2021 Guideline for the Evaluation and Diagnosis of Chest Pain

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A Selection of Tables and Figures

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AMERICAN COLLEGE of CARDIOLOGY

Advancing Heart Care Worldwide

2021 Guideline for the Evaluation and Diagnosis of Chest Pain

A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

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The ACC/AHA Joint Committee on Clinical Practice Guidelines has commissioned this guideline to focus on the evaluation of acute or stable chest pain or other anginal equivalents, in various clinical settings, with an emphasis on the diagnosis on ischemic causes. This guideline will not provide recommendations on whether revascularization is appropriate or what modality is indicated.

The following resource contains tables and figures from the 2021 Guideline for the Evaluation and Diagnosis of Chest Pain. The resource is only an excerpt from the Guideline and the full publication should be reviewed for more tables and figures as well as important context.

CITATION: J AM Coll Cardiol. Oct 2021; DOI: 10.1016/j.jacc.2021.07.053.

2021 Guideline for the Evaluation and Diagnosis of Chest Pain

Table of Contents

NOTE: All blue items are hyperlinked in this tool.

Class of Recommendation (COR)/ Level of Evidence (LOE) Table

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.

(Updated May 2019)

Master Abbreviation List

Abbreviation	Meaning/Phrase
ADAPT	Accelerated Diagnostic protocol to Assess chest Pain using Troponins
ACS	acute coronary syndrome
AMI	acute myocardial infarction
CAC	coronary artery calcium
CAD	coronary artery disease
CCTA	coronary computed tomographic angiography
CDP	clinical decision pathway
CMR	cardiovascular magnetic resonance imaging
CP	chest pain or equivalent
Cr	creatinine
CT	computed tomography
cTn	cardiac troponin
ECG	electrocardiogram
ED	emergency department
EDACS	emergency department ACS
ESC	European Society of Cardiology
FFR-CT	fractional flow reserve with CT
GDMT	guideline-directed medical therapy
GRACE	Global Registry of Acute Coronary Events
HEART	history, ECG, age, risk factors, troponin; HR, heart rate; hs, high sensitivity
hs-cTn	high-sensitivity cardiac troponin
INOCA	ischemia and no obstructive CAD

Abbreviation	Meaning/Phrase
mADAPT	modified (including TIMI scores of 1) ADAPT; NA, not applicable; neg, negative
MACE	major adverse cardiovascular events
NICE	National Institute for Health and Clinical Excellence
NORT	No Objective Testing Rule
PET	positron emission tomography
SBP	systolic blood pressure
SPECT	single-photon emission CT
SSACS	symptoms suggestive of ACS
Sx	symptoms
TIMI	thrombolysis in myocardial infarction
ULN	upper limit of normal

Top 10 Take-Home Messages *(1 of 3)*

Top 10 Take-Home Messages are written by the guideline writing committee. Corresponding guideline sections have been added by the ACC Chest Pain Guideline Dissemination Workgroup

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.

a. *Section 1.4.2. Defining Chest Pain* includes 2 recommendations and *Figure 2. Index of Suspicion that Chest "Pain" is Ischemic in Origin Based on Commonly Used Descriptors*

b. *Section 2.1. History* includes 1 recommendation and *Figure 3. Top 10 Causes of Chest Pain in Emergency Department Based on Age (Weighted Percent)* and *Table 3. Chest Pain Characteristics and Corresponding Causes*

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.

a. *Section 2.3.4. Biomarkers* includes 4 recommendations

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.

a. *Section 2.1.4. Patient-Centric Considerations includes 1 recommendation*

b. *Section 2.1. History includes* 1 recommendation and *Figure 3. Top 10 Causes of Chest Pain in Emergency Department Based on Age (Weighted Percent), Table 3. Chest Pain Characteristics and Corresponding 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.

a. *Section 4.1.7. Shared Decision-making in Patients With Acute Chest Pain* includes 2 recommendations

"Top Ten Messages" is continued in the next page.

Top 10 Take-Home Messages *(2 of 3)*

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.

a. *Section 4.1.1. Low-Risk Patients With Acute Chest Pain* includes 2 recommendations and *Table 8. Definition Used for Low-Risk Patients With Chest Pain, Figure 8. General Approach to Risk Stratification of Patients With Suspected ACS, Table 6. Sample Clinical Decision Pathways Used to Define Risk*

b. *Section 5.1.2. Low-Risk Patients With Stable Chest Pain and No Known Coronary Artery Disease* includes 3 recommendations

6

Pathways. Clinical decision pathways for chest pain in the emergency department and outpatient settings should be used routinely.

a. *Section 4. Choosing the Right Pathway With Patient-Centric Algorithms for Acute Chest Pain* is a large section with many subsections, includes *Figure 7. Patient-Centric Algorithms for Acute Chest Pain*

b. Other figures/tables in section 4: *Figure 8. General approach to risk stratification of patients with suspected ACS, Table 6. Sample Clinical Decision Pathways Used to Define Risk, Table 7. Warranty Period for Prior Cardiac Testing, Table 8. Definition Used for Low-Risk Chest Pain Patients, Figure 9. Evaluation Algorithm for Patients with suspected ACS at Intermediate Risk with No Known CAD, Figure 10. Evaluation Algorithm for Patients with suspected ACS at Intermediate Risk with Known CAD, Table 9. Differential Diagnosis of Noncardiac Chest Pain*

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.

a. *Section 2.1.1. A Focus on the Uniqueness of Chest Pain in Women* includes 2 recommendations

"Top Ten Messages" is continued in the next page.

Top 10 Take-Home Messages *(3 of 3)*

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 pre-test risk of obstructive coronary artery disease, respectively, will benefit the most from cardiac imaging and testing.

a. *Section 4.1.2. Intermediate-Risk Patients With Acute Chest Pain (includes three subsections; 4.1.2.1. Intermediate-Risk Patients With Acute Chest Pain and No Known Coronary Artery Disease; 4.1.2.1.1. Cost-Value Considerations; 4.1.2.2. Intermediate-Risk Patients With Acute Chest Pain and Known Coronary Artery Disease).* Includes *Figure 9. Evaluation Algorithm for Patients with suspected ACS at Intermediate Risk with No Known CAD,* and *Figure 10. Evaluation Algorithm for Patients with suspected ACS at Intermediate Risk with Known CAD.*

b. *Section 4.1.3. High-Risk Patients With Acute Chest Pain* includes 3 recommendations

c. *Section 5.1.3. Intermediate-High Risk Patients With Stable Chest Pain and No Known Coronary Artery Disease* includes 11 recommendations, *Figure 12. Clinical Decision Pathway for Patients With Stable Chest Pain and No Known CAD*

9

Noncardiac Is In. Atypical Is Out. "Noncardiac" should be used if heart disease is not suspected. "Atypical" is a misleading descriptor of chest pain, and its use is discouraged.

a. *Section 1.4.2. Defining Chest Pain* recommendation #2

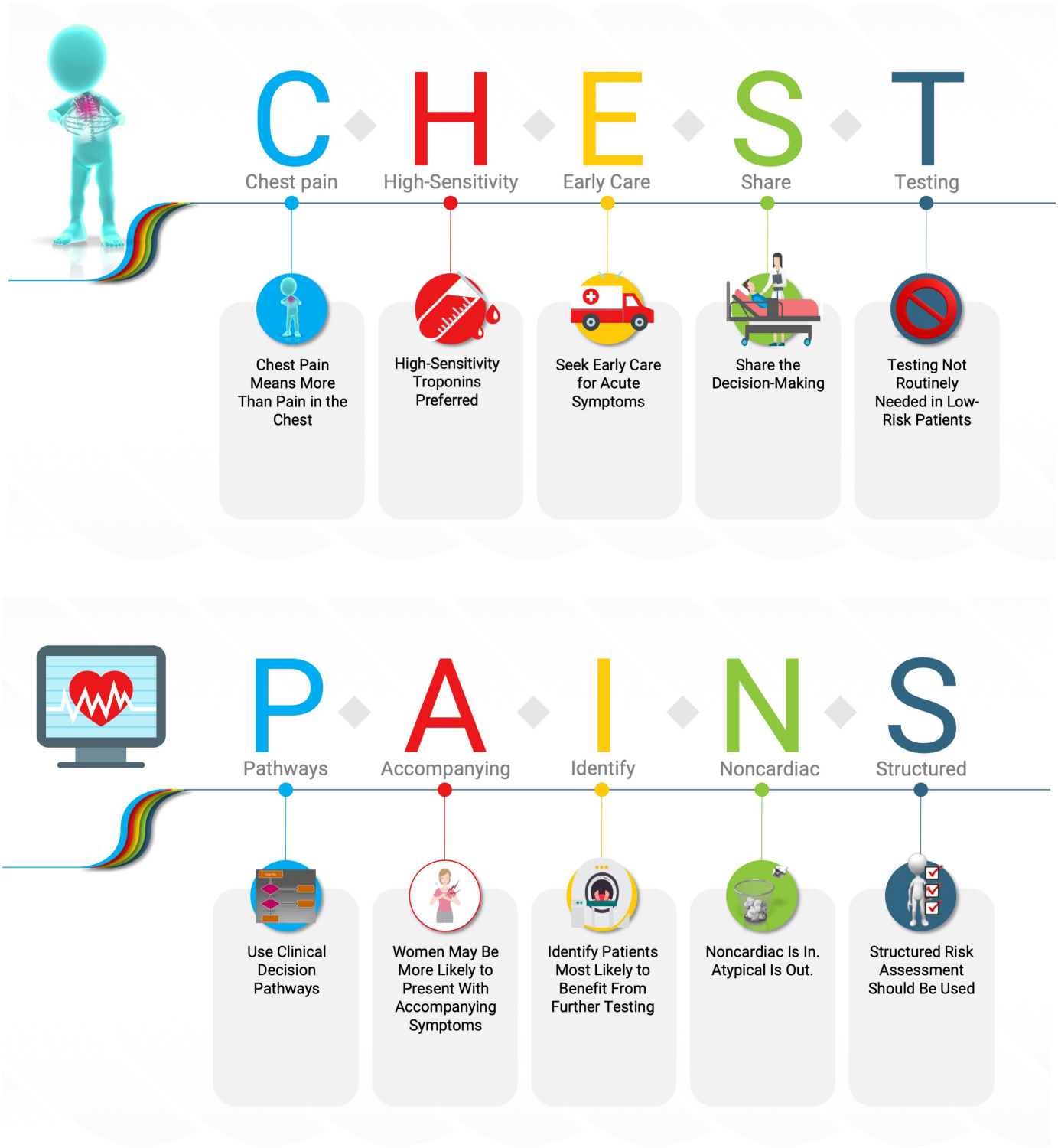
10

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.

a. *Section 4. Choosing the Right Pathway With Patient-Centric Algorithms for Acute Chest Pain* includes *Figure 7. Patient-Centric Algorithms for Acute Chest Pain which guides the user to other figures/portions of the guideline*

b. *Section 5. Evaluation of Patients With Stable Chest Pain*

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



High-Sensitivity Troponins Preferred

Recommendations from guideline section 2.3.4. Biomarkers.		
COR	LOE	Recommendations
1	B-NR	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.
1	B-NR	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.
1	C-EO	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.
3: No benefit	B-NR	With availability of cTn, creatine kinase myocardial (CK-MB) isoenzyme and myoglobin are not useful for diagnosis of acute myocardial injury.

Testing Not Needed Routinely for Low-Risk Patients

Recommendations from guideline Section 4.1.1. Low-Risk Patients With Acute Chest Pain		
COR	**LOE**	**Recommendations**
1	B-NR	1. Patients with acute chest pain and a 30-day risk of death or MACE <1% should be designated as low risk.
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.

Table 8. 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 (20)	HEART score <3, initial and serial cTn/hs-cTn < assay 99th percentile
EDACS (14)	EDACS score <16; initial and serial cTn/hs-cTn < assay 99th percentile
ADAPT (21)	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 (15)	0 factors

14. Flaws D, Than M, Scheuermeyer FX, et al. External validation of the emergency department assessment of chest pain score accelerated diagnostic pathway (EDACS-ADP). Emerg Med J. 2016;33:618-625.

15. Stopyra JP, Miller CD, Hiestand BC, et al. Validation of the no objective testing rule and comparison to the HEART Pathway. Acad Emerg Med. 2017;24:1165-1168.

20. Mahler SA, Riley RF, Hiestand BC, et al. The HEART Pathway randomized trial: identifying emergency department patients with acute chest pain for early discharge. Circ Cardiovasc Qual Outcomes. 2015;8:195-203.

21. Than M, Cullen L, Aldous S, et al. 2-Hour accelerated diagnostic protocol to assess patients with chest pain symptoms using contemporary troponins as the only biomarker: the ADAPT trial. J Am Coll Cardiol. 2012;59:2091-2098.

Figure 8. General Approach to Risk Stratification of Patients With Suspected ACS

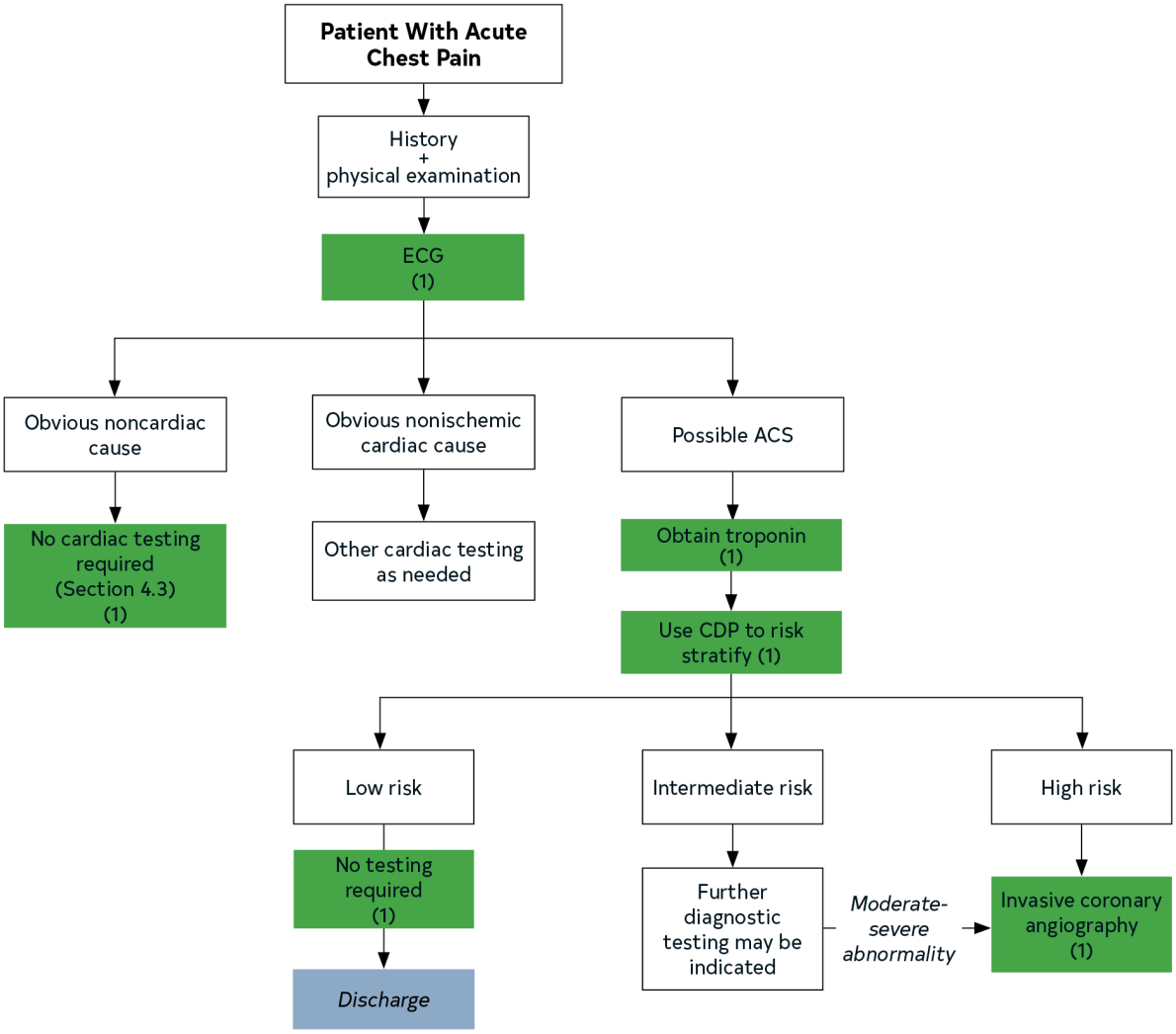


Table 6. Sample Clinical Decision Pathways Used to Define Risk

	HEART Pathway (31)	EDACS (44)	ADAPT (mADAPT) (45)	NOTR (34)	2020 ESC/ hs-cTn* (46, 47)	2016 ESC/ GRACE (11, 38)
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

Table 6 is continued in the next page.

	HEART Pathway (31)	EDACS (44)	ADAPT (mADAPT) (45)	NOTR (34)	2020 ESC/ hs-cTn* (46, 47)	2016 ESC/ GRACE (11, 38)
· High risk	HEART score 7-10	NA	TIMI score 5-7	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 (46, 47).

11. Mueller C, Giannitsis E, Christ M, et al. Multicenter evaluation of a 0-hour/1-hour algorithm in the diagnosis of myocardial infarction with high-sensitivity cardiac troponin T. Ann Emerg Med. 2016;68:76-87, e4.

31. Mahler SA, Riley RF, Hiestand BC, et al. The HEART Pathway randomized trial: identifying emergency department patients with acute chest pain for early discharge. Circ Cardiovasc Qual Outcomes. 2015;8:195-203.

34. Stopyra JP, Miller CD, Hiestand BC, et al. Validation of the no objective testing rule and comparison to the HEART Pathway. Acad Emerg Med. 2017;24:1165-1168.

38. Roffi M, Patrono C, Collet JP, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37:267-315.

44. Than MP, Pickering JW, Aldous SJ, et al. Effectiveness of EDACS versus ADAPT accelerated diagnostic pathways for chest pain: a pragmatic randomized controlled trial embedded within practice. Ann Emerg Med. 2016;68:93-102 e1.

45. Than M, Aldous S, Lord SJ, et al. A 2-hour diagnostic protocol for possible cardiac chest pain in the emergency department: a randomized clinical trial. JAMA Intern Med. 2014;174:51-58.

46. Collet JP, Thiele H, Barbato E, et al. 2020 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021;42:1289-1367.

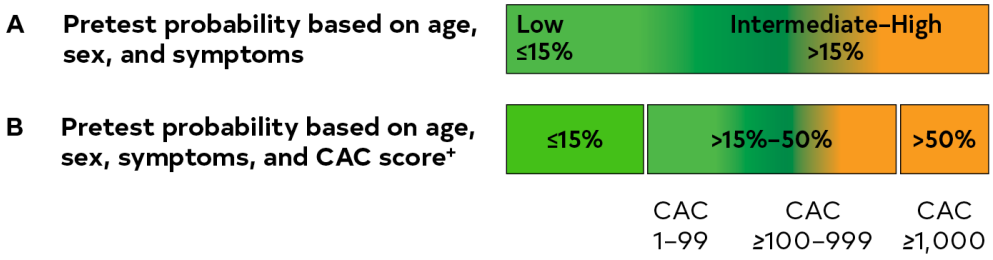
47. Twerenbold R, Costabel JP, Nestelberger T, et al. Outcome of applying the ESC 0/1-hour algorithm in patients with suspected myocardial infarction. J Am Coll Cardiol. 2019;74:483-494.

Recommendations from guideline section 5.1.2. Low-Risk Patients With Stable Chest Pain and No Known CAD		
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.
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.
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.

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

Pretest Probabilities of Obstructive CAD in Symptomatic Patients
(A) according to age, sex, and symptoms;
(B) according to age, sex, symptoms, and CAC

Age, y	Chest Pain		Dyspnea	
	Men	Women	Men	Women
30–39	≤4	≤5	0	3
40–49	≤22	≤10	12	3
50–59	≤32	≤13	20	9
60–69	≤44	≤16	27	14
70+	≤52	≤27	32	12

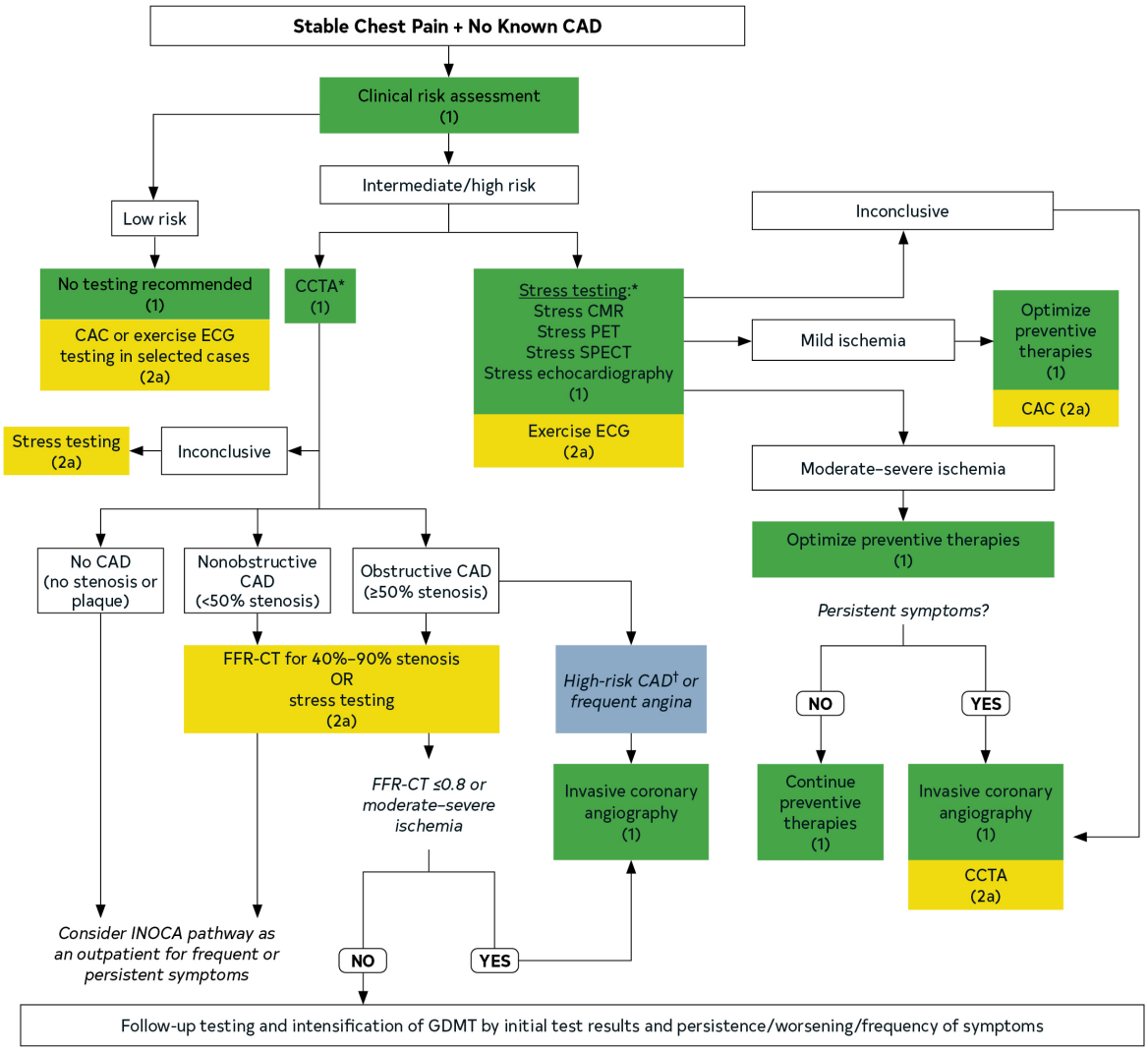


Modified from Juarez-Orozco et al. (1) and Winther et al. (2).

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 (1).
3. If CAC is available, it can also be used to estimate the pretest probability based on CAC score (2).

1. Juarez-Orozco LE, Saraste A, Capodanno D, et al. Impact of a decreasing pre-test probability on the performance of diagnostic tests for coronary artery disease. Eur Heart J Cardiovasc Imaging. 2019;20:1198-207.
2. Winther S, Schmidt SE, Mayrhofer T, et al. Incorporating coronary calcification into pre-test assessment of the likelihood of coronary artery disease. J Am Coll Cardiol. 2020;76:2421-2432.

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).

Accompanying Symptoms

Recommendations from guideline section 2.1.1. A Focus on the Uniqueness of Chest Pain in Women		
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.
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.

Noncardiac is In. Atypical Is Out

Recommendation from guideline section 1.4.2. Defining Chest Pain		
COR	LOE	Recommendations
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.