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Persistent Chest Pain in the Modern Era

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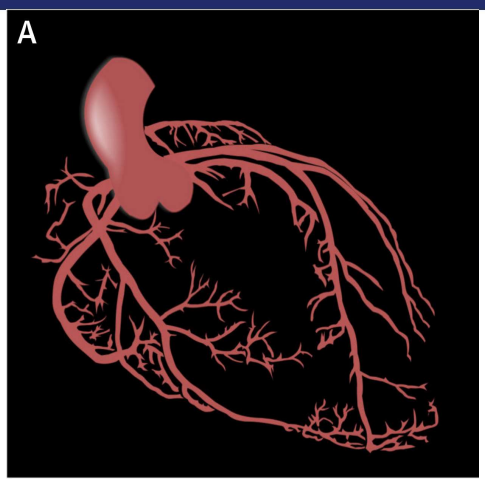
February 20, 2026

Disclosures: None

Case Example

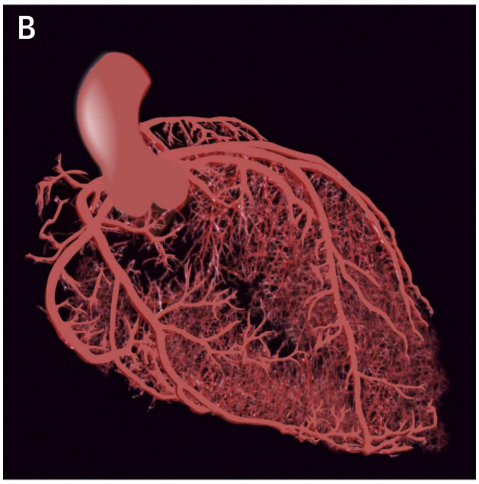
- 44y F presented with angina at rest
- Troponin was mildly elevated at 0.08
- ECG showed non-specific changes
- History of multiple similar presentations
- Coronary angiography showed mild non-obstructive CAD
- PMH of HTN, morbid obesity, and OSA

What we think the coronary arterial tree looks like…



Taqueti, V. R., & Di Carli, M. F. (2018). Coronary microvascular disease pathogenic mechanisms and therapeutic options. *Journal of the American College of Cardiology*, *72*(21), 2625–2641. https://doi.org/10.1016/j.jacc.2018.09.042

What it really looks like…



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Perspective

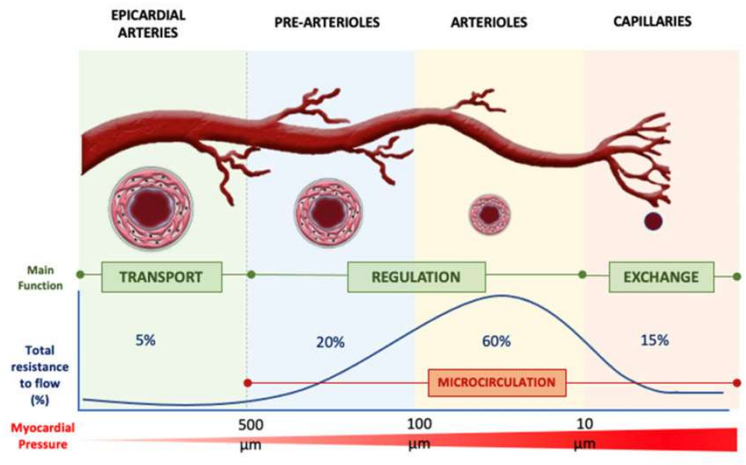
- Millions of Americans undergo evaluation for angina yearly
- Many undergo invasive coronary angiography
- 50% of them do not have obstructive epicardial disease

Samuels BA, Shah SM, Widmer RJ, et al. Comprehensive management of anoca, part 1-definition, patient population, and diagnosis: jacc state-of-the-art review. J Am Coll Cardiol. 2023;82(12):1245 1263. doi:10.1016/j.jacc.2023.06.043

Perspective

- The term ANOCA was coined to describe these patients
- ANOCA: Angina with Non-Obstructive Coronary Artery Disease
- INOCA is a derivative term that describes Ischemia with Non-Obstructive Coronary Artery Disease

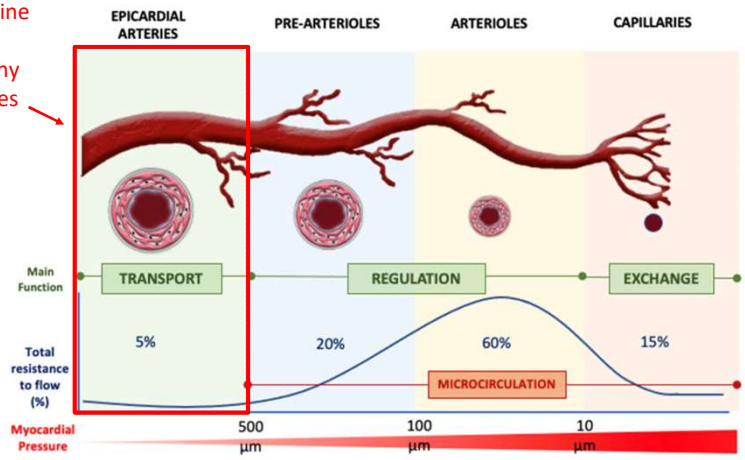
Perspective



Del Buono MG, Montone RA, Camilli M, et al. Coronary microvascular dysfunction across the spectrum of cardiovascular diseases: jacc state-of-the-art review. *J Am Coll Cardiol.* 2021;78(13):1352-1371. doi:10.1016/j.jacc.2021.07.042

Perspective

What routine coronary angiography interrogates



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Perspective

- ANOCA is caused by functional and structural alterations in the macro- and micro-circulations
- Generally divided into endothelium-dependent and endothelium-independent mechanisms

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Perspective

- Endothelium-independent disease is not well understood but likely related to smooth muscle cell hypertrophy and poor response to vasodilators
- Endothelium-dependent disease is secondary to inadequate local production of nitric oxide (NO) and/or rapid degradation of NO

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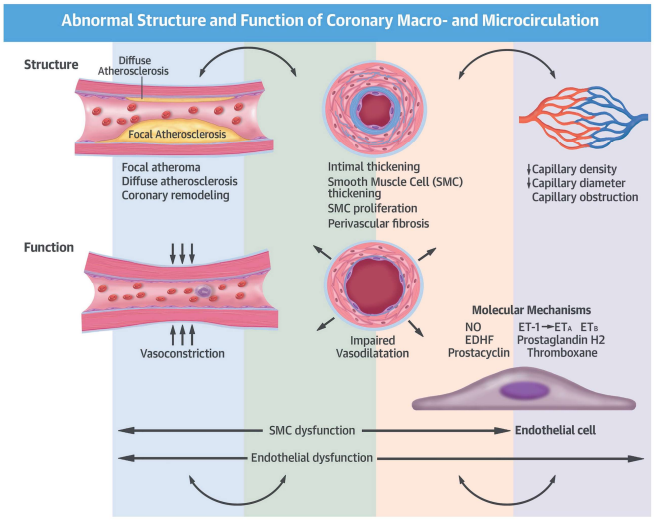
Perspective



Taqueti, V.R. et al. J Am Coll Cardiol. 2018;72(21):2625-41.

ANOCA Endotypes

- Endothelium-independent:
  - Coronary microvascular dysfunction (CMD)
- Endothelium-dependent:
  - Epicardial spasm (Prinzmetal angina)
  - Endothelial dysfunction
  - Microvascular spasm
- Myocardial bridging

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Presentation

- Most (60%) ANOCA patients present with exertional angina
- About 40% have sporadic angina or exertional dyspnea
- Symptoms are usually stable
- Many patients have had multiple evaluations (ED, PCP, cardiology)

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ANOCA Evaluation

Non-Invasive Evaluation

- Cardiac PET is the most accurate and prognostically validated non-invasive test
- Rubidium allows quantification of myocardial blood flow (mL/min/g of myocardium) and flow reserve (stress/rest flow ratio)

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Non-Invasive Evaluation

- Studies have showed coronary flow reserve (CFR) < 2 is associated with higher risk of CV events and death
- cMR and Doppler echocardiography are other non-invasive modalities
- Non-invasive testing does not allow for phenotyping of ANOCA patients

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Invasive Evaluation

- Invasive and non-invasive testing are complementary
- Invasive testing evaluates all possible pathways that affect epicardial and microvascular circulations
- Allows testing for CMD, microvascular spasm, endothelial dysfunction, epicardial spasm and myocardial bridging

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Invasive Evaluation

- Consists of measurement of LV filling pressure, coronary angiography and coronary functional testing (CFT)
- CFT assesses:
  - Epicardial spasm
  - Endothelial dysfunction
  - Microvascular spasm
  - Coronary Microvascular Dysfunction
  - Myocardial bridging

Invasive Evaluation

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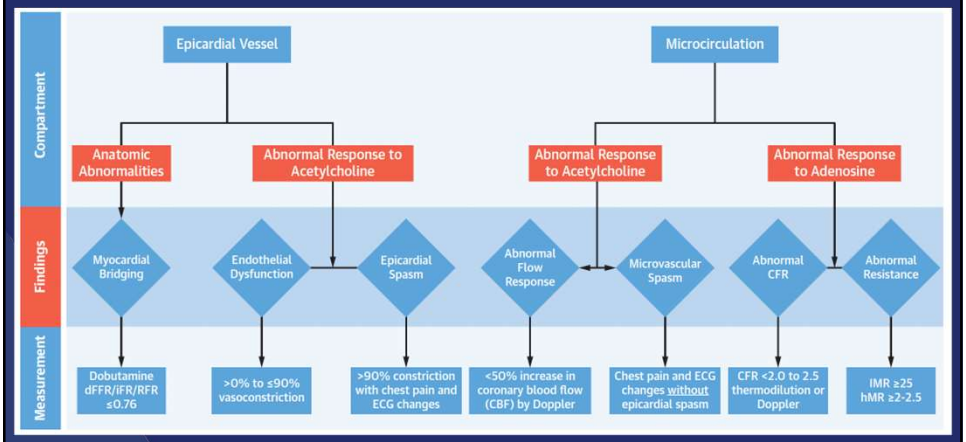
- CFT assesses:
  - Epicardial spasm
  - Endothelial dysfunction
  - Microvascular spasm

  } with acetylcholine provocation

  - Coronary microvascular dysfunction → with adenosine
  - Myocardial bridging → with intravascular ultrasound and dobutamine stress

ANOCA Endotypes and Invasive Assessment



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Coronary Spasm

- Acetylcholine (Ach) works on endothelial cells and smooth muscle cells in a counteractive manner
- In healthy endothelium, Ach induces NO release causing vasodilation, trumping the vasoconstrictive effect on smooth muscle cells
- In diseased vessels, endothelium fails to release NO causing vasoconstriction

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Coronary Spasm

- Coronary spasm can present as:
  - Epicardial spasm → >90% epicardial spasm
  - Endothelial dysfunction → 0-90% epicardial spasm
  - Microvascular spasm → No epicardial spasm
- Must be accompanied by ECG changes and angina during testing

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Coronary Microvascular Dysfunction (CMD)

- Likely related to smooth muscle cell hypertrophy and inability to vasodilate
- Assessed by evaluating coronary flow reserve (CFR) and index of microcirculatory resistance (IMR) during maximal hyperemia
- Hyperemia is induced with IV adenosine to mimic "stress"

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Coronary Microvascular Dysfunction (CMD)

- In normal coronary microvasculature, flow should increase by at least 2.5 folds with stress
- CFR < 2.5 is considered abnormal
- High resistance (IMR > 25) is also indicative of CMD, independent of CFR

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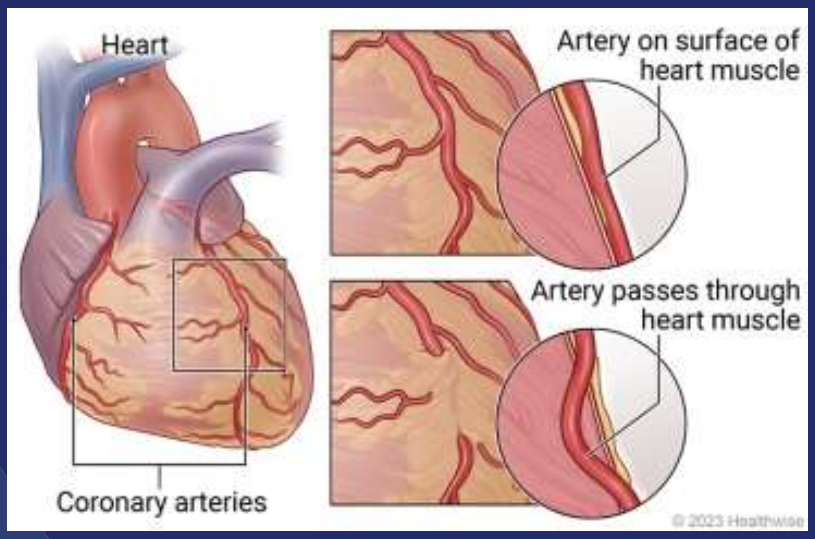
Myocardial Bridging (MB)

- A congenital anomaly in which a segment of the epicardial artery traverses through the myocardium
- Leads to systolic compression of the artery
- Most seen in the left anterior descending artery (LAD)
- Underrecognized by conventional angiography

Sternheim D, Power DA, Samtani R, Kini A, Fuster V, Sharma S. Myocardial bridging: diagnosis, functional assessment, and management: jacc state-of-the-art review. J Am Coll Cardiol. 2021;78(22):2196-2212. doi:10.1016/j.jacc.2021.09.859

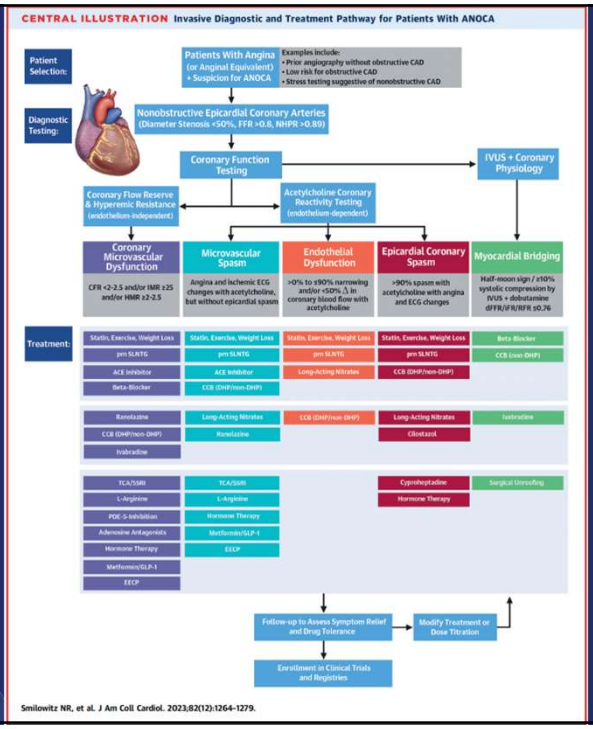


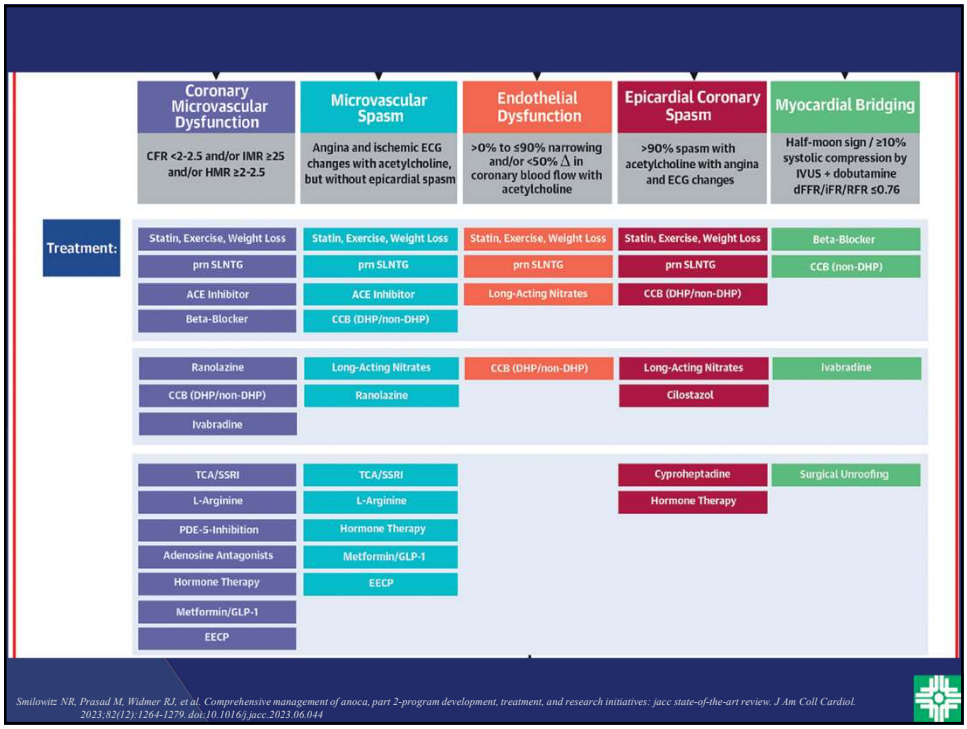
Learning about myocardial bridging | kaiser permanente. Accessed January 26, 2026. https://healthy.kaiserpermanente.org/health-wellness/health-encyclopedia/he.learning-about-myocardial-bridging.aco0525

ANOCA Management

Management

- First step is to validate patient's symptoms
- Address risk factors (obesity, smoking…Etc)
- Tailor plan to patient's unique diagnosis and co-morbidities
- CMD/spasm is a syndrome…not an isolated condition
- Cardiac rehab and weight loss are paramount
- Frequent follow-ups and medication titration are necessary





Smilowitz NR, Prasad M, Widmer RJ, et al. Comprehensive management of anoca, part 2-program development, treatment, and research initiatives: jacc state-of-the-art review. J Am Coll Cardiol. 2023;82(12):1264-1279. doi:10.1016/j.jacc.2023.06.044

CorMicA Trial (2018)

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 72, NO. 23, 2018

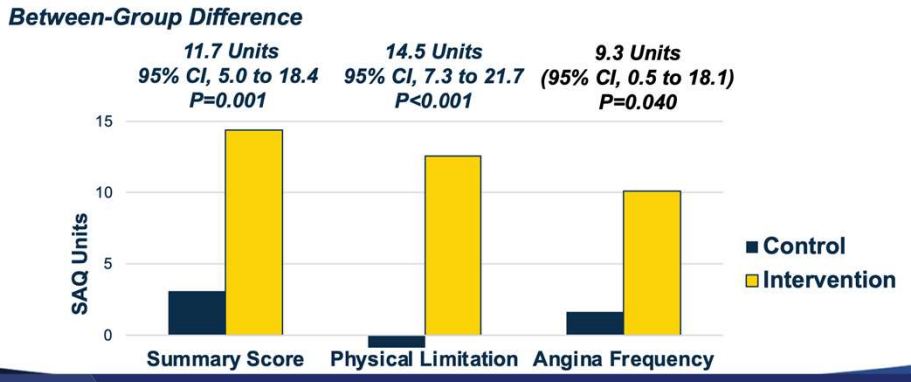
PUBLISHED BY ELSEVIER

Stratified Medical Therapy Using Invasive Coronary Function Testing in Angina

The CorMicA Trial

Thomas J. Ford, MBChB (Hons),[a,b,c] Bethany Stanley, MSc,[d] Richard Good, MD,[a] Paul Rocchiccioli, PhD,[a,b] Margaret McEntegart, PhD,[a,b] Stuart Watkins, MD,[a] Hany Eteiba, MD,[a] Aadil Shaukat, MBChB,[a] Mitchell Lindsay, MD,[a] Keith Robertson, PhD,[a] Stuart Hood, MD,[a] Ross McGeoch, MD,[e] Robert McDade, BSc,[a] Eric Yii,[b] Novalia Sidik, MBChB,[b] Peter McCartney, MBChB,[b] David Corcoran, MBChB,[b] Damien Collison, MB BCh,[a,b] Christopher Rush, MBChB,[b] Alex McConnachie, PhD,[d] Rhian M. Touyz, PhD,[b] Keith G. Oldroyd, MD (Hons),[a,b] Colin Berry, PhD[a,b]

Primary Endpoint – 6 month SAQ Change

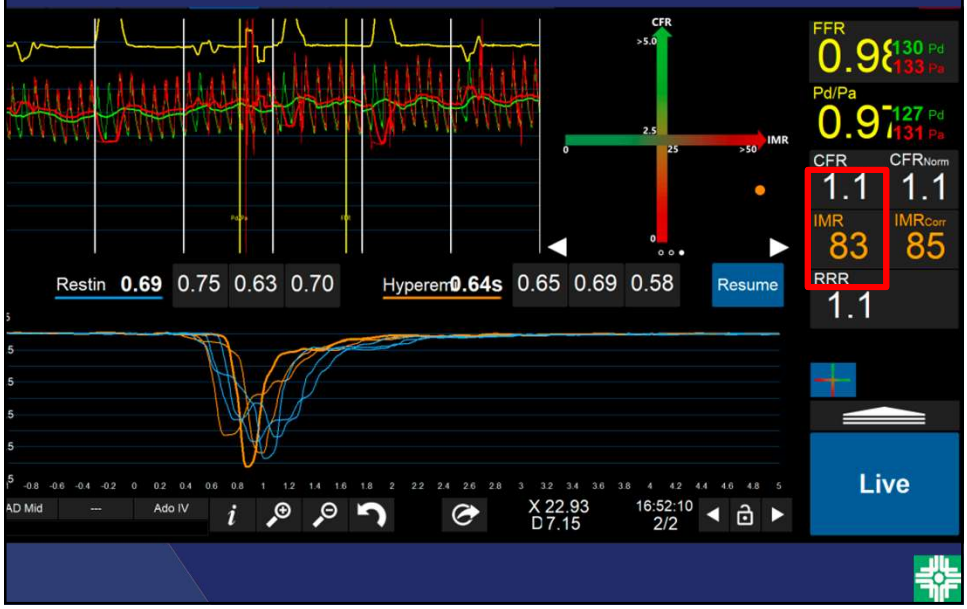


Ford TJ, Stanley B, Good R, et al. Stratified medical therapy using invasive coronary function testing in angina: the cormica trial. J Am Coll Cardiol. 2018;72(23 Pt A):2841-2855. doi:10.1016/j.jacc.2018.09.006

Case Example

- 44y F presented with angina at rest
- Troponin was mildly elevated at 0.08
- ECG showed non-specific changes
- History of multiple similar presentations
- Coronary angiography showed mild non-obstructive CAD
- PMH of HTN, morbid obesity, and OSA

Diagnosed with CMD



Take Home Message

- Lack of severe obstructive CAD does not mean chest pain is non-cardiac
- Consider further ANOCA testing in patients with recurrent angina and negative prior ischemic evaluation
- Therapy should be tailored to patient's unique condition

Thank You