



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

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# NON OBSTRUCTIVE - CAD: DIAGNOSI, TRATTAMENTO E PROGNOSI A LUNGO TERMINE

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# Disclosures/Conflicts of interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

## **Affiliation/Financial Relationship**

- Consulting Fees/Honoraria
- Research grant to my institution

## **Company**

- Abbott Vascular, Boston Scientific, Insight Lifetech, iVascular
- Astrazeneca

# Clinical CASE: Initial Presentation—2012

## 52 YO FEMALE

- Patient presents with exertional chest pain, radiating to left arm
- Past medical history:
  - Type 2 DM
  - Hypertension
  - Dyslipidaemia
  - Family history of premature CAD
  - Obesity
  - TIA
- Myocardial perfusion scan: INDUCIBLE ISCHEMIA
- Invasive coronary angiography: Anomalous CX, NO OBSTRUCTION
- Anti-anginal therapy stopped

At risk for CAD



# Low Diagnostic Yield with Invasive Coronary Angiography

At the catheterization lab, **no coronary artery disease is reported in 39.2% of patients.**<sup>1</sup>

**Coronary microvascular dysfunction** (CMD) may be present in a large proportion of patients with non-obstructive CAD (~30–50%).<sup>2</sup>

This CMD is associated with **higher rate of major adverse cardiovascular events** (MACE).<sup>3</sup>

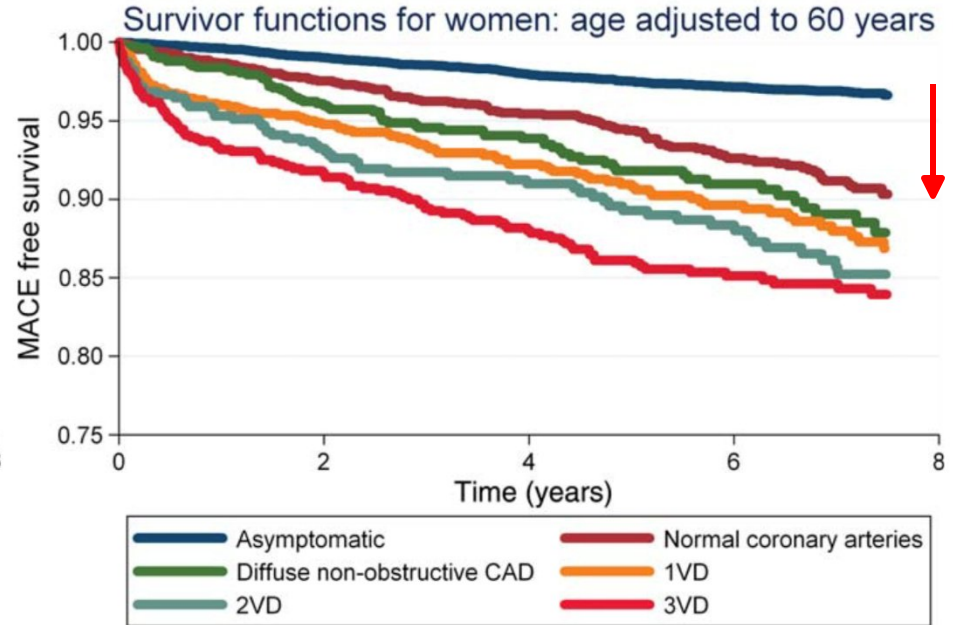
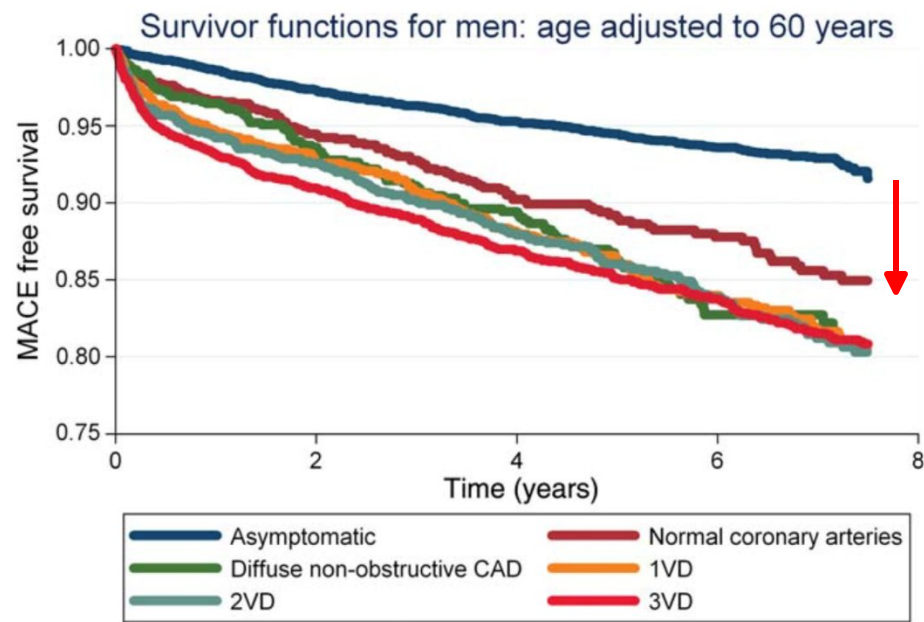
1. Patel M. NEJM 2010 ;362:886-95

2. P. Ong et al. International Journal of Cardiology 2018: 250; 16–20

3. Rahman, H., et al., Heart 2019;105:1536-1542

# INOCA Is Not Benign and Solely Having Anginal Symptoms Is Associated With MACE in Both Women and Men<sup>1</sup>

n = 11,223 patients + 5,705 healthy controls

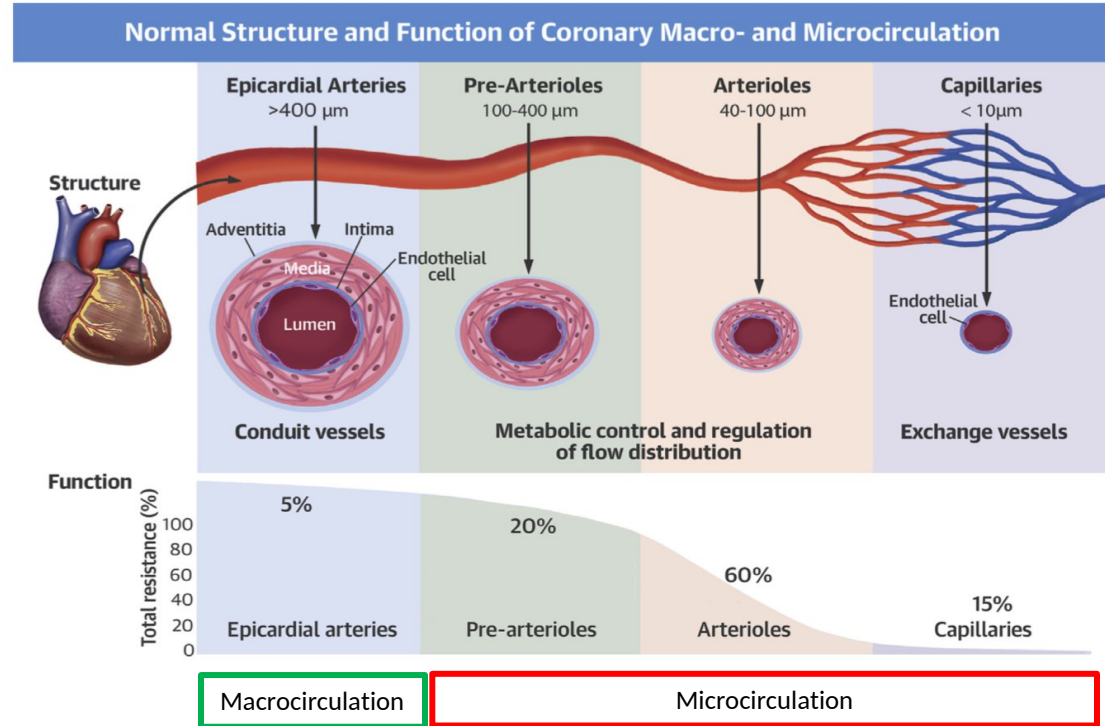


# Coronary Anatomy

## From Macrocirculation to Microcirculation

The **Macrocirculation** has a **conductance function** exhibiting minimal resistance to coronary flow.<sup>1,2</sup>

The **Microcirculation** is responsible for **regulation and distribution** of blood flow matching the needs of local tissue.<sup>1,2</sup>

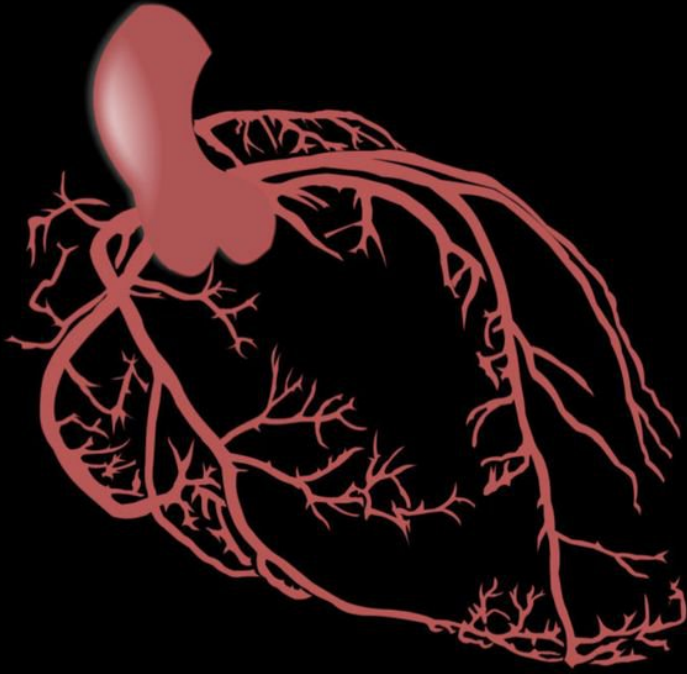


1. Taqueti et al. J Am Coll Cardiol. 2018 November 27; 72(21): 2625-2641.

2. Schelbert, H.R. Anatomy and physiology of coronary blood flow. J. Nucl. Cardiol. 17, 545-554 (2010)

# The Importance of the Microcirculation

Angiography does not show the full picture



What we see

# Definition

**ANOCA**

- **Angina**
- No obstructive coronary artery disease

**INOCA**

- **Ischemia**
- No obstructive coronary artery disease

**MINOCA**

- **Myocardial infarction**
- No obstructive coronary artery disease

# 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)

**NO OBSTRUCTION**

## Ischaemia with non obstructive coronary arteries (INOCA)

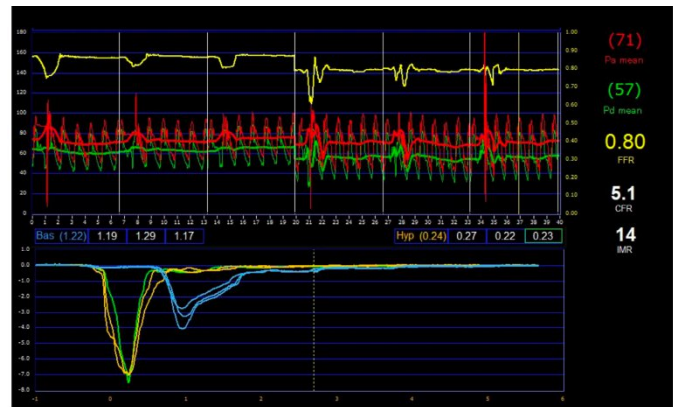
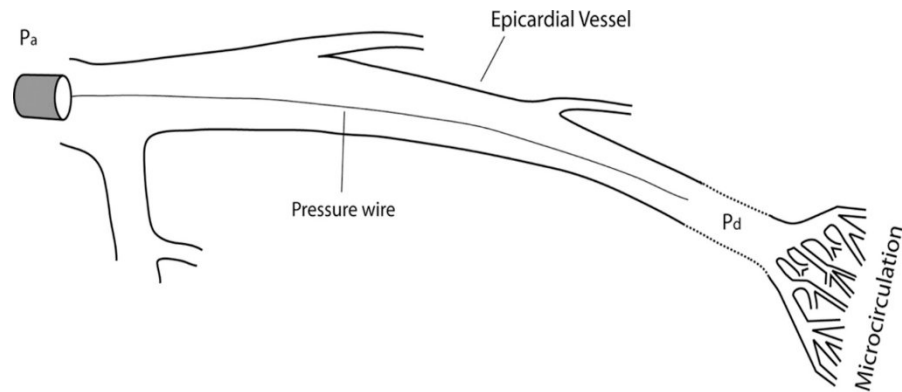
Coronary Microvascular dysfunction (CMD)/Vasospastic angina (VSA)

Non-invasive  
evaluation

Step 1: Patient evaluation

Step 2: Non-invasive evaluation  
Functional Imaging  
± Coronary CT Angiography

# IMR and CFR Measurement Steps



Resting  
CFR only

Hyperemia  
For CFR and IMR

CoroFlow<sup>†</sup> and  
PressureWire<sup>™</sup> X  
Guidewire  
setup

3x3 cc  
saline injections

Induce  
stable hyperemia

3x3 cc  
saline injections

Review  
results

5-10 minutes

# IMR & CFR

**IMR** = distal pressure (Pd) at hyperemia x  $T_{mn}$

- Resistance of the microcirculation

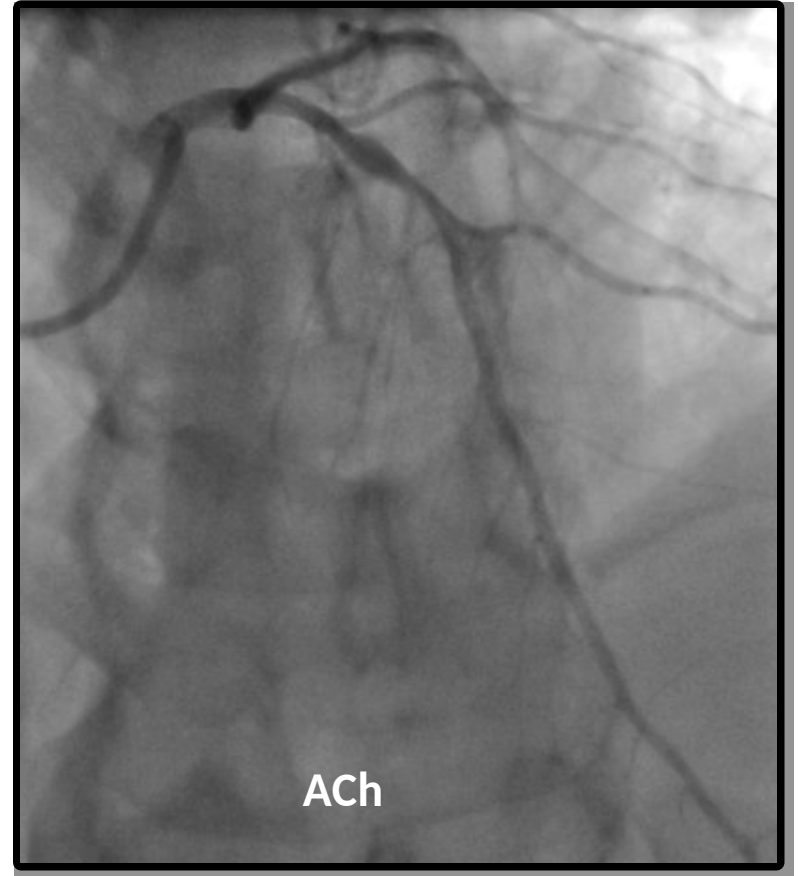
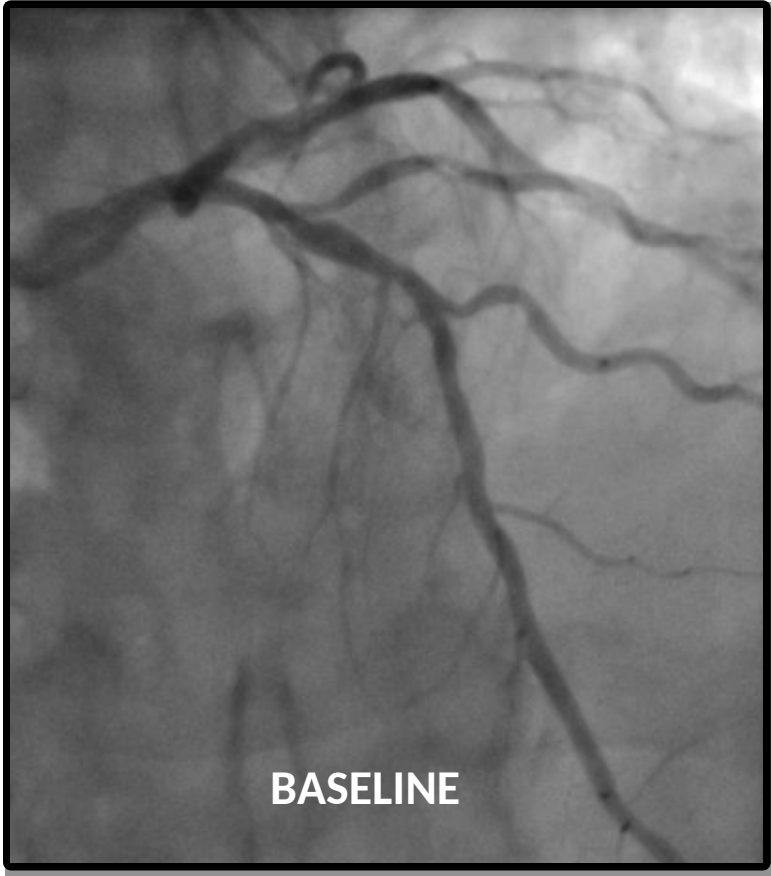
**CFR** =  $\frac{T_{mn} \text{ at rest}}{T_{mn} \text{ at hyperemia}}$

- Max increase in primary flow during effort as compared to rest

**Normal CFR:**  
**> 2.5**

FFR	Pd	Pa
0,72	72	100
Pd/Pa	Pd	Pa
0,85	82	96
CFR	CFR <sub>Norm</sub>	
3,6	4,9	
IMR	IMR <sub>Corr</sub>	
18	16	

# Vasoreactivity test



## Ischaemia with non obstructive coronary arteries (INOCA)

Coronary Microvascular dysfunction (CMD)/Vasospastic angina (VSA)

Non-invasive  
evaluation

Step 1: Patient evaluation

Step 2: Non-invasive evaluation  
Functional Imaging  
± Coronary CT Angiography

Invasive  
evaluation

Step 1: Invasive Coronary angiography

Step 2: FCA guidewire and Adenosine test

Step 3: FCA Vasoreactivity (ACH test)

## 1. Lifestyle factors



Nutrition



Exercise



Weight management



Smoking cessation



Coping with stress

## 2. Risk factor management



Hypertension

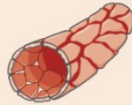


Dyslipidaemia



Diabetes mellitus

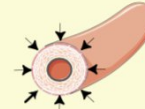
## 3. Antianginal medication



Microvascular angina

1. Betablocker
2. Calcium channel blocker
3. Nicorandil
4. Ranolazine
5. Ivabradine
6. Trimetazidine

Consider statins and  
ACEI/ARB



Vasospastic angina

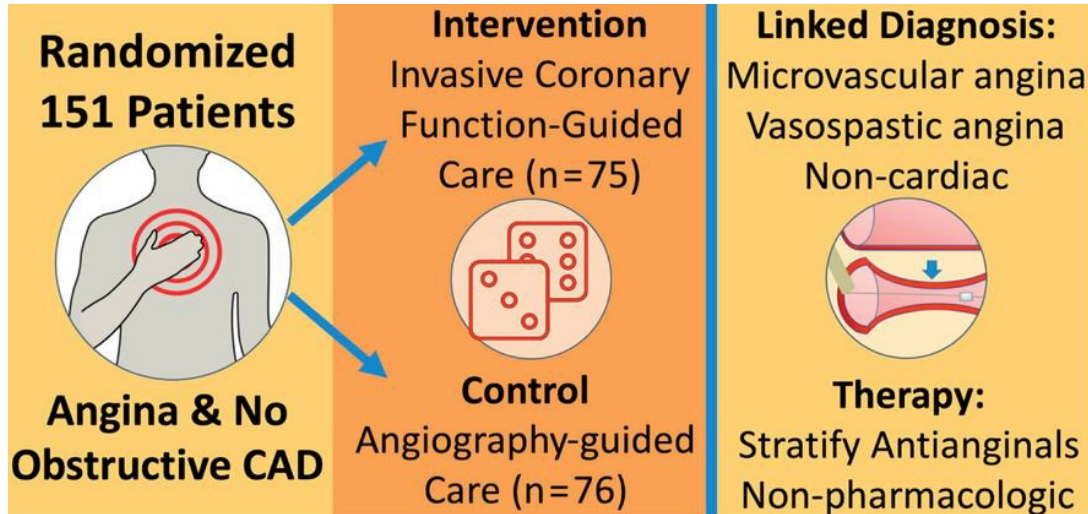
1. Calcium channel blocker
2. Long-acting nitrate
3. Nicorandil

# CorMicA Trial

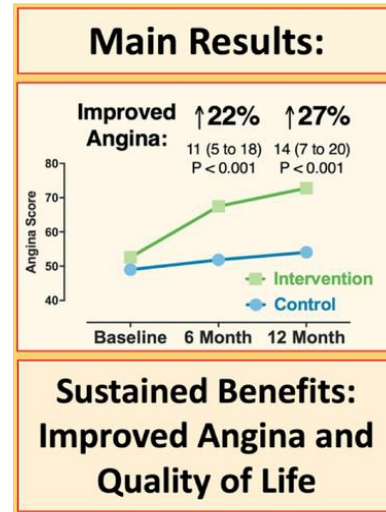
*A randomized, controlled, blinded trial of medical therapy versus standard care in INOCA patients*

**Purpose:** Test whether an interventional diagnostic procedure (IDP) linked to stratified medicine improves health status in patients with INOCA

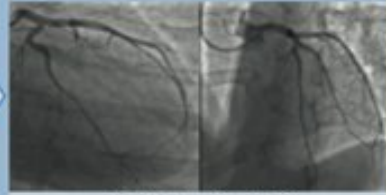
**Primary endpoint:** Mean difference in angina severity at 6 months



IDP=guidewire-based assessment of coronary flow reserve, index of microcirculatory resistance, fractional flow reserve, followed by vasoreactivity testing with acetylcholine.

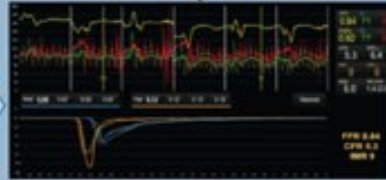


Invasive coronary angiography



No Obstructive CAD

Pressure wire assessment (adenosine)



Normal Invasive Physiology  
(FFR 0.84, CFR 5.3, IMR 9)

Vasoreactivity (acetylcholine)



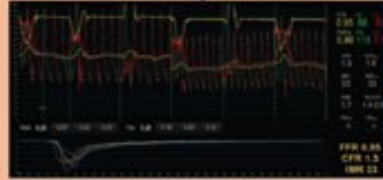
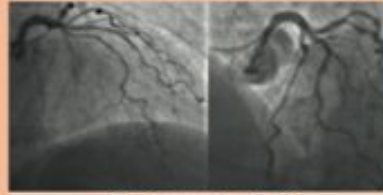
Vasospasm with ACh  
(resolves with nitrate)

Diagnosis & Management

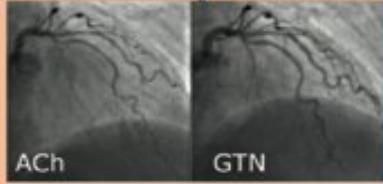
Vasospastic Angina

- Smoking cessation
- Calcium channel blocker
- Long-acting Nitrate
- Lifestyle changes

No Obstructive CAD



Coronary Microvascular Dysfunction  
(FFR 0.95, CFR 1.3, IMR 33)

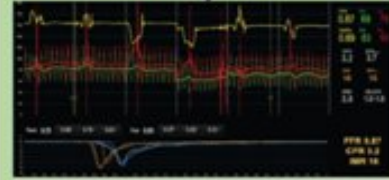
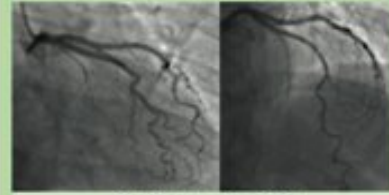


Endothelial dysfunction without  
vasospasm to ACh

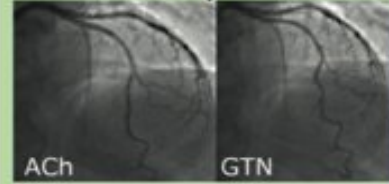
Microvascular Angina

- Betablocker (e.g. Nebivolol)
- Lifestyle changes & weight loss  
(Cardiac rehab, smoking cessation)
- Consider ACEi & Statin

No Obstructive CAD



Normal invasive physiology  
(FFR 0.87, CFR 3.2, IMR 16)



No significant response to vasoreactivity  
testing

Non-Cardiac Chest Pain

- Stop antianginal Rx
- Discharge from cardiology
- Consider non-cardiac investigation

# Clinical CASE: Initial Presentation—2012

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  - Family history of premature CAD
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- Anti-anginal therapy stopped

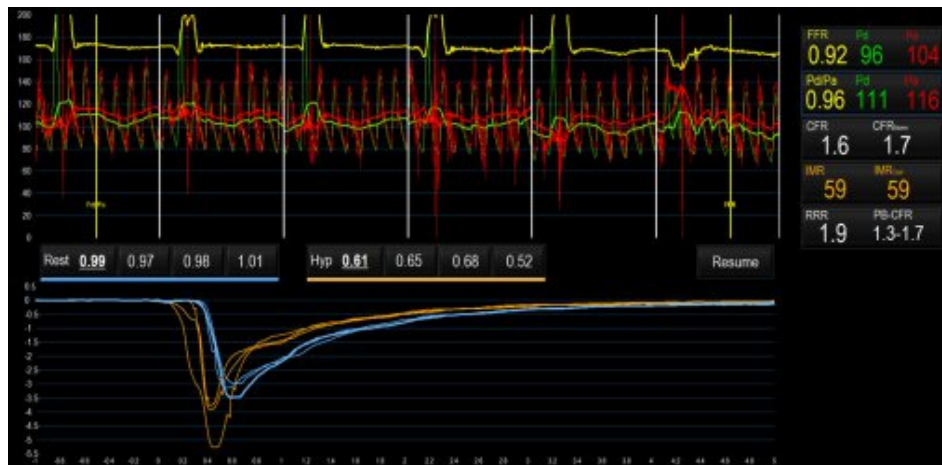
At risk for CAD



# Clinical CASE: 7 Years Later—2019

## FEMALE (NOW 59 YO)

- Presenting again after 7 years of chronic angina with radiation to left arm, symptoms worsening since 1 year
- CTCA showing mild plaque disease only
- Invasive coronary angiography + physiological assessment



**IMR= 59**

**CFR= 1.6**

**D/Microvascular Angina**

**R/ + Beta-blockers**

# Take-home messages

**Do not forget INOCA/ANOCA in case of angina/ischemia without an apparent coronary cause**

**A complete diagnosis of microvascular/vasospastic angina is feasible/safe and should not be avoided**

**The choice of the right treatment is effective**

# Thank you!



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