Chapter 48: Chest Pain

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INTRODUCTION AND EPIDEMIOLOGY

About 8 million patients with chest pain present to a U.S. ED each year.[1] Of these, 50% to 70% are placed into an observation unit or admitted to the hospital, yet only about 10% are eventually diagnosed with an acute coronary syndrome.[2,3,4,5] Still, 2% to 5% of patients with acute myocardial infarctions are missed on initial presentation and discharged from the ED.[2] We discuss the features and approach that help differentiate acute coronary syndrome from other causes of chest pain. The chapters titled "Acute Coronary Syndromes" and "Low Probability Acute Coronary Syndromes" discuss management of these specific syndromes.

Acute chest pain is the recent onset of pain, pressure, or tightness in the anterior thorax between the xiphoid, suprasternal notch, and both midaxillary lines. **Acute coronary syndrome** includes **acute myocardial infarction** and acute ischemia (unstable angina). Acute myocardial infarction is defined by myocardial necrosis with elevation of cardiac biomarkers and is classified by ECG findings as **ST-segment elevation myocardial infarction** or **non-ST-segment elevation myocardial infarction**. Unstable angina is a clinical diagnosis defined by chest pain or an equivalent (neck or upper extremity pain) from inadequate myocardial perfusion that is new, occurring with greater frequency, less activity, or at rest. Patients with unstable angina do not have pathologic ST-segment elevation on ECG or cardiac biomarker elevation, but they are at risk of eventual myocardial damage absent recognition and treatment.

PATHOPHYSIOLOGY

The chest wall, from the dermis to the parietal pleura, is innervated by somatic pain fibers. Neurons enter the spinal cord at specific levels corresponding to the skin dermatomes. Visceral pain fibers are found in internal organs, such as the heart, blood vessels, esophagus, and visceral pleura. Visceral pain fibers enter the spinal cord and map to areas on the parietal cortex corresponding to cord levels shared with somatic fibers. Stimulation of visceral or somatic afferent pain fibers results in two distinct pain syndromes. Pain from somatic fibers is usually easily described, precisely located, and often experienced as a sharp sensation. Pain from visceral fibers is generally more difficult to describe and imprecisely localized. Patients with visceral pain are more likely to use terms such as *discomfort*, *heaviness*, *pressure*, *tightness*, or *aching*. Visceral pain is often referred to an area of the body corresponding to adjacent somatic nerves, which explains why pain from an acute myocardial infarction may radiate to the neck, jaw, or arms. Factors such as age, sex, comorbid illnesses, medications, drugs, and alcohol may interact with psychological and cultural factors to alter pain perception and communication.

CLINICAL FEATURES

RISK ASSESSMENT

Patients with abnormal vital signs, concerning ECG findings (if available initially), a history of prior coronary artery disease, multiple atherosclerotic risk factors, or any abrupt, new, or severe chest pain or dyspnea should be quickly placed into a treatment bed. Initiate cardiac monitoring and IV access, and obtain an ECG, ideally within 10 minutes of arrival. Identify and treat immediate life needs like supporting the airway, breathing, and circulation. Measure vital signs promptly and at regular intervals. Administer oxygen if ambient saturation is <95%.

Once the patient is stable, focus on history, physical exam, and laboratory findings associated with cardiac (acute coronary syndrome) versus noncardiac chest pain causes. Obtain a focused history that includes symptoms, abridged past medical history, and review of systems, seeking features of life-threatening causes of chest pain, such as acute coronary syndrome, aortic dissection, pulmonary embolism, severe pneumonia, and esophageal rupture. Ask about the onset, timing, severity, radiation, and character of the chest pain; alleviating and exacerbating factors; and presence of associated symptoms, such as diaphoresis, dyspnea, nausea, vomiting, palpitations, and dizziness.

Focus the physical examination on findings pertinent to life-threatening causes of chest pain. Inspect the thorax for prior surgical incisions, chest wall deformities, and symmetric rise and fall with respiration. Palpate the chest wall for tenderness, masses, or crepitus. Auscultate to identify chest consolidation or pneumothorax, murmurs, gallops, or friction rubs, and obtain a chest x-ray immediately to identify immediate life-threatening processes.

HISTORY

Patients with serious and life-threatening intrathoracic disorders, including acute coronary syndrome, may report pain outside the chest, such as in the epigastrium, neck, jaw, shoulders, or arms. Some patients never experience chest pain or have migratory pain that is no longer in the chest at the time of medical evaluation. Patients with acute myocardial infarction who present without chest pain have diagnostic and treatment delays and have an in-hospital mortality rate more than twice that of acute myocardial infarction patients with chest pain.[6]

Classic Chest Pain

Terms such as "typical" and "atypical" symptoms are misleading because symptoms among patients with acute coronary syndrome vary and may not include classic findings. **Classic cardiac chest pain** is retrosternal left anterior chest crushing, squeezing, tightness, or pressure. Cardiac chest pain is often brought on or exacerbated by exertion and relieved by rest. Traditional teaching is that anginal pain lasts 2 to 10 minutes, unstable angina pain lasts 10 to 30 minutes, and pain from acute myocardial infarction often lasts longer than 30 minutes, but great overlap exists. Other classic features of acute coronary syndrome presentation include radiation of the pain to the arms, neck, or jaw; diaphoresis; dyspnea; and nausea or vomiting.[7]

Nonclassic Chest Pain

Patients with acute coronary syndrome frequently present without a "classic" chest pain story. The absence of classic symptoms contributes to delays in seeking care and in evaluation once they reach the ED.

Nonclassic presentations include chest pain lasting for seconds, constant pains lasting for 12 to 24 hours or more without waxing and waning intensity, or pain worsened by specific body movements or positions, such as twisting and turning of the thorax. Reports of stabbing, well-localized, positional, or pleuritic chest pain are uncommon with acute coronary syndrome but do not exclude it with certainty. The Multicenter Chest Pain Study reported that 22% of patients with acute myocardial infarction described their chest pain as sharp or stabbing.[8] **Nonclassic presentations of acute coronary syndrome occur more frequently in women, racial minorities, diabetics, the elderly, and patients with psychiatric disease or altered mental status than in other patient groups**.[6,9,10] Multiple prescription medications, drugs, alcohol, patient or provider sex, and cultural differences can impact the pain perception or reporting of symptoms.[11,12,13] For example, the term "sharp" in some cultures is interpreted to mean "severe," rather than knife-like.[14]

Premenopausal and early menopausal women with acute coronary syndrome are more likely to present with pain unrelated to exercise, pain not relieved by rest or nitroglycerin, pain relieved by antacids, palpitations without chest pain, or a chief complaint of fatigue.[15] Associated symptoms of nausea, emesis, jaw pain, neck pain, and back pain are more common in women with acute coronary syndrome, while diaphoresis is more common among men.[15]

Anginal Equivalents

One large public hospital reported that 47% of 721 consecutive patients with myocardial infarction presented complaining of symptoms other than chest pain.[10] This means ED physicians must consider potential **anginal-equivalent symptoms** like dyspnea at rest or with exertion, nausea, light-headedness, generalized weakness, acute changes in mental status, diaphoresis, or shoulder, arm, or jaw discomfort. Patients with dyspnea alone have a fourfold increased risk of sudden death from cardiac causes compared with asymptomatic patients, and a twofold increased risk compared with patients with classic angina.[16]

Epigastric or upper abdominal discomfort, even when relieved with antacids, should raise suspicion for acute coronary syndrome, especially for patients >50 years old and those with known coronary artery disease. In these two high-risk groups, include an ECG in routine evaluation of abdominal pain. Consider acute coronary syndrome in patients presenting with palpitations, because myocardial ischemia may increase automaticity and irritability, leading to dysrhythmias. Furthermore, tachycardia can cause an increase in myocardial oxygen demand, triggering myocardial ischemia.

Risk Factors

Major risk factors for coronary artery disease include age >40 years old, male or postmenopausal female, hypertension, tobacco use, hypercholesterolemia, diabetes, truncal obesity, family history, and a sedentary

lifestyle.[17,18] **Cocaine** use is associated with acute myocardial infarction even in young people with minimal or no coronary artery disease. Chronic cocaine use may accelerate atherosclerosis and severe coronary artery disease,[19] although some suggest no relationship once controlling for other cardiovascular risk factors.[20] **Human immunodeficiency virus** infection and treatment with highly active antiretroviral therapy can accelerate atherosclerosis.[21]

Although cardiac risk factors are useful in predicting coronary artery disease risk within a given population, they are less useful for diagnosing the presence or absence of acute coronary syndrome in an individual patient.[7,22,23] Patients with known coronary artery disease and prior acute coronary syndrome are at risk for another acute coronary syndrome event. So, identify previous episodes of chest pain, prior echocardiography, stress testing or coronary angiography, or prior revascularization (stent placement or coronary artery bypass graft surgery).

ACUTE MYOCARDIAL INFARCTION SIGNS AND SYMPTOMS: LIKELIHOOD RATIOS

There are no historical features with sufficient sensitivity and specificity to either diagnose or exclude acute coronary syndrome. Radiation to the arms and shoulders, particularly to the right arm or both arms, is the historical feature most strongly associated with acute coronary syndrome (likelihood ratio range of 2.3–4.7).[22,24,25] Chest pain with exertion or associated symptoms of dyspnea, diaphoresis, nausea, or vomiting are associated with twofold likelihood of acute coronary syndrome.[24,25] Pressure-like chest sensation has limited value in the prediction of acute coronary syndrome.[22] Sharp, pleuritic, positional chest pain is associated with a decreased likelihood of acute coronary syndrome but cannot eliminate the diagnosis.[22] Lack of exertional pain or pain radiation has no diagnostic value for exclusion of acute coronary syndrome.[22,25] Since classic cardiac ischemic pain is not universal and men and women both present with nonclassic symptoms, the diagnostic utility of specific chest pain descriptions does not differ significantly between men and women.[26] **Tables 48–1** and **48–2** summarize the chest pain characteristics associated with increased or decreased likelihood ratios of acute myocardial infarction.

Table 48–1

Acute Myocardial Infarction Symptoms: Positive Likelihood Ratios[22,24,25]

Pain Descriptor	Study	No. of Patients Studied	Positive Likelihood Ratio (95% Confidence Interval)
Radiation to right arm or shoulder	Chun et al.	770	4.7 (1.9–12.0)
Radiation to both arms or shoulders	Goodacre et al.	893	4.1 (2.5–6.5)
Associated with exertion	Goodacre et al.	893	2.4 (1.5–3.8)
Radiation to left arm	Panju et al.	278	2.3 (1.7–3.1)
Associated with diaphoresis	Panju et al.	8426	2.0 (1.9–2.2)
Associated with nausea or vomiting	Panju et al.	970	1.9 (1.7–2.3)
Worse than previous angina or similar to previous myocardial infarction	Chun et al.	7734	1.8 (1.6–2.0)
Described as pressure	Chun et al.	11,504	1.3 (1.2–1.5)

Table 48–2

AMI Symptoms: Negative Likelihood Ratios[22,25,27]

Pain Descriptor	Study	No. of Patients Studied	Positive Likelihood Ratio (95% Confidence Interval)
Described as pleuritic	Chun et al.	8822	0.2 (0.1–0.3)
Described as positional	Chun et al.	8330	0.3 (0.2–0.5)
Described as sharp	Chun et al.	1088	0.3 (0.2–0.5)
Reproducible with palpation	Chun et al.	8822	0.3 (0.2–0.4)
Reproducible with positioning	Chun et al.	8330	0.3 (0.2–0.5)
Inframammary location	Everts et al.	903	0.8 (0.7–0.9)
Not associated with exertion	Goodacre et al.	893	0.8 (0.6–0.9)

PHYSICAL EXAMINATION

The examination of patients with acute coronary syndrome is often normal, and there are no exam findings that are sensitive or specific enough to exclude or diagnose acute coronary syndrome. Use the exam in conjunction with history to identify or exclude other causes of chest pain and to guide therapy.

Vital sign abnormalities from acute coronary syndrome may include hyper- or hypotension, tachycardia, or bradycardia. Tachycardia may result from increased sympathetic tone and decreased left ventricular stroke volume. Bradycardia may occur due to ischemia or infarction involving the conduction system or alterations in sympathetic and parasympathetic activation of the sinoatrial or atrioventricular nodes. Patients with acute myocardial ischemia or infarction may have abnormal heart sounds due to changes in ventricular function or compliance, such as an S_3 or S_4 gallop, diminished S_1, or a paradoxically split S_2. New murmurs in patients with chest pain may be associated with acute myocardial infarction with chordae tendineae rupture or aortic root dissection. Ischemia-induced congestive heart failure may produce crackles on auscultation of the lungs.

Physical examination findings most strongly associated with acute myocardial infarction in patients presenting with acute chest pain are hypotension, S_3 gallop, and diaphoresis, although the frequency, interrater reliability, and added diagnostic value are limited.[22] Reproducible chest wall tenderness is suggestive of a musculoskeletal etiology but is reported in up to 15% of patients with confirmed acute myocardial infarction and cannot alone exclude the diagnosis of acute coronary syndrome.[28]

RESPONSE TO THERAPY

Response to medications poorly discriminates between cardiac and noncardiac chest pain. While nitroglycerin reduces anginal pain, it may also relieve the pain from noncardiac conditions such as esophageal spasm.[22,29,30,31] Similarly, relief from antacid or combination "GI cocktail" therapy does not represent a noncardiac cause of chest pain.[32,33] Combine the above responses with other features to best assess the likely presence or absence of acute coronary syndrome.

DIAGNOSIS

Life-threatening concerns in acute chest pain are acute coronary syndrome, aortic dissection, pulmonary embolism, pneumonia, tension pneumothorax, and esophageal rupture. Other diagnoses with the potential for morbidity and mortality include simple pneumothorax, myocarditis, pericarditis, aortic stenosis, perforated ulcer, and cholecystitis. Benign causes of chest pain include anxiety, musculoskeletal pain, esophagitis, and gastritis. Common causes of chest pain are listed in **Table 48–3**. **Table 48–4** summarizes the classic symptoms of the life-threatening causes of acute chest pain.

Table 48–3

Common Causes of Acute Chest Pain

Visceral Pain	Pleuritic Pain	Chest Wall Pain
Typical angina	Pulmonary embolism	Costosternal syndrome
Unstable angina	Pneumonia	Costochondritis (Tietze's syndrome)
Acute myocardial infarction	Spontaneous pneumothorax	Precordial catch syndrome
Aortic dissection	Pericarditis	Xiphodynia
Esophageal rupture	Pleurisy	Radicular syndromes
Esophageal reflux or spasm		Intercostal nerve syndromes
Mitral valve prolapse		Fibromyalgia

Table 48–4

Classic Symptoms of Potentially Life-Threatening Causes of Chest Pain*

Disorder	Pain Location	Pain Character	Radiation	Associated Signs and Symptoms
Acute coronary syndrome	Retrosternal, L chest, or epigastric	Crushing, tightness, squeezing, pressure	R or L shoulder, R or L arm/hand, jaw	Dyspnea, diaphoresis, nausea
Pulmonary embolism	Focal chest	Pleuritic	None	Tachycardia, tachypnea, hypoxia, may have hemoptysis
Aortic dissection	Midline, substernal	Ripping, tearing	Intrascapular area of back	Secondary arterial branch occlusion
Pneumonia	Focal chest	Sharp, pleuritic	None	Fever, hypoxia, may see signs of sepsis
Esophageal rupture	Substernal	Sudden, sharp, after forceful vomiting	Back	Dyspnea, diaphoresis, may see signs of sepsis
Pneumothorax	One side of chest	Sudden, sharp, lancinating, pleuritic	Shoulder, back	Dyspnea
Pericarditis	Substernal	Sharp, constant or pleuritic	Back, neck, shoulder	Fever, pericardial friction rub
Perforated peptic ulcer	Epigastric	Severe, sharp	Back, up into chest	Acute distress, diaphoresis

Abbreviations: L = left; R = right.

*Atypical presentations are common.

PULMONARY EMBOLISM

Symptoms of pulmonary embolism include sharp chest pain (may worsen with inspiration, called "pleuritic"), dyspnea, hypoxemia, syncope, or shock. There may be associated cough or hemoptysis. Patients with pulmonary embolism may be febrile and have leg swelling or pain, and some patients will report chest wall tenderness. Common physical examination findings include tachypnea, tachycardia, and hypoxemia. Pulmonary embolism risk factors include recent surgery, trauma, prolonged immobility, active cancer, estrogens from birth control pills or hormone replacement therapy (particularly when combined with smoking), procoagulant syndromes, or a history of prior pulmonary embolism or deep venous thrombosis.[34,35]

Clinical decision aids, such as the **Wells and Revised Geneva Scores,** can risk stratify patients with possible pulmonary embolism.[36,37] The **Pulmonary Embolism Rule-Out Criteria** exclude pulmonary embolism in patients with a low pretest probability without further diagnostic testing.[38] Normal **D-dimer** testing, measured by a sensitive enzyme-linked immunosorbent assay, in a hemodynamically stable low- to intermediate-risk patient (with a Revised Geneva Criteria Score of 0 to 10) makes pulmonary embolism exceptionally unlikely; in those with higher risk assessment, a negative D-dimer has limited value.[39,40] In patients with pulmonary embolism, elevated cardiac troponin (cTn) indicates ventricular dysfunction and identifies patients with an elevated risk of death and complications.[41]

In pulmonary embolism, ECG findings are nonspecific, with the most common finding being sinus tachycardia. Chest radiographs are usually normal, but in rare cases may show signs of pulmonary infarction. CT pulmonary angiography is the test of choice and is highly sensitive for the detection of large to medium-sized pulmonary emboli. See more details on pulmonary embolism in the chapter 56, "Venous Thromboembolism."

AORTIC DISSECTION

Pain from aortic dissection is classically described as a ripping or tearing sensation radiating to the interscapular area of the back. The pain is often sudden in onset, maximal at the time of symptom onset, and may migrate or be noted above and below the diaphragm. Lack of sudden-onset pain decreases the probability of aortic dissection but cannot exclude it.[42] Secondary symptoms of aortic dissection result from arterial branch occlusions and include stroke, acute myocardial infarction, or limb ischemia. Risk factors include male sex, age over 50 years, poorly controlled hypertension, cocaine or amphetamine use, a bicuspid aortic valve or prior aortic valve replacement, connective tissue disorders (Marfan's syndrome and Ehlers-Danlos syndrome), and pregnancy.[43]

Physical exam findings for aortic dissection lack sensitivity and specificity. A unilateral pulse deficit of the carotid, radial, or femoral arteries is suggestive of aortic dissection (likelihood ratio 5.7; 95% confidence interval, 1.4–23).[42] Focal neurologic deficits are rare, occurring in only 17% of patients with aortic dissection, but the combination of chest pain and a focal neurologic deficit greatly increase the likelihood of aortic dissection.[42] While a completely normal chest radiograph lowers the likelihood of aortic dissection being present, it does not exclude dissection. A negative **D-dimer** lowers the probability of aortic dissection (detecting the clotting/declotting expected), but it also cannot exclude the disease.[44] ECG changes are

common among patients with aortic dissection, with up to 40% to 50% presenting with ST-segment or T-wave changes.[45,46] Elevated cTn among patients with aortic dissection is associated with increased mortality.[47] If aortic dissection is suspected, obtain a CT aortogram or transesophageal echocardiogram. See chapter 59, "Aortic Dissection and Related Aortic Syndromes."

PNEUMONIA

Pneumonia is potentially life threatening in the elderly, immunocompromised, or patients with multiple comorbid conditions. Chest pain from pneumonia is usually described as sharp, pleuritic, and associated with fever, cough, sputum production, and possibly hypoxemia.[48] Auscultation may reveal decreased breath sounds, rales, or bronchial breath sounds over the affected areas of consolidation. A chest radiograph usually confirms the diagnosis. See chapter 65, "Pneumonia and Pulmonary Infiltrates."

ESOPHAGEAL RUPTURE (BOERHAAVE'S SYNDROME)

Patients classically present with a history of sudden-onset, sharp, substernal chest pain following forceful vomiting. Patients with esophageal rupture are usually ill-appearing and may be tachycardic, febrile, dyspneic, or diaphoretic. Physical examination may reveal crepitus in the neck or chest from subcutaneous emphysema. **Hamman's crunch**, audible crepitus that varies with the heartbeat on auscultation of the precordium, is a rare finding associated with pneumomediastinum. Chest radiography may demonstrate a pleural effusion (left more common than right), pneumothorax, pneumomediastinum, pneumoperitoneum, or subcutaneous air, although a normal x-ray cannot exclude esophageal rupture. If esophageal rupture is suspected, obtain a CT with oral water-soluble contrast. See chapter 77, "Esophageal Emergencies."

SPONTANEOUS PNEUMOTHORAX

The symptoms of spontaneous pneumothorax are sudden-onset, sharp, pleuritic chest pain with dyspnea. Classically, spontaneous pneumothorax occurs in tall, slender males. Risk factors for spontaneous pneumothorax include smoking and chronic lung diseases such as asthma and chronic obstructive pulmonary disease. Approximately 1% to 3% of patients with a spontaneous pneumothorax progress to develop a tension pneumothorax.[49] Auscultation may reveal decreased breath sounds and hyperresonance to percussion on the ipsilateral side. However, the physical exam findings of a simple pneumothorax are inconstant and cannot be used to exclude presence, with the diagnosis made by chest radiography. See chapter 68, "Pneumothorax."

ACUTE PERICARDITIS

Pain from acute pericarditis is classically described as a sharp, severe, constant pain with a substernal location. The pain may radiate to the back, neck, or shoulders; worsens by lying flat and by inspiration; and is relieved by sitting up and leaning forward. A pericardial friction rub is the most specific physical exam finding but is not always evident. The classic ECG findings are diffuse ST-segment elevation with PR depression.[50] See chapter 55, "Cardiomyopathies and Pericardial Disease."

MITRAL VALVE PROLAPSE

Symptoms attributed to mitral valve prolapse include sharp chest pain, palpitations, fatigue, anxiety, and dyspnea unrelated to exertion. A midsystolic click may be heard on auscultation. However, most patients are asymptomatic and have no consistent association of chest pain, dyspnea, or anxiety with the disorder.[51,52] See chapter 54, "Valvular Emergencies."

CHEST WALL PAIN

Musculoskeletal or chest wall pain is characterized by sharp, highly localized, and positional pain. The pain should be completely reproducible by light to moderate palpation or by specific movements and may be increased by inspiration or coughing. However, chest wall tenderness is also reported by some patients with acute coronary syndrome and pulmonary embolism. **Costochondritis (Tietze's syndrome)** is an inflammation of the costal cartilages or their sternal articulations and causes chest pain that is variably sharp, dull, and often increased with respirations. **Xiphodynia** is inflammation of the xiphoid process that causes sharp, pleuritic chest pain reproduced by light palpation. **Precordial catch syndrome** is a short, lancinating chest pain occurring in bunches lasting 1 to 2 minutes near the cardiac apex and is associated with inspiration, poor posture, and inactivity. *Pleurisy* is inflammation of the parietal pleura resulting in sharp pleuritic chest pain.

GI PAIN

GI disorders often cannot be reliably differentiated from acute coronary syndrome by history and physical examination alone.[25,53] **Gastritis** and **esophageal reflux** typically produce burning or gnawing pain in the lower half of the chest, with a brackish or acidic taste in the back of the mouth. The pain may be lessened with antacids and exacerbated by recumbency. **Peptic ulcer disease** is classically described as a postprandial, dull, boring pain in the epigastric region. Patients often describe being awakened from sleep by discomfort. Duodenal ulcer pain may be relieved after eating food, whereas gastric ulcer pain is often exacerbated by eating. Antacid medications usually provide symptomatic relief. **Acute pancreatitis** and **biliary disease** typically present with right upper quadrant or epigastric pain and tenderness but can also cause chest pain. *Esophageal spasm* is often associated with reflux disease and is characterized by a sudden onset of dull or tight substernal chest pain. The pain is frequently precipitated by consumption of hot or cold liquids or a large food bolus and may be relieved by nitroglycerin. See chapter 77, "Esophageal Emergencies" and 78, "Peptic Ulcer Disease and Gastritis."

PANIC DISORDER

Panic disorder is characterized by recurrent, unexpected, and discrete periods of intense fear or discomfort (panic attacks) with at least four of the following symptoms: chest pain, dyspnea, palpitations, diaphoresis, nausea, tremor, choking, dizziness, fear of losing control or dying, paresthesias, chills, or hot flashes. In one study, 25% of ED patients with chest pain met diagnostic criteria for panic disorder. Conversely, 9% of the patients identified as having panic disorder were ultimately diagnosed with acute coronary syndrome on hospital discharge.[54] This means panic disorder is at best a diagnosis of exclusion or a co-diagnosis with acute coronary syndrome (or another cause). Do not assume panic disorder in a patient with chest pain in the ED until further testing allows better risk stratification. See chapter 289, "Mood and Anxiety Disorders."

DIAGNOSTIC TESTING

Focus initial diagnostic testing for patients with chest pain on the exclusion or confirmation of serious pathology based on the differential diagnosis drawn from the history and physical examination. When history and exam make acute coronary syndrome a potential cause, testing commonly includes an ECG, chest x-ray, and cardiac biomarkers. Stress testing, advanced cardiac imaging, serial or continuous ECG monitoring, and serial cardiac biomarker measurements are discussed in chapter 49, "Acute Coronary Syndromes."

IMAGING

Chest radiography is commonly performed in the evaluation of ED patients with chest pain. Most patients with acute coronary syndrome have a normal chest x-ray, but the images are useful to diagnose or exclude other conditions such as pneumonia and pneumothorax.[55] Other imaging modalities such as CT help evaluate conditions such as aortic dissection or pulmonary embolism.

ECG

Guidelines recommend a screening ECG within 10 minutes of ED arrival on patients with chest pain or other symptoms concerning for acute coronary syndrome.[56] Rapid ECG screening is essential because delay in identification of an ST-segment elevation myocardial infarction is associated with increased mortality.[57] Routine triage ECG testing and prehospital ECG transmission reduce delays to ST-segment elevation myocardial infarction identification, decrease door-to-balloon or door-to-needle time, and improve patient outcomes.[58,59,60,61]

Less than 5% of patients presenting to the ED with chest pain have evidence of an ST-segment elevation myocardial infarction on ECG.[62,63] However, new ST-segment elevation of ≥1 mm in at least two contiguous leads represents an acute myocardial infarction that will benefit from rapid reperfusion interventions.[22,64] ST-segment elevation also occurs in patients with pericarditis, myocarditis, early repolarization, left ventricular hypertrophy, and ventricular aneurysms. ST-segment depression and T-wave inversions are also associated with an increase in risk of acute myocardial infarction.[22,65]

A normal ECG lacks the sensitivity to exclude acute coronary syndrome, notably unstable angina, or non-ST-segment elevation myocardial infarction. In a large multicenter observational study of 391,208 patients with an evaluable ECG and diagnosis of acute myocardial infarction, 57% had "diagnostic" ECG changes, 35% had nonspecific changes, and 8% had normal ECGs. Diagnostic changes were defined as ST-segment elevation, ST-segment depression, or left bundle-branch block.[66] Other studies document normal or near normal ECGs in 5% to 10% of patients with acute myocardial infarction.[67,68,69,70] A normal ECG is also an independent risk factor for missed acute myocardial infarction and inappropriate ED discharge (odds ratio 7.7; 95% confidence interval, 2.9–20.2).[2] However, among young patients (<40 years old) without known coronary artery disease, a normal ECG is associated with a cardiovascular event rate of less than 1% at 30 days.[71]

Misinterpretation of ECGs (i.e., failure to detect ischemic changes that are present) occurs in up to 40% of missed acute myocardial infarction cases.[70] In addition, the initial ECG represents only a single time point in a dynamic pathophysiologic process; the diagnostic value of an ECG is improved by comparing it to a prior ECG or repeating it.[72]

CARDIAC BIOMARKERS

Cardiac Troponins

Cardiac cTns are proteins essential to cardiac muscle contraction, which are complexed with actin and myosin filaments within cardiac myofibrils and are present within cardiac myocyte cytoplasm.[73] Myocardial injury resulting in the disruption of myocyte cell membrane integrity or myofibril destruction results in extracellular cTn leak, which can be detected in the patient's peripheral blood and used to identify and quantify myocardial damage.[74] Due to its high sensitivity and nearly complete cardiac specificity, cTn is the biomarker of choice for the detection of myocardial injury.[75]

Although cTn elevation is specific for myocardial necrosis, elevation does not indicate the mechanism of injury, nor does it necessarily indicate acute myocardial infarction. There are numerous nonischemic causes of cTn elevations, which are summarized in **Table 48–5**. Acute myocardial infarction can be differentiated from nonischemic cTn elevations based on the pattern of cTn elevation and the clinical context. The diagnostic criteria for acute myocardial infarction include a gradual rise and fall of cTn with a maximum value above the 99th percentile of a reference population (the upper reference limit), combined with any of the following: symptoms consistent with ischemia, characteristic acute ECG changes (ST- and T-wave changes, new left bundle-branch block, or new Q waves), or imaging evidence of a new regional wall motion abnormality or new loss of viable myocardium.[76]

Table 48–5

Conditions Associated with Elevated Cardiac Troponin Levels inthe Absence of Ischemic Heart Disease

Cardiac contusion
Cardiac procedures (surgery, ablation, pacing, stenting)
Acute or chronic congestive heart failure
Aortic dissection
Aortic valve disease
Hypertrophic cardiomyopathy
Arrhythmias (tachyarrhythmia or bradyarrhythmia)
Apical ballooning syndrome
Rhabdomyolysis with cardiac injury
Pulmonary hypertension
Pulmonary embolism
Acute neurologic disease (e.g., stroke, subarachnoid hemorrhage)
Myocardial infiltrative diseases (amyloid, sarcoid, hemochromatosis, scleroderma)
Inflammatory cardiac diseases (myocarditis, endocarditis, pericarditis)
Drug toxicity
Respiratory failure
Sepsis
Burns
Extreme exertion (e.g., endurance athletes)

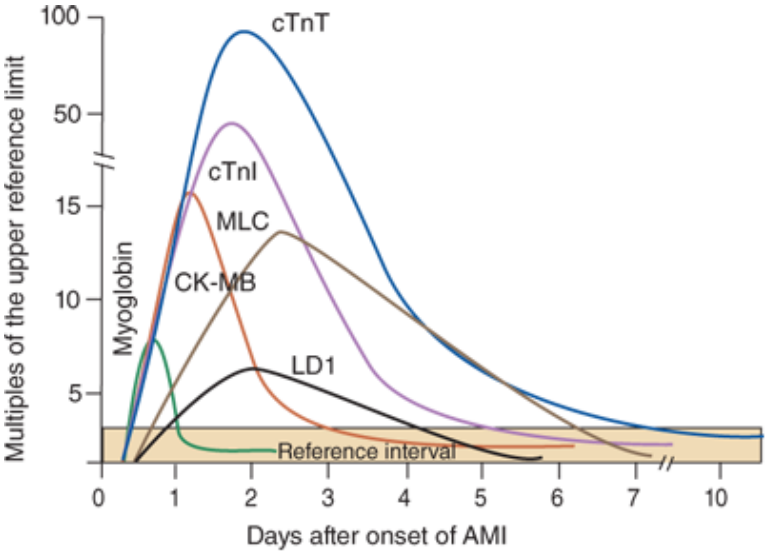
Immunoassays have been developed for the isoforms of cTnI and cTnT. Isoforms I and T provide nearly identical information, and selection between them is driven mainly by central laboratory vendor and equipment preference.[77] A single manufacturer produces the cTnT assay; however, multiple manufacturers produce cTnI assays, which differ in their upper reference limits (the cTn value above the 99th percentile of a reference population), coefficients of variability, and lower limits of detection.

Over the past 25 years, cTn assays have become more analytically sensitive, pushing down the upper reference limits (URLs) and limits of detection. For example, a "first-generation" assay, available in 1995, had a URL of 0.4 nanograms/mL, whereas a commonly used contemporary (current-generation) assay has a 10-fold lower URL (0.04 nanograms/mL).[78,79] Current commercially available contemporary cTn assays have URLs ranging from 0.023 to 0.20 nanograms/mL and lower limits of detection ranging from 0.006 to 0.15 nanograms/mL.[80] Point-of-care assays offer a shorter turnaround time but with slightly lower analytic sensitivities than conventional assays.[76,81]

With contemporary assays, cTn is detected in serum as early as 2 hours after symptom onset of an acute myocardial infarction, but elevations are not reliably present until 6 hours or more.[82] Elevations peak at approximately 48 hours from symptom onset unless repeat injury occurs, and cTns remain elevated for up to 10 days (**Figure 48–1**). This persistence makes cTn a good tool in diagnosing acute myocardial

infarction in patients with delayed presentations. However, in patients with intermittent symptoms over a period of days, an elevated cTn could represent a remote or new infarct. In this rare setting, the concomitant use of creatine kinase-MB fraction, which returns to normal sooner, can help differentiate acute from remote infarction.

FIGURE 48–1.
Typical pattern of contemporary serum marker elevation after acute myocardial infarction (AMI). CK-MB = MB fraction of creatine kinase; cTnI = cardiac troponin I; cTnT = cardiac troponin T; LD1 = lactate dehydrogenase isoenzyme 1; MLC = myosin light chain.



Obtain cardiac cTn levels in all patients with suspected acute coronary syndrome.[55] Contemporary cTn assays will identify most patients (approximately 80%) with acute myocardial infarction within 2 to 3 hours of ED arrival.[82,83,84] Patients with early presentations (within 6 hours of symptom onset) or those with intermittent symptoms should have serial measurements of cTn over time. In patients with constant symptoms for >8 to 12 hours, a single cTn may be sufficient to exclude acute myocardial infarction.[56,85] Measurement of cTn at short time intervals, such as 2 to 4 hours, to evaluate for serial change (delta cTn) is more sensitive for acute myocardial infarction than a single cTn approach.[55]

Newer high-sensitivity cTn assays have a 10-fold higher analytical sensitivity compared to contemporary assays; these are currently pending U.S. Food and Drug Administration approval.[80,87,88] Compared with contemporary assays, high-sensitivity cTn assays are more sensitive for the detection of acute myocardial infarction in all patients (94% to 96% vs. 85% to 90%) and increase the early detection of myocardial injury.[83,84] Among patients presenting within 3 hours of chest pain onset, high-sensitivity cTn assays are 92% to 94% sensitive for acute myocardial infarction compared to 76% for a contemporary assay.[83] However, the increased sensitivity of high-sensitivity cTn assays for acute myocardial infarction is balanced by the detection of more patients with non–acute myocardial infarction cTn elevations.[83,88] The overall impact on ED decision making and ultimate outcome is not yet defined or shown to be clearly superior to previous assay use.

An elevated cTn is associated with an increased risk of cardiac death or acute myocardial infarction at 30 days (odds ratio 3.4; 95% confidence interval, 2.9–4.0).[89] This elevated risk of death or cardiovascular complications is independent of ECG findings or creatine kinase-MB levels.[90] Higher cTn elevations also are associated with more adverse events, even with minimal elevations.[91]

Patients with **renal disease** often have an elevated cTnT (15% to 50%), whereas cTnI elevations are less common (<10%). After dialysis, serum levels of cTnT generally increase while cTnI levels decrease.[92] Despite these features, cTnT and cTnI assays remain highly sensitive for acute myocardial infarction in patients with renal failure, particularly when new measures can be compared with baseline measures. Furthermore, renal failure patients with elevated cTn levels are at higher risk for death and adverse events than patients with normal cTn levels.[93]

Creatine Kinase-MB and Myoglobin

Troponin testing has made these markers almost obsolete in acute coronary syndrome care. **Creatine kinase-MB** fraction levels elevate within 4 to 8 hours after acute myocardial infarction, peak between 12 and 24 hours, and return to normal between 36 and 72 hours (Figure 48–1). When used with cTn, creatine kinase-MB provides little additional information.[94] Creatine kinase-MB testing may be useful in a small subset of patients in whom the timing of infarction is unclear. Elevated creatine kinase-MB and cTn indicate an acute infarct, whereas a negative creatine kinase-MB with an elevated cTn suggests a remote or subacute infarction.

Myoglobin is a small heme-containing protein found in skeletal and cardiac muscle. After acute myocardial infarction, serum myoglobin levels rise within 3 hours of symptoms, peak at 4 to 9 hours, and return to baseline within 24 hours (Figure 48–1). False-positive results are common, and false-negative results may occur in patients with delayed presentations. Due to the improved sensitivity of contemporary cTn assays, myoglobin does not appear to have added value in the early detection of acute myocardial infarction.[95]

B-Type Natriuretic Peptide

Natriuretic peptide elevations are not specific to myocardial ischemia or infarction and will rise with any ventricular dysfunction. Patients with acute coronary syndrome and an elevated natriuretic peptide level have higher short-term mortality, although the lab test does not aid in specific patient management actions.

Other Biomarkers

High-sensitivity C-reactive protein aids long-term cardiac event prediction, but this test is not recommended for ED care.[54] A variety of other assays have been studied as cardiac biomarkers, such as ischemia-modified albumin, interleukin-6, vascular cell adhesion molecule, intercellular adhesion molecule, E-selectin, P-selectin, pregnancy-associated plasma protein A, and myeloperoxidase. Current evidence does not support the use of these novel biomarkers for ED chest pain evaluations.

CLINICAL RISK SCORES AND DECISION AIDS

The **Thrombosis in Myocardial Infarction** risk score or **Global Registry of Acute Coronary Events** score can aid acute coronary syndrome risk stratification (**Figure 48–2**).[56] The Thrombosis in Myocardial Infarction and Global Registry of Acute Coronary Events scores were drawn from groups with acute coronary syndrome present or strongly suspected, and then were applied to a wider population. Each stratifies patients into low-, intermediate-, or high-risk groups for acute coronary syndrome. However, a low-risk score is not sensitive enough to exclude acute coronary syndrome or identify patients for early discharge without further evaluation.[96,97]

FIGURE 48–2.
Thrombosis in Myocardial Infarction (TIMI) score and the Global Registry of Acute Coronary Events (GRACE) score. ACS = acute coronary syndrome; Cr = creatinine; HR = heart rate; SBP = systolic blood pressure.

TIMI Score	Yes 1 point	No 0 points
Age ≥65		
≥3 Risk factors for ACS; hypertension, hyperlipidemia, smoking, diabetes, family history		
Use of aspirin in last 7 days		
Prior coronary stenosis >50%		
≥2 angina events in 24 hours or persisting discomfort		
ST-segment deviation of ≥0.05 mV on initial ECG		
Elevated cardiac biomarkers		
Total Score		

Low Risk	0-2
Intermediate Risk	3-4
High Risk	5-7

GRACE Score									
Age	Points	**HR**	Points	**SBP**	Points	**Cr**	Points	**Killip Class**	Points
<39	0	<70	0	<80	40	0.0-0.39	1	I	0
40-49	18	70-89	5	80-99	37	0.4-0.79	4	II	15
50-59	36	90-109	10	100-119	30	0.8-1.19	7	III	29
60-69	55	110-149	17	120-139	23	1.2-159	10	IV	44
70-79	73	150-199	26	140-159	17	1.6-1.99	13	**Cardiac arrest**	30
80-89	91	≥200	34	160-199	7	2.0-3.99	21	**Elevated cardiac markers**	13
>90	100	-	-	≥200	0	≥4	28	**St-segment deviation**	17

Low Risk	1-88
Intermediate Risk	89-118
High Risk	≥119

The **HEART** score, **ADAPT**, and the **North American Chest Pain Rule** (**Figure 48–3**) combine clinical information to risk stratify patients and guide key decisions, notably discharge with follow-up for the lowest risk patients or observation/admission for the remaining patients. Although these decision support tools may improve the quality and efficiency of chest pain care in the ED, they require further impact assessment before routine use.[98,99,100]

FIGURE 48–3.

ADAPT, the North American Chest Pain Rule (NACPR), and the HEART score. With ADAPT and NACPR, a patient is considered low risk if the patient has none of the high-risk criteria. For ADAPT, risk factors include family history of coronary disease, hypertension, hypercholesterolemia, diabetes mellitus, and current smoker. With the HEART score, low risk is a score of 0 to 3, and high risk is a score of 4 or greater. Risk factors include currently treated diabetes mellitus, current or recent (<90 days) smoker, diagnosed and/or treated hypertension, diagnosed hypercholesterolemia, family history of coronary artery disease, obesity (body mass index >30), or a history of significant atherosclerosis (coronary revascularization, myocardial infarction, stroke, or peripheral arterial disease). ACS = acute coronary syndrome; TIMI = Thrombosis in Myocardial Infarction score.

ADAPT		
High risk criteria	**Yes**	**No**
1. TIMI Score >0		
a. Age ≥65		
b. ≥3 Risk factors		
c. Use of aspirin in last 7 days		
d. Significant coronary stenosis (prior stenosis ≥50%)		
e. ≥2 angina events in 24 hours or persisting discomfort		
f. ST-segment deviation of ≥0.05 mV on initial ECG		
g. Increased initial troponin		
2. Positive troponin test at 0 or 2 hours		
3. New ischemic ECG changes		

HEART Score		Points
History	Highly Suspicious	2
	Moderately Suspicious	1
	Slightly Suspicious	0
ECG	Significant ST-depression	2
	Non-specific repolarization abnormality	1
	Normal	0
Age	≥65	2
	45-65	1
	≤45	0
Risk factors	3 or more risk factors	2
	1-2 risk factors	1
	No risk factors	0
Troponin	≥3× normal limit	2
	1-3× normal limit	1
	≤ normal limit	0
Total		

North American Chest Pain Rule		
High risk criteria	**Yes**	**No**
Age ≥50		
Acute ischemic ECG changes		
Known coronary artery disease		
Pain typical for ACS		
Any troponin >99th percentile		

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