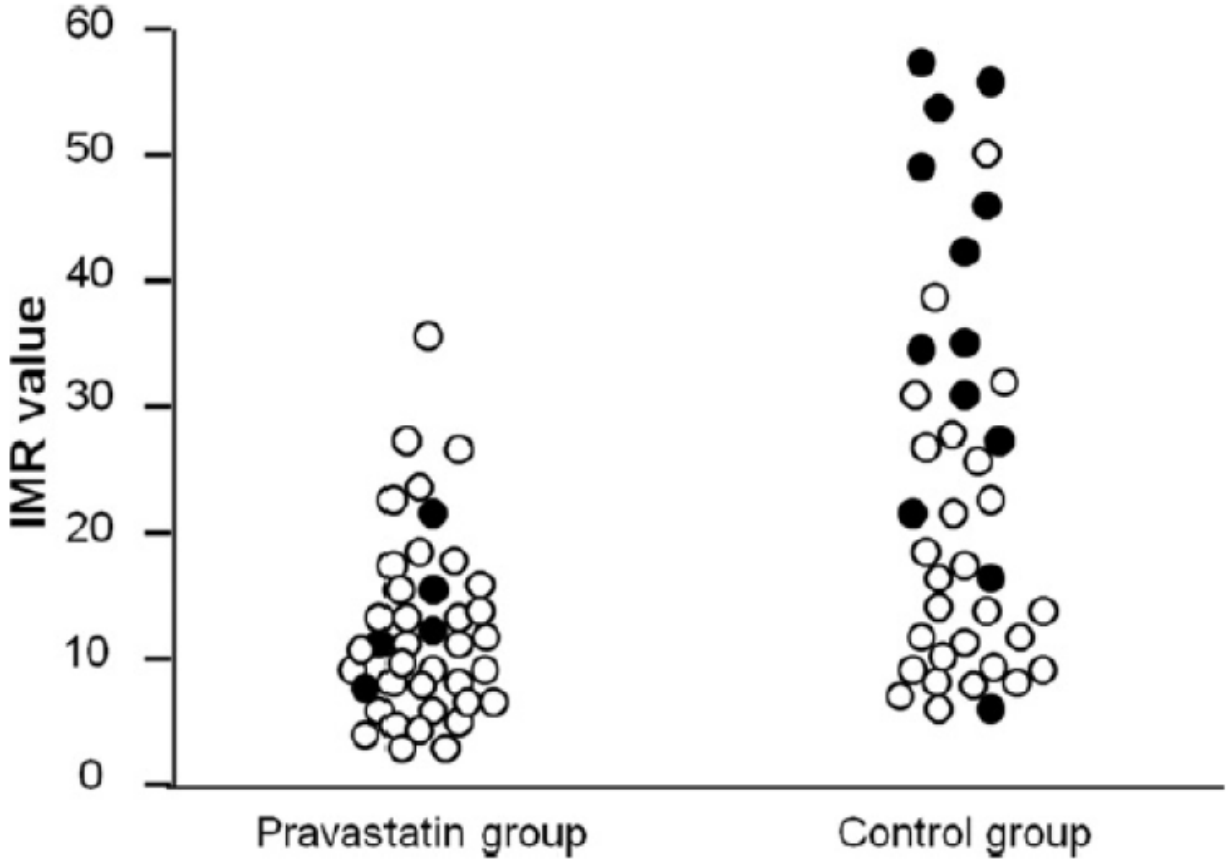


No. at risk:				
IMR ≤40	173	154	149	84
IMR >40	80	69	63	33

Circulation 2013; 127:2436-2441.

IMR improves with Statin Therapy

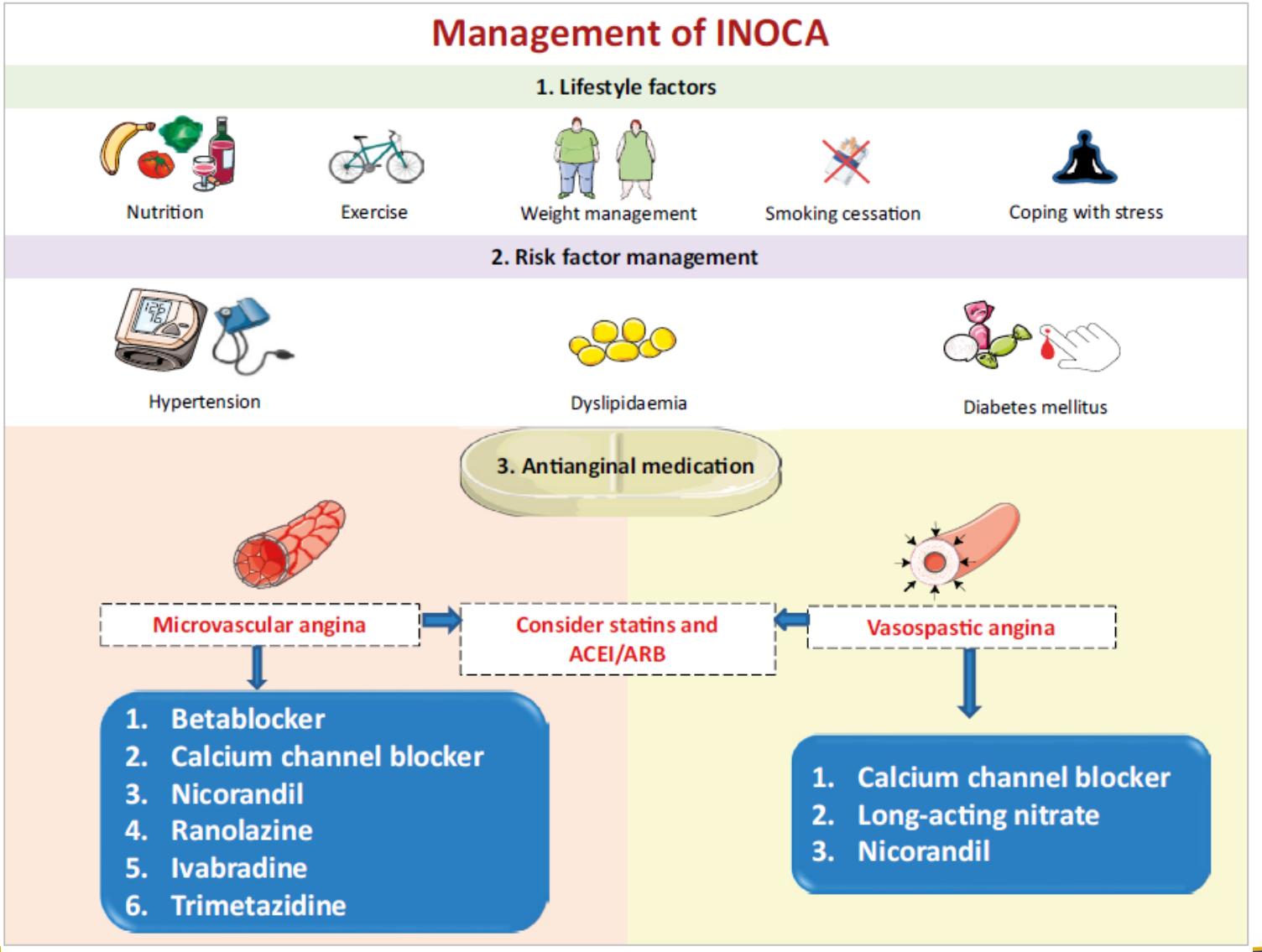
IMR measured after PCI in 80 patients randomized to either 1 month pretreatment with pravastatin or placebo



Fujii, et al. J Am Coll Cardiol Intv 2011; 4:513-20.

Treatment

Management Consensus for the INOCA Patient



1. Kunadian, Vijay; EAPCI Expert Consensus Document *EHJ & Eurointervention* 2020: ehaa503

Conclusions

- The microvasculature is a complex entity, which is challenging to investigate.
- Measurement of IMR is easy, specific for the microvasculature, quantitative, reproducible, and independent of hemodynamic changes.
- Measurement of IMR may help guide treatment in patients with “normal coronaries” and chest pain. IMR predicts outcomes in acute MI; emerging data suggest its utility in stable PCI patients, as well.