ESC CCS guidelines, 2019

ESC guidelines, Chronic Coronary Syndromes
Angina without obstructive disease in the epicardial coronary arteries - INOCA

Recommendations	Class	Level
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.	IIa	B
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.	IIb	B
Transthoracic Doppler of the LAD, CMR, and PET may be considered for non-invasive assessment of CFR.	IIb	B

Following society guidelines for IMR and CFR

ESC guidelines recommend measuring IMR and CFR using a guidewire-based approach for symptomatic patients who exhibit no significant evidence of epicardial stenosis.

Recommendations	Class[a]	Level[b]
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 stenosis with preserved iwFR (instantaneous wave-free ratio)/FFR.	IIa	B

a Class of recommendation. **b** Level of evidence.

CFR = coronary flow reserve; iwFR = instantaneous wave-free ratio; FFR = fractional flow reserve

The PressureWire™ X Guidewire has the capability to wirelessly measure both indices of epicardial disease (FFR, RFR) and microvascular dysfunction (IMR, CFR) using its pressure and temperature sensors.

Microvascular angina (MVA)

International standardization of diagnostic criteria for microvascular angina☆

Peter Ong [a,*,1], Paolo G. Camici [b,1], John F. Beltrame [c], Filippo Crea [d], Hiroaki Shimokawa [e], Udo Sechtem [a], Juan Carlos Kaski [f], C. Noel Bairey Merz [g,*], On behalf of the Coronary Vasomotion Disorders International Study Group (COVADIS)

Int J Cardiol 2017

1. Symptoms of myocardial ischaemia	○ Effort and/or rest angina ○ Angina equivalents (i.e. SOB)
2. Absence of obstructive CAD (>50% diameter reduction or FFR <0.80) by	○ Coronary CTCA ○ Invasive coronary angiography
3. Objective evidence of myocardial ischaemia	○ Ischemic ECG changes during an episode of chest pain ○ Stress-induced chest pain and/or ischemic ECG changes in the presence or absence of transient/reversible abnormal myocardial perfusion and/or wall motion abnormality
4. Evidence of impaired coronary microvascular function	○ Impaired coronary flow reserve (cut-off values depending on methodology use between ≤2.0 and ≤2.5) ○ Coronary microvascular spasm, defined as reproduction of symptoms, ischemic ECG shifts but no epicardial spasm during acetylcholine testing. ○ Abnormal coronary microvascular resistance indices (e.g. IMR >25, HMR ≥2.5 mm Hg·cm-1·s) ○ Coronary slow flow phenomenon, defined as TIMI frame count >25.

* 1 – 3 = probable MVA, 1 – 4 = definite MVA

CB. Dec 2020

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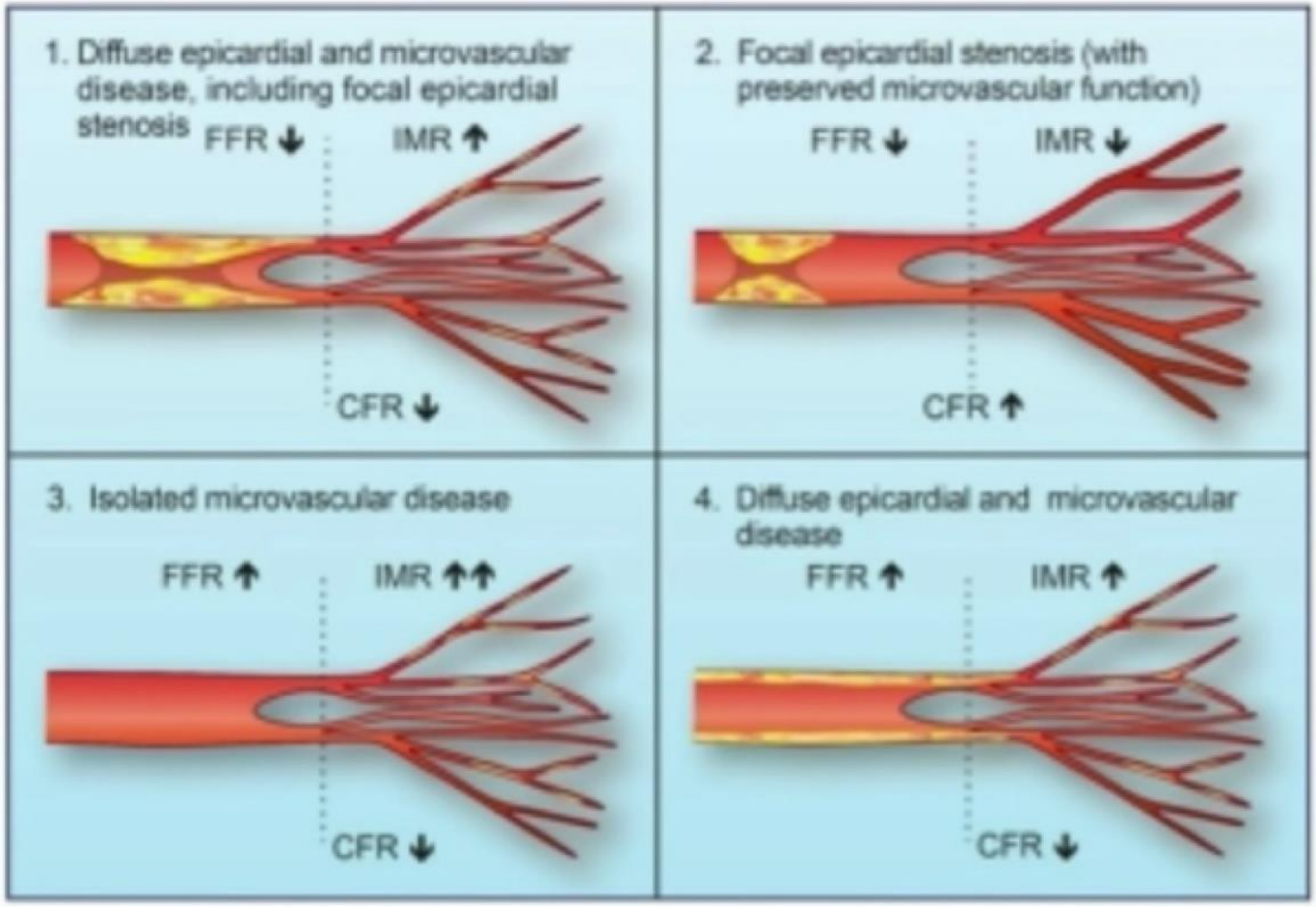
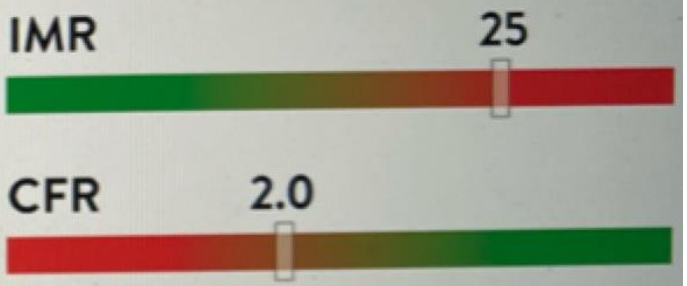
Coronary endotypes



Ford, Corcoran, Berry. EHJ 2017

Coronary Microvascular Dysfunction

IMR and CFR cutoffs in a population of ischemia with no obstructive coronary artery disease (INOCA) patients are shown on the right (based on CorMicA trial).[2]



Green indicates normal values, red indicates abnormal values
Cutoff values are specific for INOCA patients
INOCA: Ischemia with no obstructive coronary artery disease

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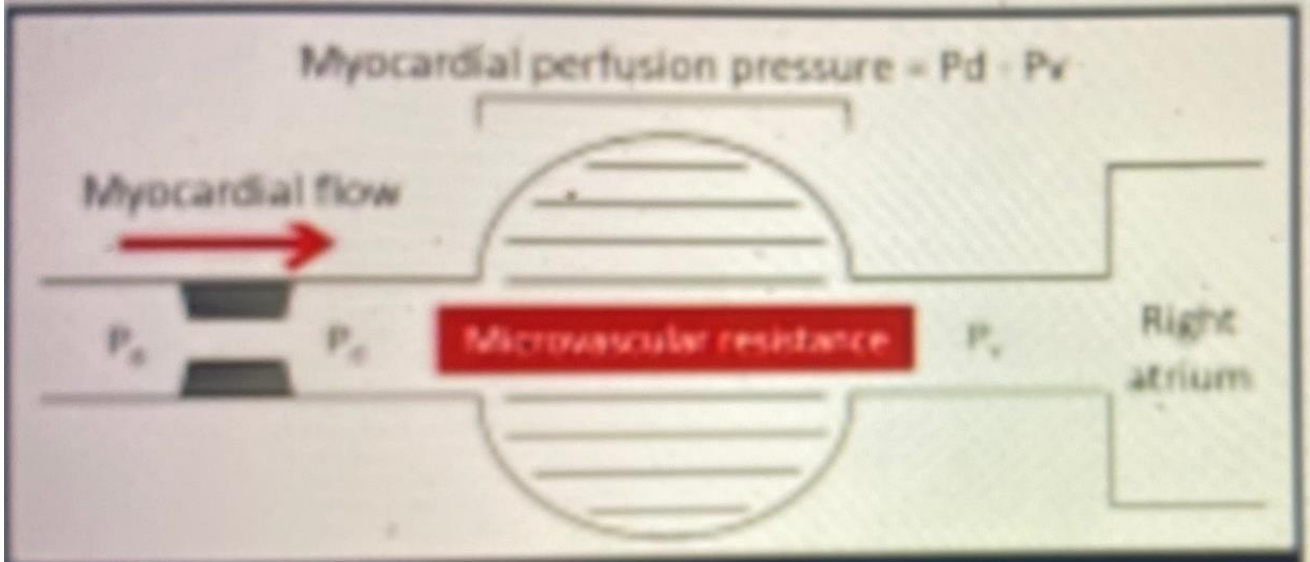
How coronary microvascular resistance is calculated



Thermodilution

β = Tmn-1

IMR = $(Pd \times Tmn)_{hyp}$

Doppler

HMR = $(Pd/V)_{hyp}$

Ohm's Law:

R = Pressure / Flow

Coronary microvascular Resistance:

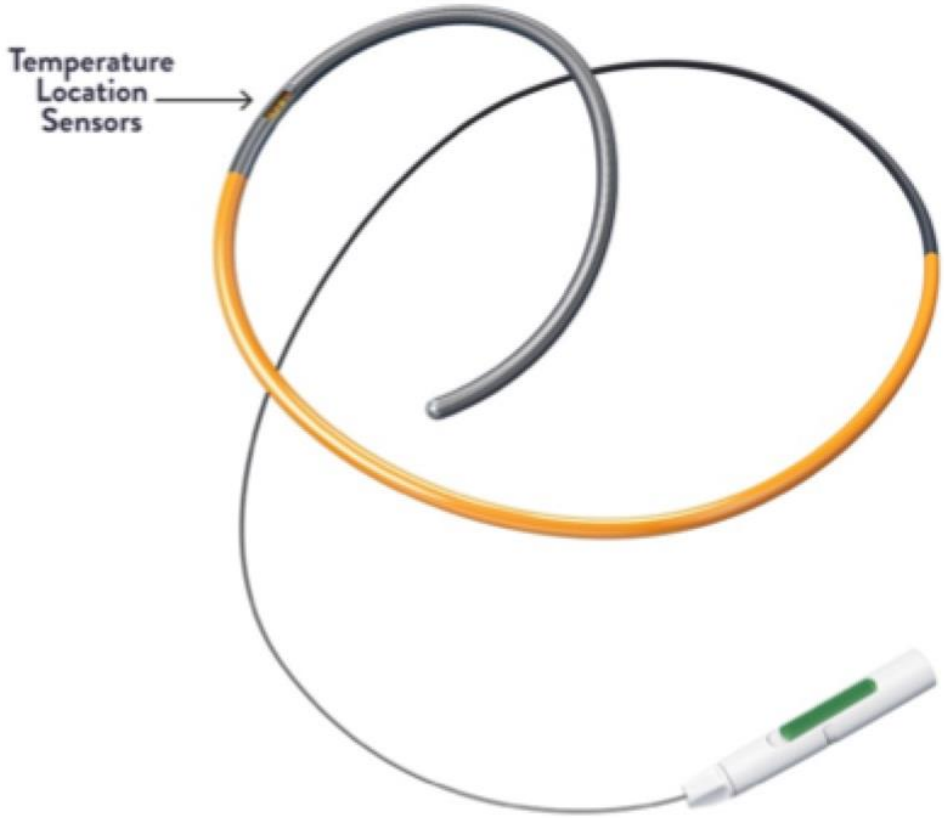
$$R = \frac{Pd - Pv}{\text{Myocardial Flow}}$$

↓

Pd>>>>>Pv

↓

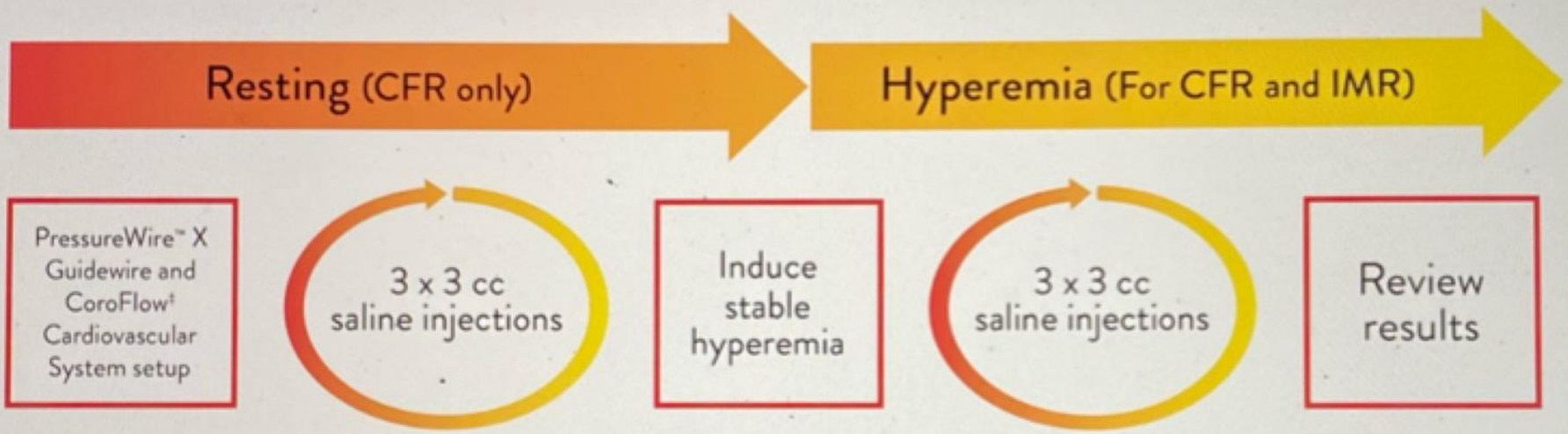
$$R = \frac{Pd}{\beta}$$



Using thermodilution to evaluate IMR and CFR

Measuring IMR and CFR

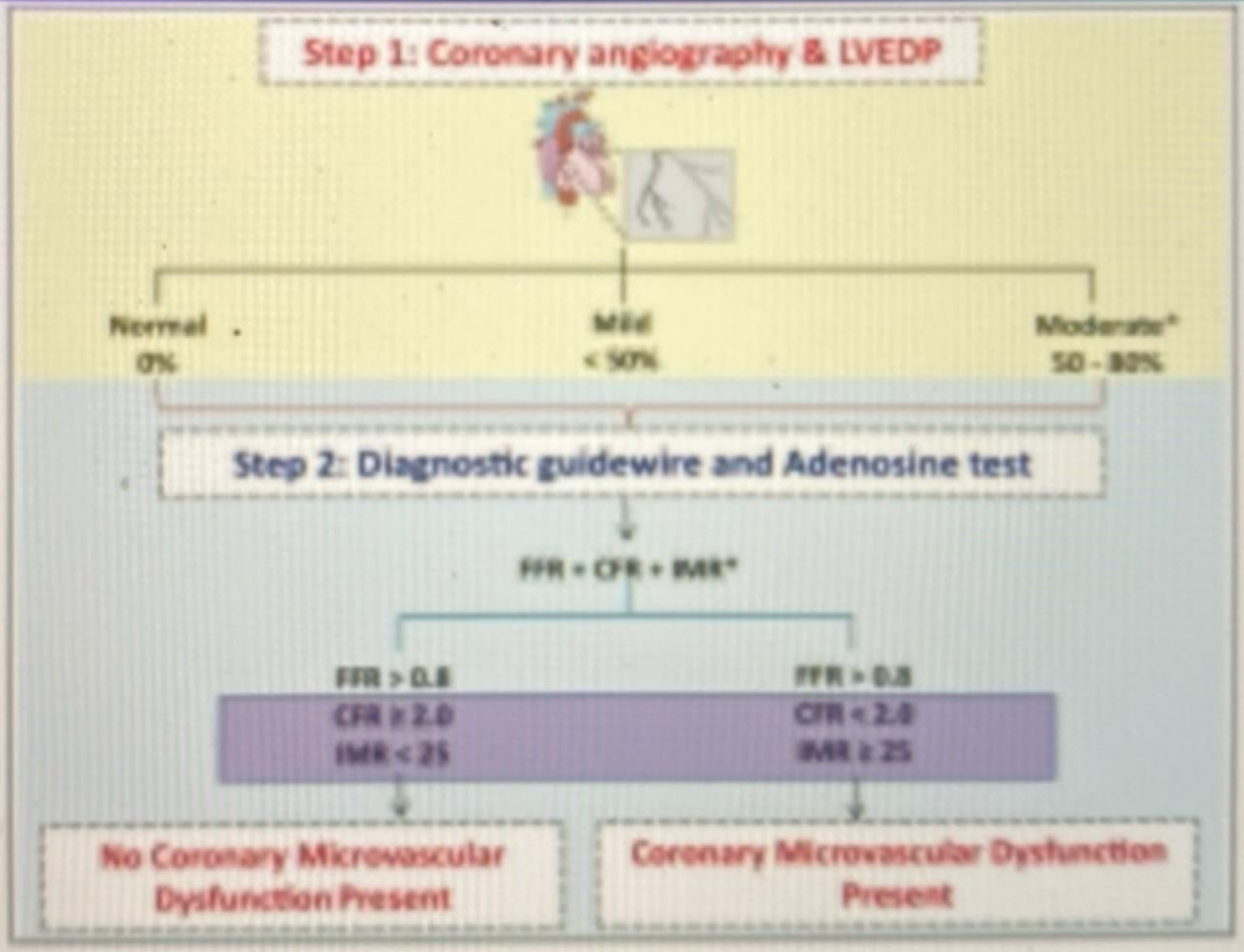
Measuring IMR and CFR is straightforward, requiring just a few minutes.



After being recorded, measurements are then displayed for review.

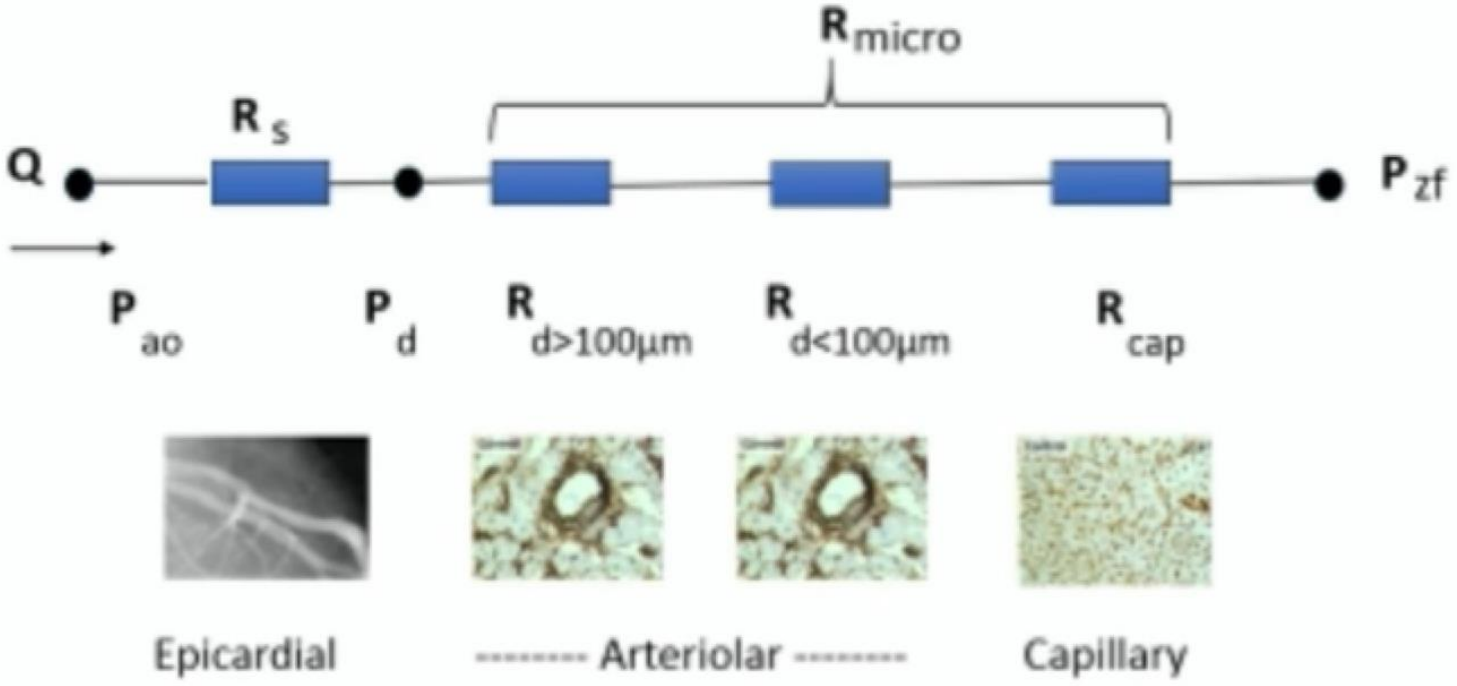
IMR = Blood Flow in Microvasculature
CFR = Blood Flow in Epicardial Vessels + Microvasculature

Threshold for CFR and microvascular resistance indices



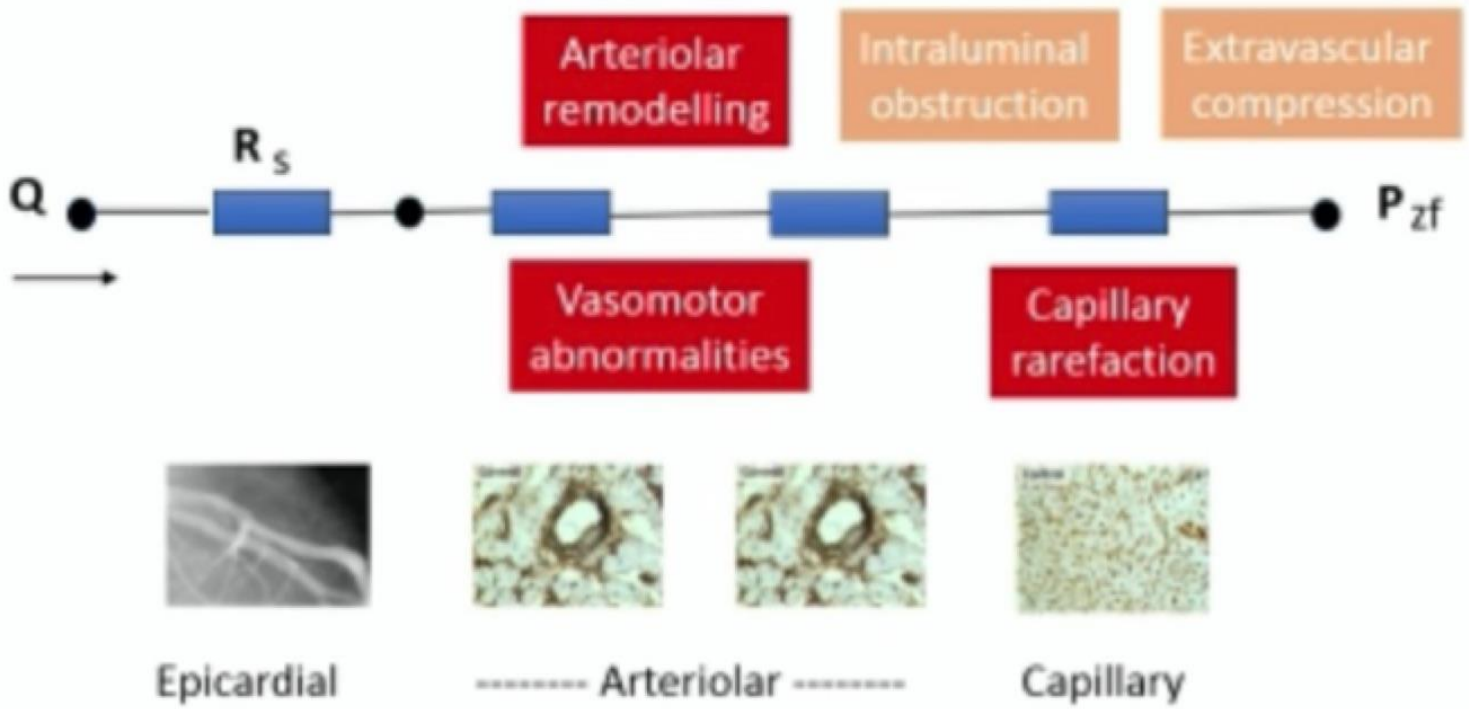
Kunadian, Chieffo et al. Eur Heart J. 2020 Oct 1;41(37):3504-3520

A resistive map of the coronary circulation



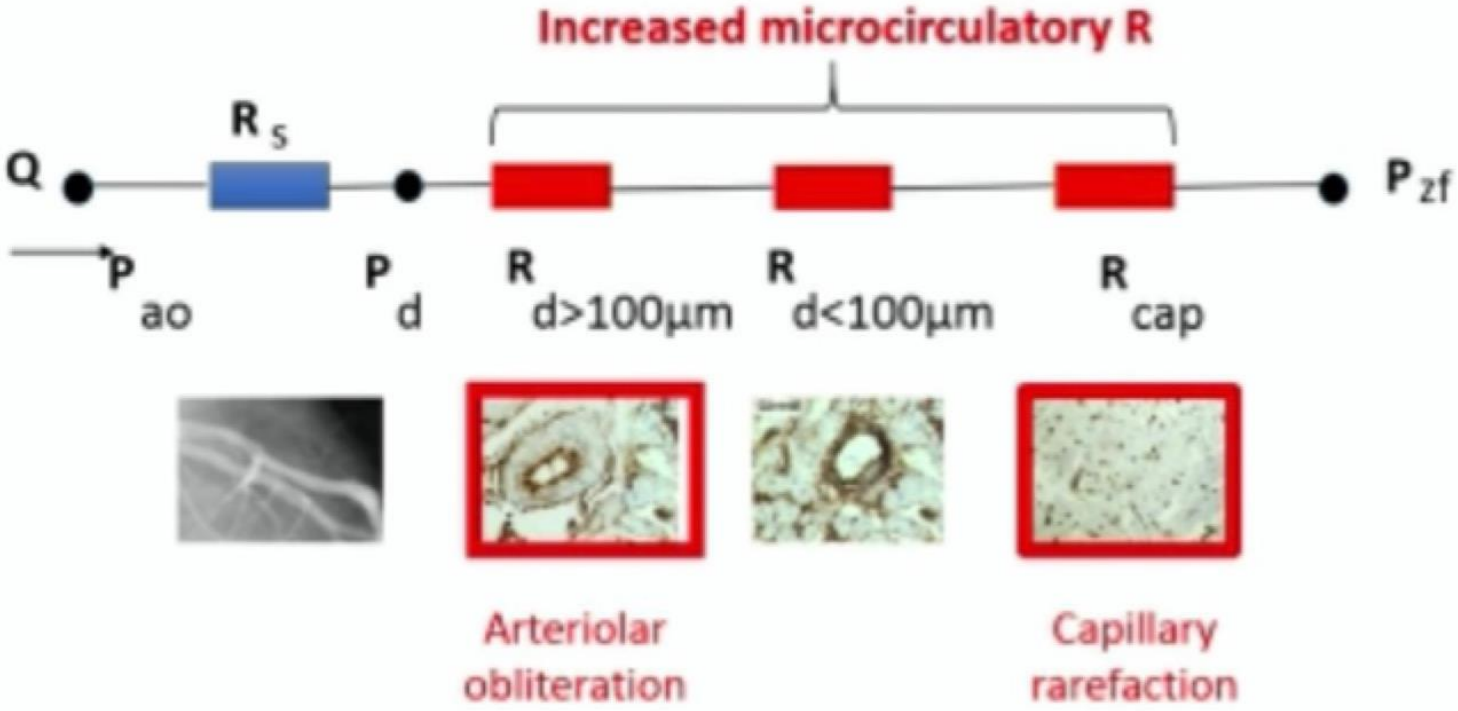
Mejia-Renteria H, Escaned J et al. Int J Cardiovasc Imaging 2017 / DOI 10.1007

Mechanisms of microvascular dysfunction



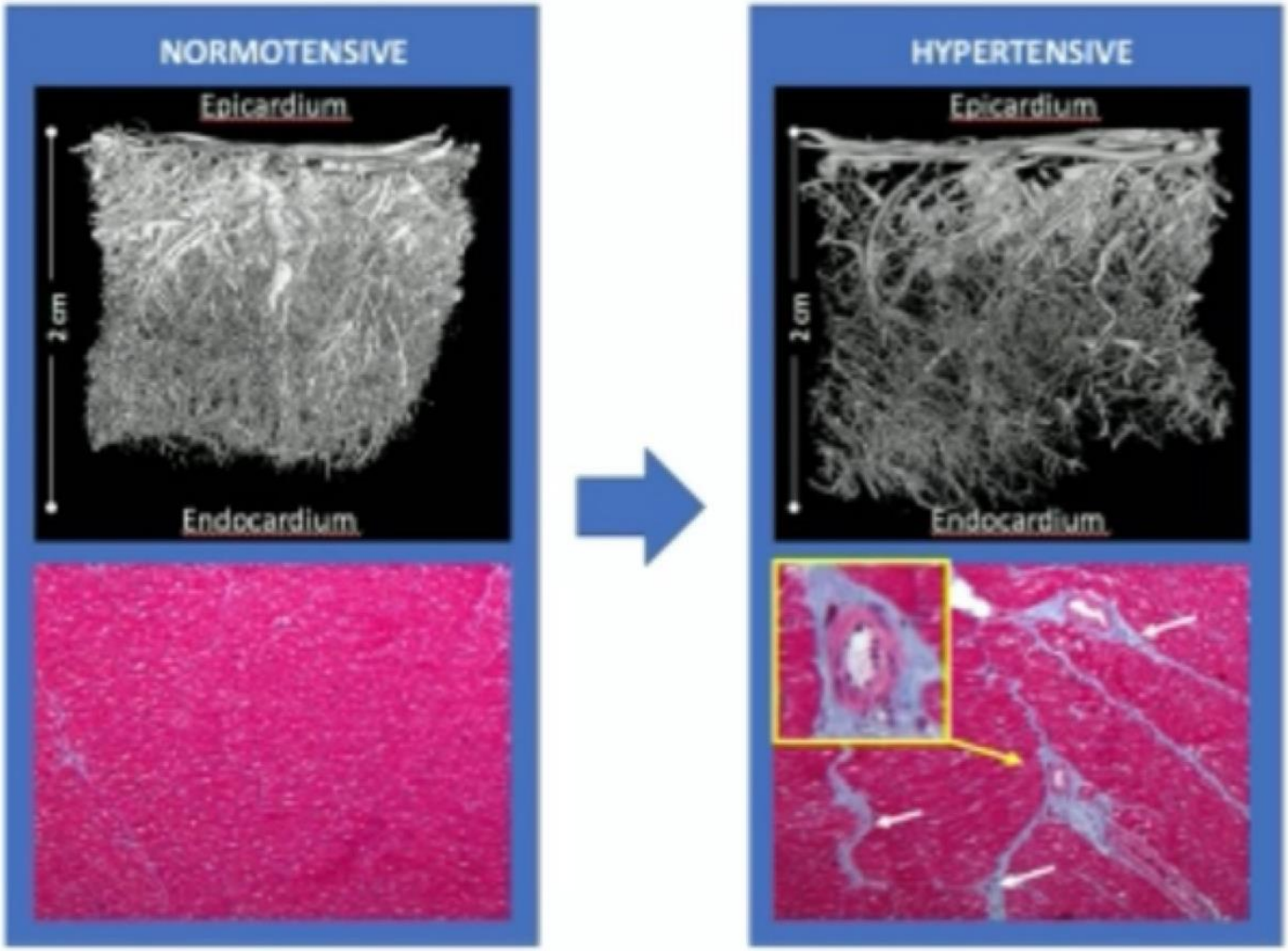
Meja-Renteria H, Escaned J et al. Int J Cardiovasc Imaging 2017 / DOI 10.1007

Structural remodelling of arterioles and capillaries



Mejia-Renteria H, Escaned J et al. Int J Cardiovasc Imaging 2017 / DOI 10.1007

Structural microcirculatory changes in HTN



Escaned J, Lerman LO Eur Heart J 2020

Conditions associated to microvascular dysfunction

- Arterial hypertension
- Diabetes mellitus
- Dyslipidaemia
- Oestrogen withdrawal
- LV hypertrophy
- Lipid-rich atherosclerosis
- Chronic coronary occlusion
- Myocardial bridges
- Myocarditis
- Cardiac allograft vasculopathy

Case 2: INOCA

Clinical Characteristics

Age 69 yrs, female, BMI 34.3 kg/m²

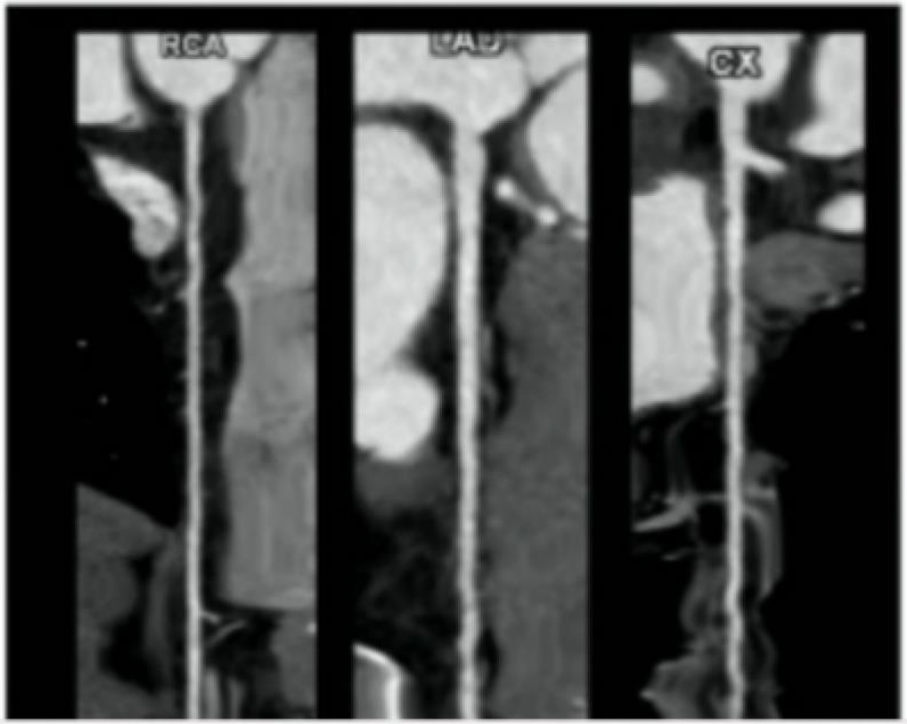
Medical history: Hyperlipidemia, hypertension, Sleep Apnea Syndrome

Atypical angina

Creatinine 1.52 mg/dL (eGFR 36 mL/min/1.73m²)

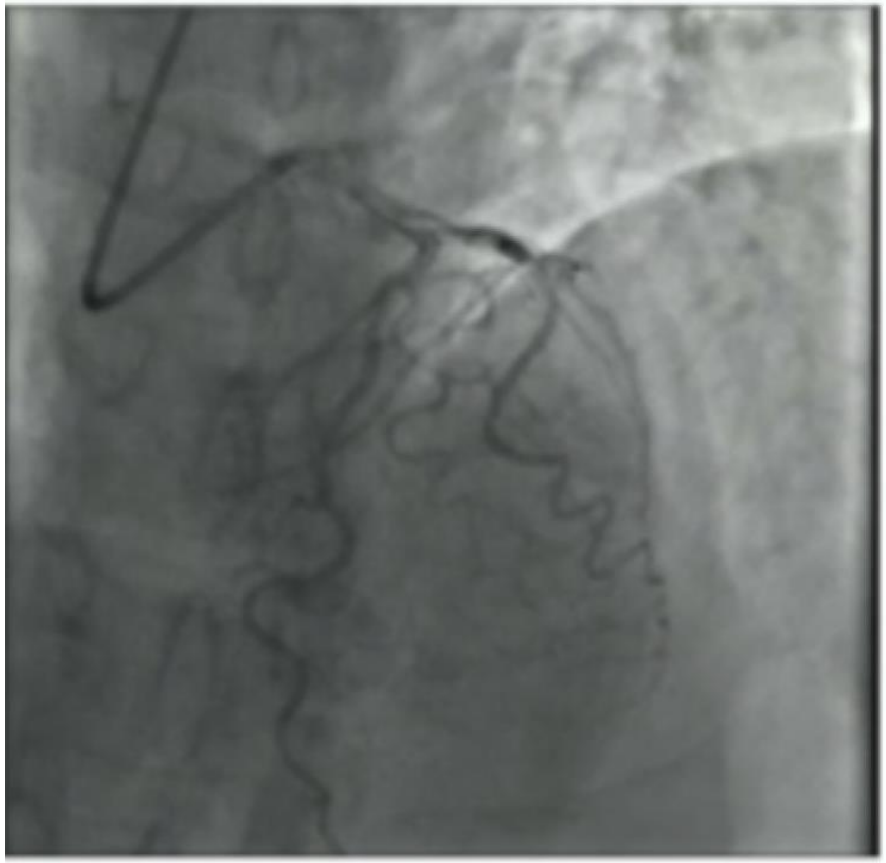
'Normal' invasive diagnostic angiography 2017

Coronary CTA 2020



PCR webinars Acetylcholine (ACh) spasm provocation test

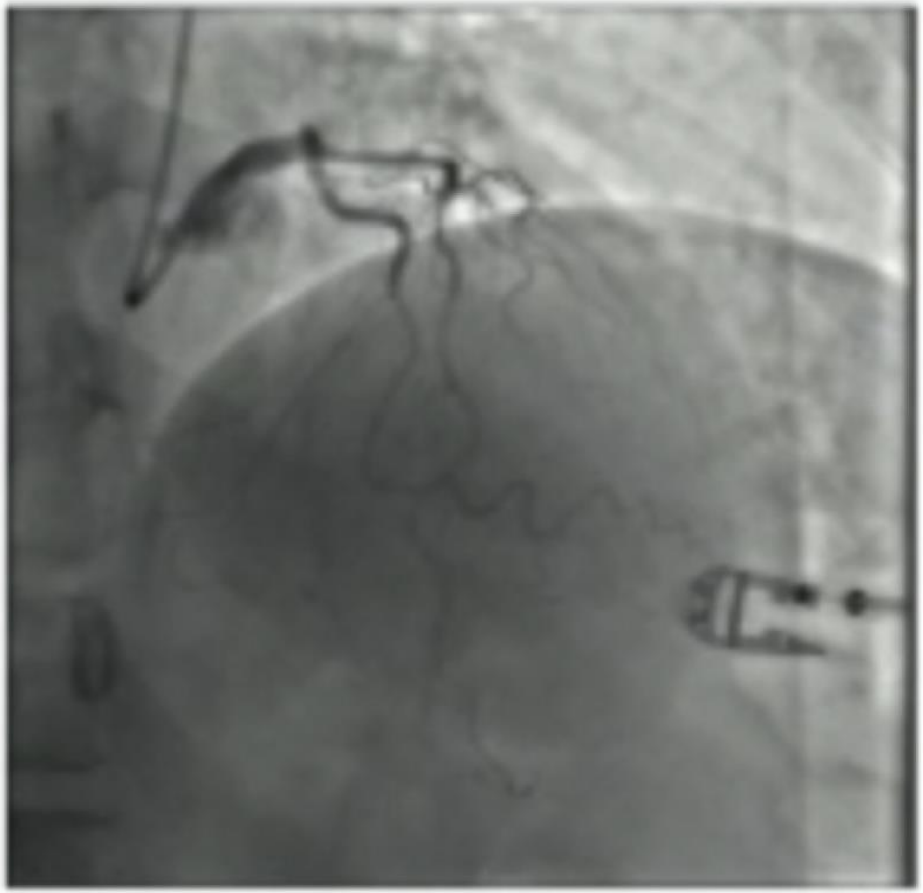
Baseline Angiography

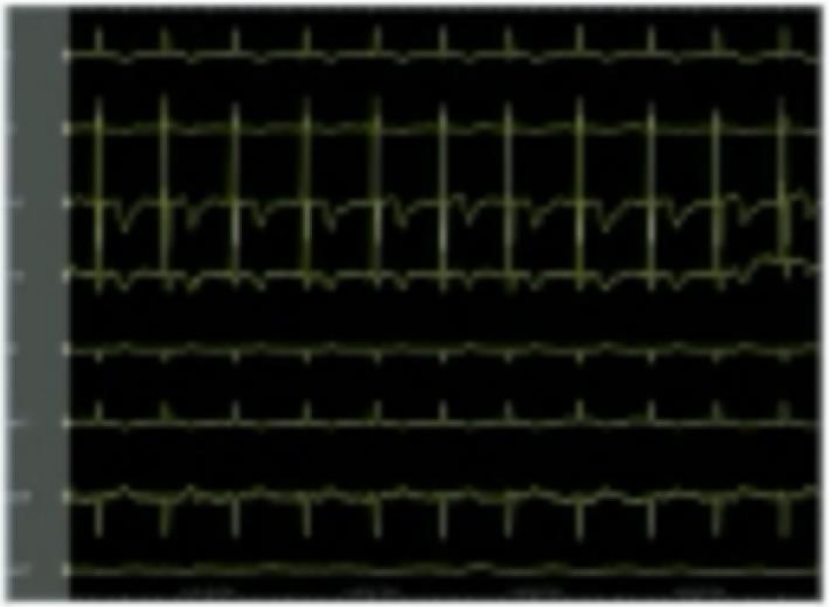


ECG

PCR webinars Acetylcholine (ACh) spasm provocation test

Acetylcholine 100 µg IC

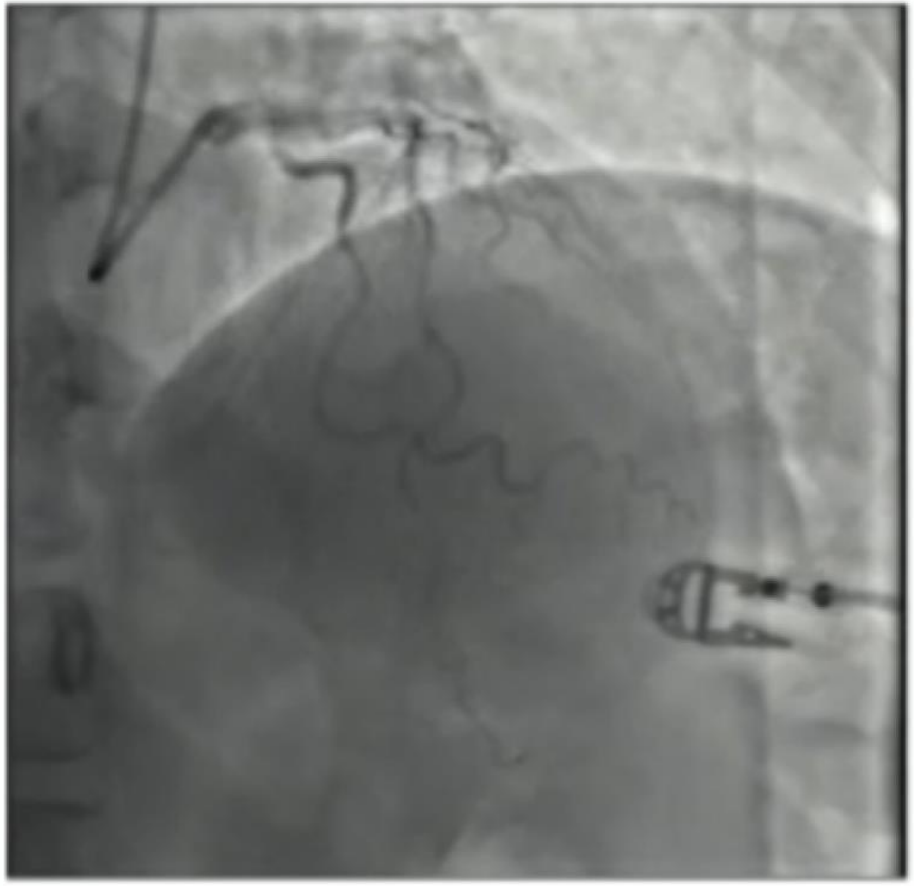




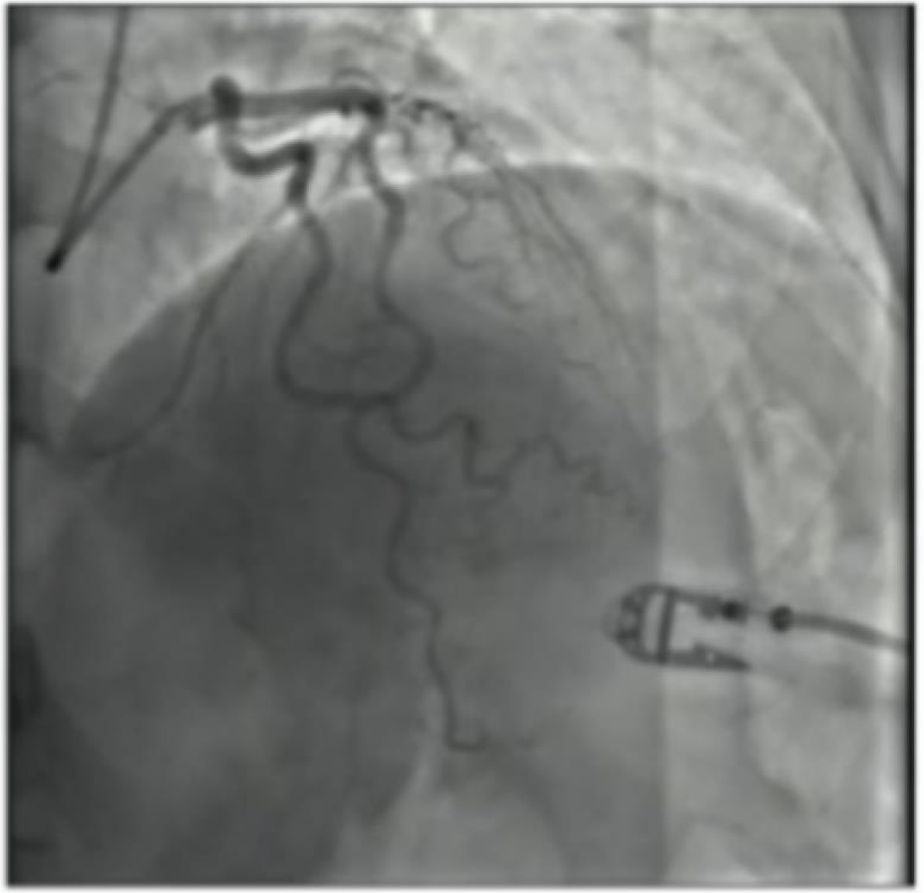
Chest Pain

PCR webinars Acetylcholine (ACh) spasm provocation test

Acetylcholine 100 µg IC



After nitrates



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Case 2: INOCA

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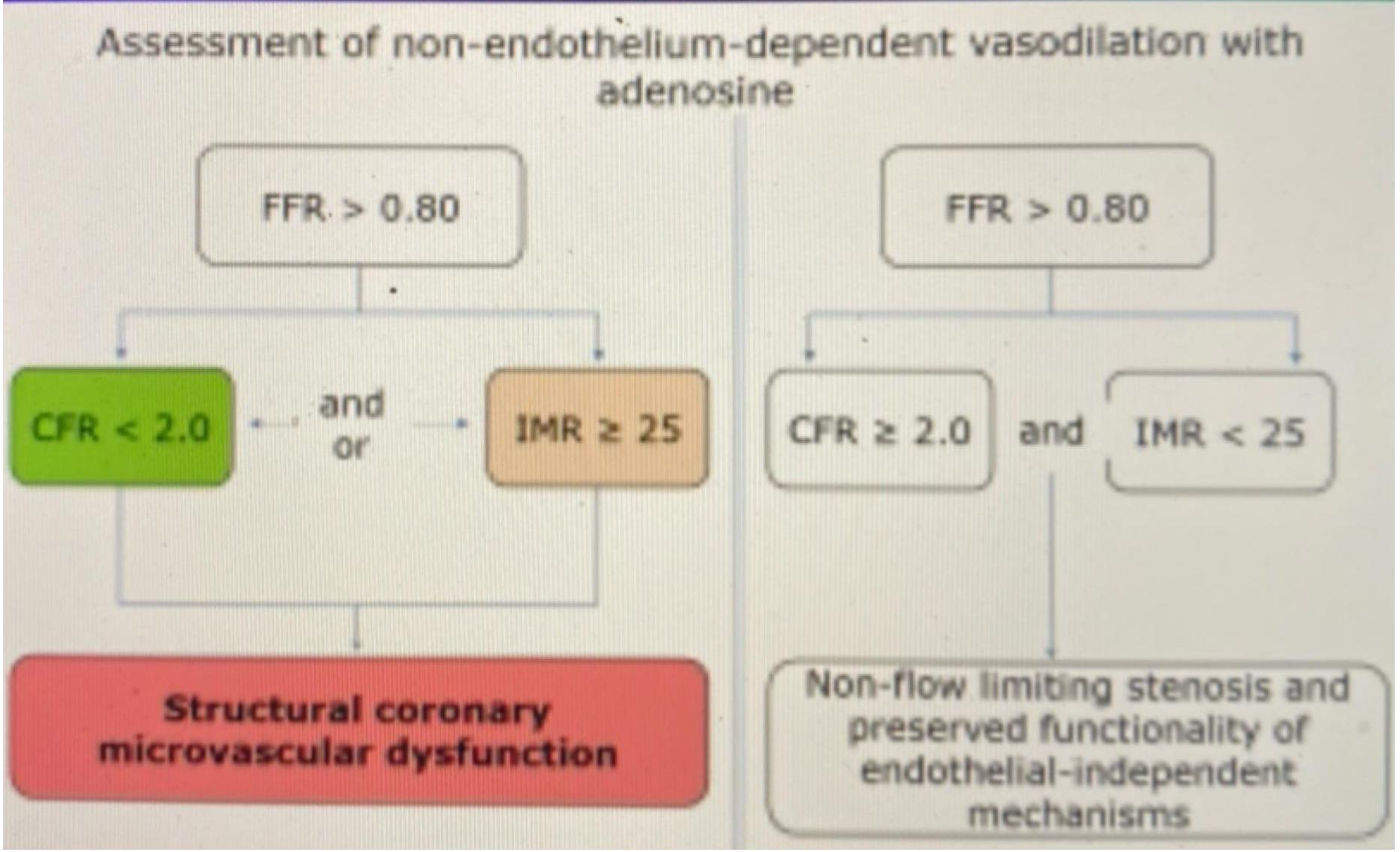
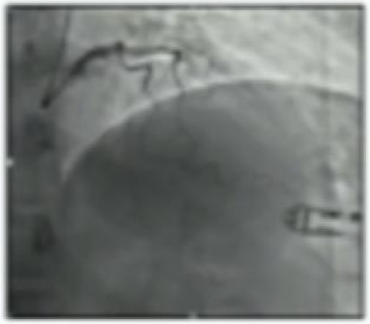
Invasive assessment of INOCA with CFR and microvascular resistance indices



Case 2 Epicardial spasm and microvascular dysfunction

Angina

No CAD
(%DS<50% or FFR >0.80)



Epicardial stenosis >90%
ACh
+ ECG + Pain

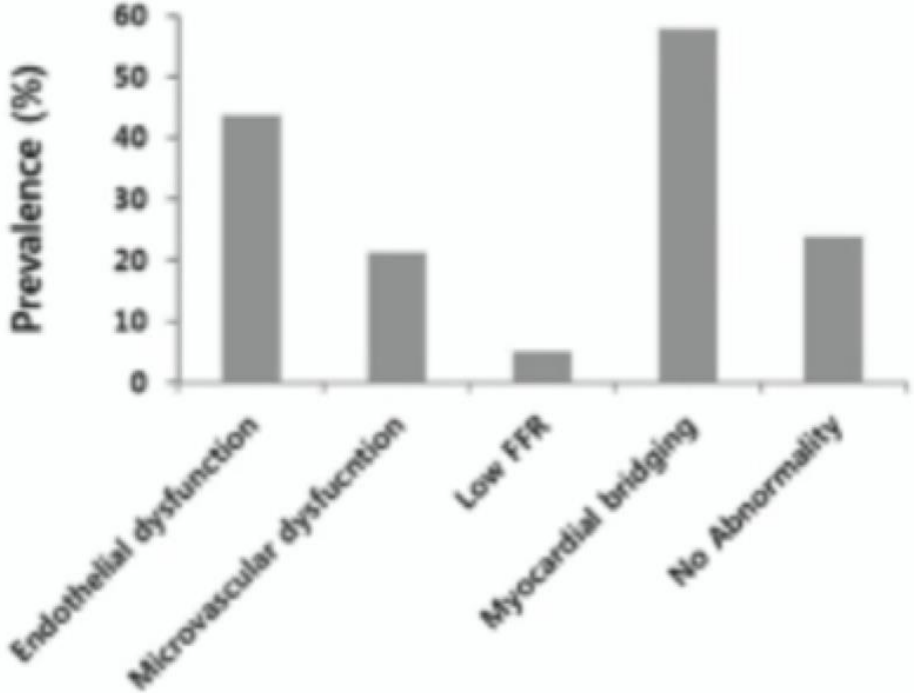
Impaired microvascular function
IMR >25

Management

Diltiazem 240 mg
Olmesartan 20mg
Rosuvastatin 10 mg
Aspirin 80 mg

Myocardial Bridges

- A commonly overlooked cause of angina in patients without obstructive CAD
- Even when we do vascular function testing, ~½ of patients remain without a diagnosis
- Disproportionally high prevalence of MBs in these patients (~60%) vs. ~30% in the general population



Lee, Tremmel, et al. Circulation 2015;131:1054-106

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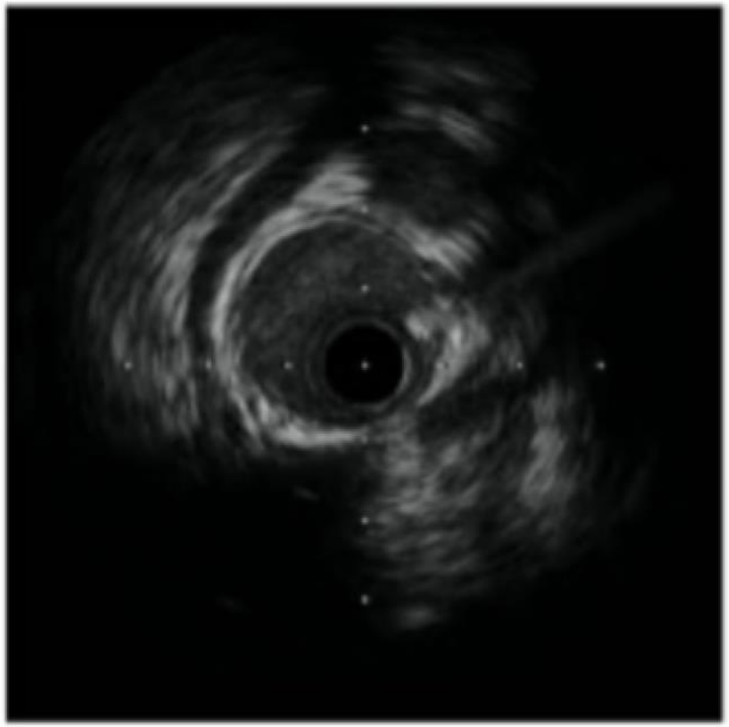
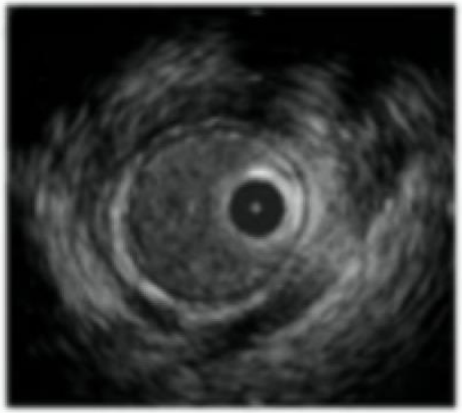
Why are MBs overlooked?

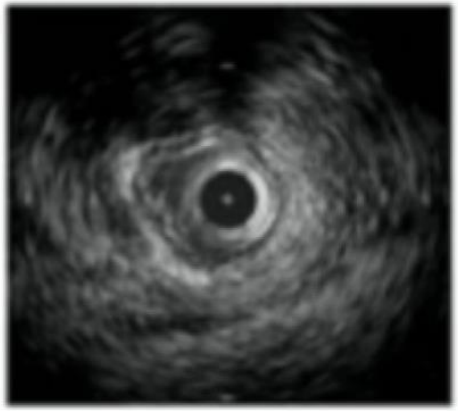
- We are taught that bridges are inconsequential
- Can be challenging to diagnose
  - Only a minority are seen on invasive angiography (sometimes mistaken for a stenosis) and often not mentioned on CCTA (although non-invasive gold standard)
  - Common in the general population
    - Must determine if hemodynamically significant or simply incidental
  - Rarely identified on routine stress testing
    - Reports of anteroseptal ischemia on nuclear perfusion scans, septal ischemia/infarction on MRI and autopsy
    - Focal septal buckling with apical sparing on stress echo

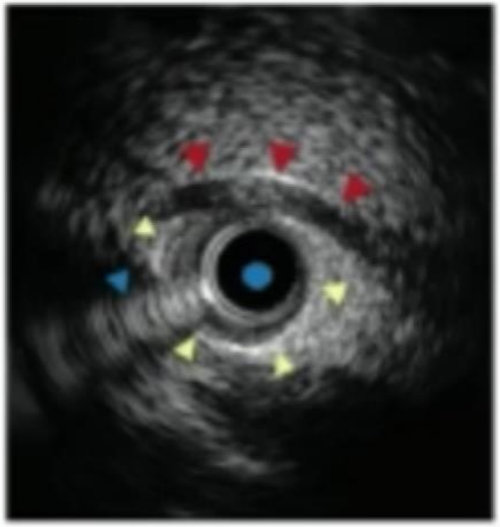
Forsdahl, Tremmel, et al. Circulation Journal 2017;81:1894-1900
Pargaonkar, Tremmel, et al. Int J Cardiol 2019;282:7–15

IVUS: Invasive Gold Standard for Diagnosis







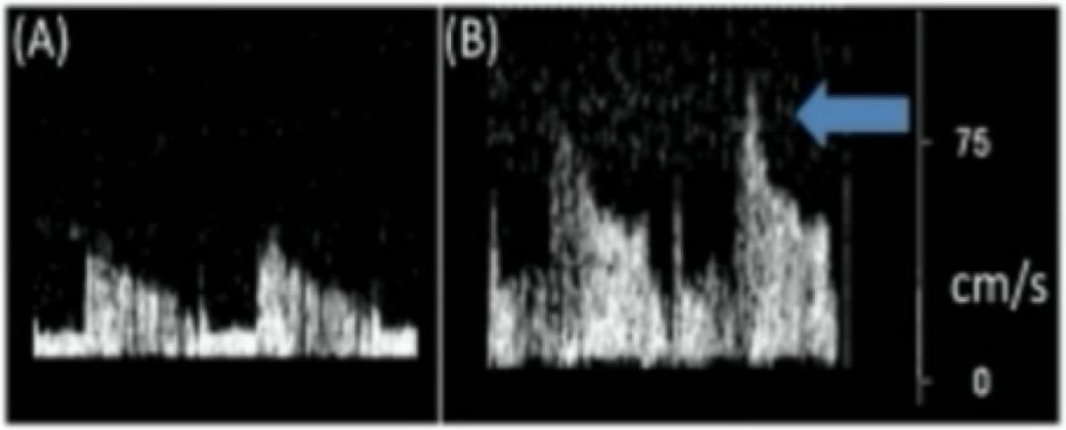


- Echo-lucent half moon sign (halo)→felt to be pathognomonic, but not 100% sensitive
- ≥10% systolic compression

Lin, Tremmel et al. J Am Heart Assoc 2013;2:e000097

Compressive Effects Not Limited to Systole

- Systolic compression extends into early-diastole resulting in a delayed relaxation in diastole
- Characteristic diastolic flow pattern with increased diastolic velocities ("fingertip")



Costello et al. Cathet Cardiovasc Interv 2008;71:590-593
Ge et al. Circulation 1994;89:1725-32

Assessing the Hemodynamic Significance of a Myocardial Bridge

- MBs are dynamic rather than fixed
- For a fixed stenosis, adenosine (a vasodilator) is sufficient, whereas an MB requires inotropy and chronotropy (dobutamine or exercise)
- For a fixed stenosis, systole and diastole are equally affected, so mean FFR is sufficient
- With an MB, the main pressure drop is in diastole (and there can actually be an overshoot in systole), so mean FFR is insufficient—need dFFR (ratio of Pd/Pa in diastole)

Escaned et al. J Am Coll Cardiol 2003;42:226-33
Hakeem et al. Catheter Cardiovasc Interv. 2010;75(2):229-36

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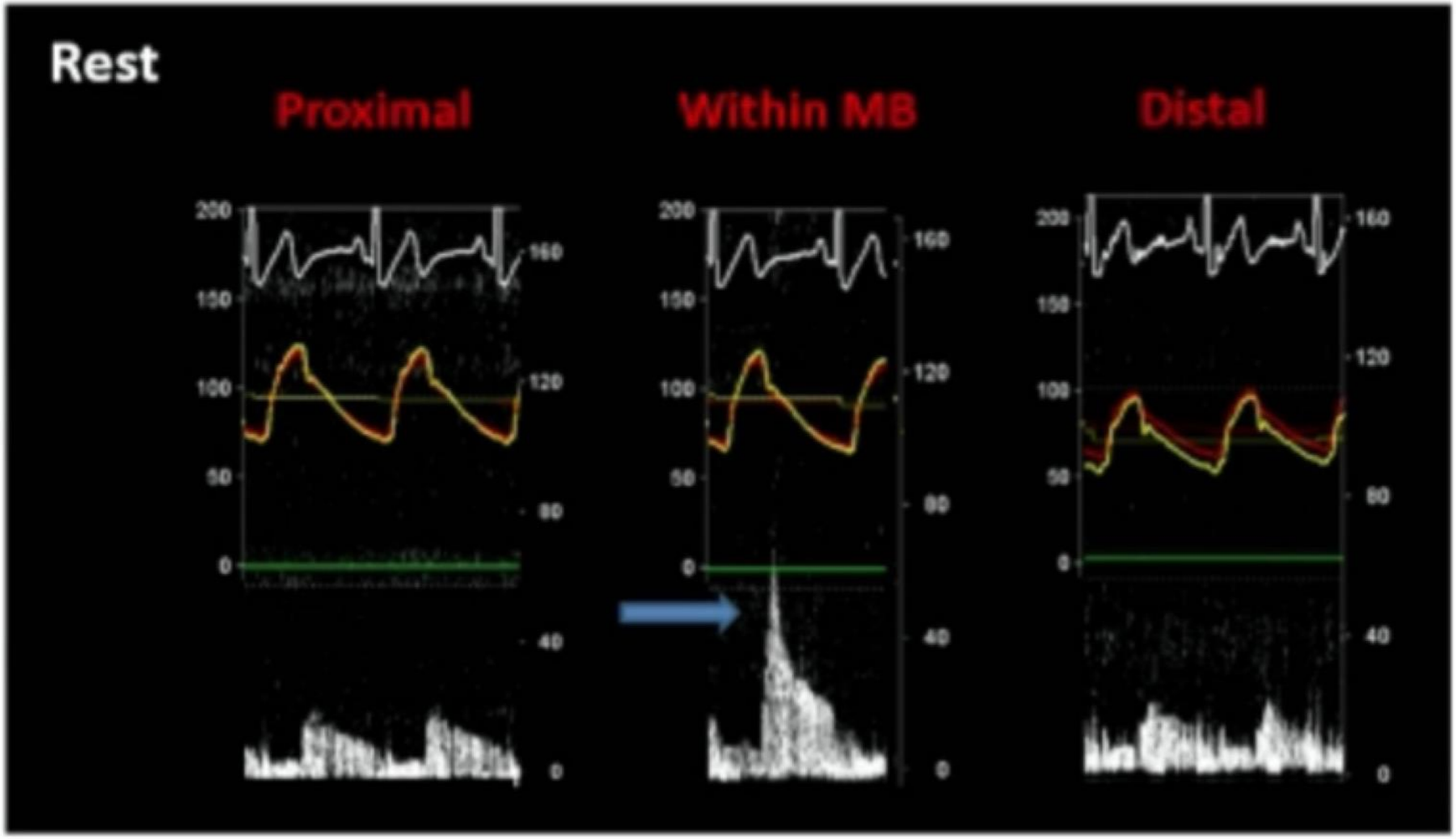
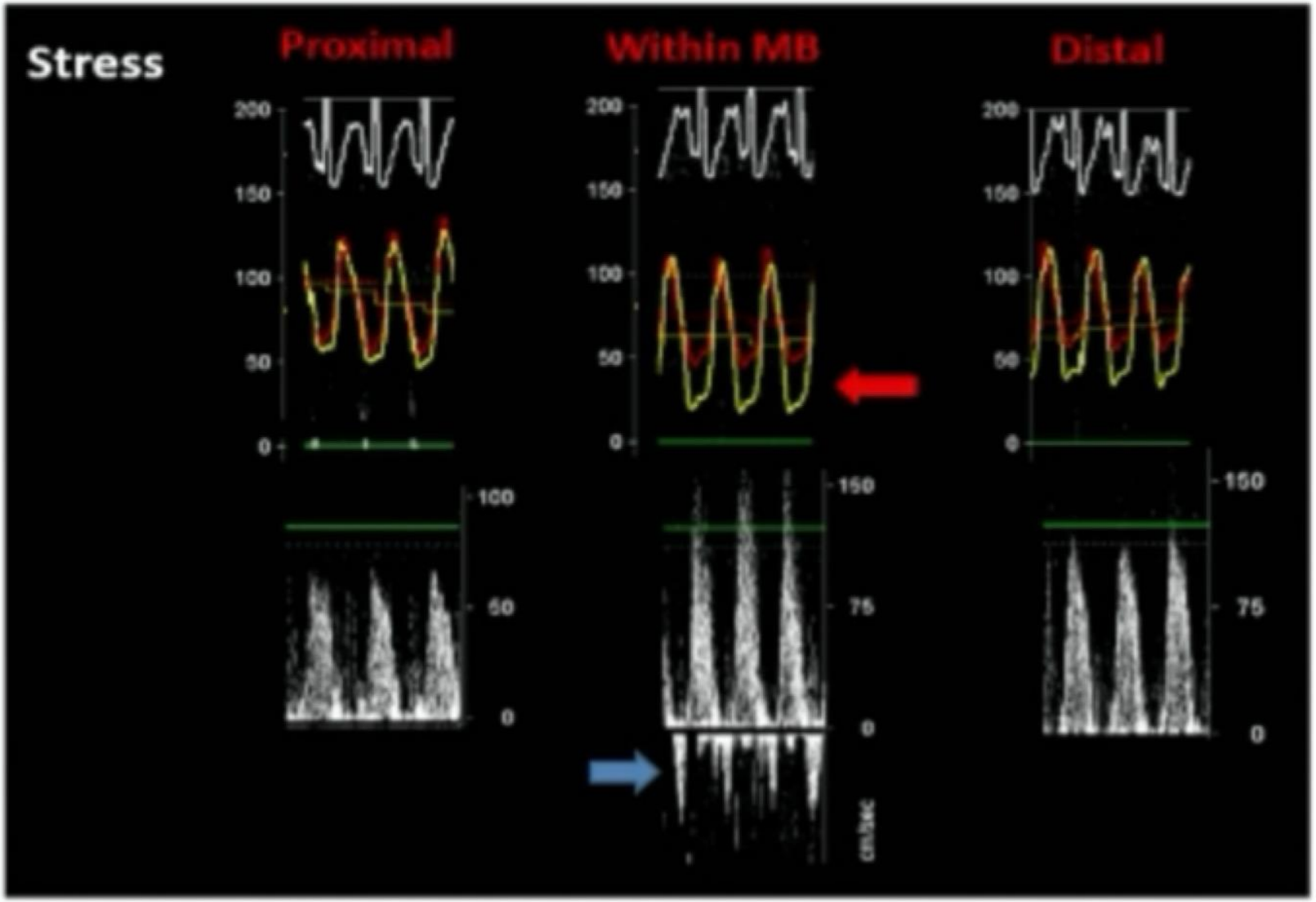
dFFR and Doppler at Rest

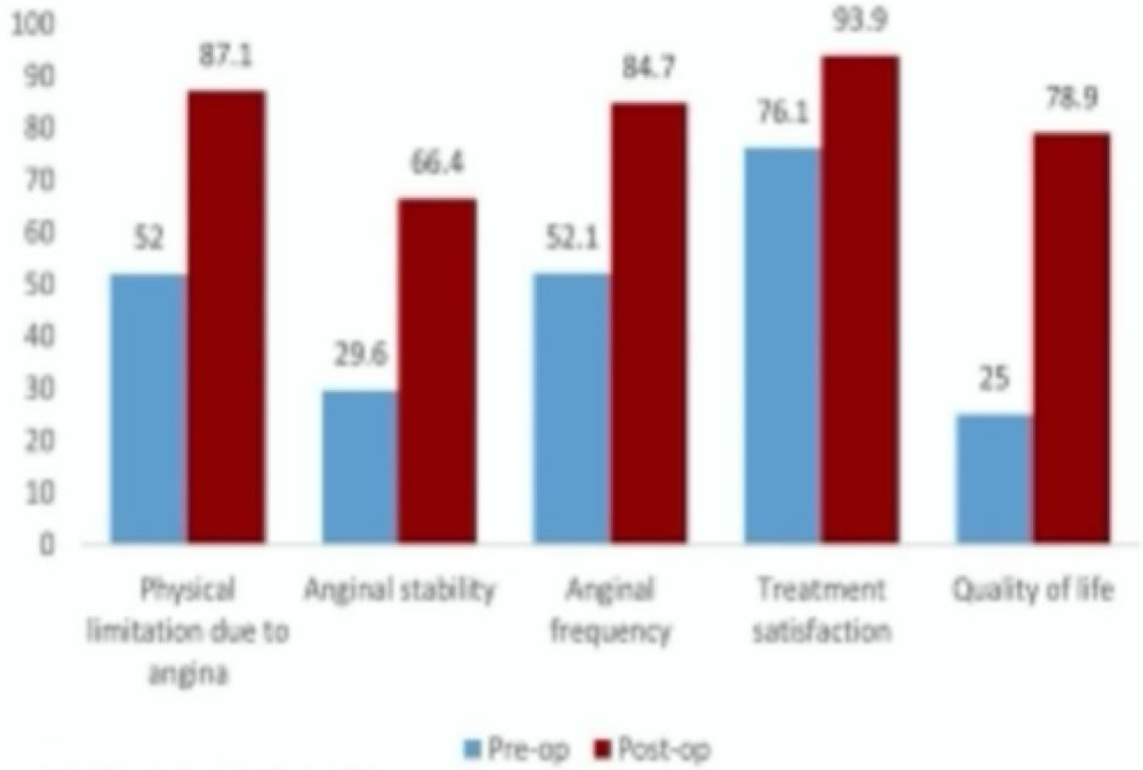


dFFR with Dobutamine Stress



Treatment of Symptomatic MBs

- Medical management: BB (nebivolol), CCB, +/- nitrates
- Stenting? CABG?
- Surgical unroofing



Boyd, Tremmel, et al. Ann Thorac Surg 2017;103:1443-1450

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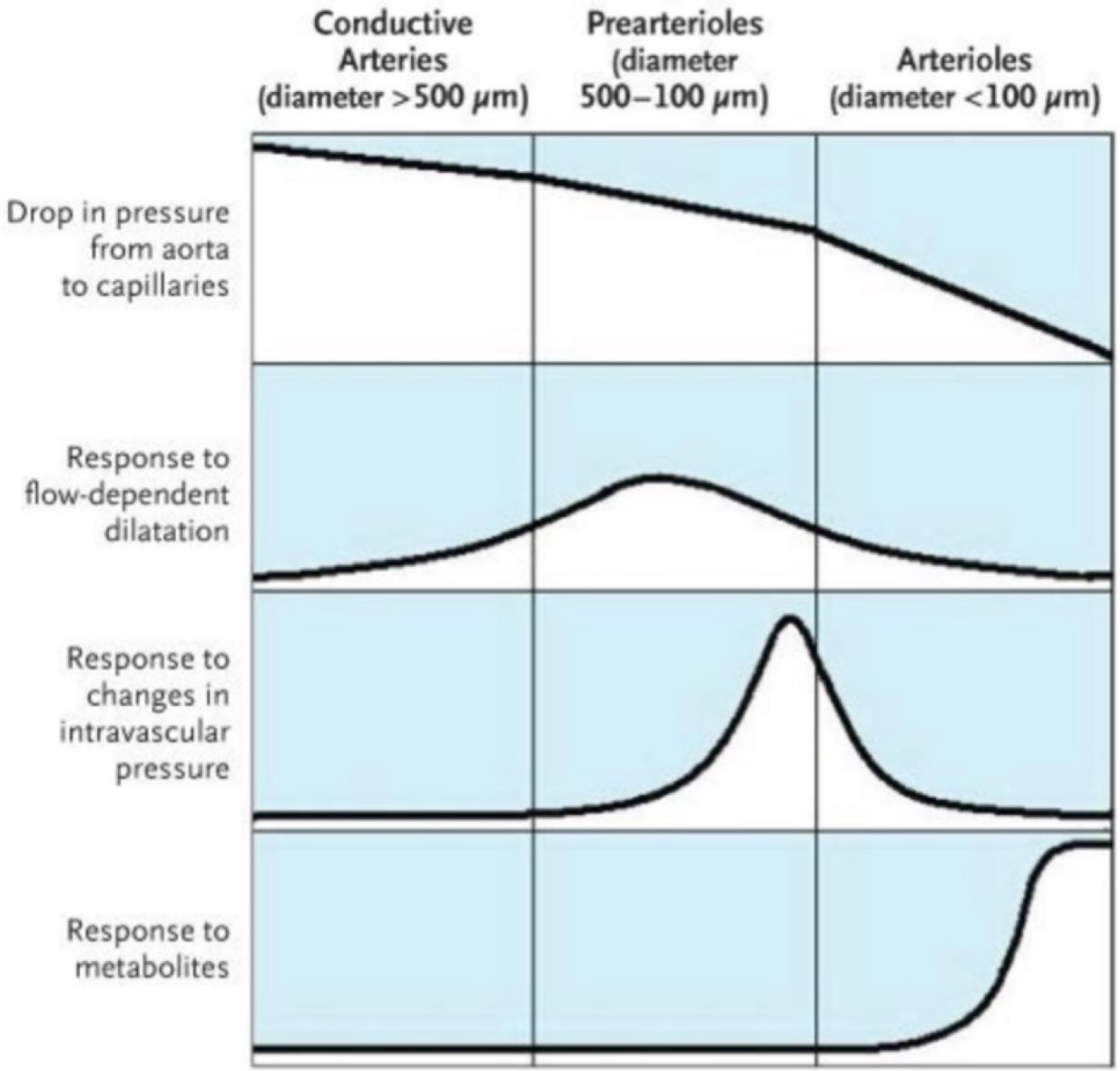
Conclusions

- Consider myocardial bridging as an etiology in your patients with angina and non-obstructive CAD
- Don't rely on coronary angiography for the diagnosis
- Understand that MBs can have compressive effects that extend into diastole
- The presence of an MB in someone with angina does not mean that it is hemodynamically significant—requires physiologic testing
  - Diastolic testing with dobutamine (or exercise) to target HR
- May be associated with endothelial dysfunction
- Medical management/surgical unroofing


Conductive Arteries (diameter >500 μm)
Prearterioles (diameter 500–100 μm)
Arterioles (diameter <100 μm)
Drop in pressure from aorta to capillaries
Response to flow-dependent dilatation
Response to changes in intravascular pressure
Response to metabolites