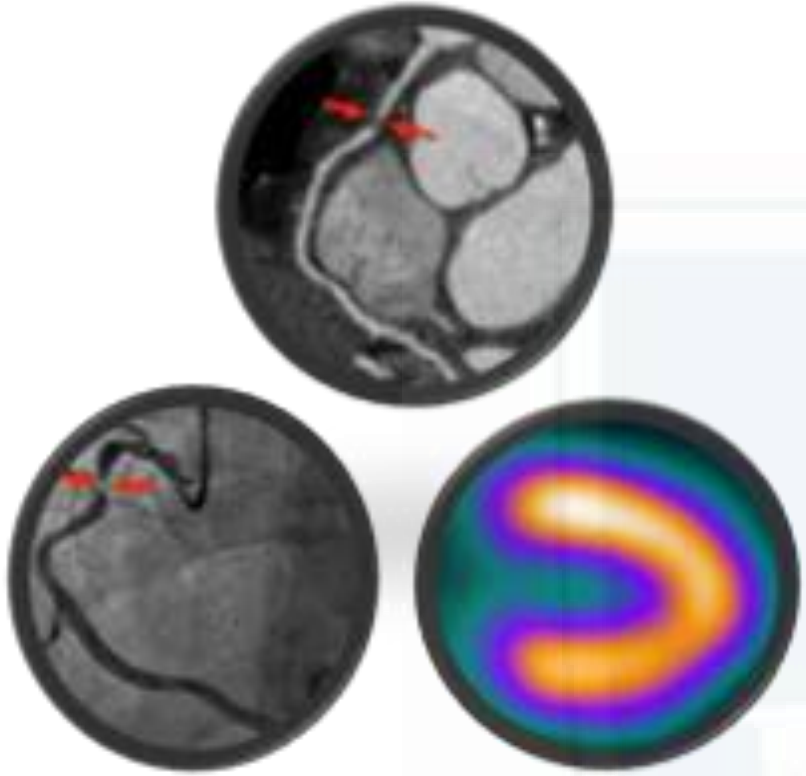


Chapter 3:

Select diagnostics that confirm disease and estimate death.

Strategy: ***Confirm the diagnosis of coronary artery disease and estimate the risk of death.***

Audience Question #3

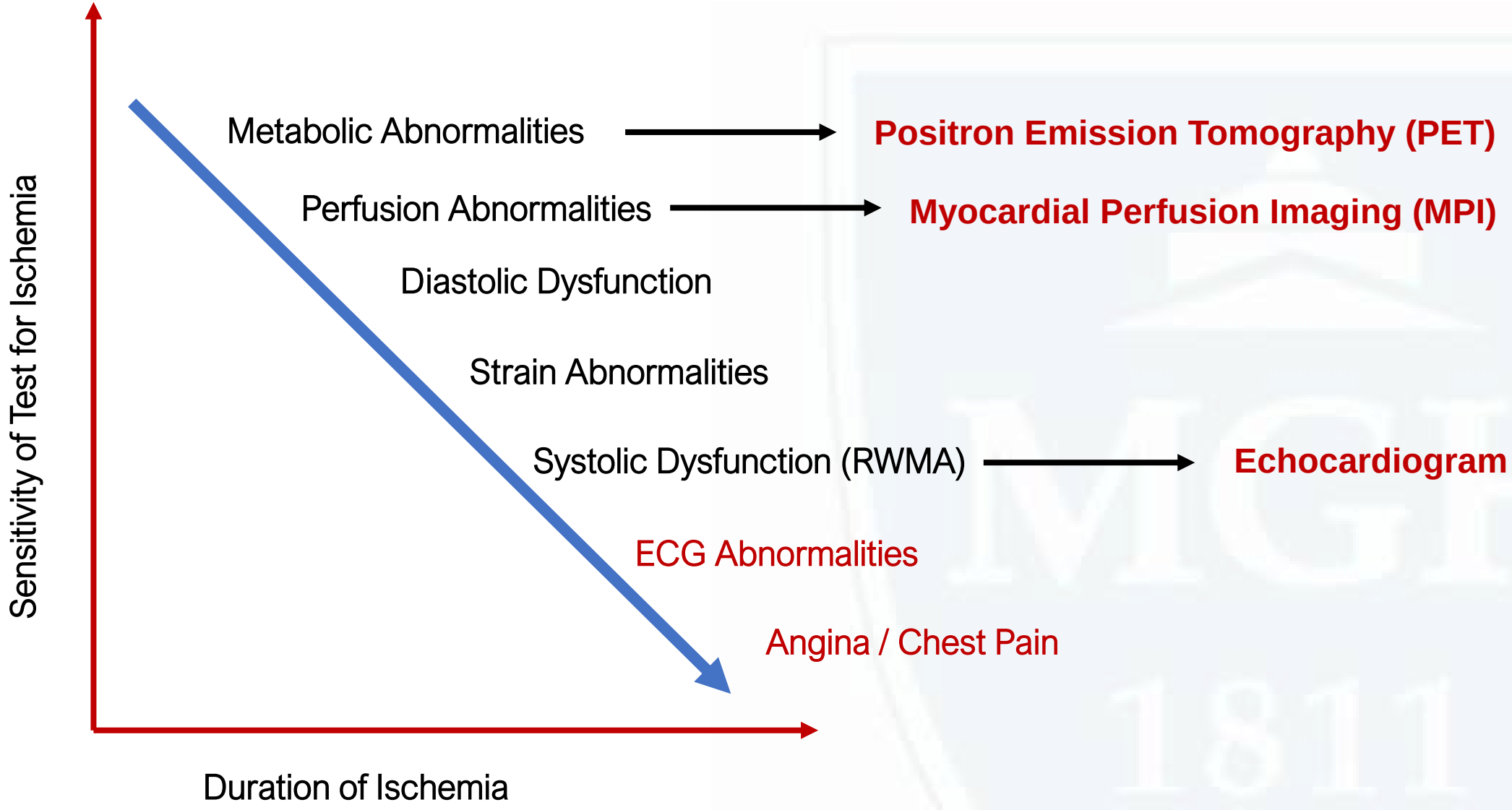
After the onset of ischemia, all of the following occur. Which of the following happens last?

a. ECG changes
b. Chest Pain
c. Systolic Dysfunction (RWMA)
d. Diastolic Dysfunction

Answer (B): Chest Pain

The ischemic cascade teaches us that angina or chest pain is a late and not an early first manifestation of ischemia. ECG abnormalities come just before.

The Ischemic Cascade



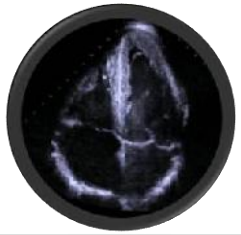
If you are taking the Internal Medicine Certification Examination …

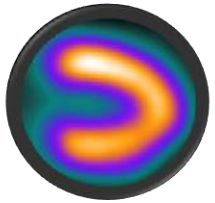
For a patient who is able to exercise and has a normal baseline electrocardiogram, an **exercise treadmill stress test** is the most appropriate noninvasive study to evaluate for coronary artery disease.

Test	Stress electrocardiography
Requirements and considerations	Exercise stress on a treadmill Requires interpretable electrocardiogram (eg, no left bundle-branch block or major ST- and T-wave changes) at baseline
Sensitivity	**0.58** (95% CI, 0.46-0.69)
Specificity	**0.62** (95% CI, 0.54-0.69)
Findings indicating high risk	>2-mm ST-segment depressions at low workload ST-segment elevations or ventricular tachycardia or ventricular fibrillation

- Exercise ECG has a sensitivity of **only 58%.**
- It **misses 42%** of patients with CAD.
- Its sensitivity is even **less in woman** since false negative results occur most often in those with less disease.
- Reminder: Its diagnostic value is lost **when the ECG is abnormal** (e.g. left bundle branch block).

Joshi and de Lemos. JAMA. 2021.

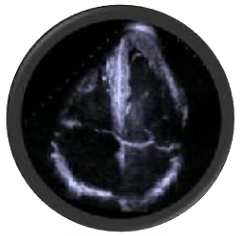


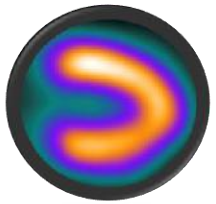


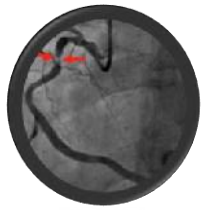
Test	Stress echocardiography	Stress myocardial perfusion imaging
Requirements and considerations	Exercise or pharmacological stress (dobutamine [with atropine if necessary to achieve target heart rate] or adenosine derivatives) For patients with poor-quality echocardiographic images, contrast may improve the interpretability of the test	Exercise or pharmacological stress (vasodilator) Higher radiation exposure than other noninvasive tests
Sensitivity	**0.85** (95% CI, 0.80-0.89)	**0.87** (95% CI, 0.83-0.90)
Specificity	**0.82** (95% CI, 0.72-0.89)	**0.70** (95% CI, 0.63-0.76)
Findings indicating high risk	Decrease in left ventricular ejection fraction (LVEF) >10% or left ventricular (LV) dilation Wall motion abnormalities in multiple coronary territories Baseline LV dysfunction	Decrease in LVEF >10% or LV dilation Perfusion defect in >10% of myocardium Baseline LV dysfunction

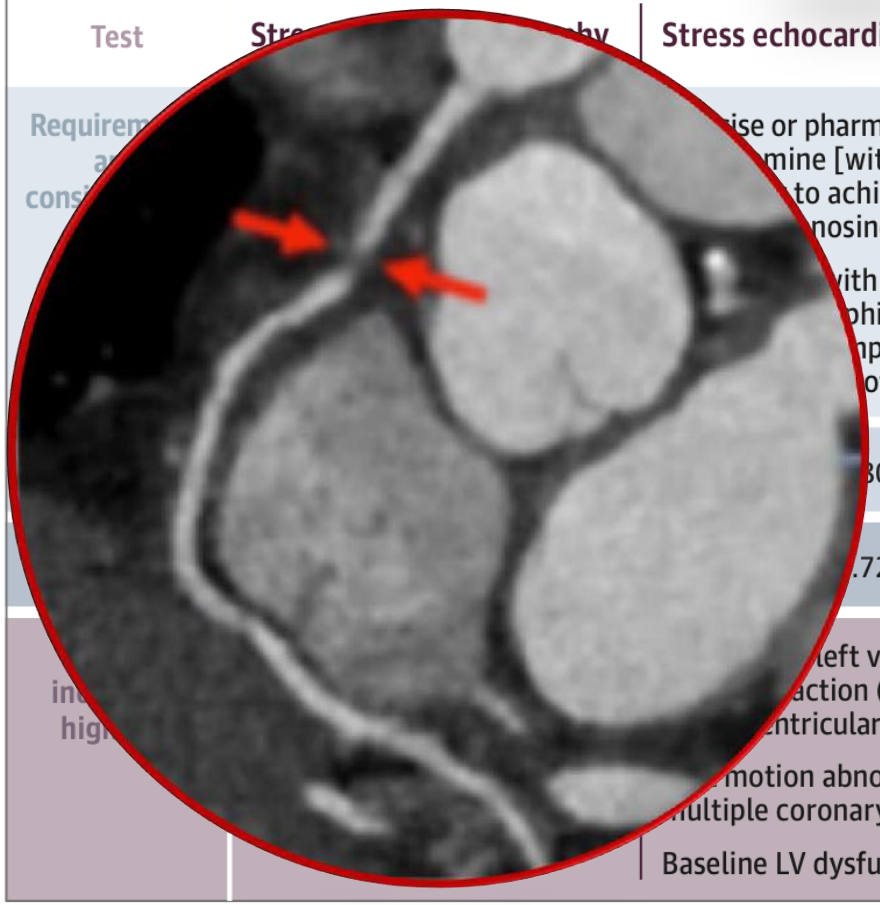
- Higher sensitivity and specificity
- **Fewer** catheterization referrals
- Offers **functional evidence** of ischemia which is typically required to support revascularization. Can **guide revascularization**.
- Useful particularly in patients with **known CAD**.

Joshi and de Lemos. JAMA. 2021.







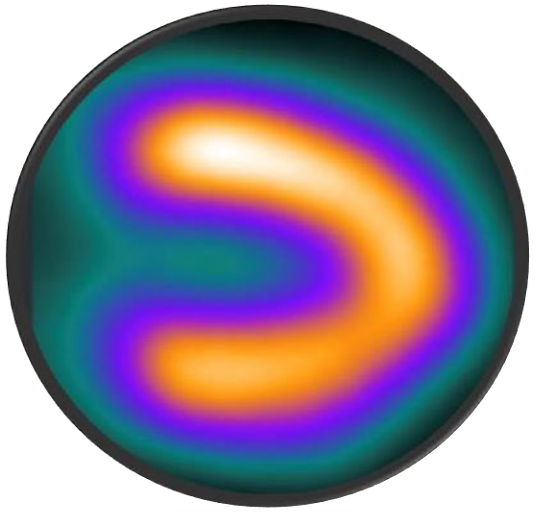


- **More than CAC scoring**. Coronary CTA offers visualization of the lumen and wall of of the coronary artery. **Lesion are not always ischemic**.
- When non-obstructive CAD which can provide prognostic information and **guide preventive therapy**. (e.g. no obstruction, abundant atherosclerosis, start statin therapy).
- Often best when 1. lower clinical likelihood of CAD, 2. **no previous CAD diagnosis**, and 3. anticipate good image quality.

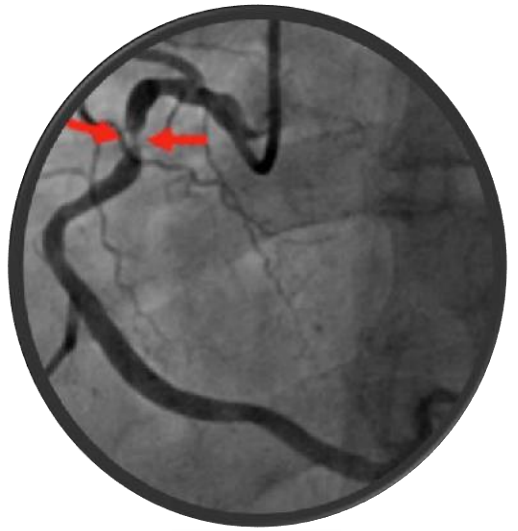
Joshi and de Lemos. JAMA. 2021.

Which Test to Choose?

Anatomical Non-invasive



Functional Non-invasive



Invasive Angiography

European Guidelines

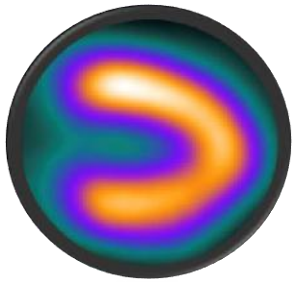
Use of diagnostic imaging tests in the initial diagnostic management of symptomatic patients with suspected coronary artery disease

Recommendations	Class[a]	Level[b]
Non-invasive functional imaging for myocardial ischaemia[c] or coronary CTA is recommended as the initial test to diagnose CAD in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone.[4,5,55,73,78–80]	I	B

Cor CTA

OR

Stress Perfusion



Knuuti and others. 2019 ESC Guidelines.

Circulation

AHA/ACC CLINICAL PRACTICE GUIDELINE

2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

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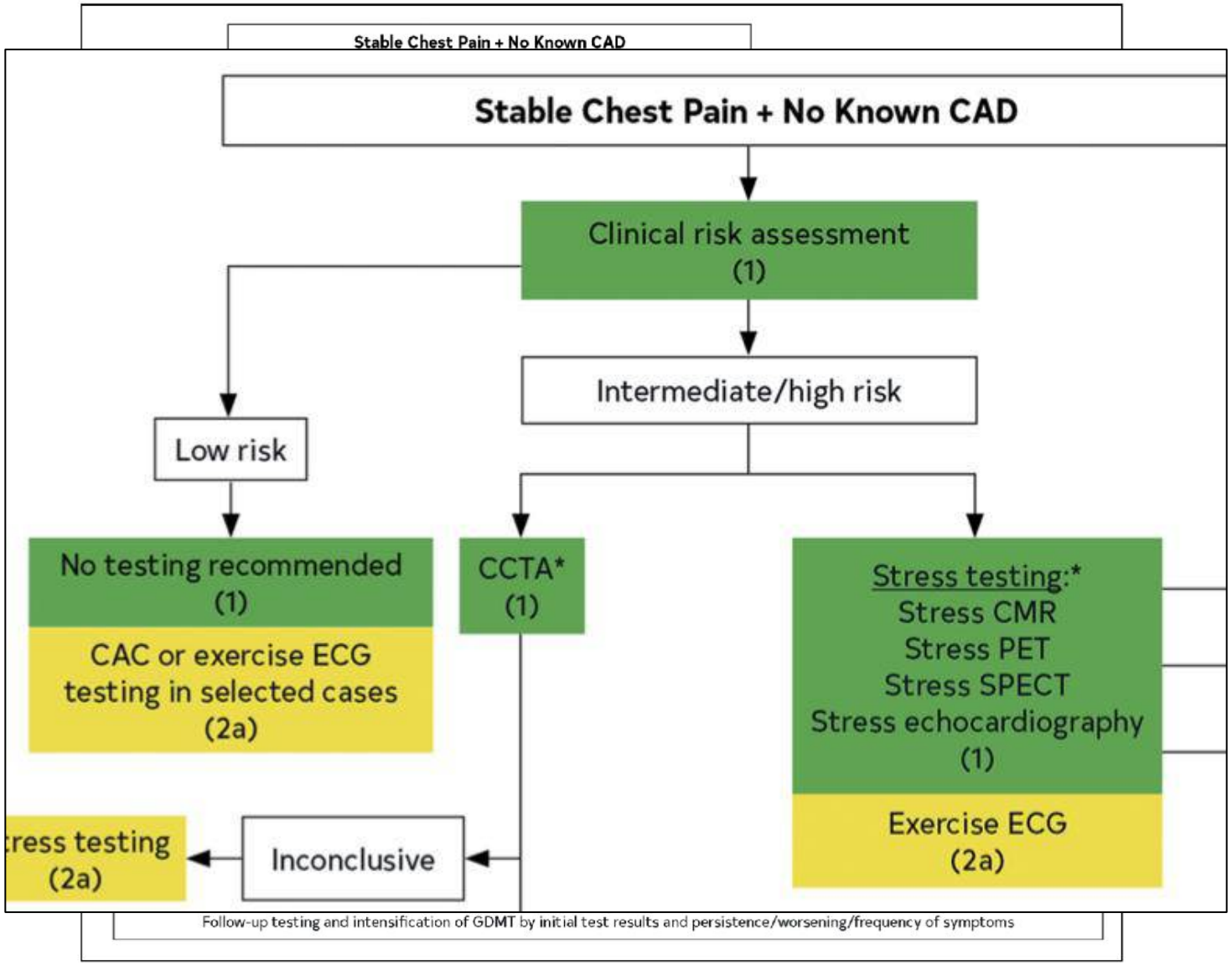
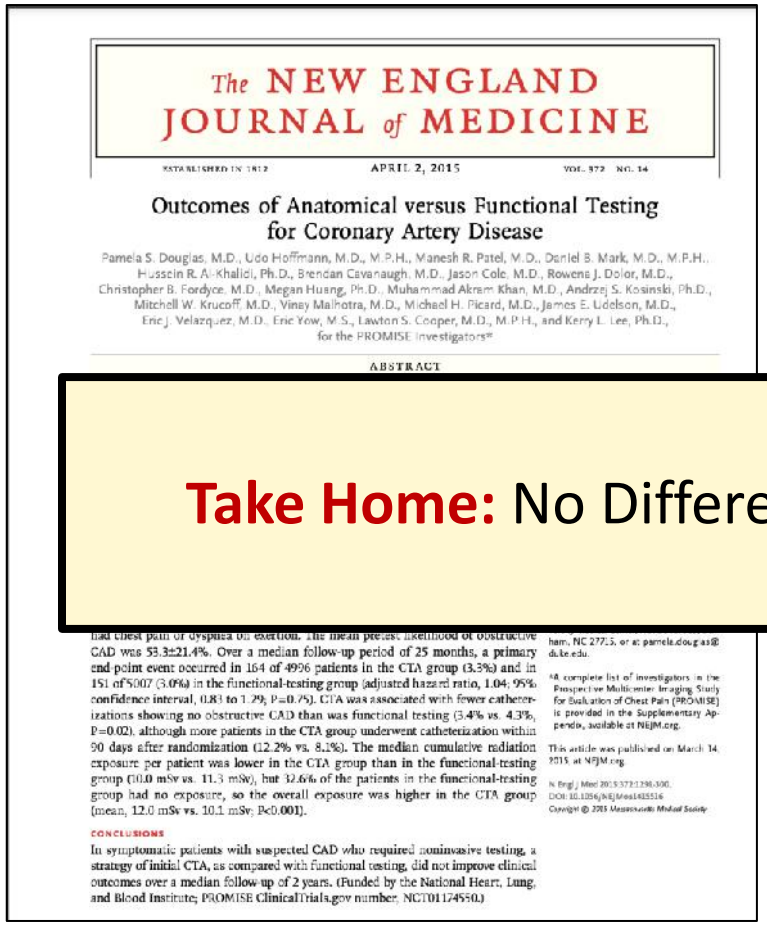
Your patient does not have known CAD


Stable Chest Pain + No Known CAD
Clinical risk assessment
(1)
Intermediate/high risk
Low risk
No testing recommended
(1)
CAC or exercise ECG
testing in selected cases
(2a)
CCTA*
(1)
Stress testing:*
Stress CMR
Stress PET
Stress SPECT
Stress echocardiography
(1)
Exercise ECG
(2a)
Inconclusive
ress testing
(2a)
Follow-up testing and intensification of GDMT by initial test results and persistence/worsening/frequency of symptoms

Why many are choosing a CTA first approach …

Anatomical Non-invasive



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 2, 2015 VOL. 372 NO. 14

Outcomes of Anatomical versus Functional Testing for Coronary Artery Disease

Pamela S. Douglas, M.D., Udo Hoffmann, M.D., M.P.H., Manesh R. Patel, M.D., Daniel B. Mark, M.D., M.P.H., Hussein R. Al-Khalidi, Ph.D., Brendan Cavanaugh, M.D., Jason Cole, M.D., Rowena J. Dolor, M.D., Christopher B. Fordyce, M.D., Megan Huang, Ph.D., Muhammad Akram Khan, M.D., Andrzej S. Kosinski, Ph.D., Mitchell W. Krucoff, M.D., Vinay Malhotra, M.D., Michael H. Picard, M.D., James E. Udelson, M.D., Eric J. Velazquez, M.D., Eric Yow, M.S., Lawton S. Cooper, M.D., M.P.H., and Kerry L. Lee, Ph.D., for the PROMISE Investigators*

ABSTRACT

had chest pain or dyspnea on exertion. The mean pretest likelihood of obstructive CAD was 53.3±21.4%. Over a median follow-up period of 25 months, a primary end-point event occurred in 164 of 4996 patients in the CTA group (3.3%) and in 151 of 5007 (3.0%) in the functional-testing group (adjusted hazard ratio, 1.04; 95% confidence interval, 0.83 to 1.29; P=0.75). CTA was associated with fewer catheterizations showing no obstructive CAD than was functional testing (3.4% vs. 4.3%, P=0.02), although more patients in the CTA group underwent catheterization within 90 days after randomization (12.2% vs. 8.1%). The median cumulative radiation exposure per patient was lower in the CTA group than in the functional-testing group (10.0 mSv vs. 11.3 mSv), but 32.6% of the patients in the functional-testing group had no exposure, so the overall exposure was higher in the CTA group (mean, 12.0 mSv vs. 10.1 mSv; P<0.001).

CONCLUSIONS

In symptomatic patients with suspected CAD who required noninvasive testing, a strategy of initial CTA, as compared with functional testing, did not improve clinical outcomes over a median follow-up of 2 years. (Funded by the National Heart, Lung, and Blood Institute; PROMISE ClinicalTrials.gov number, NCT01174550.)

ham, NC 27715, or at pamela.douglas@duke.edu.

A complete list of investigators in the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) is provided in the Supplementary Appendix, available at NEJM.org.

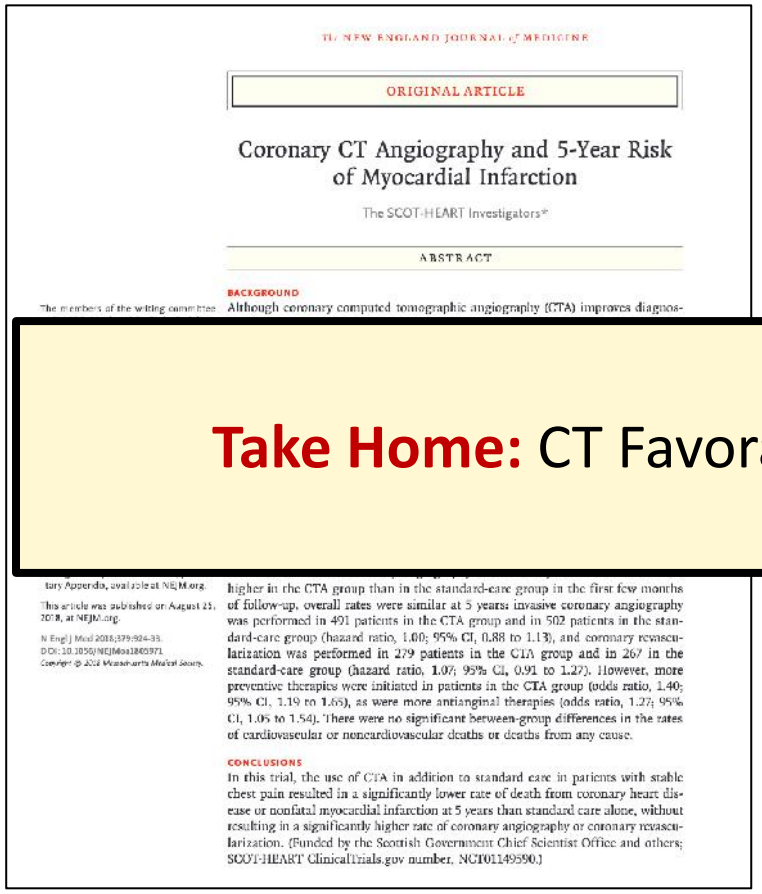
This article was published on March 14, 2015, at NEJM.org.

N Engl J Med 2015;372:1291-300.
DOI: 10.1056/NEJMoa1415516

PROMISE

- N = 10K symptomatic outpatients
- RCT: Cor CT vs Functional Stress
- *functional:
- Outcome: Death, MI, UA, Proc Cx
- CCTA (3.3%), Fxn (3.0%)

Take Home: No Difference between CT and Functional Stress



THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Coronary CT Angiography and 5-Year Risk of Myocardial Infarction

The SCOT-HEART Investigators*

ABSTRACT

BACKGROUND

Although coronary computed tomographic angiography (CTA) improves diagnos-

The members of the writing committee

tory Appendix, available at NEJM.org.

This article was published on August 25, 2018, at NEJM.org.

N Engl J Med 2018;379:924-33.
DOI: 10.1056/NEJMoa1805971
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higher in the CTA group than in the standard-care group in the first few months of follow-up, overall rates were similar at 5 years: invasive coronary angiography was performed in 491 patients in the CTA group and in 502 patients in the standard-care group (hazard ratio, 1.00; 95% CI, 0.88 to 1.13), and coronary revascularization was performed in 279 patients in the CTA group and in 267 in the standard-care group (hazard ratio, 1.07; 95% CI, 0.91 to 1.27). However, more preventive therapies were initiated in patients in the CTA group (odds ratio, 1.40; 95% CI, 1.19 to 1.65), as were more antianginal therapies (odds ratio, 1.27; 95% CI, 1.05 to 1.54). There were no significant between-group differences in the rates of cardiovascular or noncardiovascular deaths or deaths from any cause.

CONCLUSIONS

In this trial, the use of CTA in addition to standard care in patients with stable chest pain resulted in a significantly lower rate of death from coronary heart disease or nonfatal myocardial infarction at 5 years than standard care alone, without resulting in a significantly higher rate of coronary angiography or coronary revascularization. (Funded by the Scottish Government Chief Scientist Office and others; SCOT-HEART ClinicalTrials.gov number, NCT01149590.)

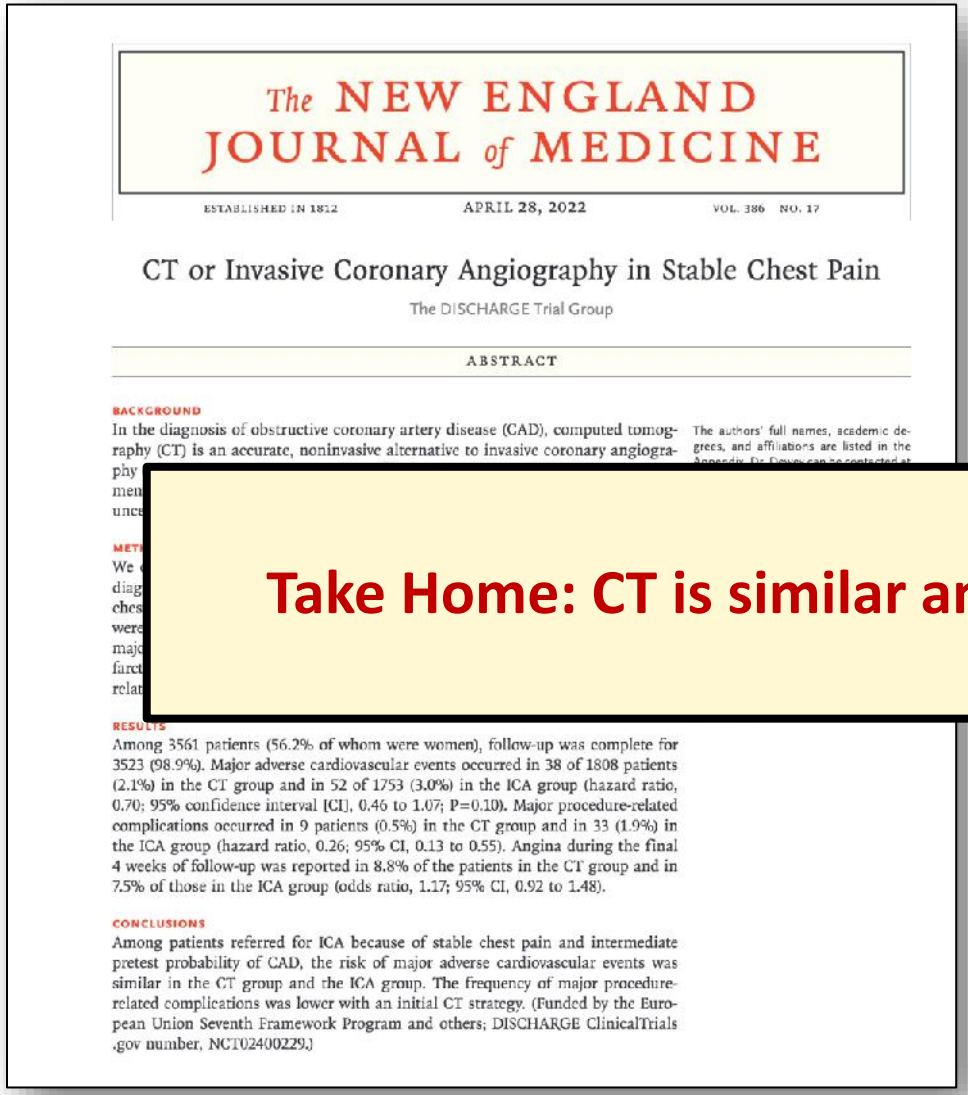
SCOT-HEART

- N = 4.2 K stable angina
- RCT: Cor CT vs Usual Care
- *usual care:

Take Home: CT Favorable to Exercise ECG in Stable CAD

Outcome: Fatal or Nonfatal MI

- 2 Yrs: HR, 0.62 (0.38 – 1.01)^{NS}
- 5 Yrs: HR, 0.59 (0.41 - 0.84)**



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 28, 2022 VOL. 386 NO. 17

CT or Invasive Coronary Angiography in Stable Chest Pain

The DISCHARGE Trial Group

ABSTRACT

BACKGROUND

In the diagnosis of obstructive coronary artery disease (CAD), computed tomography (CT) is an accurate, noninvasive alternative to invasive coronary angiography

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Davies can be contacted at

RESULTS

Among 3561 patients (56.2% of whom were women), follow-up was complete for 3523 (98.9%). Major adverse cardiovascular events occurred in 38 of 1808 patients (2.1%) in the CT group and in 52 of 1753 (3.0%) in the ICA group (hazard ratio, 0.70; 95% confidence interval [CI], 0.46 to 1.07; P=0.10). Major procedure-related complications occurred in 9 patients (0.5%) in the CT group and in 33 (1.9%) in the ICA group (hazard ratio, 0.26; 95% CI, 0.13 to 0.55). Angina during the final 4 weeks of follow-up was reported in 8.8% of the patients in the CT group and in 7.5% of those in the ICA group (odds ratio, 1.17; 95% CI, 0.92 to 1.48).

CONCLUSIONS

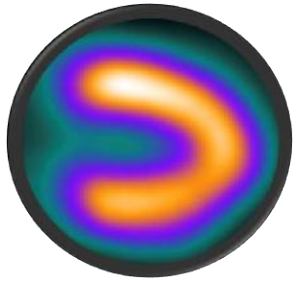
Among patients referred for ICA because of stable chest pain and intermediate pretest probability of CAD, the risk of major adverse cardiovascular events was similar in the CT group and the ICA group. The frequency of major procedure-related complications was lower with an initial CT strategy. (Funded by the European Union Seventh Framework Program and others; DISCHARGE ClinicalTrials.gov number, NCT02400229.)

DISCHARGE

- N = 3.6 K stable angina (56% women)
- RCT: Cor CT vs Invasive Angiography
- HR, 0.70 (0.46 to 1.07; p = 0.10)
- Cx: 0.5% (CT) and 1.9% (ICA)
- HR, 0.26 (0.13 – 0.55)

Take Home: CT is similar and safer compared to invasive ”cath”

Radiation Estimates



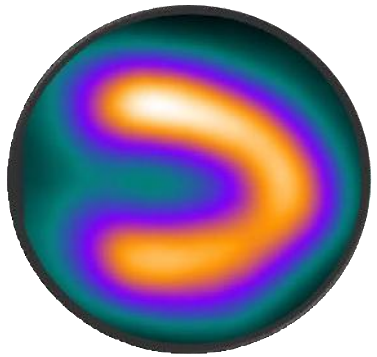
- Measurable Radiation Risk **> 100** mSV (cumulative)
- Nuclear Stress Test (US median) **11.6** mSV
- Annual Radiation (Boston, MA) **3.4** mSv
- Annual Radiation (Denver, CO) **7 - 8** mSv
- Coronary CT Angio **1.5 – 2** mSv

Your Patient has Known CAD

Which Strategy to Choose?

Conservative

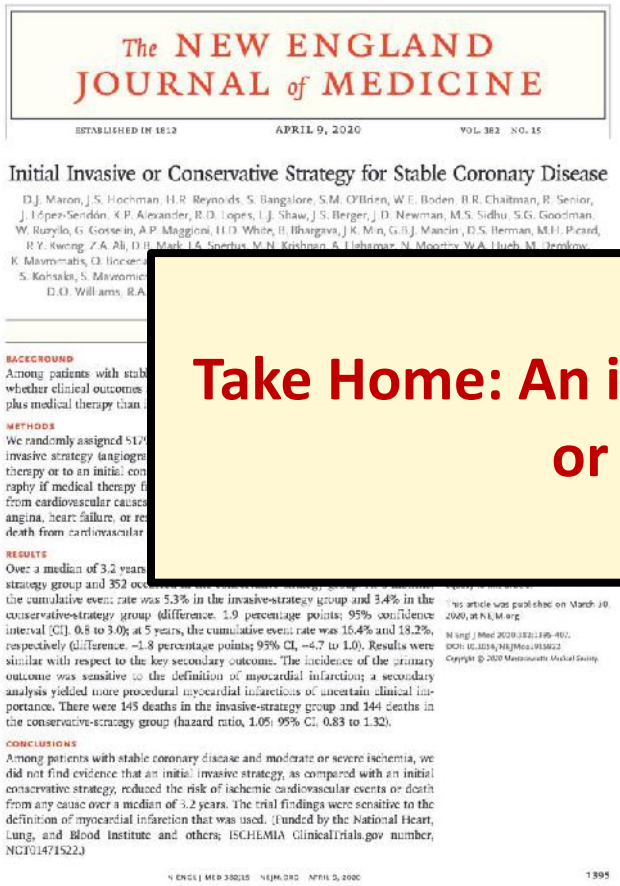
Anatomical Non-invasive



Functional Non-invasive

Invasive

Invasive Angiography



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 9, 2020 VOL. 382 NO. 15

Initial Invasive or Conservative Strategy for Stable Coronary Disease

D.J. Maron, J.S. Hochman, H.R. Reynolds, S. Bangalore, S.M. O'Brien, W.E. Boden, R.R. Chaitman, R. Senior, J. López-Sendón, K.P. Alexander, R.D. Lopes, L.J. Shaw, J.S. Berger, J.D. Newman, M.S. Sidhu, S.G. Goodman, W. Ruzyllo, G. Gosselin, A.P. Maggioni, H.D. White, B. Bhargava, J.K. Min, G.B.J. Mancini, D.S. Berman, M.H. Picard, R.Y. Kwong, Z.A. Ali, D.B. Mark, I.A. Spertus, V.N. Krishnan, A. Ljungman, N. Moorthy, W.A. Lluch, M. Demkow, K. Mavromatis, O. Ilcewicz, S. Kohsaka, S. Mavromichalis, D.O. Williams, R.A.

BACKGROUND

Among patients with stab... whether clinical outcomes ... plus medical therapy than ...

METHODS

We randomly assigned 51... invasive strategy (angiogra... therapy or to an initial con... raphy if medical therapy fi... from cardiovascular causes ... angina, heart failure, or re... death from cardiovascular ...

RESULTS

Over a median of 3.2 years ... strategy group and 352 occ... the cumulative event rate was 5.3% in the invasive-strategy group and 3.4% in the conservative-strategy group (difference, 1.9 percentage points; 95% confidence interval [CI], 0.8 to 3.0); at 5 years, the cumulative event rate was 16.4% and 13.2%, respectively (difference, −1.8 percentage points; 95% CI, −4.7 to 1.0). Results were similar with respect to the key secondary outcome. The incidence of the primary outcome was sensitive to the definition of myocardial infarction; a secondary analysis yielded more procedural myocardial infarctions of uncertain clinical importance. There were 145 deaths in the invasive-strategy group and 144 deaths in the conservative-strategy group (hazard ratio, 1.05; 95% CI, 0.83 to 1.32).

CONCLUSIONS

Among patients with stable coronary disease and moderate or severe ischemia, we did not find evidence that an initial invasive strategy, as compared with an initial conservative strategy, reduced the risk of ischemic cardiovascular events or death from any cause over a median of 3.2 years. The trial findings were sensitive to the definition of myocardial infarction that was used. (Funded by the National Heart, Lung, and Blood Institute and others; ISCHEMIA ClinicalTrials.gov number, NCT01471522.)

This article was published on March 10, 2020, at NEJM.org

N Engl J Med 2020;382:1395-407.

DOI: 10.1056/NEJMoa1915922

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N ENGL J MED 382;15 NEJM.ORG APRIL 9, 2020

1395

ISCHEMIA

N = 5.2K with moderate to severe ischemia

Take Home: An initial invasive strategy does not reduce CV events or mortality over a 3-year time period.

Invasive group: 145 deaths

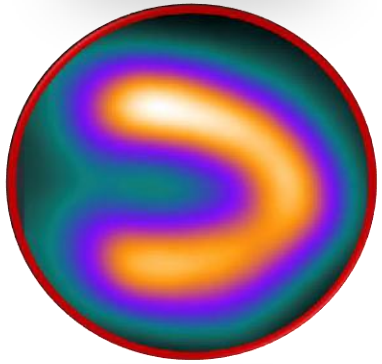
Conservative Group: 144 deaths

Has CAD been previously confirmed?

No? →

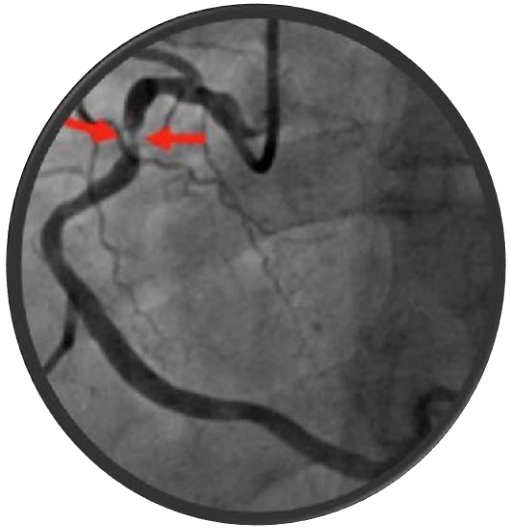
Anatomical study (CTA) because of its low false negative rate. SPECT/Echo may miss disease and patients may then miss beneficial OMT.

Yes? →

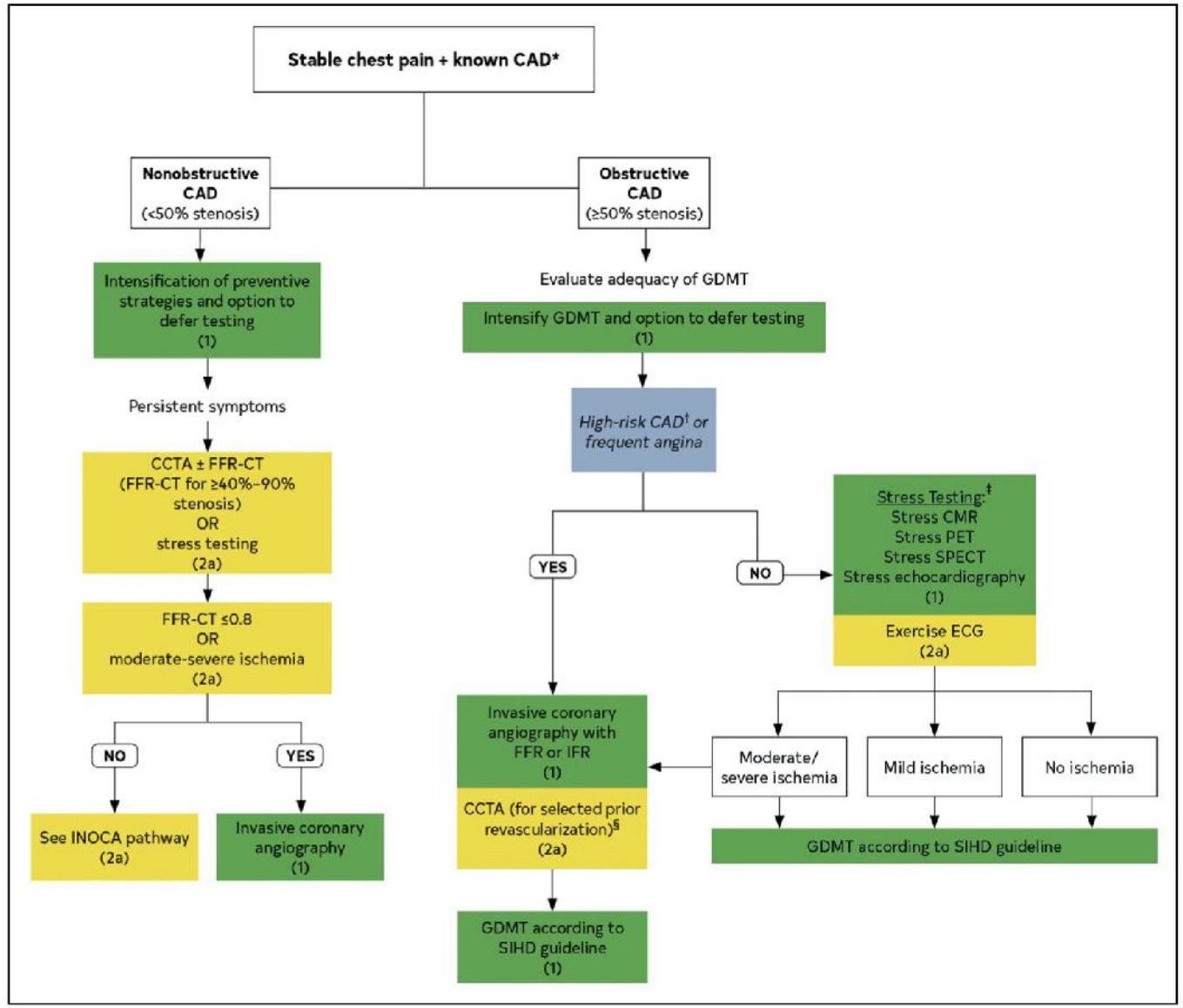


Functional study (SPECT, stress echo) to understand if there's a physiological reason for the syndrome. Is there ischemia to explain the chest discomfort?

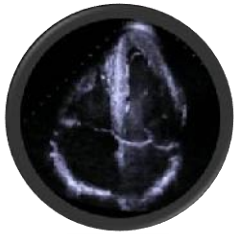
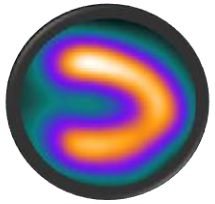
When might you choose an “Invasive First” Strategy?

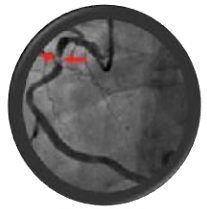


Invasive Angiography


Stable chest pain + known CAD*
Nonobstructive CAD (<50% stenosis)
Obstructive CAD (≥50% stenosis)
Intensification of preventive strategies and option to defer testing (1)
Persistent symptoms
CCTA ± FFR-CT (FFR-CT for ≥40%–90% stenosis) OR stress testing (2a)
FFR-CT ≤0.8 OR moderate-severe ischemia (2a)
NO
YES
See INOCA pathway (2a)
Invasive coronary angiography (1)
Evaluate adequacy of GDMT
Intensify GDMT and option to defer testing (1)
High-risk CAD† or frequent angina
YES
NO
Stress Testing:‡ Stress CMR Stress PET Stress SPECT Stress echocardiography (1)
Exercise ECG (2a)
Invasive coronary angiography with FFR or IFR (1)
CCTA (for selected prior revascularization)§ (2a)
GDMT according to SIHD guideline (1)
Moderate/ severe ischemia
Mild ischemia
No ischemia
GDMT according to SIHD guideline

Who is high risk?

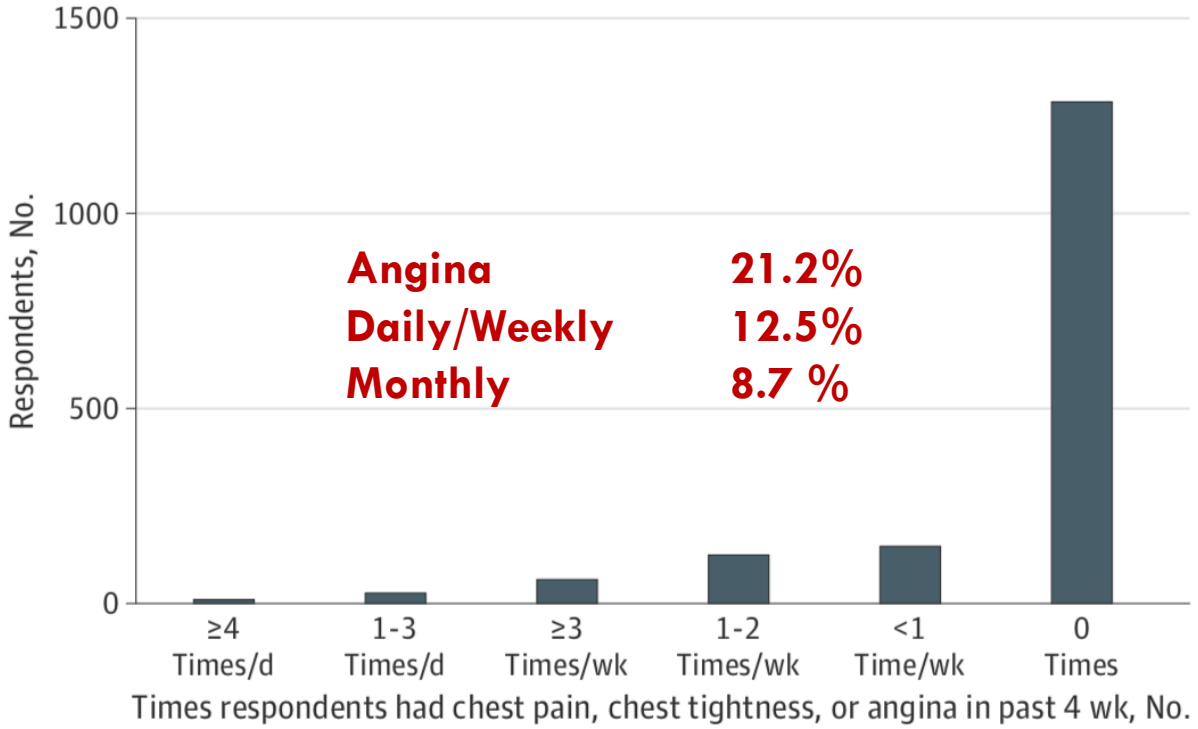


Test	Stress electrocardiography	Stress echocardiography	Stress myocardial perfusion imaging	Coronary computed tomographic angiography	Invasive coronary angiography
Findings indicating high risk	>2-mm ST-segment depressions at low workload ST-segment elevations or ventricular tachycardia or ventricular fibrillation	Decrease in left ventricular ejection fraction (LVEF) >10% or left ventricular (LV) dilation Wall motion abnormalities in multiple coronary territories Baseline LV dysfunction	Decrease in LVEF >10% or LV dilation Perfusion defect in >10% of myocardium Baseline LV dysfunction	Multiple coronary arteries with ≥70% stenosis Left main stenosis ≥50%	Multiple coronary arteries with ≥70% stenosis Left main stenosis ≥50%

Adapted from Joshi and de Lemos. JAMA. 2021.

~1 in 5 patients in primary care offices with a CAD diagnosis experience at least monthly angina

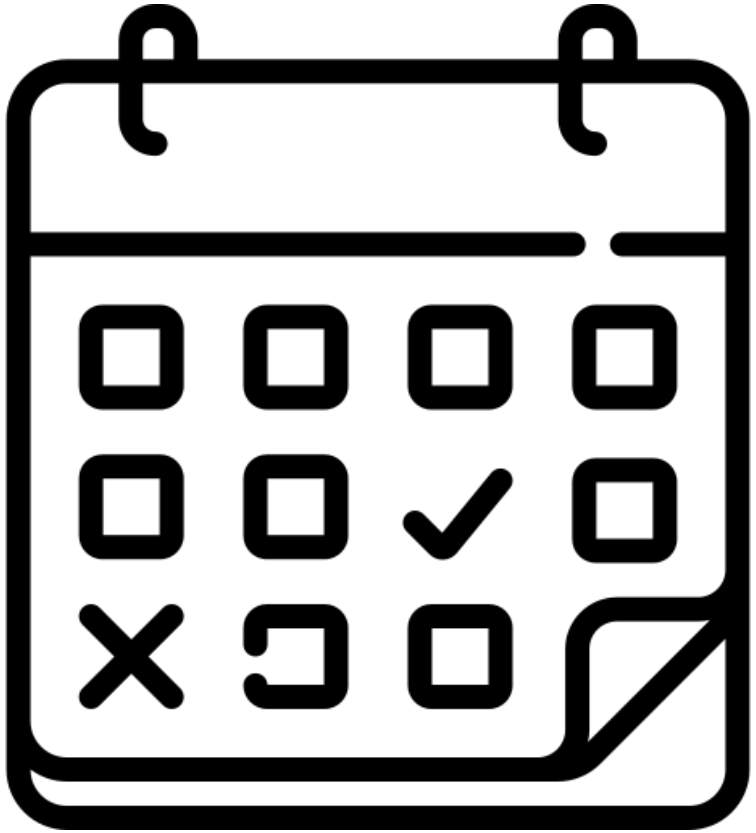
Figure 2. Frequency of Angina Among Seattle Angina Questionnaire–7 Respondents

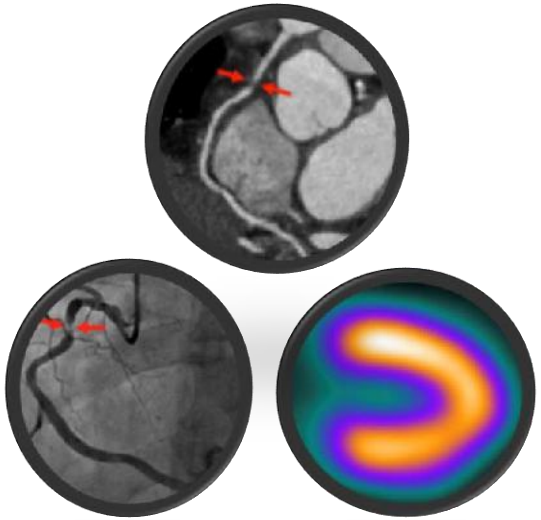


Blumenthal DM and others. **JAMA Network Open.** 2021.

What is the symptom frequency?

- Monthly
- Weekly
- Daily





- ❑If no hx of CAD, consider CTA first strategy.
- ❑ If known CAD and an eye towards revascularization, consider a functional study.
- ❑ Refractory Sx. High Risk Anatomy. ↑ Angina.

Chapter 3: Confirm disease. Estimate risk of death.

Chapter 1:

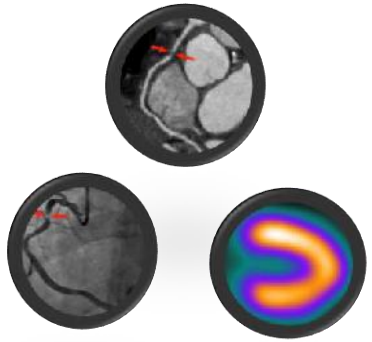
Assess Syndrome Stability

Exclude ACS

Chapter 2:

Estimate CAD probability

(low risk → non-CAD approach)



Chapter 3:

Confirm Disease and Mortality Risk

Select a diagnostic test

Best Approaches in the Evaluation of Patients with Coronary Artery Disease

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