

2026 WNEACC

Seeing the Invisible

Ischemia and Nonobstructive Coronary Arteries (INOCA)

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Disclosures

Within the prior 24 months, I have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

Nature of Financial Relationship

Grant/Research Support

Abbott Vascular

Consultant Fees/Honoraria

Abbott Vascular; Medtronic; Edwards Lifesciences;
Shockwave Medical; Vahaticor; Philips

Individual Stock(s)/Stock Options

Intellia Therapeutics, Vahaticor

Royalties/Patent Beneficiary

Executive Role/Ownership Interest

Angiomedix, Inc

Other Financial Benefit

This presentation will include discussion of off label use of Miochol E (acetylcholine chloride)

Background

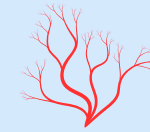
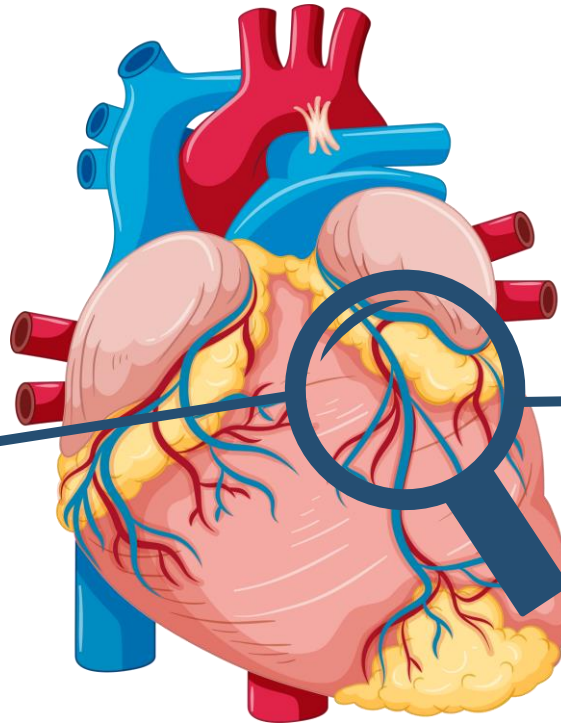
- Each year more than **10 million patients** are evaluated for chest pain
 - 20-40% of all people will experience chest pain at some point
 - One of the most common complaints in the ER (women > men)
- Determining the cause of chest pain is essential:
 - It can be a symptom of a **lack of blood flow to the heart**
 - **Chest pain** can be a stable symptom or a sign of a heart attack
- Cardiovascular disease is the **leading cause of death** in women and men

Ischemic Heart Disease

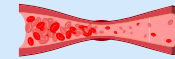
Coronary Artery Disease (Atherosclerosis)



- 18 million people in the US
- Diagnosed with stress tests, CT scans, or cardiac catheterization
- Can be treated with medications, stents, or bypass surgery



Coronary Microvascular Dysfunction (CMD)



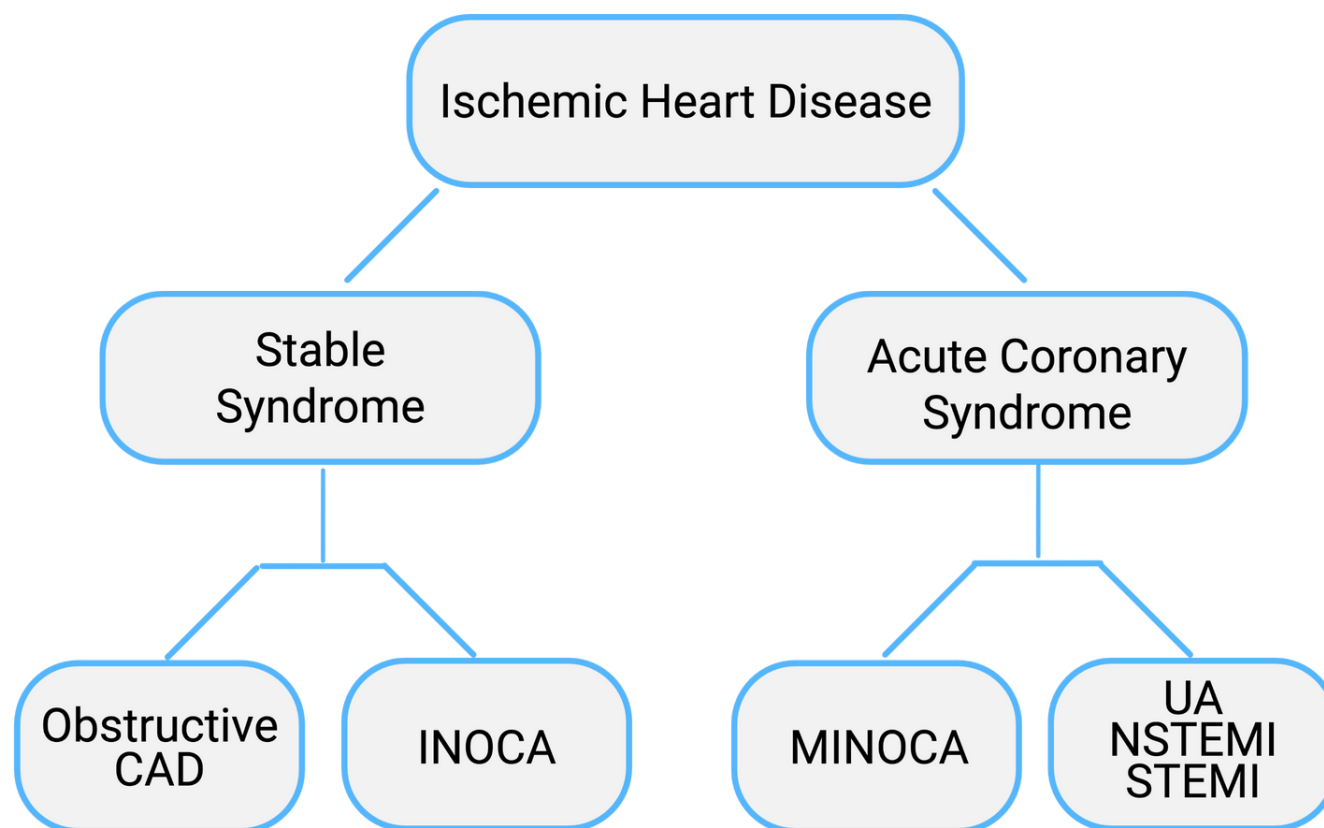
Coronary Vasospasm



Myocardial Bridging

- Increasingly recognized with new diagnostic tests
- Unknown prevalence
- Treated with medications and lifestyle changes

Nomenclature



INOCA VS. MINOCA

- **INOCA (or ANOCA)** is due to coronary microvascular dysfunction (CMD), coronary vasospasm, myocardial bridging
- **MINOCA** is due to plaque erosion, cardiomyopathies, vasospasm

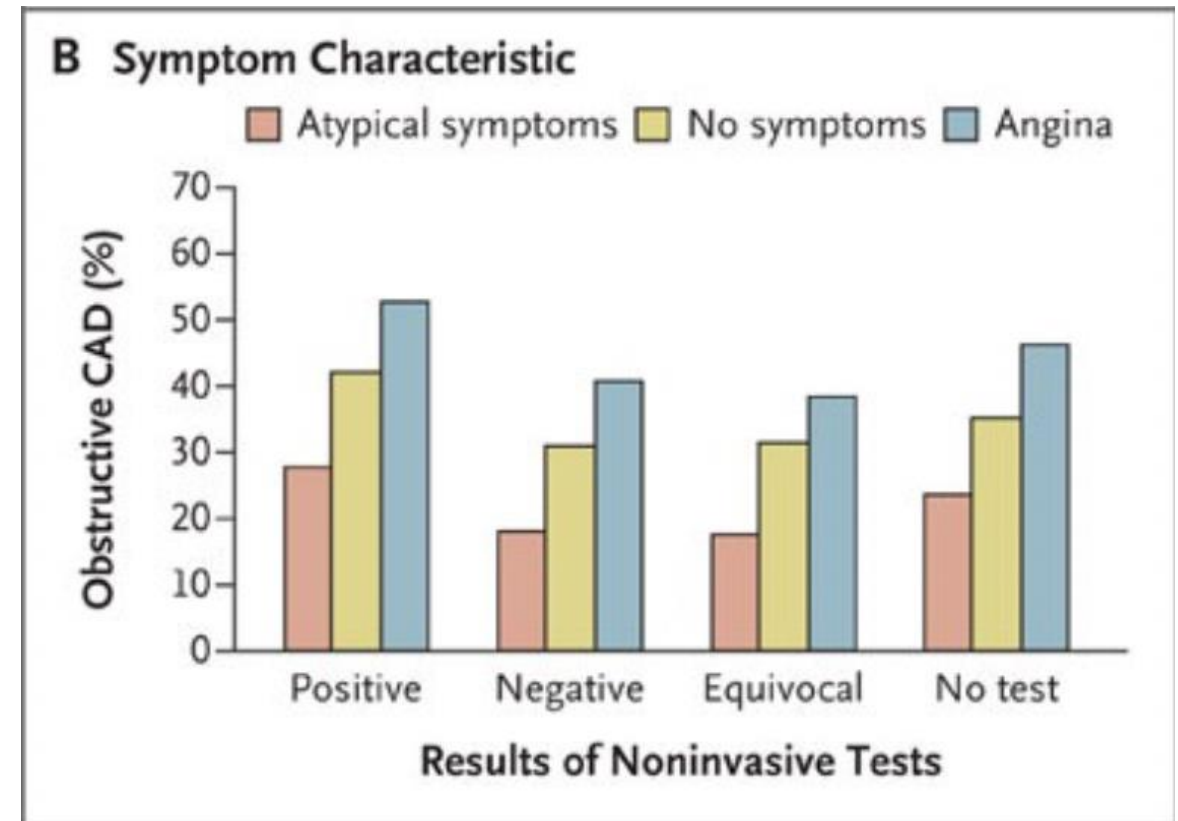
Chest pain in the absence of coronary artery disease is common

2010

Low prevalence of coronary artery disease in the cath lab

Data from 664 hospitals and 400,000 patients

- 59% of patients did not have any stenosis **greater than 50%**
- Only 38% of patients had a stenosis **greater than 70%**



Did not include pre-op, known CAD, prior MI, prior PCI, or CABG

N Engl J Med 2010; 362:886-895

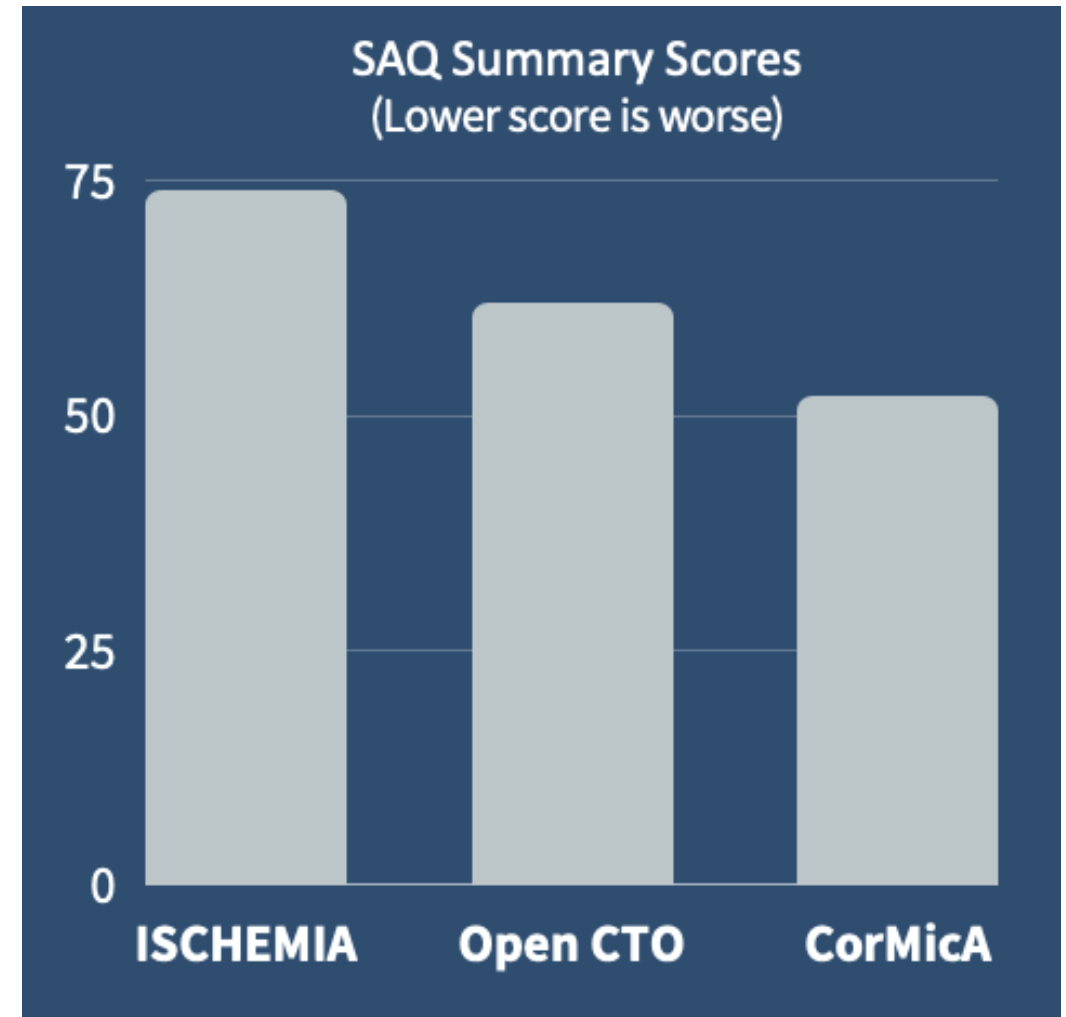
INOCA is not benign

- Patients may be more symptomatic than those with obstructive CAD
- **Prognosis:**
 - MI, Death (4x mortality)
 - Symptoms, QoL

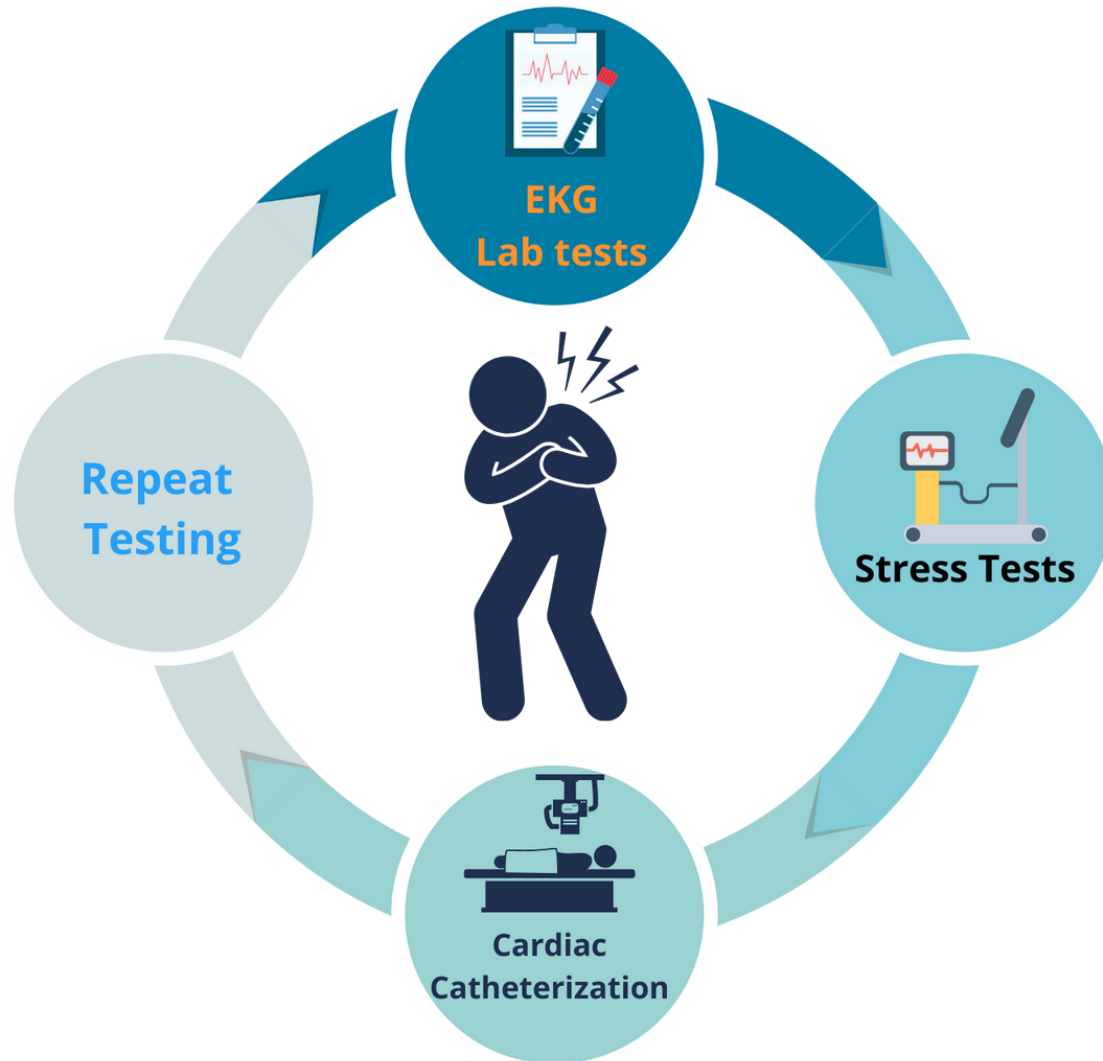
Ford et al., J Am Coll Cardiol. 2018 Dec 11;72(23 Pt A):2841-2855

Saponitis et al., J Am Coll Cardiol Interv. 2017 Aug, 10 (15) 1523–1534

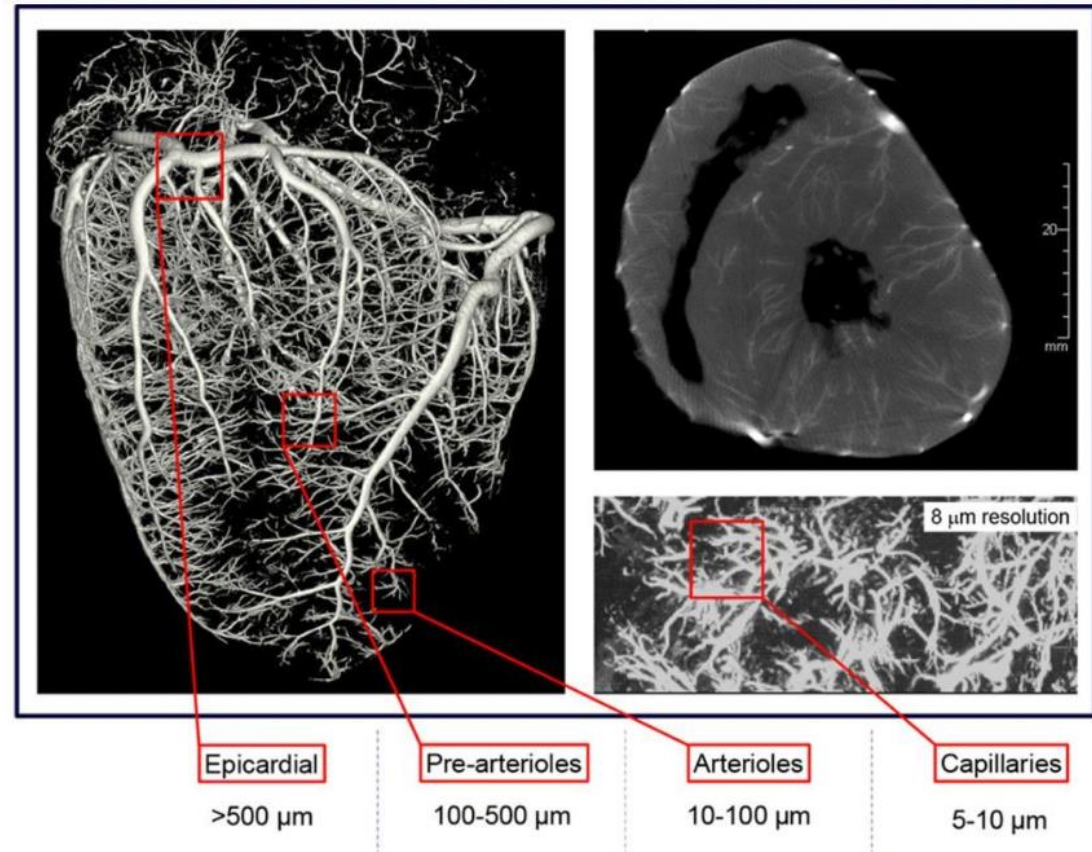
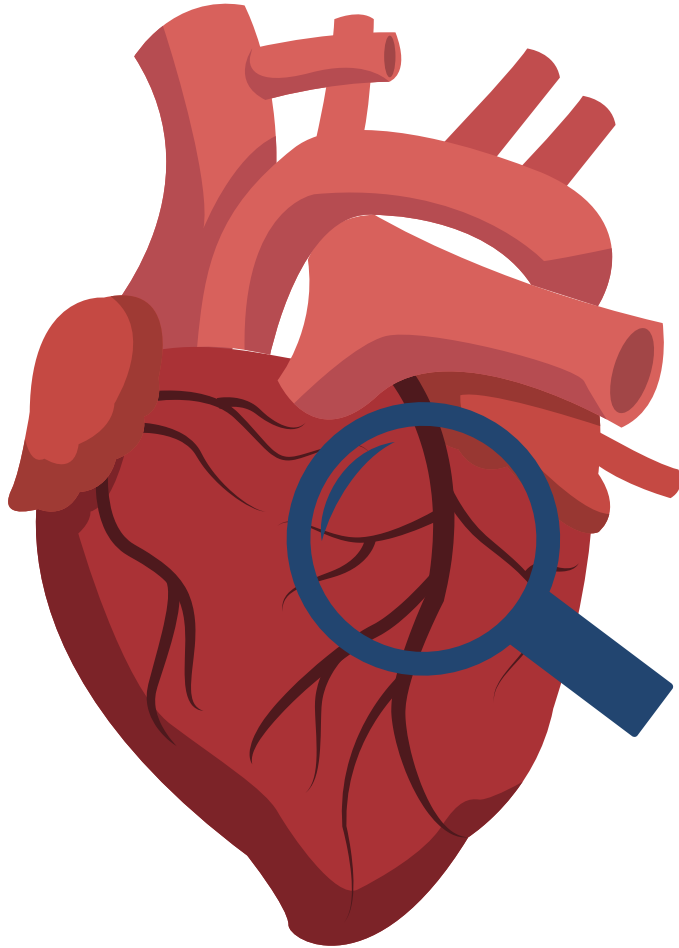
Spertus et al., N Engl J Med 2020; 382:1408-1419



Standard Diagnostic Approach

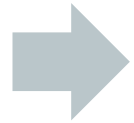


Blood Supply to the Heart

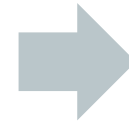


Coronary Function Testing (CFT)

**Suspected Ischemic
Heart Disease**



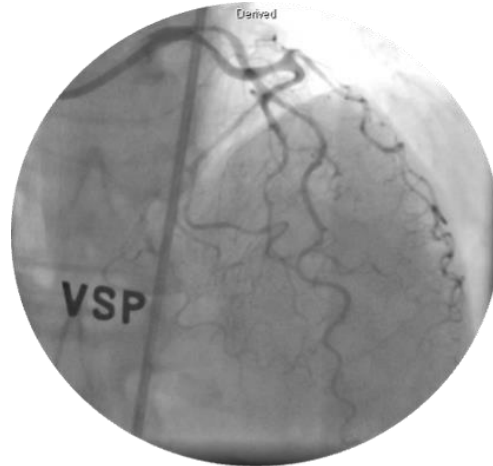
**Acetylcholine
Testing**



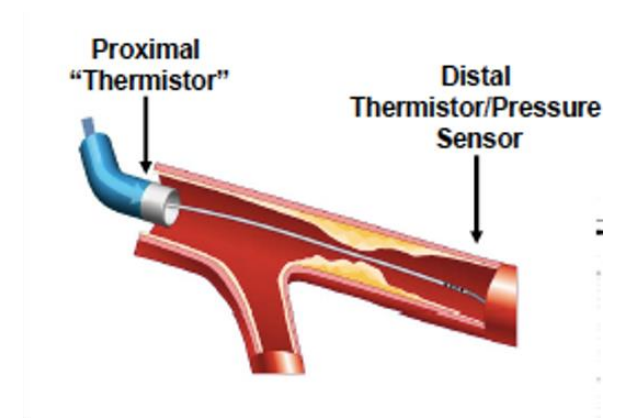
**Guidewire Testing
FFR/CFR/IMR**



**Diagnostic
Angiography**

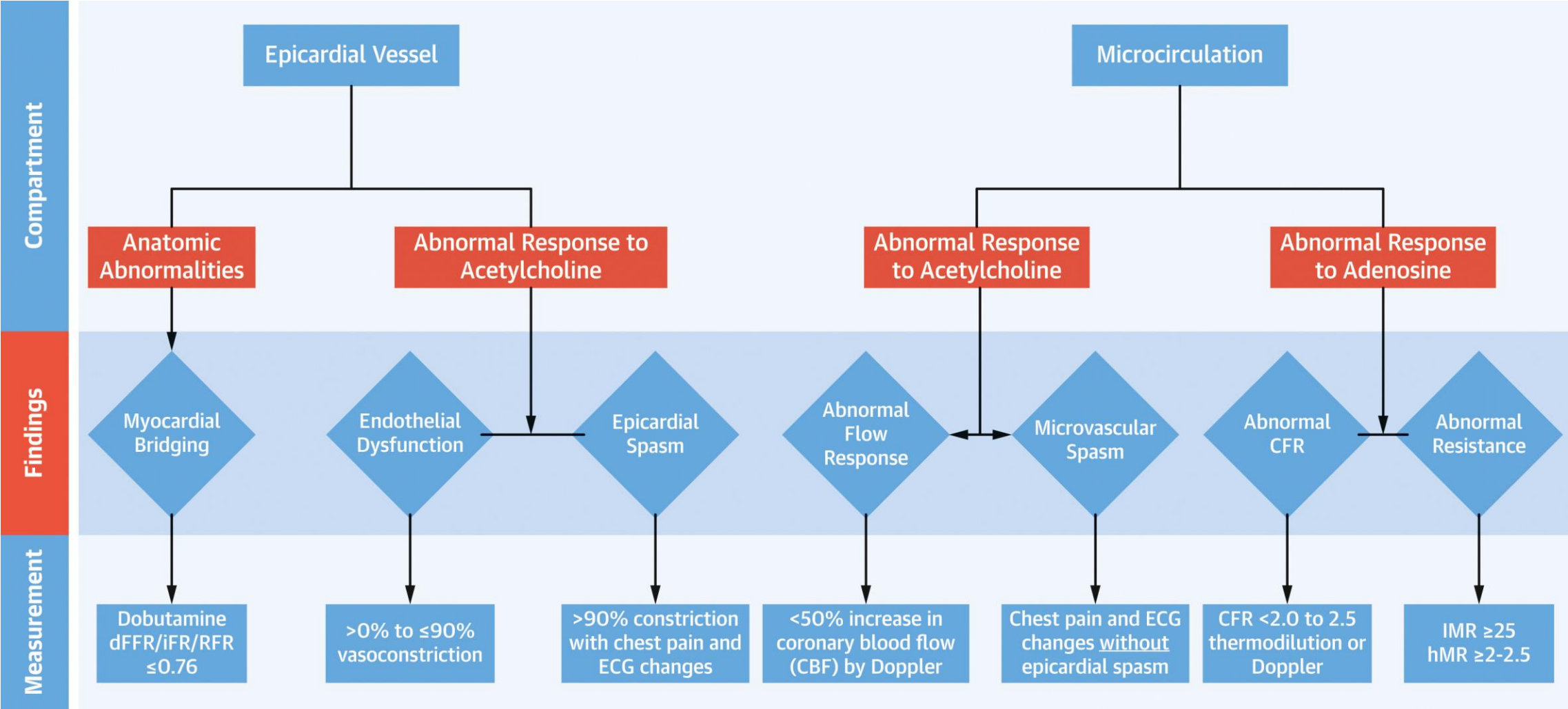


**Coronary
Vasospasm**



**Microvascular
Disease**

Comprehensive Assessment



Case Example

A 67-year-old man with **hypertension** and **diabetes mellitus**, and **prior COVID-19** presents to the emergency department with **chest pressure** and **shortness of breath**

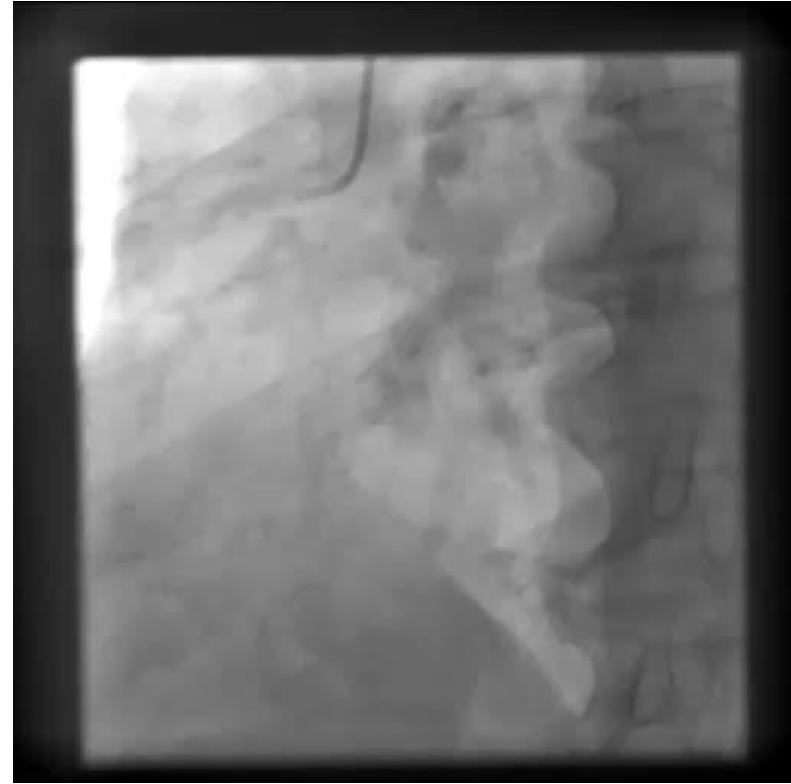
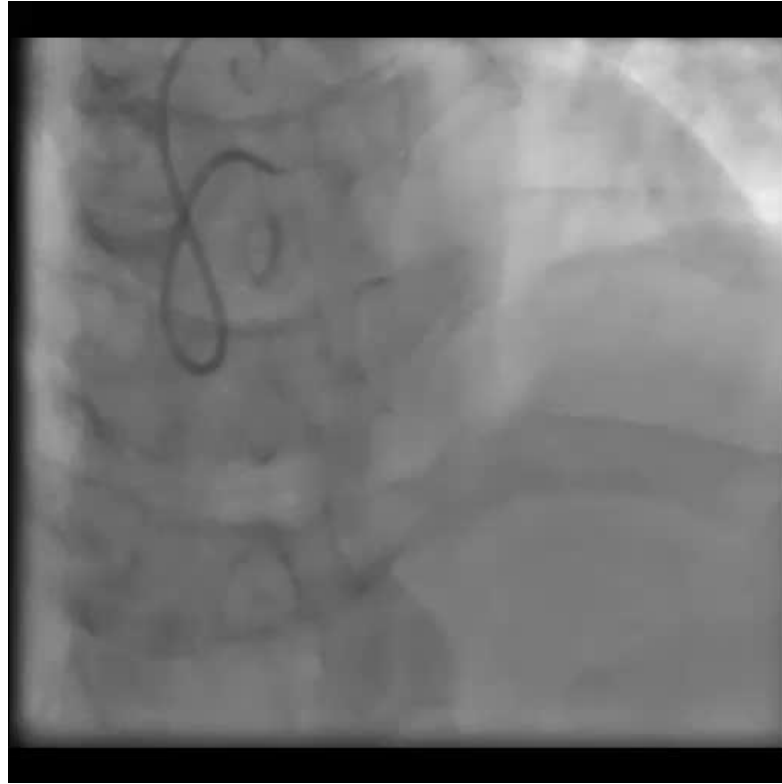


Initial presentation
EKG: non-specific
Troponin: Negative

Exercise SPECT
7.2 METs
5/10 chest pain
Inferior ischemia

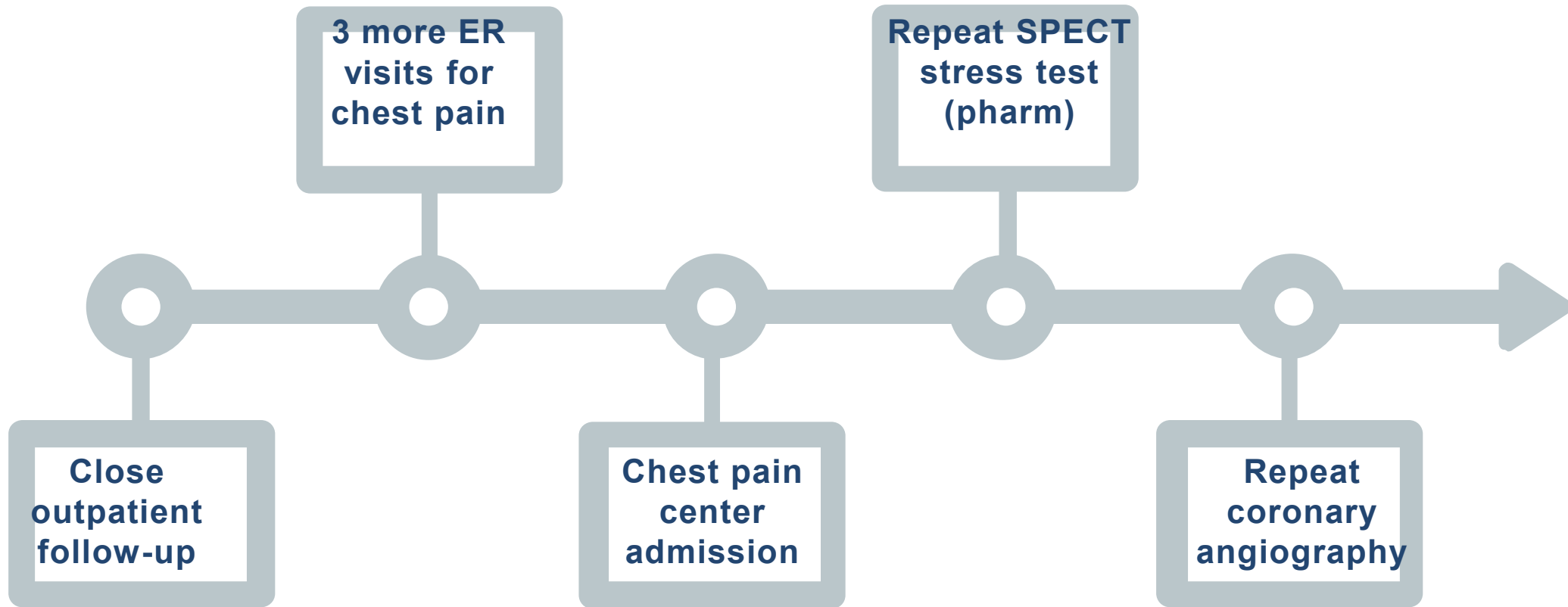
Referred for diagnostic
coronary angiography

Coronary Angiogram #1

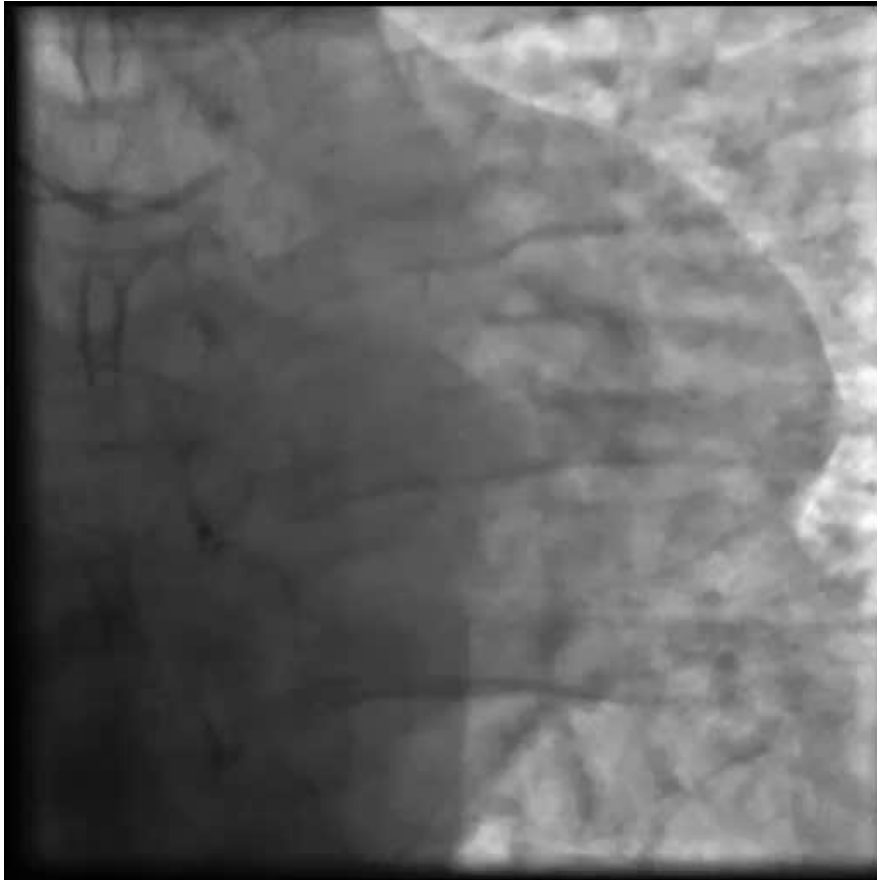


Pressure wire assessment of the RCA: iFR 0.91
[Ref: > 0.89]

Ongoing Symptoms



Coronary Angiogram #2



Pressure wire assessment of the LAD: **FFR 0.87**

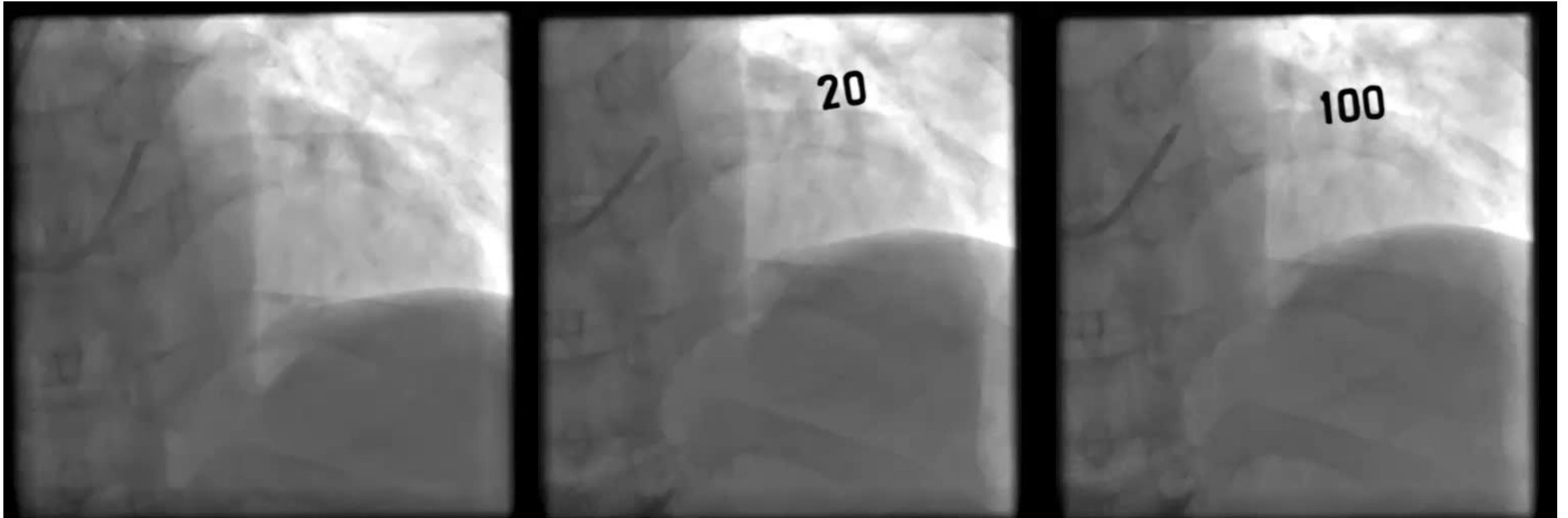
[Ref: > 0.80]

Evaluation

- 2 hospital admissions
- 5 ER visits for chest pain
- 2 coronary angiograms
- 2 SPECT stress tests
- GI referral and endoscopy

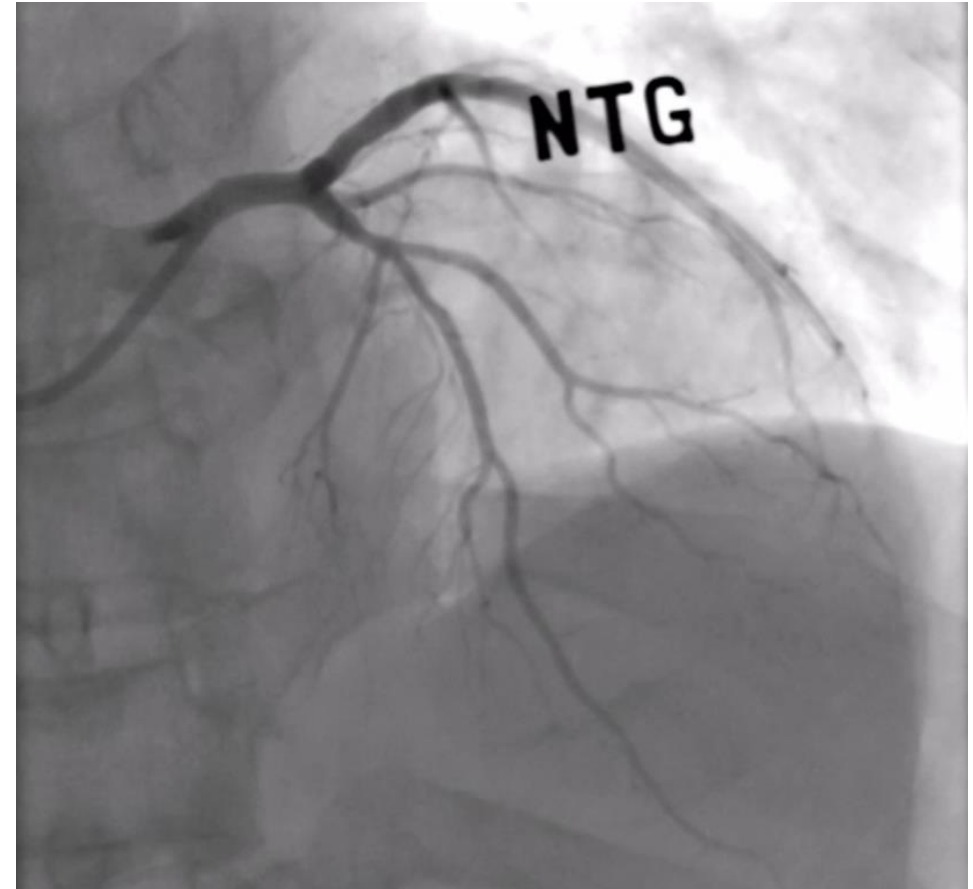
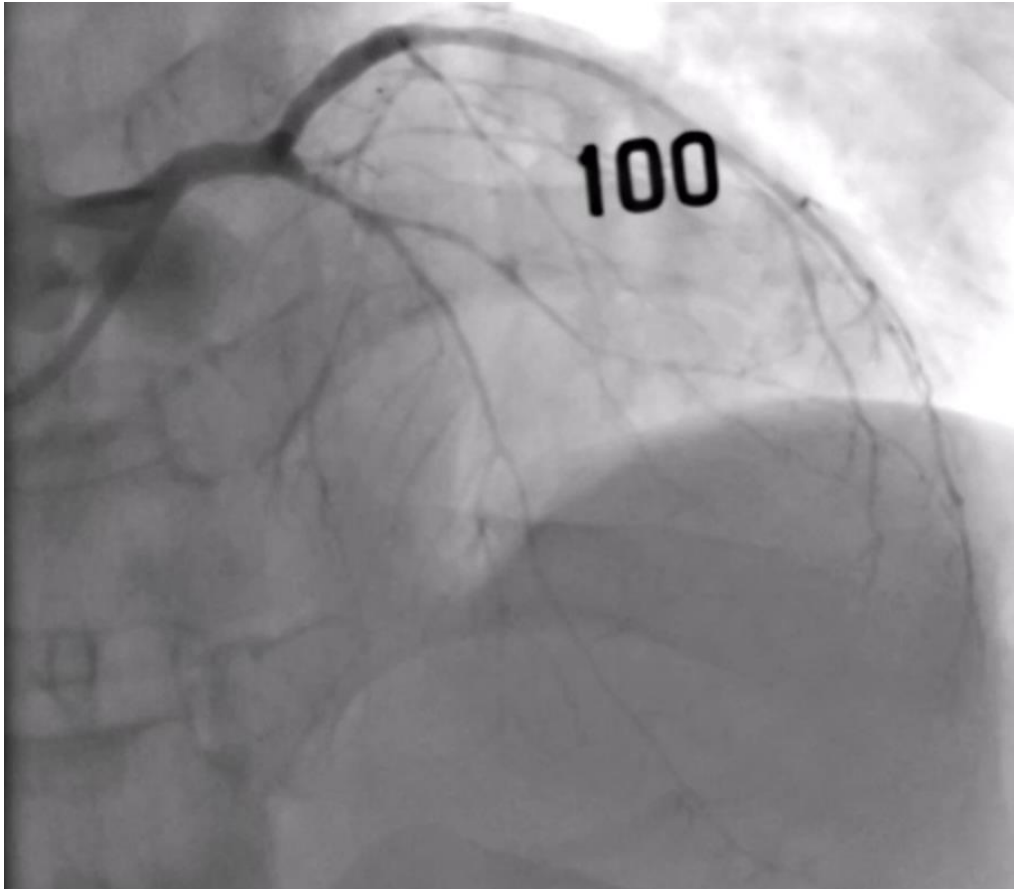
"Should he have recurrent chest pain further evaluation for microvascular disease would be warranted."

Coronary Angiogram #3: Acetylcholine provocation



**Severe vasospasm of the entire LAD and
Diagonal**

Coronary Angiogram #3 (continued)

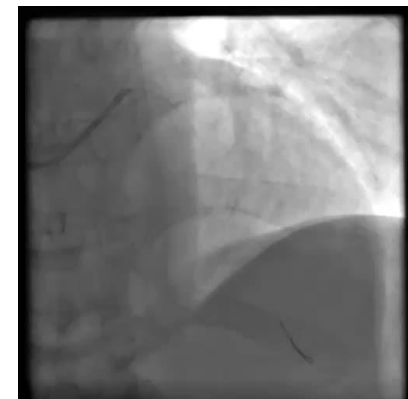


**ST elevation and chest pain, resolved with
nitroglycerin**

Coronary Angiogram #3 (continued)



Coronary microvascular dysfunction (IMR > 25)



Symptom relief

"He reports that his chest discomfort has completely resolved. He comments that he feels "really good" now. He has been performing his usual daily activities and has remained active."

Giving Patients an Accurate Diagnosis

- **Phenotypes of INOCA** include:
 - Coronary microvascular dysfunction (CMD)
 - Vasospastic angina (VSA)
 - Diffuse, physiologically significant coronary artery disease
 - Symptomatic myocardial bridging
 - Endothelial Dysfunction
 - Other disorders such as elevated resting flow or abnormal nociception
- Recent trials (**CorMicA**, **CHAMP-CMD**) have demonstrated improved symptom burden and quality of life if medical therapy is based on a specific phenotype

2024 ESC Class I

Recommendations	Class ^a	Level ^b
Diagnosis of ANOCA/INOCA endotypes		
In persistently symptomatic patients despite medical treatment with suspected ANOCA/INOCA (i.e. anginal symptoms with normal coronary arteries or non-obstructive lesions at non-invasive imaging, or intermediate stenoses with normal FFR/iFR at coronary arteriography) and poor quality of life, invasive coronary functional testing is recommended to identify potentially treatable endotypes and to improve symptoms and quality of life, considering patient choices and preferences. ^{36,37,298,930,939,985}	I	B

J Am Coll Cardiol 2018 Dec 11;72(23 Pt A):2841-2855

Circulation 2024 Jan 2;149(1):36-47

Conclusions

- Ischemia and nonobstructive coronary arteries (INOCA) is increasingly recognized, and coronary function testing can be used to give patients a clear diagnosis *and* better treatment
- Patients who present for evaluation of new or persistent cardiovascular symptoms *likely* have a cardiovascular diagnosis
- This is a patient population that is highly symptomatic, at risk for repeat presentation, and may be difficult to identify
- We are trying to better understand the long-term hazard of INOCA with **DISCOVER INOCA**

Thank you

Treatment (Yale Experience)

Table 3. Definitions for endotypes of ANOCA based on invasive coronary function testing.

ANOCA endotypes	Definitions based on invasive coronary function testing ^{10,81}	Treatment
Coronary microvascular dysfunction	Based on coronary Doppler or thermodilution techniques: • CFR < 2.0-2.5 and/or • IMR ≥ 25 /or • hMR ≥ 2-2.5	• Beta-blocker (carvedilol, metoprolol) • ACE inhibitor or ARB • Statin • Ranolazine • Cardiac rehabilitation
Microvascular spasm	Based on acetylcholine provocation testing: • Chest pain and/or • Absence of epicardial artery constriction • Ischemic ECG changes (ST-segment depression or elevation ≥0.1 mV in at least 2 contiguous leads)	• Calcium-channel blocker (verapamil, amlodipine, diltiazem) • ACE inhibitor or ARB • Statin • Short-acting nitrates as needed • Smoking cessation
Endothelial dysfunction	Based on acetylcholine provocation testing: • >0% and ≤90% epicardial artery narrowing and/or • <50% augmentation in coronary blood flow by Doppler	• Statin • Cardiac rehabilitation • ACE inhibitor or ARB • Short-acting nitrates as needed
Epicardial coronary spasm	Based on acetylcholine provocation testing: • Chest pain and/or • >90% epicardial artery spasm and/or • ECG changes (ST-segment depression or elevation ≥0.1 mV in at least 2 contiguous leads)	• Calcium-channel blocker (verapamil, amlodipine, diltiazem) • ACE inhibitor or ARB • Statin • Short-acting nitrates as needed • Smoking cessation
Myocardial bridging	• Half-moon sign on IVUS • ≥10% systolic compression by IVUS • Dobutamine dFFR/iFR/RFR ≤ 0.76	• Beta-blocker • Calcium-channel blocker • Ivabradine • Surgical unroofing (select cases)

What is the prevalence of ANOCA?

Center	Diagnostic Modality	Prevalence
Mayo Clinic (1998)	Doppler	59%
WISE (2001)	Doppler + ACh infusion	47%
ACOVA (2012)	ACh Infusion	62%
Stanford (2015)	Bolus ACh + Thermodilution	77%
CorMicA (2019)	ACh Infusion + Thermodilution	89%
Radboud University (2021)	Bolus ACh + Thermodilution	86%

Hasdai et al., *Mayo Clinic Proceedings*. Vol. 73. No. 12., 1998

Reis et al., *American Heart Journal*. 2001;141(5):735–741

Ong et al., *J Am Coll Cardiol*. 2012 Feb 14;59(7):655-62

Lee et al., *Circulation*. 2015 Mar 24;131(12):1054-60

Ford et al., *Circ Cardiovasc Interv*. 2019 Dec; 12(12): e008126

Konst et al., *International Journal of Cardiology* 333 (2021): 14-20