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CLINICAL PRACTICE GUIDELINE: EXECUTIVE SUMMARY

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

Writing Committee Members*

Martha Gulati, MD, MS, FACC, FAHA, *Chair*†
Phillip D. Levy, MD, MPH, FACC, FAHA, *Vice Chair*†
Debabrata Mukherjee, MD, MS, FACC, FAHA, *Vice Chair*†

Ezra Amsterdam, MD, FACC†
Deepak L. Bhatt, MD, MPH, FACC, FAHA†
Kim K. Birtcher, MS, PharmD, AACC‡
Ron Blankstein, MD, FACC, MSCCT§
Jack Boyd, MD†
Renee P. Bullock-Palmer, MD, FACC, FAHA, FASE, FSCCT†
Theresa Conejo, RN, BSN, FAHA‖
Deborah B. Diercks, MD, MSc, FACC¶
Federico Gentile, MD, FACC#
John P. Greenwood, MBChB, PhD, FSCMR, FACC**
Erik P. Hess, MD, MSc†
Steven M. Hollenberg, MD, FACC, FAHA, FCCP††
Wael A. Jaber, MD, FACC, FASE‡‡
Hani Jneid, MD, FACC, FAHA§§
José A. Joglar, MD, FAHA, FACC‡
David A. Morrow, MD, MPH, FACC, FAHA†
Robert E. O'Connor, MD, MPH, FAHA†
Michael A. Ross, MD, FACC†
Leslee J. Shaw, PhD, FACC, FAHA, MSCCT†

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry may apply; see Appendix 1 for detailed information. †ACC/AHA Representative. ‡ACC/AHA Joint Committee on Clinical Practice Guidelines Liaison. §Society of Cardiovascular Computed Tomography Representative. ‖Lay Patient Representative. ¶Society for Academic Emergency Medicine Representative. #Former ACC/AHA Joint Committee member; current member during the writing effort. **Society for Cardiovascular Magnetic Resonance Representative. ††American College of Chest Physicians Representative. ‡‡American Society of Echocardiography Representative. §§Task Force on Performance Measures, Liaison.

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ABSTRACT

AIM This executive summary of the clinical practice guideline for the evaluation and diagnosis of chest pain provides recommendations and algorithms for clinicians to assess and diagnose chest pain in adult patients.

METHODS A comprehensive literature search was conducted from November 11, 2017, to May 1, 2020, encompassing studies, reviews, and other evidence conducted on human subjects that were published in English from PubMed, EMBASE, the Cochrane Collaboration, Agency for Healthcare Research and Quality reports, and other relevant databases. Additional relevant studies, published through April 2021, were also considered.

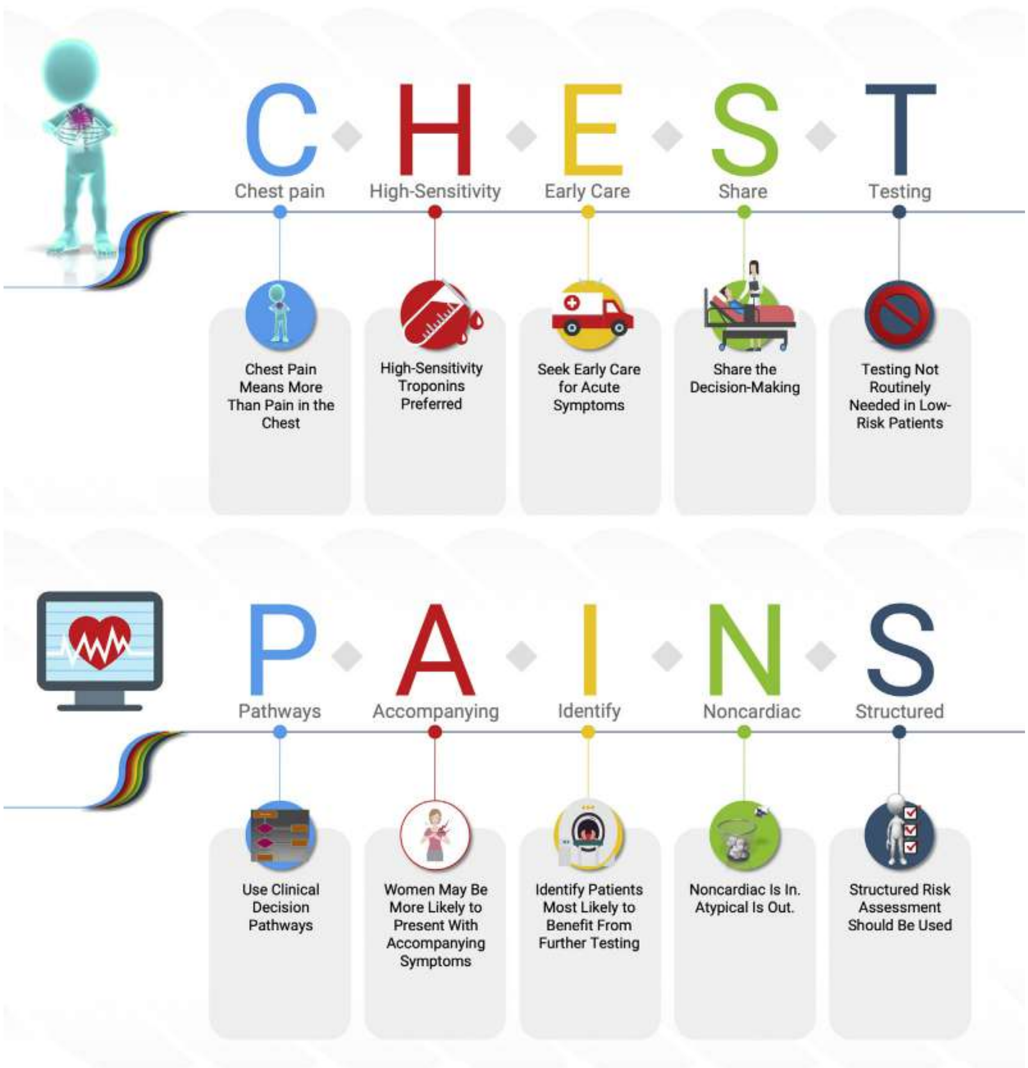
STRUCTURE Chest pain is a frequent cause for emergency department visits in the United States. The "2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain" provides recommendations based on contemporary evidence on the assessment and evaluation of chest pain. These guidelines present an evidence-based approach to risk stratification and the diagnostic workup for the evaluation of chest pain. Cost-value considerations in diagnostic testing have been incorporated and shared decision-making with patients is recommended.

CONTENTS

TOP 10 TAKE-HOME MESSAGES FOR THE EVALUATION AND DIAGNOSIS OF CHEST PAIN

1. **Chest Pain Means More Than Pain in the Chest.** Pain, pressure, tightness, or discomfort in the chest, shoulders, arms, neck, back, upper abdomen, or jaw, as well as shortness of breath and fatigue should all be considered anginal equivalents.
2. **High-Sensitivity Troponins Preferred.** High-sensitivity cardiac troponins are the preferred standard for establishing a biomarker diagnosis of acute myocardial infarction, allowing for more accurate detection and exclusion of myocardial injury.
3. **Early Care for Acute Symptoms.** Patients with acute chest pain or chest pain equivalent symptoms should seek medical care immediately by calling 9-1-1. Although most patients will not have a cardiac cause, the evaluation of all patients should focus on the early identification or exclusion of life-threatening causes.
4. **Share the Decision-Making.** Clinically stable patients presenting with chest pain should be included in decision-making; information about risk of adverse events, radiation exposure, costs, and alternative options should be provided to facilitate the discussion.
5. **Testing Not Needed Routinely for Low-Risk Patients.** For patients with acute or stable chest pain determined to be low risk, urgent diagnostic testing for suspected coronary artery disease is not needed.
6. **Pathways.** Clinical decision pathways for chest pain in the emergency department and outpatient settings should be used routinely.
7. **Accompanying Symptoms.** Chest pain is the dominant and most frequent symptom for both men and women ultimately diagnosed with acute coronary syndrome. Women may be more likely to present with accompanying symptoms such as nausea and shortness of breath.
8. **Identify Patients Most Likely to Benefit From Further Testing.** Patients with acute or stable chest pain who are at intermediate risk or intermediate to high pretest risk of obstructive coronary artery disease, respectively, will benefit the most from cardiac imaging and testing.
9. **Noncardiac Is In. Atypical Is Out.** "Noncardiac" should be used if heart disease is not suspected.

FIGURE 1 Take-Home Messages for the Evaluation and Diagnosis of Chest Pain



"Atypical" is a misleading descriptor of chest pain, and its use is discouraged.

10. **Structured Risk Assessment Should Be Used.** For patients presenting with acute or stable chest pain, risk for coronary artery disease and adverse events should be estimated using evidence-based diagnostic protocols.

Figure 1 illustrates the take-home messages.

1. PURPOSE OF THE EXECUTIVE SUMMARY

The charge of the writing committee was to develop a guideline for the evaluation of acute or stable chest pain or other anginal equivalents, in a variety of clinical settings, with an emphasis on the diagnosis on ischemic causes (1). The guideline will not provide recommendations on whether revascularization is appropriate, or what modality is indicated (1). Such recommendations can be found in the forthcoming American Heart Association (AHA)/American College of Cardiology (ACC) coronary artery revascularization guideline (1a).

After injuries, chest pain is the second most common reason for adults to present to the emergency department (ED) in the United States and accounts for >6.5 million visits, which is 4.7% of all ED visits (2). Chest pain also leads to nearly 4 million outpatient visits annually in the United States (3). Chest pain remains a diagnostic challenge in the ED and outpatient setting and requires thorough clinical evaluation. Although the cause of chest pain is often noncardiac, coronary artery disease (CAD) affects >18.2 million adults in the United States and remains the leading cause of death for men and women,

TABLE 1 Applying ACC/AHA Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

CLASS (STRENGTH) OF RECOMMENDATION	
CLASS 1 (STRONG)	**Benefit >>> Risk**
Suggested phrases for writing recommendations: • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	
CLASS 2a (MODERATE)	**Benefit >> Risk**
Suggested phrases for writing recommendations: • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	
CLASS 2b (WEAK)	**Benefit ≥ Risk**
Suggested phrases for writing recommendations: • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	
CLASS 3: No Benefit (MODERATE) **(Generally, LOE A or B use only)**	**Benefit = Risk**
Suggested phrases for writing recommendations: • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	
Class 3: Harm (STRONG)	**Risk > Benefit**
Suggested phrases for writing recommendations: • Potentially harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	

LEVEL (QUALITY) OF EVIDENCE‡	
LEVEL A	
• High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies	
LEVEL B-R	**(Randomized)**
• Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs	
LEVEL B-NR	**(Nonrandomized)**
• Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies	
LEVEL C-LD	**(Limited Data)**
• Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects	
LEVEL C-EO	**(Expert Opinion)**
• Consensus of expert opinion based on clinical experience	

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

accounting for >365,000 deaths annually (4). Distinguishing between serious and benign causes of chest pain is imperative. The lifetime prevalence of chest pain in the United States is 20% to 40% (5), and women experience this symptom more often than men (6). Of all ED patients with chest pain, only 5.1% will have an acute coronary syndrome (ACS) and more than half will ultimately be found to have a noncardiac cause (7). Nonetheless, chest pain is the most common symptom of CAD in both men and women.

1.1. Document Review and Approval

This document was reviewed by 16 official reviewers nominated by the ACC, AHA, the American College of Emergency Physicians, American Society of Echocardiography (ASE), American Society of Nuclear Cardiology (ASNC), American College of Chest Physicians (CHEST), Society for Academic Emergency Medicine (SAEM), Society of Cardiovascular Computed Tomography (SCCT), and Society for Cardiovascular Magnetic Resonance (SCMR), and 39 individual content reviewers. Authors' relationships with industry and other entities information is published in Appendix 1 of the full guideline (1). Reviewers' relationships with industry and other entities information is published in Appendix 2 of the full guideline (1).

1.2. Class of Recommendations and Level of Evidence

The Class of Recommendation (COR) indicates the strength of recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk. The Level of Evidence (LOE) rates the quality of scientific evidence supporting the intervention on the basis of the type, quantity, and consistency of data from clinical trials and other sources (Table 1) (8).

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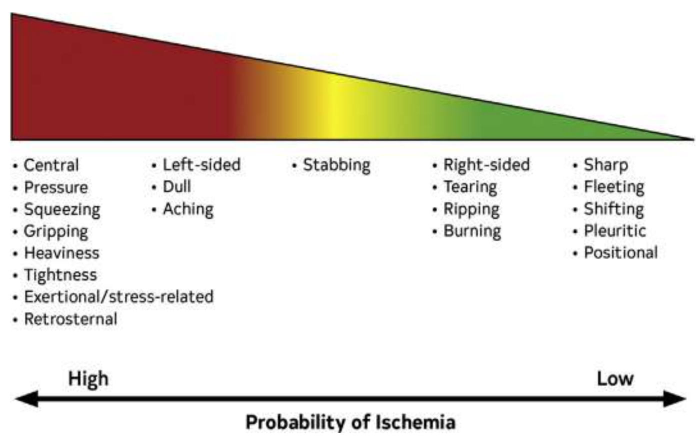
1.3. Defining Chest Pain

Figure 2 presents an index of suspicion that chest "pain" is ischemic in origin based on commonly used descriptors.

Recommendations for Defining Chest Pain
Referenced studies that support the recommendations are summarized in Online Data Supplements 1 and 2.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. An initial assessment of chest pain is recommended to triage patients effectively on the basis of the likelihood that symptoms may be attributable to myocardial ischemia (9-15).
1	C-LD	2. Chest pain should not be described as atypical, because it is not helpful in determining the cause and can be misinterpreted as benign in nature. Instead, chest pain should be described as cardiac, possibly cardiac, or noncardiac because these terms are more specific to the potential underlying diagnosis.

FIGURE 2 Index of Suspicion That Chest "Pain" Is Ischemic in Origin on the Basis of Commonly Used Descriptors



2. INITIAL EVALUATION

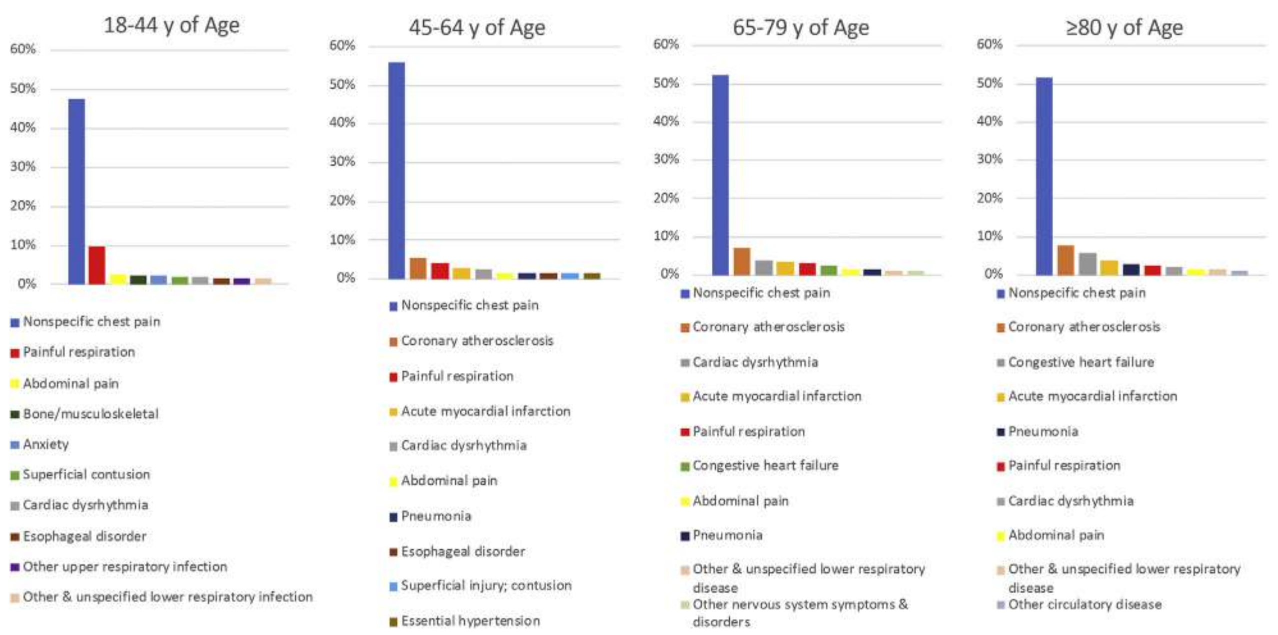
2.1. History

Figure 3 presents the top 10 causes of chest pain in ED based on age. Table 2 presents chest pain characteristics and corresponding causes.

Recommendation for History

COR	LOE	RECOMMENDATION
1	C-LD	1. In patients with chest pain, a focused history that includes characteristics and duration of symptoms relative to presentation as well as associated features, and cardiovascular risk factor assessment should be obtained.

FIGURE 3 Top 10 Causes of Chest Pain in the ED Based on Age (Weighted Percentage)



Created using data from Hsia, RY, et al. (7). ED indicates emergency department.

TABLE 2 Chest Pain Characteristics and Corresponding Causes

Nature	
	Anginal symptoms are perceived as retrosternal chest discomfort (e.g., pain, discomfort, heaviness, tightness, pressure, constriction, squeezing) (See Section 1.4.2, Defining Chest Pain, in the full guideline (1)).
	Sharp chest pain that increases with inspiration and lying supine is unlikely related to ischemic heart disease (e.g., these symptoms usually occur with acute pericarditis).
Onset and duration	
	Anginal symptoms gradually build in intensity over a few minutes.
	Sudden onset of ripping chest pain (with radiation to the upper or lower back) is unlikely to be anginal and is suspicious of an acute aortic syndrome.
	Fleeting chest pain—of few seconds' duration—is unlikely to be related to ischemic heart disease.
Location and radiation	
	Pain that can be localized to a very limited area and pain radiating to below the umbilicus or hip are unlikely related to myocardial ischemia.
Severity	
	Ripping chest pain ("worse chest pain of my life"), especially when sudden in onset and occurring in a hypertensive patient, or with a known bicuspid aortic valve or aortic dilation, is suspicious of an acute aortic syndrome (e.g., aortic dissection).
Precipitating factors	
	Physical exercise or emotional stress are common triggers of anginal symptoms.
	Occurrence at rest or with minimal exertion associated with anginal symptoms usually indicates ACS.
	Positional chest pain is usually nonischemic (e.g., musculoskeletal).
Relieving factors	
	Relief with nitroglycerin is not necessarily diagnostic of myocardial ischemia and should not be used as a diagnostic criterion.
Associated symptoms	
	Common symptoms associated with myocardial ischemia include, but are not limited to, dyspnea, palpitations, diaphoresis, lightheadedness, presyncope or syncope, upper abdominal pain, or heartburn unrelated to meals and nausea or vomiting.
	Symptoms on the left or right side of the chest, stabbing, sharp pain, or discomfort in the throat or abdomen may occur in patients with diabetes, women, and elderly patients.

ACS indicates acute coronary syndrome.

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2.1.1. A Focus on the Uniqueness of Chest Pain in Women

Recommendations for a Focus on the Uniqueness of Chest Pain in Women
Referenced studies that support the recommendations are summarized in Online Data Supplements 3 and 4.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. Women who present with chest pain are at risk for underdiagnosis, and potential cardiac causes should always be considered (11,12,14,16-19).
1	B-NR	2. In women presenting with chest pain, it is recommended to obtain a history that emphasizes accompanying symptoms that are more common in women with ACS (11,12,14,16-19).

2.1.2. Considerations for Older Patients With Chest Pain

Recommendation for Considerations for Older Patients With Chest Pain

COR	LOE	RECOMMENDATION
1	C-LD	1. In patients with chest pain who are >75 years of age, ACS should be considered when accompanying symptoms such as shortness of breath, syncope, or acute delirium are present, or when an unexplained fall has occurred (20).

2.1.3. Considerations for Diverse Patient Populations With Chest Pain

Recommendations for Considerations for Diverse Patient Populations With Chest Pain

COR	LOE	RECOMMENDATIONS
1	C-LD	1. Cultural competency training is recommended to help achieve the best outcomes in patients of diverse racial and ethnic backgrounds who present with chest pain.
1	C-LD	2. Among patients of diverse race and ethnicity presenting with chest pain in whom English may not be their primary language, addressing language barriers with the use of formal translation services is recommended.

2.1.4. Patient-Centric Considerations

Recommendation for Patient-Centric Considerations

COR	LOE	RECOMMENDATION
1	C-LD	1. In patients with acute chest pain, it is recommended that 9-1-1 be activated by patients or bystanders to initiate transport to the closest ED by emergency medical services (EMS) (21).

2.2. Physical Examination

Table 3 presents physical examination in patients with chest pain.

Recommendation for Physical Examination

COR	LOE	RECOMMENDATION
1	C-EO	1. In patients presenting with chest pain, a focused cardiovascular examination should be performed initially to aid in the diagnosis of ACS or other potentially serious causes of chest pain (e.g., aortic dissection, pulmonary embolism (PE), or esophageal rupture) and to identify complications.

TABLE 3 Physical Examination in Patients With Chest Pain

Clinical Syndrome	Findings
Emergency	
ACS	Diaphoresis, tachypnea, tachycardia, hypotension, crackles, S3, MR murmur (22); examination may be normal in uncomplicated cases
PE	Tachycardia + dyspnea—>90% of patients; pain with inspiration (23)
Aortic dissection	Connective tissue disorders (e.g., Marfan syndrome), extremity pulse differential (30% of patients, type A>B) (24) Severe pain, abrupt onset + pulse differential + widened mediastinum on CXR >80% probability of dissection (25) Frequency of syncope >10% (24), AR 40%-75% (type A) (26)
Esophageal rupture	Emesis, subcutaneous emphysema, pneumothorax (20% patients), unilateral decreased or absent breath sounds
Other	
Noncoronary cardiac: AS, AR, HCM	AS: Characteristic systolic murmur, tardus or parvus carotid pulse AR: Diastolic murmur at right of sternum, rapid carotid upstroke HCM: Increased or displaced left ventricular impulse, prominent *a* wave in jugular venous pressure, systolic murmur
Pericarditis	Fever, pleuritic chest pain, increased in supine position, friction rub
Myocarditis	Fever, chest pain, heart failure, S3
Esophagitis, peptic ulcer disease, gall bladder disease	Epigastric tenderness Right upper quadrant tenderness, Murphy sign
Pneumonia	Fever, localized chest pain, may be pleuritic, friction rub may be present, regional dullness to percussion, egophony
Pneumothorax	Dyspnea and pain on inspiration, unilateral absence of breath sounds
Costochondritis, Tietze syndrome	Tenderness of costochondral joints
Herpes zoster	Pain in dermatomal distribution, triggered by touch; characteristic rash (unilateral and dermatomal distribution)

ACS indicates acute coronary syndrome; AR, aortic regurgitation; AS, aortic stenosis; CXR, chest x-ray; LR, likelihood ratio; HCM, hypertrophic cardiomyopathy; MR, mitral regurgitation; PE, pulmonary embolism; and PUD, peptic ulcer disease.

2.3. Diagnostic Testing

2.3.1. Setting Considerations

Recommendations for Setting Considerations
Referenced studies that support the recommendations are summarized in Online Data Supplement 5.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. Unless a noncardiac cause is evident, an ECG should be performed for patients seen in the office setting with stable chest pain; if an ECG is unavailable the patient should be referred to the ED so one can be obtained (27-31).

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(continued)

COR	LOE	RECOMMENDATIONS
1	C-LD	2. Patients with clinical evidence of ACS or other life-threatening causes of acute chest pain seen in the office setting should be transported urgently to the ED, ideally by EMS (27-35).
1	C-LD	3. In all patients who present with acute chest pain regardless of the setting, an ECG should be acquired and reviewed for ST-segment-elevation myocardial infarction (STEMI) within 10 minutes of arrival (27-29,32,33,36).
1	C-LD	4. In all patients presenting to the ED with acute chest pain and suspected ACS, cTn should be measured as soon as possible after presentation (34,35).
3: Harm	C-LD	5. For patients with acute chest pain and suspected ACS initially evaluated in the office setting, delayed transfer to the ED for cTn or other diagnostic testing should be avoided.

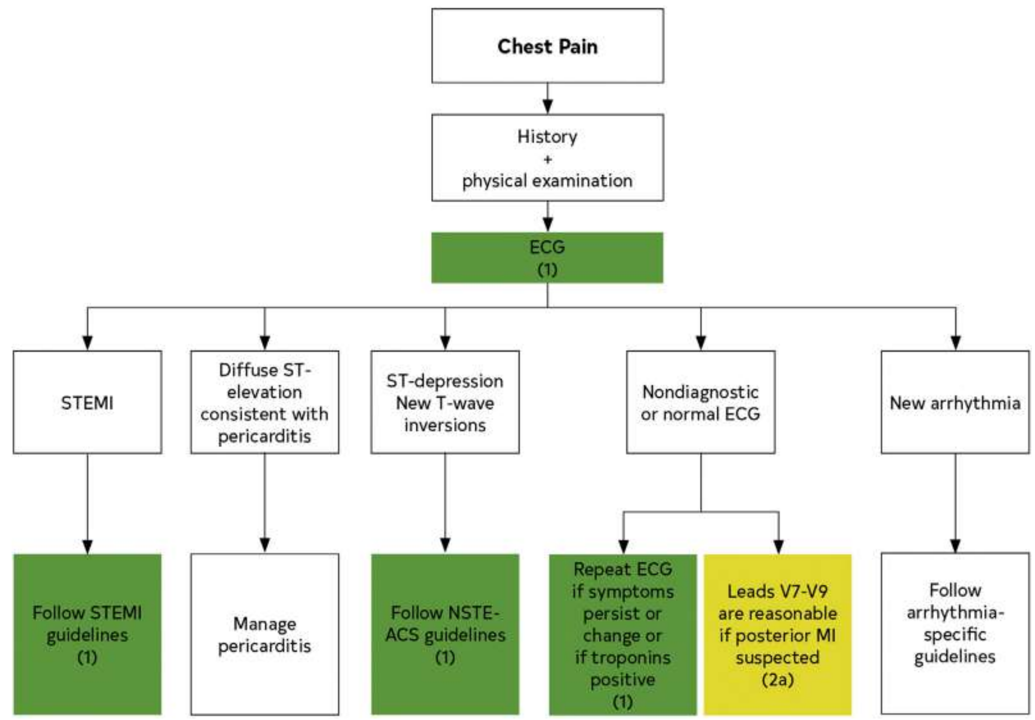
2.3.2. Electrocardiogram

Figure 4 presents electrocardiographic-directed management of chest pain.

Recommendations for Electrocardiogram (ECG)
Referenced studies that support the recommendations are summarized in Online Data Supplement 6.

COR	LOE	RECOMMENDATIONS
1	C-EO	1. In patients with chest pain in which an initial ECG is nondiagnostic, serial ECGs to detect potential ischemic changes should be performed, especially when clinical suspicion of ACS is high, symptoms are persistent, or the clinical condition deteriorates (33).
1	C-EO	2. Patients with chest pain in whom the initial ECG is consistent with an ACS should be treated according to STEMI and non-ST-segment-elevation ACS guidelines (32,33).
2a	B-NR	3. In patients with chest pain and intermediate-to-high clinical suspicion for ACS in whom the initial ECG is nondiagnostic, supplemental electrocardiographic leads V_7 to V_9 are reasonable to rule out posterior myocardial infarction (MI) (37-39).

FIGURE 4 Electrocardiographic-Directed Management of Chest Pain



ECG indicates electrocardiogram; NSTE-ACS, non-ST-segment-elevation acute coronary syndrome; MI, myocardial infarction; and STEMI, ST-segment-elevation myocardial infarction.

2.3.3. Chest Radiography

Recommendation for Chest Radiography

COR	LOE	RECOMMENDATION
1	C-EO	1. In patients presenting with acute chest pain, a chest radiograph is useful to evaluate for other potential cardiac, pulmonary, and thoracic causes of symptoms.

2.3.4. Biomarkers

Recommendations for Biomarkers
Referenced studies that support the recommendations are summarized in Online Data Supplement 7.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In patients presenting with acute chest pain, serial cTn I or T levels are useful to identify abnormal values and a rising or falling pattern indicative of acute myocardial injury (35,40-59).
1	B-NR	2. In patients presenting with acute chest pain, high-sensitivity cTn is the preferred biomarker because it enables more rapid detection or exclusion of myocardial injury and increases diagnostic accuracy (35,56,60-63).

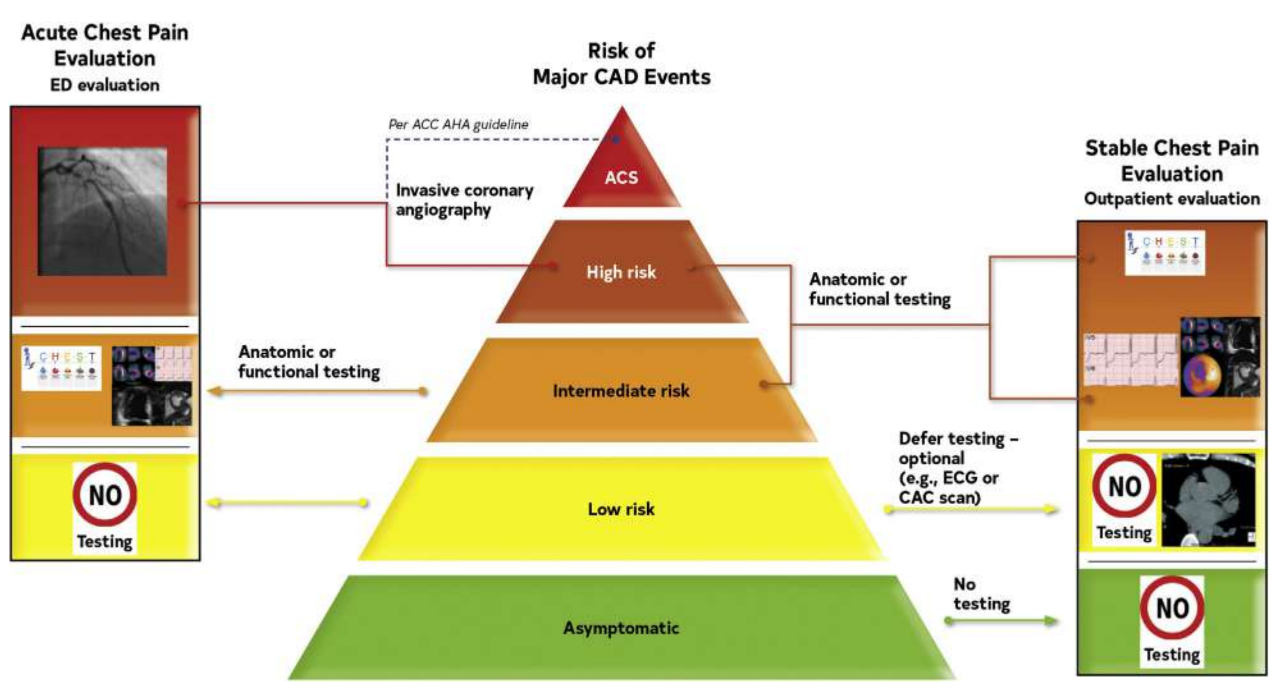
(continued)

1	C-EO	3. Clinicians should be familiar with the analytical performance and the 99th percentile upper reference limit that defines myocardial injury for the cTn assay used at their institution (34,61).
3: No benefit	B-NR	4. With availability of cTn, creatine kinase myocardial (CK-MB) isoenzyme and myoglobin are not useful for diagnosis of acute myocardial injury (64-69).

3. CARDIAC TESTING GENERAL CONSIDERATIONS

The approach outlined in this guideline focuses on selective use of testing, optimization of lower cost evaluations, reducing layered testing, and deferring or eliminating testing when the diagnostic yield is low (Figure 5). Figure 6 display choosing the right diagnostic test. Table 4 presents contraindication by type of imaging modality.

FIGURE 5 Chest Pain and Cardiac Testing Considerations



The choice of imaging depends on the clinical question of importance, to either a) ascertain the diagnosis of CAD and define coronary anatomy or b) assess ischemia severity among patients with an expected higher likelihood of ischemia with an abnormal resting ECG or those incapable of performing maximal exercise. ACS indicates acute coronary syndrome; CAC, coronary artery calcium; CAD, coronary artery disease; and ECG, electrocardiogram.

FIGURE 6 **Choosing the Right Diagnostic Test**

Pretest likelihood of CAD	Low →	No testing necessary →		Option for CAC for ASCVD risk stratification		
	Intermediate-high →	Younger patient (<65 y of age)	**OR**	Less obstructive CAD suspected	→	CCTA favored
	Intermediate-high →	Older patient (≥65 y of age)	**OR**	More obstructive CAD suspected	→	Stress testing favored

	Favors use of CCTA	Favors use of stress imaging
Goal	• Rule out obstructive CAD • Detect nonobstructive CAD	• Ischemia-guided management
Availability and expertise	• High-quality imaging and expert interpretation routinely available	• High-quality imaging and expert interpretation routinely available
Likelihood of obstructive CAD	• Age <65 y	• Age ≥65 y
Prior test results	• Prior functional study inconclusive	• Prior CCTA inconclusive
Other compelling indications	• Anomalous coronary arteries • Require evaluation of aorta or pulmonary arteries	• Suspect scar (especially if PET or stress CMR available) • Suspect coronary microvascular dysfunction (when PET or CMR available)

Stress testing information

	ETT	Stress echocardiography	SPECT MPI	PET MPI	Stress CMR MPI
Patient capable of exercise	✓	✓	✓		
Pharmacologic stress indicated		✓	✓	✓	✓
Quantitative flow				✓	✓
LV dysfunction/scar		✓	✓	✓	✓

ASCVD indicates atherosclerotic cardiovascular disease; CAD, coronary artery disease; CAC, coronary artery calcium; CCTA, coronary computed tomography angiography; CMR, cardiovascular magnetic resonance; ETT, exercise tolerance test; LV, left ventricular; MPI, myocardial perfusion imaging; PET, positron emission tomography; and SPECT, single-photon emission computed tomography.

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TABLE 4 Contraindication by Type of Imaging Modality and Stress Protocol

Exercise ECG	Stress Nuclear (70)*	Stress Echocardiography (71-73a)	Stress CMR (74)	CCTA (75)*

■ Abnormal ST changes on resting ECG, digoxin, left bundle branch block, Wolff-Parkinson-White pattern, ventricular paced rhythm (unless test is performed to establish exercise capacity and not for diagnosis of ischemia)
■ Unable to achieve ≥5 METs or unsafe to exercise
■ High-risk unstable angina or AMI (<2 d) i.e., active ACS
■ Uncontrolled heart failure
■ Significant cardiac arrhythmias (e.g., VT, complete atrioventricular block) or high risk for arrhythmias caused by QT prolongation
■ Severe symptomatic aortic stenosis
■ Severe systemic arterial hypertension (e.g., ≥200/110 mm Hg)
■ Acute illness (e.g., acute PE, acute myocarditis/pericarditis, acute aortic dissection)
	■ High-risk unstable angina, complicated ACS or AMI (<2 d)
	■ Contraindications to vasodilator administration
	  ▪ Significant arrhythmias (e.g., VT, second- or third-degree atrioventricular block) or sinus bradycardia <45 bpm
	  ▪ Significant hypotension (SBP <90 mm Hg)
	  ▪ Known or suspected bronchoconstrictive or bronchospastic disease
	  ▪ Recent use of dipyridamole or dipyridamole-containing medications
	  ▪ Use of methylxanthines (e.g., aminophylline, caffeine) within 12 h
	  ▪ Known hypersensitivity to adenosine, regadenoson
	■ Severe systemic arterial hypertension (e.g., ≥200/110 mm Hg)
		■ Limited acoustic windows (e.g., in COPD patients)
		■ Inability to reach target heart rate
		■ Uncontrolled heart failure
		■ High-risk unstable angina, active ACS or AMI (<2 d)
		■ Serious ventricular arrhythmia or high risk for arrhythmias attributable to QT prolongation
		■ Respiratory failure
		■ Severe COPD, acute pulmonary emboli, severe pulmonary hypertension
		■ Contraindications to dobutamine (if pharmacologic stress test needed)
		  ▪ Atrioventricular block, uncontrolled atrial fibrillation
		  ▪ Critical aortic stenosis†
		  ▪ Acute illness (e.g., acute PE, acute myocarditis/pericarditis, acute aortic dissection)
		  ▪ Hemodynamically significant LV outflow tract obstruction
		  ▪ Contraindications to atropine use:
		    ▪ Narrow-angle glaucoma
		    ▪ Myasthenia gravis
		    ▪ Obstructive uropathy
		    ▪ Obstructive gastrointestinal disorders
		■ Severe systemic arterial hypertension (e.g., ≥200/110 mm Hg)
		Use of Contrast Contraindicated in:
		■ Hypersensitivity to perflutren
		■ Hypersensitivity to blood, blood products, or albumin (for Optison only)
			■ Reduced GFR (<30 mL/min/1.73 m^2)
			■ Contraindications to vasodilator administration
			■ Implanted devices not safe for CMR or producing artifact limiting scan quality/interpretation
			■ Significant claustrophobia
			■ Caffeine use within past 12 h
				■ Allergy to iodinated contrast
				■ Inability to cooperate with scan acquisition and/or breath-hold instructions
				■ Clinical instability (e.g., acute myocardial infarction, decompensated heart failure, severe hypotension)
				■ Renal impairment as defined by local protocols
				■ Contraindication to beta blockade in the presence of an elevated heart rate and no alternative medications available for achieving target heart rate
				■ Heart rate variability and arrhythmia
				■ Contraindication to nitroglycerin (if indicated)

For all the imaging modalities, inability to achieve high-quality images should be considered, in particular for obese patients

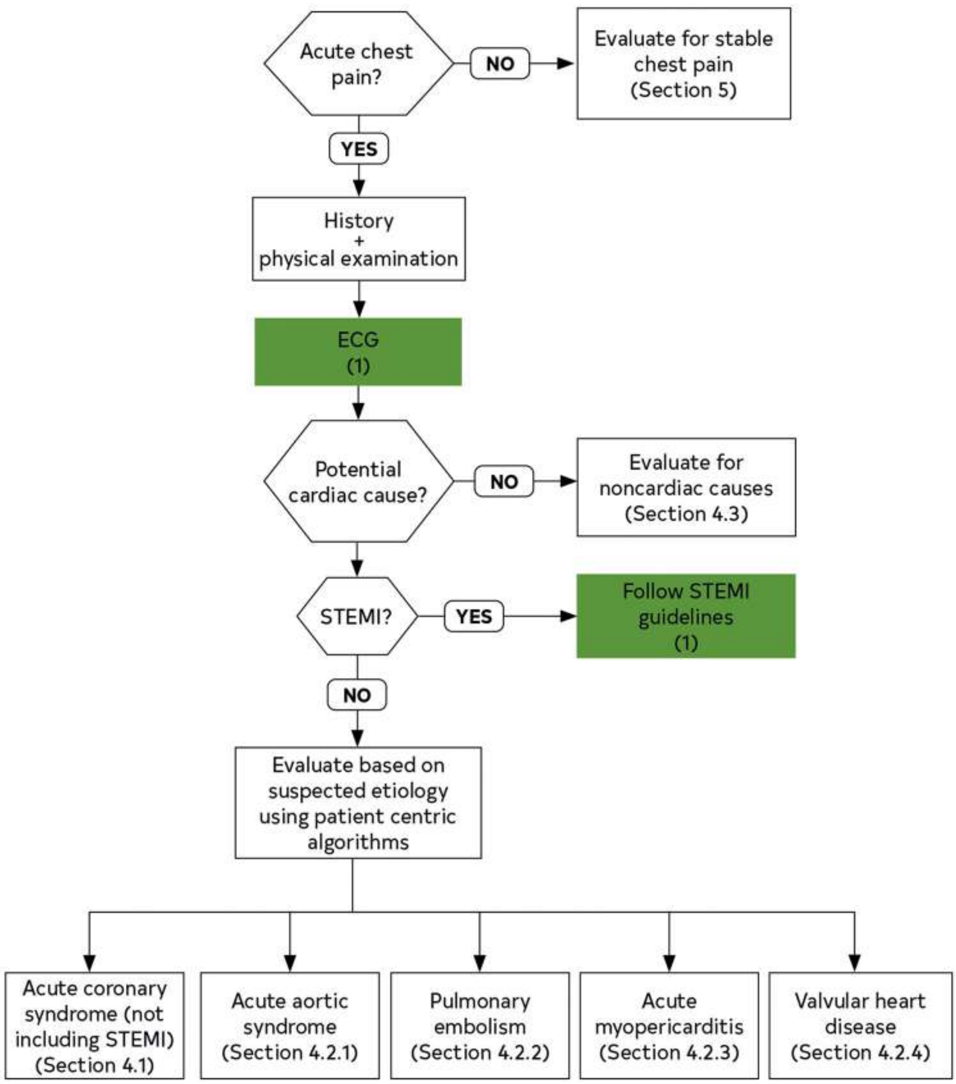
*Screening for potential pregnancy by history and/or pregnancy testing should be performed according to the local imaging facilities policies for undertaking radiological examinations that involve ionizing radiation in women of child-bearing age.
†Low-dose dobutamine may be useful for assessing for low-gradient AS.

ACS indicates acute coronary syndrome; AMI, acute myocardial infarction; AS, aortic stenosis; CCTA, coronary computed tomography angiography; CMR, cardiovascular magnetic resonance imaging; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; LV, left ventricular; MET, metabolic equivalent; MRI, magnetic resonance imaging; PE, pulmonary embolism; SBP, systolic blood pressure; and VT, ventricular tachycardia.

4. CHOOSING THE RIGHT PATHWAY WITH PATIENT-CENTRIC ALGORITHMS FOR ACUTE CHEST PAIN

Figure 7 provides an overview of a patient-centric algorithm for acute chest pain.

FIGURE 7 Patient-Centric Algorithms for Acute Chest Pain



ECG indicates electrocardiogram; and STEMI, ST-segment-elevation myocardial infarction.

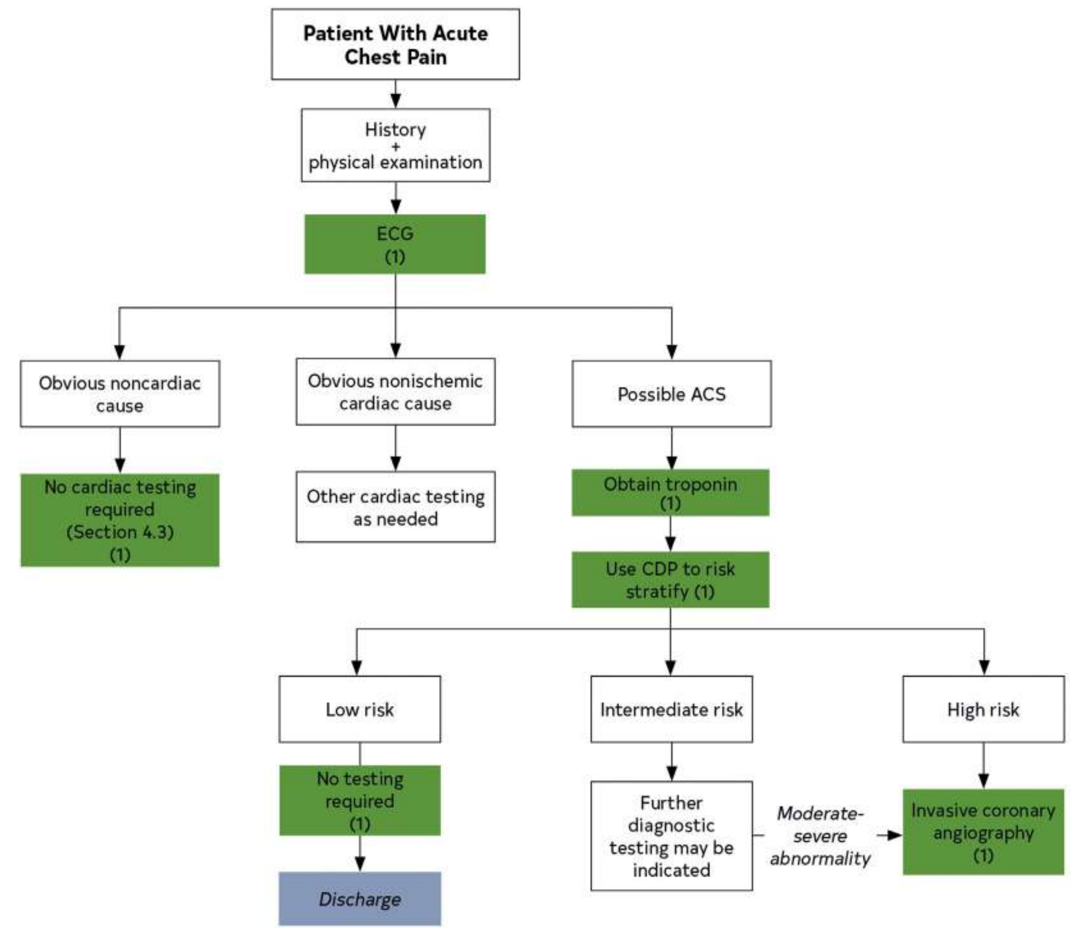
4.1. Patients With Acute Chest Pain and Suspected Acute Coronary Syndrome (Not Including STEMI)

Recommendations for Patients With Acute Chest Pain and Suspected ACS (Not Including STEMI)
Referenced studies that support the recommendations are summarized in Online Data Supplements 8 and 9.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In patients presenting with acute chest pain and suspected ACS, clinical decision pathways (CDPs) should categorize patients into low-, intermediate-, and high-risk strata to facilitate disposition and subsequent diagnostic evaluation (40-52,76).
1	B-NR	2. In the evaluation of patients presenting with acute chest pain and suspected ACS for whom serial troponins are indicated to exclude myocardial injury, recommended time intervals after the initial troponin sample collection (time zero) for repeat measurements are: 1 to 3 hours for high-sensitivity troponin and 3 to 6 hours for conventional troponin assays (35,56,77).
1	C-LD	3. To standardize the detection and differentiation of myocardial injury in patients presenting with acute chest pain and suspected ACS, institutions should implement a CDP that includes a protocol for troponin sampling based on their particular assay (78,79)
1	C-LD	4. In patients with acute chest pain and suspected ACS, previous testing when available should be considered and incorporated into CDPs (80-84).
2a	B-NR	5. For patients with acute chest pain, a normal ECG, and symptoms suggestive of ACS that began at least 3 hours before ED arrival, a single hs-cTn concentration that is below the limit of detection on initial measurement (time zero) is reasonable to exclude myocardial injury (51,85-89).

Patients with acute chest pain and suspected ACS cover a spectrum of disease likelihood and stratification into low- versus intermediate- or high-risk groups once STEMI has been excluded (**Figure 8**). Chest pain risk scores provide a summative assessment combining clinical information, such as age, ST-segment changes on ECG, symptoms, CAD risk factors, and cTn (**Table 5**) to estimate a patient's probability of ACS or risk of 30-day major adverse cardiovascular events (MACE) (90-95). The warranty period of prior cardiac testing should be considered, when symptoms are unchanged (**Table 6**). Low-risk chest pain has been defined in **Table 7**.

FIGURE 8 General Approach to Risk Stratification of Patients With Suspected ACS



ACS indicates acute coronary syndrome; CDP, clinical decision pathway; and ECG, electrocardiogram.

TABLE 5 Sample Clinical Decision Pathways Used to Define Risk

	HEART Pathway (91)	EDACS (96)	ADAPT (mADAPT) (97)	NOTR (94)	2020 ESC/hs-cTn* (98,99)	2016 ESC/ GRACE (49,100)
Target population	Suspected ACS	Suspected ACS, CP >5 min, planned serial troponin	Suspected ACS, CP >5 min, planned observation	Suspected ACS, ECG, troponin ordered	Suspected ACS, stable	Suspected ACS, planned serial troponin
Target outcome	↑ ED discharge without increasing missed 30-d or 1-y MACE	↑ ED discharge rate without increasing missed 30-d MACE	↑ ED discharge rate without increasing missed 30-d MACE	↑ Low-risk classification without increasing missed 30-d MACE	Early detection of AMI; 30-d MACE	Early detection of AMI
Patients with primary outcome in study population, %	6-22	12	15	5-8	9.8	10-17
Troponin	cTn, hs-cTn	hs-cTn	cTn, hs-cTn	cTn, hs-cTn	hs-cTn	cTn, hs-cTn
Variables used	History ECG Age Risk factors Troponin (0, 3 h)	Age Sex Risk factors History Troponin (0, 2 h)	TIMI score 0-1 No ischemic ECG changes Troponin (0, 2 h)	Age Risk factors Previous AMI or CAD Troponin (0, 2 h)	History ECG hs-cTn (0, 1 or 2 h)	Age HR, SBP Serum Cr Cardiac arrest ECG Cardiac biomarker Killip class
Risk thresholds:						
■ Low risk	HEART score <3 Neg 0, 3-h cTn Neg 0, 2-h hs-cTn	EDACS score <16 Neg 0, 2 h hs-cTn No ischemic ECG Δ	TIMI score 0 (or <1 for mADAPT) ■ Neg 0, 2-h cTn or hs-cTn ■ No ischemic ECG Δ	Age <50 y <3 risk factors Previous AMI or CAD Neg cTn or hs-cTn (0, 2 h)	■ Initial hs-cTn is "very low" and Sx onset >3 h ago **Or** ■ Initial hs-cTn "low" and 1- or 2-h hs-cTn Δ is "low"	Chest pain free, GRACE <140 ■ Sx <6 h - hs-cTn <ULN (0, 3 h) ■ Sx >6 h - hs-cTn <ULN (arrival)
■ Intermediate risk	HEART score 4-6	NA	TIMI score 2-4	NA	■ Initial hs-cTn is between "low" and "high" **And/Or** ■ 1- or 2-h hs-cTn Δ is between low and high thresholds	■ T0 hs-cTn = 12-52 ng/L or ■ 1-h Δ = 3-5 ng/L
■ High risk	HEART score 7-10 (101,102)	NA	TIMI score 5-7 (102)	NA	■ Initial hs-cTn is "high" **Or** ■ 1- or 2-h hs-cTn Δ is high	■ T0 hs-cTn >52 ng/L or ■ Δ 1 h >5 ng/L
Performance	↑ ED discharges by 21% (40% versus 18%) ↓ 30-d objective testing by 12% (69% versus 57%) ↓ length of stay by 12 h (9.9 versus 21.9 h)	More patients identified as low risk versus ADAPT (42% versus 31%)	ADAPT: More discharged ≤6 h (19% versus 11%)	30-d MACE sensitivity =100% 28% eligible for ED discharge	AMI sensitivity >99% 62% Ruled out (0.2% 30-d MACE) 25% Observe 13% Rule in	AMI sensitivity >99% 30-d MACE not studied
AMI sensitivity, %	100	100	100	100	>99	96.7
cTn accuracy: 30-d MACE sensitivity, %	100	100	100	100	NA	NA
hs-cTn accuracy: 30-d MACE sensitivity, %	95	92	93	99	99	-
ED discharge, %	40	49	19 (ADAPT) 39 (mADAPT)	28	-	-

*The terms "very low," "low," "high," "1 h Δ," and "2 h Δ" refer to hs-cTn assay-specific thresholds published in the ESC guideline (98,99).

ACS indicates acute coronary syndrome; ADAPT, Accelerated Diagnostic protocol to Assess chest Pain using Troponins; AMI, acute myocardial infarction; CP, chest pain or equivalent; Cr, creatinine; cTn, cardiac troponin; hs-cTn, high-sensitivity cardiac troponin; ECG, electrocardiogram; ED, emergency department; EDACS, emergency department ACS; ESC, European Society of Cardiology; GRACE, Global Registry of Acute Coronary Events; HEART, history, ECG, age, risk factors, troponin; HR, heart rate; hs, high sensitivity; MACE, major adverse cardiovascular events; mADAPT, modified (including TIMI scores of 1) ADAPT; NA, not applicable; neg, negative; NICE, National Institute for Health and Clinical Excellence; NOTR, No Objective Testing Rule; SBP, systolic blood pressure; SSACS, symptoms suggestive of ACS; Sx, symptoms; and ULN, upper limit of normal.

TABLE 6 Warranty Period for Prior Cardiac Testing

Test Modality	Result	Warranty Period
Anatomic	Normal coronary angiogram CCTA with no stenosis or plaque	2 y
Stress testing	Normal stress test (given adequate stress)	1 y

CCTA indicates coronary computed tomographic angiography.

TABLE 7 Definition Used for Low-Risk Patients With Chest Pain

	Low Risk (<1% 30-d Risk for Death or MACE)
hs-cTn Based	
T-0	T-0 hs-cTn below the assay limit of detection or "very low" threshold if symptoms present for at least 3 h
T-0 and 1- or 2-h Delta	T-0 hs-cTn and 1- or 2-h delta are both below the assay "low" thresholds (>99% NPV for 30-d MACE)
Clinical Decision Pathway Based	
HEART Pathway (91)	HEART score ≤3, initial and serial cTn/hs-cTn < assay 99th percentile
EDACS (105)	EDACS score ≤16; initial and serial cTn/hs-cTn < assay 99th percentile
ADAPT (90)	TIMI score 0, initial and serial cTn/hs-cTn < assay 99th percentile
mADAPT	TIMI score 0/1, initial and serial cTn/hs-cTn < assay 99th percentile
NOTR (94)	0 factors

ADAPT indicates 2-hour Accelerated Diagnostic Protocol to Access Patients with Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarkers; cTn, cardiac troponin; EDACS, Emergency Department Acute Coronary Syndrome; HEART Pathway, History, ECG, Age, Risk Factors, Troponin; hs-cTn, high-sensitivity cardiac troponin; MACE, major adverse cardiovascular events; mADAPT, modified 2-hour Accelerated Diagnostic Protocol to Access Patients with Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarkers; NOTR, No Objective Testing Rule; NPV, negative predictive value; and TIMI, Thrombolysis in Myocardial Infarction.

4.1.1. Low-Risk Patients With Acute Chest Pain

Recommendations for Low-Risk Patients With Acute Chest Pain
Referenced studies that support the recommendations are summarized in Online Data Supplements 10 and 11.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. Patients with acute chest pain and a 30-day risk of death or major adverse cardiovascular events (MACE) <1% should be designated as low risk (34,41,45,49,51,52,54,55,57,85,103).
2a	B-R	2. In patients with acute chest pain and suspected ACS who are deemed low-risk (<1% 30-day risk of death or MACE), it is reasonable to discharge home without admission or urgent cardiac testing (60,94,97,104,105).

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4.1.2. Intermediate-Risk Patients With Acute Chest Pain

Recommendations for Intermediate-Risk Patients With Acute Chest Pain
Referenced studies that support the recommendations are summarized in Online Data Supplements 12 and 13.

COR	LOE	RECOMMENDATIONS
1	C-EO	1. For intermediate-risk patients with acute chest pain, transthoracic echocardiography (TTE) is recommended as a rapid, bedside test to establish baseline ventricular and valvular function, evaluate for wall motion abnormalities, and to assess for pericardial effusion.
2a	A	2. For intermediate-risk patients with acute chest pain, management in an observation unit is reasonable to shorten length of stay and lower cost relative to an inpatient admission (106-112).

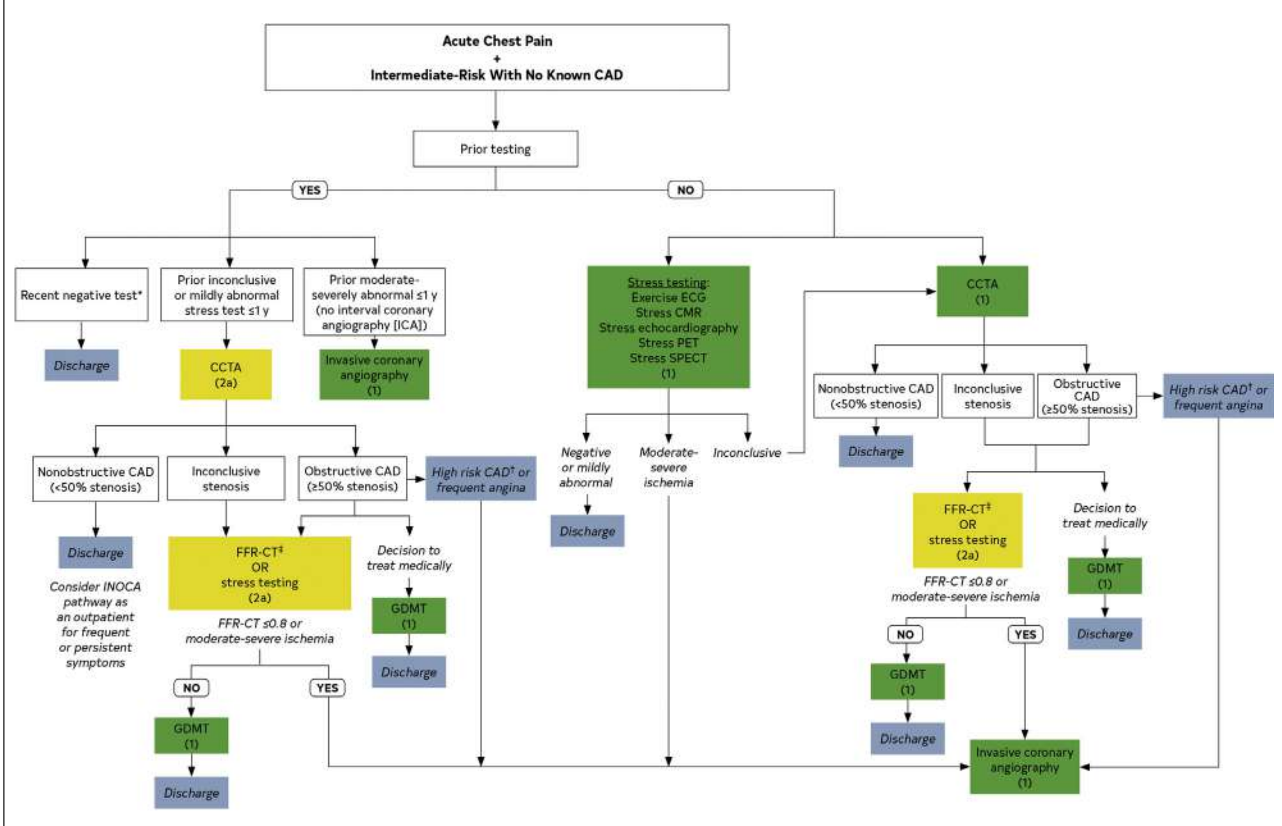
4.1.2.1. Intermediate-Risk Patients With Acute Chest Pain and No Known Coronary Artery Disease

Figure 9 presents an evaluation algorithm for patients with suspected ACS at intermediate risk with no known CAD.

Recommendations for Intermediate-Risk Patients With No Known CAD
Referenced studies that support the recommendations are summarized in Online Data Supplements 14 and 15.

COR	LOE	RECOMMENDATIONS
		Index Diagnostic Testing
		Anatomic Testing
1	A	1. For intermediate-risk patients with acute chest pain and no known CAD eligible for diagnostic testing after a negative or inconclusive evaluation for ACS, coronary computed tomography angiography (CCTA) is useful for exclusion of atherosclerotic plaque and obstructive CAD (113-123).
1	C-EO	2. For intermediate-risk patients with acute chest pain, moderate-severe ischemia on current or prior (≤1 year) stress testing, and no known CAD established by prior anatomic testing, invasive coronary angiography (ICA) is recommended.
2a	C-LD	3. For intermediate-risk patients with acute chest pain with evidence of previous mildly abnormal stress test results (≤1 year), CCTA is reasonable for diagnosing obstructive CAD (124,125).
		Stress Testing
1	B-NR	4. For intermediate-risk patients with acute chest pain and no known CAD who are eligible for cardiac testing, either exercise ECG, stress echocardiography, stress positron emission tomography (PET)/single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI), or stress CMR is useful for the diagnosis of myocardial ischemia (33,107,111,113,116,122,126-145).
		Sequential or Add-on Diagnostic Testing
2a	B-NR	5. For intermediate-risk patients with acute chest pain and no known CAD, with a coronary artery stenosis of 40% to 90% in a proximal or middle coronary artery on CCTA, fractional flow reserve computed tomography (FFR-CT) can be useful for the diagnosis of vessel-specific ischemia and to guide decision-making regarding the use of coronary revascularization (146-152).
2a	C-EO	6. For intermediate-risk patients with acute chest pain and no known CAD, as well as an inconclusive prior stress test, CCTA can be useful for excluding the presence of atherosclerotic plaque and obstructive CAD.
2a	C-EO	7. For intermediate-risk patients with acute chest pain and no known CAD, with an inconclusive CCTA, stress imaging (with echocardiography, PET/SPECT MPI, or CMR) can be useful for the diagnosis of myocardial ischemia.

FIGURE 9 Evaluation Algorithm for Patients With Suspected ACS at Intermediate Risk With No Known CAD



Test choice should be guided by local availability and expertise. *Recent negative test: normal CCTA ≤2 years (no plaque/no stenosis) OR negative stress test ≤1 year, given adequate stress. †High-risk CAD means left main stenosis ≥50%; anatomically significant 3-vessel disease (≥ 70% stenosis). ‡For FFR-CT, turnaround times may impact prompt clinical care decisions. However, the use of FFR-CT does not require additional testing, as would be the case when adding stress testing. CAD indicates coronary artery disease; CCTA, coronary CT angiography; CMR, cardiovascular magnetic resonance imaging; CT, computed tomography; FFR-CT, fractional flow reserve with CT; GDMT, guideline-directed medical therapy; ICA, invasive coronary angiography; INOCA, ischemia and no obstructive coronary artery disease; PET, positron emission tomography; and SPECT, single-photon emission CT.

4.1.2.2. Intermediate-Risk Patients With Acute Chest Pain and Known Coronary Artery Disease

Recommendations for Intermediate-Risk Patients With Acute Chest Pain and Known CAD
Referenced studies that support the recommendations are summarized in Online Data Supplements 16 and 17.

COR	LOE	RECOMMENDATIONS
1	A	1. For intermediate-risk patients with acute chest pain who have known CAD and present with new onset or worsening symptoms, guideline-directed medical therapy (GDMT) should be optimized before additional cardiac testing is performed (153,154).
1	A	2. For intermediate-risk patients with acute chest pain who have worsening frequency of symptoms with significant left main, proximal left anterior descending stenosis, or multivessel CAD on prior anatomic testing or history of prior coronary revascularization, ICA is recommended (113-115,119,155,156).
2a	B-NR	3. For intermediate-risk patients with acute chest pain and known nonobstructive CAD, CCTA can be useful to determine progression of atherosclerotic plaque and obstructive CAD (157-159).

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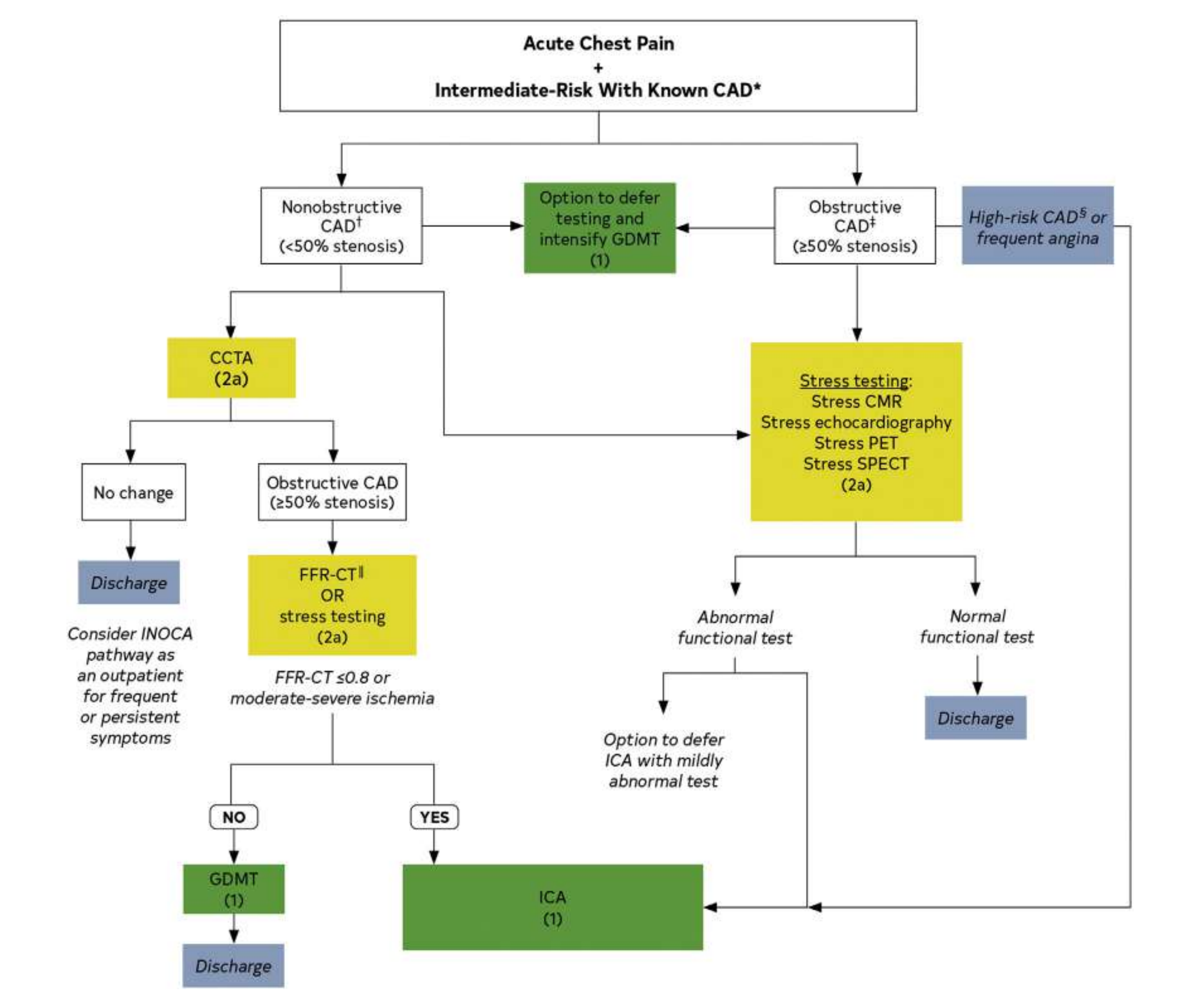
(continued)

2a	B-NR	4. For intermediate-risk patients with acute chest pain and coronary artery stenosis of 40% to 90% in a proximal or middle segment on CCTA, FFR-CT is reasonable for diagnosis of vessel-specific ischemia and to guide decision-making regarding the use of coronary revascularization (146,148,149,151,152,160).
2a	B-NR	5. For intermediate-risk patients with acute chest pain and known CAD who have new onset or worsening symptoms, stress imaging (PET/SPECT MPI, CMR, or stress echocardiography) is reasonable (120,126,129,142).

Figure 10 includes the evaluation algorithm for patients with known CAD, including patients with nonobstructive and obstructive CAD.

FIGURE 10 Evaluation Algorithm for Patients With Suspected ACS at Intermediate Risk With Known CAD



Test choice should be guided by local availability and expertise. *Known CAD is prior MI, revascularization, known obstructive or nonobstructive CAD on invasive or CCTA. †If extensive plaque is present a high-quality CCTA is unlikely to be achieved, and stress testing is preferred. ‡Obstructive CAD includes prior coronary artery bypass graft/percutaneous coronary intervention. §High-risk CAD means left main stenosis ≥50%; anatomically significant 3-vessel disease (≥70% stenosis). ‖FFR-CT turnaround times may impact prompt clinical care decisions. ACS indicates acute coronary syndrome; CAD, coronary artery disease; CCTA, coronary CT angiography; CMR, cardiovascular magnetic resonance; CT, computed tomography; FFR-CT, fractional flow reserve with CT; GDMT, guideline-directed medical therapy; ICA, invasive coronary angiography; INOCA, ischemia and no obstructive coronary artery disease; PET, positron emission tomography; and SPECT, single-photon emission CT.

4.1.3. High-Risk Patients With Acute Chest Pain

Recommendations for High-Risk Patients With Acute Chest Pain
Referenced studies that support the recommendations are summarized in Online Data Supplements 18 and 19.

COR	LOE	RECOMMENDATIONS
		Recommendations for High-Risk Patients, Including Those With High-Risk Findings on CCTA or Stress Testing
1	B-NR	1. For patients with acute chest pain and suspected ACS who have new ischemic changes on electrocardiography, troponin-confirmed acute myocardial injury, new-onset left ventricular systolic dysfunction (ejection fraction <40%), newly diagnosed moderate-severe ischemia on stress testing, hemodynamic instability, and/or a high CDP risk score should be designated as high risk for short-term MACE (161-163).
1	C-EO	2. For patients with acute chest pain and suspected ACS who are designated as high risk, ICA is recommended (33,164-166).
2a	B-NR	3. For high-risk patients with acute chest pain who are troponin positive in whom obstructive CAD has been excluded by CCTA or ICA, CMR or echocardiography can be effective in establishing alternative diagnoses (167-171).

4.1.4. Acute Chest Pain in Patients With Prior Coronary Artery Bypass Graft (CABG) Surgery

Recommendations for Acute Chest Pain in Patients With Prior CABG Surgery

COR	LOE	RECOMMENDATIONS
1	C-LD	1. In patients with prior CABG surgery presenting with acute chest pain who do not have ACS, performing stress imaging is effective to evaluate for myocardial ischemia or CCTA for graft stenosis or occlusion (172-178).
1	C-LD	2. In patients with prior CABG surgery presenting with acute chest pain, who do not have ACS (165,179-184) or who have an indeterminate/nondiagnostic stress test, ICA is useful (179).

4.1.5. Evaluation of Patients With Acute Chest Pain Receiving Dialysis

Recommendation for Evaluation of Patients With Acute Chest Pain Receiving Dialysis
Referenced studies that support the recommendation are summarized in Online Data Supplement 20.

COR	LOE	RECOMMENDATION
1	B-NR	1. In patients who experience acute unremitting chest pain while undergoing dialysis, transfer by EMS to an acute care setting is recommended (185-189).

4.1.6. Evaluation of Acute Chest Pain in Patients With Cocaine and Methamphetamine Use

Recommendation for Evaluation of Acute Chest Pain in Patients With Cocaine and Methamphetamine Use
Referenced studies that support the recommendation are summarized in Online Data Supplement 21.

COR	LOE	RECOMMENDATION
2a	B-NR	1. In patients presenting with acute chest pain, it is reasonable to consider cocaine and methamphetamine use as a cause of their symptoms (190-192).

4.1.7. Shared Decision-Making in Patients With Acute Chest Pain

Recommendations for Shared Decision-Making in Patients With Acute Chest Pain
Referenced studies that support the recommendations are summarized in Online Data Supplement 22.

COR	LOE	RECOMMENDATIONS
1	B-R	1. For patients with acute chest pain and suspected ACS who are deemed low risk by a CDP, patient decision aids are beneficial to improve understanding and effectively facilitate risk communication (193,194).
1	B-R	2. For patients with acute chest pain and suspected ACS who are deemed intermediate risk by a CDP, shared decision-making between the clinician and patient regarding the need for admission, for observation, discharge, or further evaluation in an outpatient setting is recommended for improving patient understanding and reducing low-value testing (193,194).

4.2. Evaluation of Acute Chest Pain With Nonischemic Cardiac Pathologies

Recommendation for Evaluation of Acute Chest Pain With Nonischemic Cardiac Pathologies

COR	LOE	RECOMMENDATION
1	C-EO	1. In patients with acute chest pain in whom other potentially life-threatening nonischemic cardiac conditions are suspected (e.g., aortic pathology, pericardial effusion, endocarditis), TTE is recommended for diagnosis.

4.2.1. Acute Chest Pain With Suspected Acute Aortic Syndrome

Recommendations for Acute Chest Pain With Suspected Acute Aortic Syndrome

COR	LOE	RECOMMENDATIONS
1	C-EO	1. In patients with acute chest pain where there is clinical concern for aortic dissection, computed tomography angiography (CTA) of the chest, abdomen, and pelvis is recommended for diagnosis and treatment planning.
1	C-EO	2. In patients with acute chest pain where there is clinical concern for aortic dissection, transesophageal echocardiography (TEE) or CMR should be performed to make the diagnosis if CT is contraindicated or unavailable.

4.2.2. Acute Chest Pain With Suspected PE

Recommendations for Acute Chest Pain With Suspected PE
Referenced studies that support the recommendations are summarized in Online Data Supplement 23.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In stable patients with acute chest pain with high clinical suspicion for PE, CTA using a PE protocol is recommended (195-198).
1	C-EO	2. For patients with acute chest pain and possible PE, need for further testing should be guided by pretest probability.

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4.2.3. Acute Chest Pain With Suspected Myopericarditis

Recommendations for Acute Chest Pain With Suspected Myopericarditis
Referenced studies that support the recommendations are summarized in Online Data Supplement 24.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In patients with acute chest pain and myocardial injury who have nonobstructive coronary arteries on anatomic testing, CMR with gadolinium contrast is effective to distinguish myopericarditis from other causes, including myocardial infarction and nonobstructive coronary arteries (MINOCA) (168,170,171,199-201).
1	B-NR	2. In patients with acute chest pain with suspected acute myopericarditis, CMR is useful if there is diagnostic uncertainty, or to determine the presence and extent of myocardial and pericardial inflammation and fibrosis (202-207).
1	C-EO	3. In patients with acute chest pain and suspected myopericarditis, TTE is effective to determine the presence of ventricular wall motion abnormalities, pericardial effusion, valvular abnormalities, or restrictive physiology.
2b	C-LD	4. In patients with acute chest pain with suspected acute pericarditis, noncontrast or contrast cardiac CT scanning may be reasonable to determine the presence and degree of pericardial thickening (202,203,208).

4.2.4. Acute Chest Pain With Valvular Heart Disease (VHD)

Recommendations for Acute Chest Pain With VHD

COR	LOE	RECOMMENDATIONS
1	C-EO	1. In patients presenting with acute chest pain with suspected or known history of VHD, TTE is useful in determining the presence, severity, and cause of VHD.
1	C-EO	2. In patients presenting with acute chest pain with suspected or known VHD in whom TTE diagnostic quality is inadequate, TEE (with 3D imaging if available) is useful in determining the severity and cause of VHD.
2a	C-EO	3. In patients presenting with acute chest pain with known or suspected VHD, CMR imaging is reasonable as an alternative to TTE and/or TEE is nondiagnostic.

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4.3. Evaluation of Acute Chest Pain With Suspected Noncardiac Causes

Recommendation for Evaluation of Acute Chest Pain With Suspected Noncardiac Causes

COR	LOE	RECOMMENDATION
1	C-EO	1. Patients with acute chest pain should be evaluated for noncardiac causes if they have persistent or recurring symptoms despite a negative stress test or anatomic cardiac evaluation, or a low-risk designation by a CDP.

The differential diagnosis for noncardiac causes of acute chest pain is quite broad, and includes respiratory, musculoskeletal, gastrointestinal, psychological, and other causes (Table 8).

TABLE 8 Differential Diagnosis of Noncardiac Chest Pain

Respiratory
Pulmonary embolism
Pneumothorax/hemothorax
Pneumomediastinum
Pneumonia
Bronchitis
Pleural irritation
Malignancy
Gastrointestinal
Cholecystitis
Pancreatitis
Hiatal hernia
Gastroesophageal reflux disease/gastritis/esophagitis
Peptic ulcer disease
Esophageal spasm
Dyspepsia
Chest wall
Costochondritis
Chest wall trauma or inflammation
Herpes zoster (shingles)
Cervical radiculopathy
Breast disease
Rib fracture
Musculoskeletal injury/spasm
Psychological
Panic disorder
Anxiety
Clinical depression
Somatization disorder
Hypochondria
Other
Hyperventilation syndrome
Carbon monoxide poisoning
Sarcoidosis
Lead poisoning
Prolapsed intervertebral disc
Thoracic outlet syndrome
Adverse effect of certain medications (e.g., 5-fluorouracil)
Sickle cell crisis

4.3.1. Evaluation of Acute Chest Pain With Suspected Gastrointestinal Syndromes

Recommendation for Evaluation of Acute Chest Pain With Suspected Gastrointestinal Syndromes

COR	LOE	RECOMMENDATION
2a	C-LD	1. In patients with recurrent acute chest pain without evidence of a cardiac or pulmonary cause, evaluation for gastrointestinal causes is reasonable.

4.3.2. Evaluation of Acute Chest Pain With Suspected Anxiety and Other Psychosomatic Considerations

Recommendation for Evaluation of Acute Chest Pain With Suspected Anxiety and Other Psychosomatic Considerations
Referenced studies that support the recommendation are summarized in Online Data Supplement 25.

COR	LOE	RECOMMENDATION
2a	B-R	1. For patients with recurrent, similar presentations for acute chest pain with no evidence of a physiological cause on prior diagnostic evaluation including a negative workup for myocardial ischemia, referral to a cognitive-behavioral therapist is reasonable (209-222).

4.3.3. Evaluation of Acute Chest Pain in Patients With Sickle Cell Disease

Recommendations for Evaluation of Acute Chest Pain in Patients With Sickle Cell Disease
Referenced studies that support the recommendations are summarized in Online Data Supplement 26.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In patients with sickle cell disease who report acute chest pain, emergency transfer by EMS to an acute care setting is recommended (223-227).
1	C-LD	2. In patients with sickle cell disease who report acute chest pain, ACS should be excluded (225-227).

5. EVALUATION OF PATIENTS WITH STABLE CHEST PAIN

5.1. Patients With No Known CAD Presenting With Stable Chest Pain

Stable chest pain is a symptom of myocardial ischemia characterized by chest pain that is provoked with stress (physical or emotional). Risk status in stable ischemic heart disease (SIHD) is not well defined. **Figure 11** provides a description of SIHD risk estimates (228).

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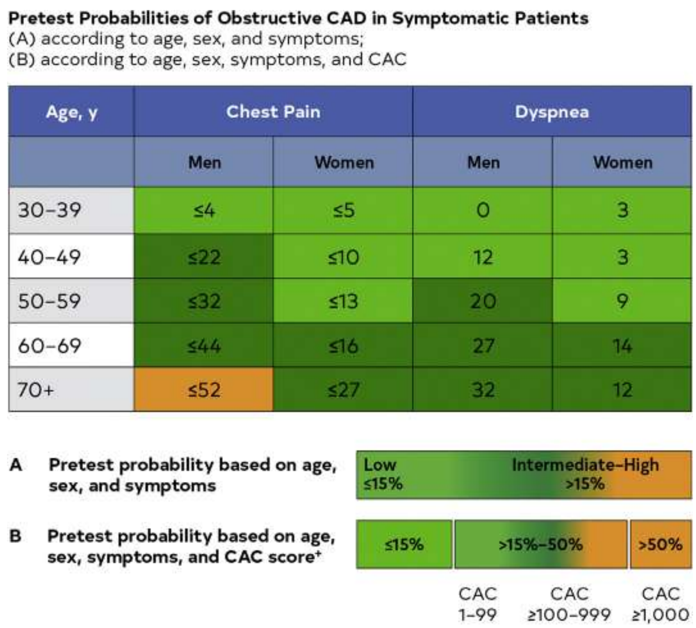
FIGURE 11 **Pretest Probabilities of Obstructive CAD in Symptomatic Patients According to Age, Sex, and Symptoms**



Modified from Juarez-Orozco, et al. (228) and Winther S, et al. (229). 1) The pretest probability shown is for patients with anginal symptoms. Patients with lower-risk symptoms would be expected to have lower pretest probability. 2) The darker green- and orange-shaded regions denote the groups in which noninvasive testing is most beneficial (pretest probability >15%). The light green-shaded regions denote the groups with pretest probability of CAD ≤15% in which the testing for diagnosis may be considered based on clinical judgment (228). 3) If CAC is available, it can also be used to estimate the pretest probability based on CAC score (229). CAC indicates coronary artery calcium; and CAD, coronary artery disease.

5.1.2. Low-Risk Patients With Stable Chest Pain and No Known CAD

Recommendations for Low-Risk Patients With Stable Chest Pain and No Known CAD
Referenced studies that support the recommendations are summarized in Online Data Supplements 27 and 28.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. For patients with stable chest pain and no known CAD presenting to the outpatient clinic, a model to estimate pretest probability of obstructive CAD is effective to identify patients at low risk for obstructive CAD and favorable prognosis in whom additional diagnostic testing can be deferred (228-232).
2a	B-R	2. For patients with stable chest pain and no known CAD categorized as low risk, CAC testing is reasonable as a first-line test for excluding calcified plaque and identifying patients with a low likelihood of obstructive CAD (233-236).
2a	B-NR	3. For patients with stable chest pain and no known CAD categorized as low risk, exercise testing without imaging is reasonable as a first-line test for excluding myocardial ischemia and determining functional capacity in patients with an interpretable ECG (237).

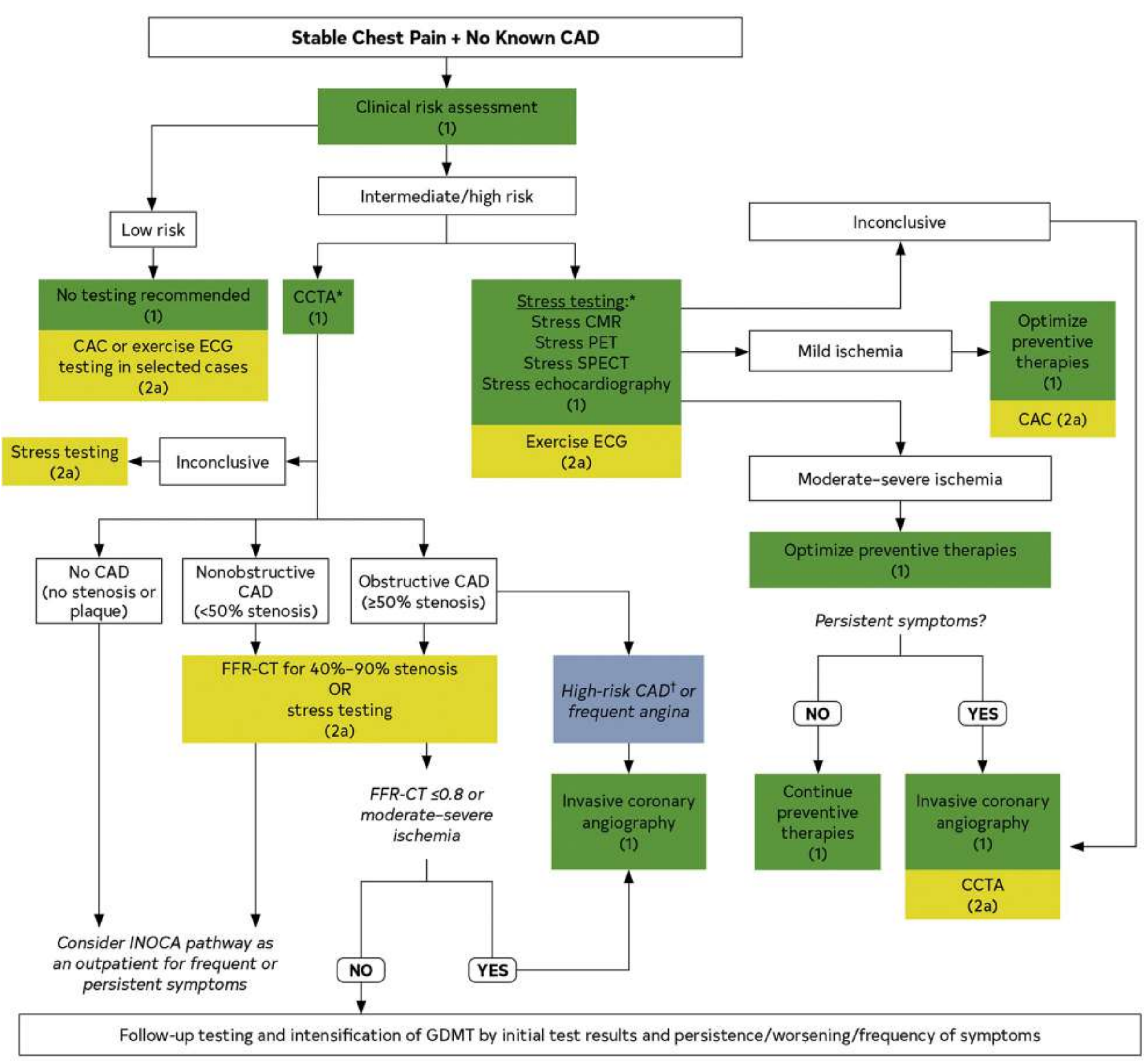
5.1.3. Intermediate-High Risk Patients With Stable Chest Pain and No Known CAD

Figure 12 presents a CDP for patients with stable chest pain and no known CAD.

Recommendations for Intermediate-High Risk Patients With Stable Chest Pain and No Known CAD
Referenced studies that support the recommendations are summarized in Online Data Supplements 29 and 30.

COR	LOE	RECOMMENDATIONS
		Index Diagnostic Testing
		Anatomic Testing
1	A	1. For intermediate-high risk patients with stable chest pain and no known CAD, CCTA is effective for diagnosis of CAD, for risk stratification, and for guiding treatment decisions (160,238-248).
		Stress Testing
1	B-R	2. For intermediate-high risk patients with stable chest pain and no known CAD, stress imaging (stress echocardiography, PET/SPECT MPI or CMR) is effective for diagnosis of myocardial ischemia and for estimating risk of MACE (124,245,249-270).
2a	B-R	3. For intermediate-high risk patients with stable chest pain and no known CAD for whom rest/stress nuclear MPI is selected, PET is reasonable in preference to SPECT, if available to improve diagnostic accuracy and decrease the rate of nondiagnostic test results (271-274).
2a	B-R	4. For intermediate-high risk patients with stable chest pain and no known CAD with an interpretable ECG and ability to achieve maximal levels of exercise (≥5 metabolic equivalent [MET]s), exercise electrocardiography is reasonable (181,237,245,249,251,275-278).
2b	B-NR	5. In intermediate-high risk patients with stable chest pain selected for stress MPI using SPECT, the use of attenuation correction or prone imaging may be reasonable to decrease the rate of false-positive findings (279-284).
		Assessment of Left Ventricular Function
1	B-NR	6. In intermediate-high risk patients with stable chest pain who have pathological Q waves, symptoms or signs suggestive of heart failure, complex ventricular arrhythmias, or a heart murmur with unclear diagnosis, use of TTE is effective for diagnosis of resting left ventricular systolic and diastolic ventricular function and detection of myocardial, valvular, and pericardial abnormalities (249,250,285).
		Sequential or Add-on Testing: What to Do If Index Test Results Are Positive or Inconclusive
2a	B-NR	7. For intermediate-high risk patients with stable chest pain and known coronary stenosis of 40% to 90% in a proximal or middle coronary segment on CCTA, FFR-CT can be useful for diagnosis of vessel-specific ischemia and to guide decision-making regarding the use of coronary revascularization (146,148,149,160,286-288).
2a	B-NR	8. For intermediate-high risk patients with stable chest pain after an inconclusive or abnormal exercise ECG or stress imaging study, CCTA is reasonable (84,154,242,289-291).
2a	B-NR	9. For intermediate-high risk patients with stable chest pain and no known CAD undergoing stress testing, the addition of CAC testing can be useful (235,292-297).
2a	B-NR	10. For intermediate-high risk patients with stable chest pain after inconclusive CCTA, stress imaging is reasonable (237,249,250,255-258,298-303).
2b	C-EO	11. For intermediate-high risk patients with stable chest pain after a negative stress test but with high clinical suspicion of CAD, CCTA or ICA may be reasonable.

FIGURE 12 Clinical Decision Pathway for Patients With Stable Chest Pain and No Known CAD



Test choice should be guided by local availability and expertise. *Test choice guided by patient's exercise capacity, resting electrocardiographic abnormalities; CCTA preferable in those <65 years of age and not on optimal preventive therapies; stress testing favored in those ≥65 years of age (with a higher likelihood of ischemia). †High-risk CAD means left main stenosis ≥50%; anatomically significant 3-vessel disease (≥70% stenosis). CAD indicates coronary artery disease; CCTA, coronary CT angiography; CMR, cardiovascular magnetic resonance imaging; CT, computed tomography; FFR-CT, fractional flow reserve with CT; GDMT, guideline-directed medical therapy; INOCA, ischemia and no obstructive CAD; PET, positron emission tomography; and SPECT, single-photon emission CT.

5.2. Patients With Known CAD Presenting With Stable Chest Pain

Recommendations for Patients With Known CAD Presenting With Stable Chest Pain
Referenced studies that support the recommendations are summarized in Online Data Supplement 31.

COR	LOE	RECOMMENDATIONS
1	A	1. For patients with obstructive CAD and stable chest pain, it is recommended to optimize GDMT (153,154,304).
1	C-EO	2. For patients with known nonobstructive CAD and stable chest pain, it is recommended to optimize preventive therapies (305,306).

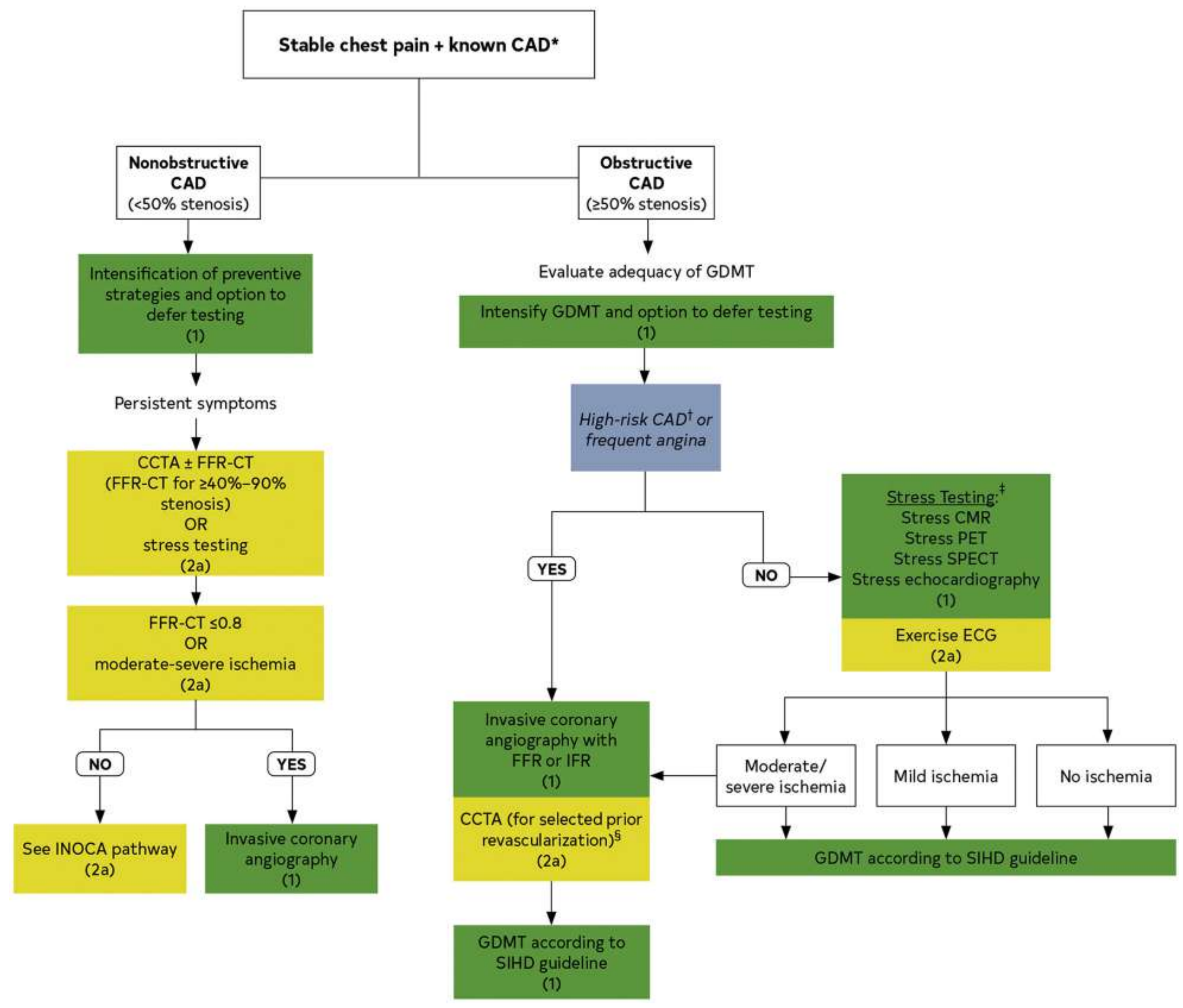
5.2.1. Patients With Obstructive CAD Who Present With Stable Chest Pain

Recommendations for Patients With Obstructive CAD Who Present With Stable Chest Pain
Referenced studies that support the recommendations are summarized in Online Data Supplements 32 and 33.

COR	LOE	RECOMMENDATIONS
		Index Diagnostic Testing
		Anatomic Testing
1	A	1. For patients with obstructive CAD who have stable chest pain despite GDMT and moderate-severe ischemia, ICA is recommended for guiding therapeutic decision-making (153,154,304,307).
1	A	2. For patients with obstructive CAD who have stable chest pain despite optimal GDMT, those referred for ICA without prior stress testing benefit from FFR or instantaneous wave free ratio (307-310).
1	B-R	3. For symptomatic patients with obstructive CAD who have stable chest pain with CCTA-defined ≥50% stenosis in the left main coronary artery, obstructive CAD with FFR with CT ≤0.80, or severe stenosis (≥70%) in all 3 main vessels, ICA is effective for guiding therapeutic decision-making (154,165).
2a	B-NR	4. For patients who have stable chest pain with previous coronary revascularization, CCTA is reasonable to evaluate bypass graft or stent patency (for stents ≥3 mm) (288,311-314).
		Stress Testing
1	B-NR	5. For patients with obstructive CAD who have stable chest pain despite optimal GDMT, stress PET/SPECT MPI, CMR, or echocardiography is recommended for diagnosis of myocardial ischemia, estimating risk of MACE, and guiding therapeutic decision-making (265,272,315-335).
2a	B-R	6. For patients with obstructive CAD who have stable chest pain despite optimal GDMT, when selected for rest/stress nuclear MPI, PET is reasonable in preference to SPECT, if available, to improve diagnostic accuracy and decrease the rate of nondiagnostic test results (261).
2a	B-NR	7. For patients with obstructive CAD who have stable chest pain despite GDMT, exercise treadmill testing can be useful to determine if the symptoms are consistent with angina pectoris, assess the severity of symptoms, evaluate functional capacity and select management, including cardiac rehabilitation (154,336-338).
2a	B-NR	8. For patients with obstructive CAD who have stable chest pain symptoms undergoing stress PET MPI or stress CMR, the addition of myocardial blood flow reserve is useful to improve diagnosis accuracy and enhance risk stratification (272,331-335).

Imaging should be considered in those with new onset or persistent stable chest pain (Figure 13).

FIGURE 13 Clinical Decision Pathway for Patients With Stable Chest Pain (or Equivalent) Symptoms With Prior MI, Prior Revascularization, or Known CAD on Invasive Coronary Angiography or CCTA, Including Those With Nonobstructive CAD



Test choice should be guided by local availability and expertise. *Known CAD means prior MI, revascularization, known obstructive CAD, nonobstructive CAD. †High-risk CAD means left main stenosis ≥50%; or obstructive CAD with FFR-CT ≤0.80. ‡Test choice guided by the patient's exercise capacity, resting electrocardiographic abnormalities. §Patients with prior CABG or stents >3.0 mm. *Follow-up Testing and Intensification of GDMT Guided by Initial Test Results and Persistence / Worsening / Frequency of Symptoms and Shared Decision Making*. CABG indicates coronary artery bypass graft; CAD, coronary artery disease; CCTA, coronary CT angiography; CMR, cardiovascular magnetic resonance imaging; CT, computed tomography; ECG, electrocardiogram; FFR-CT, fractional flow reserve with CT; GDMT, guideline-directed medical therapy; ICA, invasive coronary angiography; iFR, instant wave-free ratio; INOCA, ischemia and no obstructive coronary artery disease; MI, myocardial infarction; MPI, myocardial perfusion imaging; PET, positron emission tomography; SIHD, stable ischemic heart disease; and SPECT, single-photon emission CT.

5.2.1.1. Patients With Prior CABG Surgery With Stable Chest Pain

Recommendations for Patients With Prior CABG Surgery With Stable Chest Pain

COR	LOE	RECOMMENDATIONS
1	C-LD	1. In patients who have had prior CABG surgery presenting with stable chest pain whose noninvasive stress test results show moderate-to-severe ischemia (165,179-184), or in those suspected to have myocardial ischemia with indeterminate/nondiagnostic stress test, ICA is recommended for guiding therapeutic decision-making (179).
2a	C-LD	2. In patients who have had prior CABG surgery presenting with stable chest pain who are suspected to have myocardial ischemia, it is reasonable to perform stress imaging or CCTA to evaluate for myocardial ischemia or graft stenosis or occlusion (172-178,339).

5.2.2. Patients With Known Nonobstructive CAD Presenting With Stable Chest Pain

Recommendations for Patients With Known Nonobstructive CAD Presenting With Stable Chest Pain
Referenced studies that support the recommendations are summarized in Online Data Supplements 34 and 35.

COR	LOE	RECOMMENDATIONS
		Index Diagnostic Testing
		Anatomic Testing
2a	B-NR	1. For symptomatic patients with known nonobstructive CAD who have stable chest pain, CCTA is reasonable for determining atherosclerotic plaque burden and progression to obstructive CAD, and guiding therapeutic decision-making (124,158,159,340-343).
2a	B-NR	2. For patients with known coronary stenosis from 40% to 90% on CCTA, FFR can be useful for diagnosis of vessel-specific ischemia and to guide decision-making regarding the use of ICA (146,148,149,160,286-288).
		Stress Testing
2a	C-LD	3. For patients with known extensive nonobstructive CAD with stable chest pain symptoms, stress imaging (PET/SPECT, CMR, or echocardiography) is reasonable for the diagnosis of myocardial ischemia (272,328,331-334,344-347).

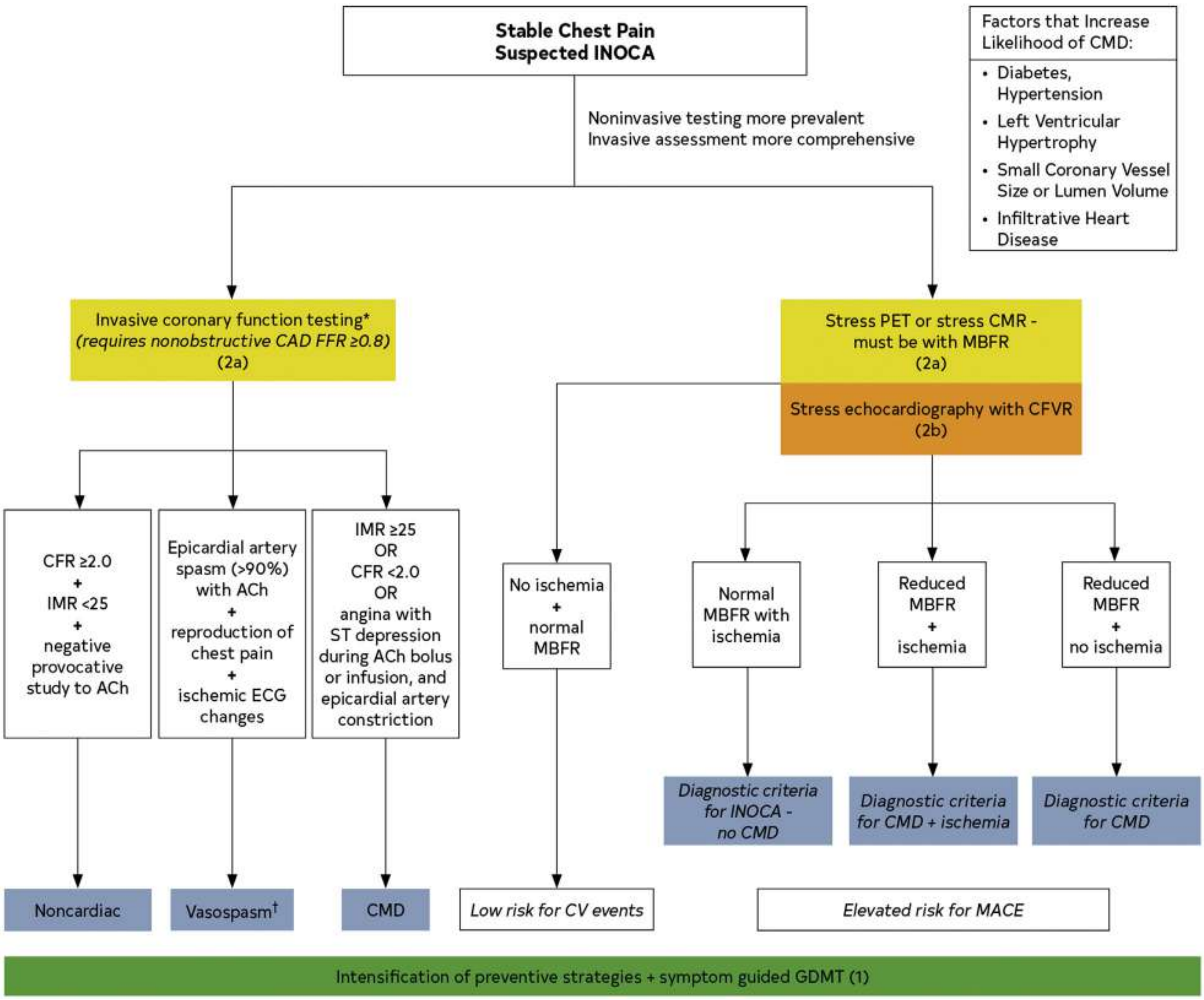
5.2.3. Patients With Suspected Ischemia and No Obstructive CAD (INOCA)

Recommendations for Patients With Suspected INOCA
Referenced studies that support the recommendations are summarized in Online Data Supplements 36 and 37.

COR	LOE	RECOMMENDATIONS
2a	B-NR	1. For patients with persistent stable chest pain and nonobstructive CAD and at least mild myocardial ischemia on imaging, it is reasonable to consider invasive coronary function testing to improve the diagnosis of coronary microvascular dysfunction and to enhance risk stratification (348-351).
2a	B-NR	2. For patients with persistent stable chest pain and nonobstructive CAD, stress PET MPI with myocardial blood flow reserve is reasonable to diagnose microvascular dysfunction and enhance risk stratification (272,331-334,344,345).
2a	B-NR	3. For patients with persistent stable chest pain and nonobstructive CAD, stress CMR with the addition of myocardial blood flow reserve measurement is reasonable to improve diagnosis of coronary myocardial dysfunction and for estimating risk of MACE (328,346,347).
2b	C-EO	4. For patients with persistent stable chest pain and nonobstructive CAD, stress echocardiography with the addition of coronary flow velocity reserve measurement may be reasonable to improve diagnosis of coronary myocardial dysfunction and for estimating risk of MACE.

A proposed diagnostic evaluation pathway is outlined in Figure 14.

FIGURE 14 **Clinical Decision Pathway for INOCA**



Test choice should be guided by local availability and expertise. *Ford T, et al. (352). †Cannot exclude microvascular vasospasm. ACh indicates acetylcholine; CAD, coronary artery disease; CFR, coronary flow reserve; CFVR, coronary flow velocity reserve; CMD, coronary microvascular dysfunction; CV, cardiovascular; ECG, electrocardiographic; FFR, fractional flow reserve; GDMT, guideline-directed medical therapy; IMR, index of microcirculatory restriction; INOCA, ischemia and no obstructive CAD; MACE, major adverse cardiovascular events; and MBFR, myocardial blood flow reserve.

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