Diagnosis and Early Management of Chest Pain and Acute Coronary Syndromes

Series Editor and Author:
Kendal Williams, MD, MPH
Clinical Assistant Professor
University of Pennsylvania School of Medicine
Philadelphia, PA

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Cover Illustration by brand x pictures
**INTRODUCTION**

Despite significant advances in the prevention, diagnosis, and treatment of coronary artery disease (CAD), it remains the leading cause of mortality in the Western world and is having an increasing impact on developing countries. The majority of patients with CAD will at some point experience an acute coronary syndrome (ACS)—unstable angina (UA), non–ST segment myocardial infarction (NSTEMI), or ST segment myocardial infarction (STEMI). ACS represents the rupture of an unstable cholesterol plaque, resulting in complete or near-complete obstruction of the coronary lumen with the potential for downstream ischemia. In most cases, these patients will present with the syndrome of “chest pain” and require further evaluation to determine the best management strategy. This manual focuses on the diagnosis, classification, and early management of chest pain and ACS. Part 2 of this volume will discuss the therapeutic advances that are at long last reducing the case-fatality rate of this devastating disease.

**CASE STUDY**

**INITIAL PRESENTATION**

A 68-year-old woman with a history of chronic obstructive pulmonary disease, hypertension, and anxiety presents to the emergency department (ED) complaining of intermittent chest discomfort for the past 3 weeks.

**HISTORY**

The patient describes her pain as a “tightness” that begins in her mid-chest and radiates to her neck and jaw and is associated with nausea and palpitations. She denies shortness of breath, diaphoresis, or vomiting but does admit to feeling “anxious” when the pain occurs. There is no radiation to her shoulder or arms. The pain first occurred while the patient was cooking and was minimally relieved when she took her sister’s sublingual nitroglycerin. She has experienced multiple similar episodes since then, each lasting a minute or two, but none have been as severe or prolonged as the first. There is no exertional component. The last episode occurred 6 hours prior to presentation, and the patient has been free from chest pain since then.

The patient reports that she is a 50 pack-year smoker and that both a brother and sister had myocardial infarctions (MI) in their sixth decade. She cannot recall her serum cholesterol values from her last lipid profile. Her only medications are an albuterol metered-dose inhaler as needed and hydrochlorothiazide.

**PHYSICAL EXAMINATION**

Physical examination reveals a well-nourished, well-developed, pleasant but anxious-appearing woman in no apparent distress. Her blood pressure is 156/94 mm Hg, heart rate is 76 bpm, respiratory rate is 20 bpm, and oxygen saturation is 92% on room air. Jugular venous pulse is appreciated and normal at 9 cm. Chest examination reveals mildly increased anteroposterior diameter with slight end-expiratory wheezes and prolonged expiratory phase but no rales or rhonchi. Heart sounds are normal with an S1 and S2 and no evidence of S3, S4, murmurs, or rub. Her carotid pulses are brisk. Abdominal, extremity, and skin examinations are normal.

- **What are initial steps in the evaluation of the patient with chest pain?**

**EARLY ASSESSMENT**

The chest pain symptom complex presents a unique challenge because it is extremely common but also may be the harbinger of acute life-threatening illness that will require immediate intervention. The first goal of the initial evaluation is to distinguish potentially lethal diagnoses, particularly ACS, pulmonary embolus, aortic dissection, and pneumothorax, from each other and from the more common benign causes of anterior
CHEST PAIN AND ACUTE CORONARY SYNDROMES

Any patient presenting to the ED complaining of chest pain should have a brief history, physical examination, and electrocardiogram (ECG) done within minutes. Although patients presenting to outpatient clinics with chest pain have a higher prevalence of benign and chronic causes, any patient complaining of chest pain of acute onset should be evaluated promptly. Upon arrival in the evaluation room, vital signs, including blood pressure in both arms, should be recorded. The physical examination should focus on the cardiopulmonary system, looking for decreased breath sounds from pneumothorax, evidence of congestive heart failure, or a pericardial friction rub. The presence of an S3 has been shown to raise the likelihood of coronary ischemia. An S4 has classically been described in patients with MI because of decreased left ventricular wall compliance, but it is probably most helpful as a sign of left ventricular hypertrophy (LVH), the presence of which can occasionally confound the ECG reading for ischemia. A short, mid or late systolic mitral regurgitation murmur can be seen in an MI with mitral valve compromise, but it is more important to ascertain the presence of a murmur and carotid pulse findings suggestive of advanced aortic stenosis. The carotid pulsation in a patient with severe aortic stenosis will be slow and delayed, whereas the more benign aortic sclerosis will not exhibit any carotid pulse findings. If severe or critical aortic stenosis is present, the use of nitroglycerin will reduce preload and could worsen any ischemia that might be present, possibly spiraling the patient into irreversible hypotension.

The interview of a patient with chest pain should begin with open-ended questions that allow the patient to describe their symptoms without prompting or interruption, such as “Can you please tell me about your chest pain?” As the interview proceeds and the physician seeks to clarify historical information, the questions should become more pointed, with either yes/no or menu-type options. The type of onset, duration, nature, and location of the discomfort as well as any associated symptoms (nausea, diaphoresis, dyspnea) should be assessed.

The history of a patient with chest pain also should include an assessment for CAD risk factors and other comorbidities. However, the well-known predictors of CAD in population-based studies (ie, elevated cholesterol, hypertension, family history of CAD, and smoking) have not been shown to predict cardiac ischemia in the acute setting, with the notable exception of a personal history of CAD. Thus, when evaluating a patient with chest pain concerning for ischemia, physicians should put the most weight on the patient’s symptoms, signs, and ECG findings. The comorbidities of diabetes and hypertension do confer a poorer prognosis for patients who have an ACS and should be noted. Once the initial history and physical exam are complete, the physician should have developed a presumptive impression as to the probability of an ACS and the other life-threatening diagnoses.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of acute chest pain is quite broad. Only those entities considered immediately life-threatening will be discussed here, with particular focus on the distinctive presenting features of pulmonary embolism, thoracic artery dissection, and ACS.

Classically, the chest pain of ACS has been described as a pressure or tightness felt in the substernal location or left chest with or without radiation of the pain to the shoulders, left arm, or throat. There may be associated dyspnea, nausea, vomiting, or diaphoresis. The relief of pain with nitroglycerin has traditionally been thought to be virtually diagnostic of ischemia. While this classical description of angina holds true in many cases, a large minority of patients will present with atypical symptoms. In addition, even within the categories of myocardial ischemia (ie, stable angina, UA, and MI), patients may present with various degrees of chest discomfort and associated symptoms. Indeed, some patients with ischemia have no pain at all. Absence of pain is more frequent in the elderly at the extreme of age and in diabetics but can be seen in any patient group.

Numerous studies have been performed to refine our ability to distinguish cardiac ischemia from other causes of chest pain. These have been summarized in 2 recent systematic reviews. The first review—from the Journal of the American Medical Association’s “Rational Clinical Examination” series—showed that the most helpful historical feature predictive of an acute MI is radiation of pain to the arm and shoulder (Table 1). Surprisingly, radiation to the right shoulder is more suggestive than radiation to the left, with radiation to both simultaneously being the most predictive. Nausea, vomiting, and diaphoresis increase the odds of an acute MI by twofold. Chest pain that is pleuritic, sharp, stabbing, positional, or reproduced by palpation reduces the likelihood of ischemia (Table 2). It does not rule out ischemia, however, and it is important to note that a small minority of patients with an ACS will describe their pain in this way.

Contrary to the traditional teaching, one recent study concluded that the response of chest pain to
nitroglycerin does not predict the presence of active CAD. It has also been shown that esophageal spasm, a well-known mimic of ischemia, also responds to nitroglycerin. Until further work is done in this area, it would be prudent not to rely heavily on this traditional clinical marker. Little data exist regarding the predictive ability of the duration of pain. One study found that pain lasting longer than 30 minutes without other evidence of MI reduced the likelihood of ischemia a significant degree (negative likelihood ratio = 0.1), whereas pain less than 5 minutes increased the odds (positive likelihood ratio = 2.4). The old saying that “pain that lasts less than a minute is not angina, and pain that lasts greater than 20 minutes is either an MI or nonischemic” likely still holds true. Finally, clinicians probably underappreciate the constitutional symptoms of malaise, fatigue, and weakness in acute ischemia, although they have been reported to occur in up to 40% of MI patients.

Pulmonary embolism can present with either dyspnea or acute chest discomfort that is often described as “sharp” and pleuritic. Unfortunately, no symptoms or signs commonly associated with pulmonary embolism (pleuritic chest pain, dyspnea, tachycardia) have been shown to be specific for the diagnosis, and the pretest probability ultimately is determined by the presence of risk factors for venous thromboembolism.

Thoracic aortic dissection can be similarly difficult to detect by history alone. Only approximately one third of thoracic dissections are suspected on initial evaluation, resulting in diagnostic delays that frequently exceed 24 hours. Approximately 90% of patients experience some form of sudden-onset chest or back pain, which one third of patients will describe as “ripping” or “tearing.” The absence of sudden-onset pain can be helpful in ruling out the diagnosis, but no other historical feature is meaningful. The presence of pulse deficits or focal neurologic deficits are suggestive when they are present, but frequently they are not.

If there is concern for pulmonary embolus and/or thoracic dissection, a contrasted computed tomography (CT) scan, if available, or a ventilation/perfusion scan should be performed. Magnetic resonance imaging and transesophageal echocardiography are also appropriate if there is a high level of suspicion for dissection.

**Considerations in Specific Groups**

As discussed, atypical presentations of ACS are not unusual, particularly in women. Compared with men, women with ACS are more likely to present with greater emphasis on the associated symptoms—nausea, vomiting, and dyspnea. Chest pain with exertion, a clinical sign that suggests angina in men, is less helpful in women as they frequently experience ischemic chest

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**Table 1. Clinical Features that Increase the Probability of a Myocardial Infarction in Patients Presenting with Acute Chest Pain**

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Likelihood Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain in chest or left arm</td>
<td>2.7*</td>
</tr>
<tr>
<td>Chest pain radiation</td>
<td></td>
</tr>
<tr>
<td>Right shoulder</td>
<td>2.9 (1.4–6.0)</td>
</tr>
<tr>
<td>Left arm</td>
<td>2.3 (1.7–3.1)</td>
</tr>
<tr>
<td>Both left and right arm</td>
<td>7.1 (3.6–14.2)</td>
</tr>
<tr>
<td>Chest pain most important symptom</td>
<td>2.0*</td>
</tr>
<tr>
<td>History of myocardial infarction</td>
<td>1.5–3.0†</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>1.9 (1.7–2.3)</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>2.0 (1.9–2.2)</td>
</tr>
<tr>
<td>S3 on auscultation</td>
<td>3.2 (1.6–6.5)</td>
</tr>
<tr>
<td>Hypotension (systolic blood pressure, ≤ 80 mm Hg)</td>
<td>3.1 (1.8–5.2)</td>
</tr>
<tr>
<td>Pulmonary crackles on auscultation</td>
<td>2.1 (1.4–3.1)</td>
</tr>
</tbody>
</table>

*Data not available to calculate confidence intervals.
†In heterogeneous studies, the likelihood ratios are reported as ranges.

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**Table 2. Clinical Features that Decrease the Probability of a Myocardial Infarction in Patients Presenting with Acute Chest Pain**

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Likelihood Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleuritic chest pain</td>
<td>0.2 (0.2–0.3)</td>
</tr>
<tr>
<td>Chest pain sharp or stabbing</td>
<td>0.3 (0.2–0.5)</td>
</tr>
<tr>
<td>Positional chest pain</td>
<td>0.3 (0.2–0.4)</td>
</tr>
<tr>
<td>Chest pain reproduced by palpation</td>
<td>0.2–0.4*</td>
</tr>
</tbody>
</table>

*In heterogeneous studies, the likelihood ratios are reported as ranges.
pain at rest. Overall, women experience more frequent “atypical” chest pains from vasospasm, microvascular angina, or other nonischemic causes of pain (eg, mitral valve prolapse, anxiety), making it more difficult to detect angina when it is present. When women do have an ACS, they are more likely than men to present with UA or NSTEMI than STEMI.7 Thus, physicians should be careful not to discount atypical presentations in women as they are in fact normative.

Younger patients (age < 40 years) with chest pain also represent a distinct group. Pneumothorax and pulmonary embolism remain in the differential diagnosis, but aortic dissection is less likely in younger people unless there is a predisposing condition (ie, Marfan’s syndrome). In a retrospective study of young patients (age < 40 years) presenting to the ED with an acute MI,12 90% of patients had substernal chest pain and 80% had radiation to the shoulders, arms, or jaw; 80.8% were male and 81.3% were smokers. The high prevalence of smoking in younger patients with acute MI has also been seen in other studies.

Younger patients are also more likely to have used illicit drugs, particularly cocaine. The management of “cocaine chest pain” is different from routine chest pain in that the sensitivity of the history and the ECG for myocardial ischemia is reduced and creatine kinase (CK) levels and MB fraction are often elevated from rhabdomyolysis.13,14 For these reasons, patients with chest pain related to cocaine use often require hospital admission or more extended observation periods (12 hours) until serial troponin measurements are obtained. In principle, β blockers should be avoided, although there is little empirical evidence from human studies on this issue.10

**PHYSICIAN’S IMPRESSION AND ECG RESULTS**

The case patient’s history has some features that raise the probability of ischemia, including the description of her pain as “tightness,” the radiation to the jaw, and the associated diaphoresis. The fact that she had some relief with nitroglycerin adds little diagnostic value. The lack of an exertional component is similarly unhelpful in women. There is little in the history to clearly suggest pulmonary embolism or aortic dissection but little to rule them out as well. The ECG done promptly upon the patient’s arrival in the ED reveals a normal sinus rhythm, normal axis, and normal intervals. There is no evidence of ST elevation or depression, but there are T wave inversions in the lateral leads (V4–V6).

- What is the role of ECG in evaluation of chest pain?

The ECG is the most important single diagnostic test in the initial evaluation of acute chest pain. It should be done immediately following the physical exam and within 10 minutes of patient arrival. Both a misunderstanding of the ECG manifestations of ischemia and ischemia mimics as well as a misplaced appreciation of ECG findings in the diagnostic reasoning process can lead to error (see pages 6 and 7 for “Essentials of Diagnostic Reasoning”). Like any diagnostic test in clinical medicine, ECG findings are not diagnostic in themselves but simply serve to raise or lower the probability of the suspected disease and must be interpreted in the context of the patient’s overall symptoms and signs. ECG findings in patients with acute chest pain fall into 4 basic categories:

1. Findings highly suggestive of an ACS requiring immediate intervention:
   - ST elevations greater than 1 mm in 2 contiguous anatomic leads
   - New left bundle branch block (LBBB) in a patient with an otherwise high probability for an ACS

2. Findings suggestive of an ACS requiring consideration of the initiation of anti-ischemic therapy:
   - ST depressions
   - T wave inversions

3. Findings suggestive of a diagnosis other than acute coronary ischemia:
   - For example, diffuse ST elevations of pericarditis

4. Findings that lower but do not eliminate the probability of ischemia:
   - Normal ECG
   - Abnormal ECG with nonischemic findings (eg, LVH)

**ECG MANIFESTATIONS OF STEMI**

The physician’s determination that ischemic ST elevations are present on an ECG in a patient with acute chest pain leads necessarily to interventions that can be of great benefit or pose great risk (eg, systemic thrombolytic therapy). Thus, it is essential that physicians be able to properly distinguish between ischemic ST elevations and ST elevations that are consistent with a more benign entity. This section reviews both the patterns of ST elevations in MI and causes of ST elevations other than MI.

**Ischemic Changes**

The ECG in a patient with an acutely obstructed
The appropriate evaluation of chest pain and other symptoms involves careful attention to the predictive value of a variety of diagnostic tests. Sound diagnostic reasoning is thus an essential element of good patient care. This section will review the fundamentals of diagnostic reasoning with emphasis on sensitivity, specificity, likelihood ratios, and the application of Bayes’ theorem.

Before entering the clinical arena, all diagnostic tests are evaluated to determine their operating characteristics—sensitivity, specificity, and the derived likelihood ratios. This evaluation involves doing clinical research studies in which patients undergo both the diagnostic test of interest and a “gold standard” test that defines the disease. The “gold standard” is often another test that the proposed test seeks to replace, because it is felt to be too invasive, inconvenient, or costly. Each patient must undergo both tests and each test should be interpreted without knowledge of the results of the other. The results allow the formation of the famous 2 × 2 table, as follows (hypothetical results are in parentheses):

<table>
<thead>
<tr>
<th>Gold Standard Result</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive</strong></td>
<td><strong>Negative</strong></td>
</tr>
<tr>
<td><strong>Positive Test</strong></td>
<td></td>
</tr>
<tr>
<td>A = true positive (84)</td>
<td>B = false positive (10)</td>
</tr>
<tr>
<td><strong>Negative Test</strong></td>
<td></td>
</tr>
<tr>
<td>C = false negative (16)</td>
<td>D = true negative (90)</td>
</tr>
</tbody>
</table>

A + C = total with disease (100)  
B + D = total without disease (100)

Sensitivity and specificity can be calculated from the data in the table:

\[
\text{Sensitivity} = \frac{A}{A + C} = \frac{84}{84 + 16} = 84\%
\]

Specificity = \(\frac{D}{B + D} = \frac{90}{90 + 10} = 90\%\)

The sensitivity of a test tells you how good it is at identifying disease when it is present, whereas the specificity tells you how good a test correctly identifies the absence of disease. Both are properties of the test itself and should largely be independent of the patient population. Somewhat counterintuitively, tests with high sensitivity are most helpful when they are negative, as they can rule out disease (SnOut). Tests with high specificity rule in disease when they are positive (SpIn).

Whereas sensitivity and specificity essentially define the quality of a diagnostic test, physicians most often are faced with a test result that requires interpretation. In this case, we are not primarily interested in a test’s operating characteristics but rather the significance of the result. Positive predictive value answers the question, given this positive test result, how likely is my patient to have the disease? We thus read horizontally across the table to obtain the proportion of patients with positive test results who actually have the disease. Negative predictive value is derived from a similar calculation for a negative test.

\[
\text{Positive predictive value} = \frac{A}{A + B} = \frac{84}{84 + 10} = 89\%
\]

\[
\text{Negative predictive value} = \frac{D}{C + D} = \frac{90}{90 + 16} = 86\%
\]

Increasingly, sensitivity and specificity are combined in a calculated measure known as the likelihood ratio:

Positive likelihood ratio = \(\frac{\text{sensitivity}}{1 - \text{specificity}}\)  
Negative likelihood ratio = \(1 - \frac{\text{sensitivity}}{\text{specificity}}\)

A likelihood ratio tells you how likely a given test result is to occur in a patient with the disorder as opposed to without the disorder. The larger the positive likelihood ratio, the higher the probability that a patient with a positive test has the disease. The smaller the negative likelihood ratio, the less
likely a patient with a negative test has the disease.

Likelihood ratios are given practical expression when used in the context of Bayes’ theorem, named for the 18th-century mathematician Thomas Bayes. The theorem as it is applied in medical decision making simply expresses that the probability of a disease being present or absent after a diagnostic test (posttest probability) depends on the pretest probability and the power of the test to alter that probability (the likelihood ratio).

Posttest probability (expressed as odds) = Pretest probability (odds) × likelihood ratio

Tests with high or low likelihood ratios have the greatest ability to change our probability estimates. Although this calculation can be easily performed, the Bayes’ nomogram (Figure) allows us to do this without any calculation at all. First, one specifies a pretest probability of the disease being present. This estimate is usually based on the clinical signs and symptoms as well the prevalence of disease in the population the patient represents. By lining up the pretest probability with the known likelihood ratio, the posttest probability becomes apparent. We can then decide whether that new probability solidifies our management strategy or whether further testing is required.

It is often the case that the pretest probability falls between 30% and 70%. Depending on the clinical scenario, probabilities higher or lower than that would often dictate a management strategy, making further testing unnecessary. As can be seen from the nomogram, within that 30% to 70% range, positive likelihood ratios greater than 10 make the diagnosis virtually certain and negative likelihood ratios less than 0.1 make it highly unlikely. These 2 values are good benchmarks when judging the reported diagnostic power of a test.

The use of Bayes’ theorem gives quantitative expression to sound diagnostic reasoning. It emphasizes that no test is absolute but must be interpreted in the context of the patient’s overall probability of disease. By classifying and reporting the likelihood ratios of various diagnostic tests, physicians also now have an intuitive method of quantitatively comparing the discriminative power of diagnostic tests. Its influence and importance in medicine will undoubtedly increase.
coronary vessel and resulting transmural ischemia will initially exhibit hyperacute “peaked” T waves in the anatomic distribution of the affected vessel, followed and occasionally accompanied by ischemic ST elevations in the same leads. Hyperacute T waves are infrequently seen, however, because they are a very early change that has usually resolved by the time the patient presents to care. The initial ST changes involve an elevation of the J point and the ST segment, which then progresses from being concave to convex in appearance (Figure 1).

The ST segment may remain elevated for hours to days unless the patient undergoes rapid coronary intervention that restores blood flow and causes the ST segments to resolve more quickly. If infarction does occur, then as the ST elevation resolves, the leads that exhibit ST elevations will show the formation of T wave inversions, usually followed by significant Q waves that can persist indefinitely (Figure 2). Persistence of ST elevations beyond 2 weeks is suggestive of a residual left ventricular aneurysm. The leads involved with these changes reflect the anatomic area of the heart supplied by the affected vessel (Table 3), which also shows the appropriate “reciprocal changes.”

**Inferior Wall MI**

Inferior wall MI is the most common form of MI and has a more favorable prognosis compared with MI involving the anterior wall. The vessel affected and the resulting extent of the infarct depends on the coronary anatomy. In 80% of the population, the right coronary artery supplies the left ventricular inferior wall, the interventricular septum, and the right side of the heart. The posterior descending artery branches from the right coronary artery and supplies the posterior septum and posterior left ventricle. In 10% to 20% of people, the right coronary artery is not the dominant artery supplying the inferior and posterior wall, with either a codominant circulation or the posterior descending artery branching off of the left circumflex rather than the right coronary artery. Due largely to this anatomic variation, the inferior wall MI is actually a heterogeneous group of MIs with variable involvement of the right ventricle and posterior wall with or without associated conduction disturbances.

ST elevations in II, III, and aVF—the classic changes suggesting inferior wall MI—will be associated with reciprocal changes in the precordial leads in 50% of patients with inferior wall MI. Absence of reciprocal changes portends a better prognosis overall. The presence of reciprocal changes increases the positive predictive value of the ECG for MI to greater than 90% and also suggests a larger infarct with the potential for increased MI complications (ie, hypotension, congestive heart failure, arrhythmias). Reciprocal changes
seen in the anterolateral leads (V₄–V₆) indicates that the patient may have multivessel disease that will require more extensive intervention.

The pattern of ST elevations in inferior wall MI can also predict the culprit vessel with relatively high sensitivity and specificity. As shown in Figure 3, ST elevation that is greater in lead III than II with reciprocal ST depressions in lead I, aVL, or both suggests right coronary artery involvement (with the potential for associated right ventricular infarction). A left circumflex occlusion, on the other hand, will cause the ST elevation in lead II to be equal or greater than that in III, with an isoelectric or elevated ST segment in aVL. Nonischemic causes of ST elevation also will fail to show the pattern of greater ST elevation in lead III than II, which can be helpful if one is trying to distinguish between ischemia from right coronary artery occlusion and nonischemic causes of ST elevation.

Sinus bradycardia and atrioventricular conduction delays, largely due to increased vagal tone in the early MI period, are commonly seen in inferior wall MI and will usually resolve within 24 hours. If bradycardia is significant, atropine may be given. Later in the course of the MI, edema around the conduction system can lead to first-, second-, or third-degree atrioventricular block that may require a temporary pacer, but this will also resolve within 2 weeks.

### Posterior Wall MI

Posterior wall infarction complicates inferior wall MI in approximately one third of patients but can also be seen in isolation or with anterolateral MI caused by occlusion of the left circumflex artery (in a left dominant patient). The recognition of its presence in an inferior or lateral MI is important because it means that a patient is experiencing a larger infarct with the potential for increased complications. It is absolutely essential to recognize the rare occurrence of a posterior wall MI in isolation because the patient would then require immediate reperfusion interventions. The unique and sometimes subtle ECG manifestations of a posterior MI in the anterior leads, essentially the mirror image of ST elevations, are frequently missed by clinicians who lack an appropriate level of suspicion for the entity.

In the standard 12-lead ECG, the presence of horizontal ST depressions in V₁, V₂, or V₃ with or without a tall and upright T wave, and tall R waves with an R/S ratio greater than 1.0 in V₂, can indicate a posterior infarct.

Confirmation of the presence of a posterior infarct can be obtained by placing 3 “posterior leads” immediately inferior to the left scapula with the middle lead (V₈) placed inferior to the tip of the scapula and the flanking leads (V₇ and V₉) placed approximately 3 cm from V₈ on each side. In these leads, ischemia will

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**Table 3. ECG Changes Seen in Different MIs**

<table>
<thead>
<tr>
<th>Anatomical Location of Infarct</th>
<th>Primary ECG Changes</th>
<th>Reciprocal Changes</th>
<th>Vessel(s) Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inferior wall MI</td>
<td>ST elevations II, III, aVF</td>
<td>ST segment depression may be seen in V₁–V₃ (or V₂–V₄), I, aVL</td>
<td>RCA (80%), Left circumflex (20%)</td>
</tr>
<tr>
<td>Anterior wall MI</td>
<td>ST elevations may be seen in V₁–V₆</td>
<td>ST segment depression in II, III, aVF</td>
<td>LAD artery, Left circumflex</td>
</tr>
<tr>
<td>Anteroseptal MI</td>
<td>ST elevations in V₁–V₂</td>
<td>ST segment depression in II, III, aVF</td>
<td>LAD artery</td>
</tr>
<tr>
<td>Anterolateral MI</td>
<td>ST elevations in V₄–V₆, I, aVL</td>
<td>ST segment depression in II, III, aVF</td>
<td>Branch of LAD or left circumflex</td>
</tr>
<tr>
<td>Posterior wall MI</td>
<td>Increased R wave V₁–V₂, ST depressions in V₁–V₂, ST elevations in posterior leads V₇–V₉</td>
<td>Anterior ST depressions are reciprocal changes and the only way to detect a posterior infarction in anterior leads</td>
<td>RCA or left circumflex</td>
</tr>
<tr>
<td>Right ventricular wall MI</td>
<td>ST elevation in II, III, aVF (inferior wall MI)</td>
<td>ST elevation in V₄R of right-sided leads</td>
<td>RCA in virtually all cases</td>
</tr>
</tbody>
</table>

LAD = left anterior descending; MI = myocardial infarction; RCA = right coronary artery.
manifest as ST elevations, although they are often more subtle than anterior elevations because of the increased distance from the posterior ventricular wall.

In summary, posterior wall infarction should be suspected in any patient who presents with evidence of an inferior or a lateral wall MI or with a chest pain syndrome concerning for MI with prominent R waves with or without ST depressions in leads V₁ to V₃. It can be confirmed by the use of posterior leads demonstrating ST elevations in leads V₈ or V₉.

Right Ventricular Infarction

Right ventricular infarction is also often associated with inferior wall MI but can rarely occur in isolation or with anterior wall MI. Classically, right ventricular infarction has been known by the clinical triad of elevated jugular venous distention (JVD), clear lung fields, and hypotension with or without atrioventricular conduction delay. Clinicians often encounter it in the setting of an inferior wall MI with hypotension or an exaggerated hypotensive response to nitroglycerin. Right ventricular infarction almost always results from the proximal occlusion of the right coronary artery leading to ischemia of both the right ventricle and the inferior wall. As noted, in approximately 20% of the population the inferior wall is supplied by the left circumflex artery with the smaller, nondominant right coronary artery supplying only the right ventricle. Occlusion of this nondominant right coronary artery can present with ST elevations in leads V₁ through V₅ and right ventricular infarction with no inferior changes, but this is rare.

The ECG diagnosis of right ventricular infarction involves the placement of rightsided leads that mirror the lead placement on the left chest (Figure 4). An ST elevation of greater than 1 mm with an upright T wave can then be seen in V₄R (Figure 5). As noted in Figure 3, an ST elevation in V₁, V₄R, or both in the presence of ST elevations inferiorly is 79% sensitive and 100% specific for right ventricular infarction. It should be noted that the changes in V₄R are transient and will rarely be seen beyond 12 hours. ST elevation in V₄R is also a much less consistent finding when right ventricular infarction complicates anterior ischemia. Nevertheless, the essential message is that clinicians should have a high suspicion for right ventricular involvement in the setting of an inferior wall MI and take the time to place rightsided leads. When the ST segment is elevated in V₄R, consideration should be given to volume loading, if appropriate, and
nitroglycerin should be used cautiously because the right ventricular is preload dependent.

**Anterior Wall MI**

The anterior wall is supplied primarily by the large left anterior descending artery (LAD) and laterally by the smaller left circumflex artery. Occlusion of the LAD will result in ST elevations in the “anteroseptal” leads, V₁ to V₃. ST segment depressions in II, III, and aVF, or reciprocal changes, will also be seen with a proximal LAD lesion. Associated ST elevations in II, III, and aVF, an infarction pattern, can also be seen if the occlusion is in a distal LAD that wraps around to supply the inferior wall. ST segment elevations in the anterolateral area, leads V₄ to V₆, I, and aVL, most often suggest proximal occlusion of the left circumflex artery (whereas distal occlusion will produce an inferior infarct). Occlusion of the left main coronary artery, which gives rise to both the LAD and the circumflex, will result in massive myocardial ischemia involving the entire anterior wall.

Anterior infarcts are less complex but more lethal than inferior infarcts. Associated right or posterior ventricular infarction is rare. As with inferior infarcts, conduction defects can be seen, but the defects are more ominous because they represent septal ischemia and possibly necrosis of the distal conduction system. Patients who present with anterior ischemia and new-onset LBBB have a very high mortality rate. The development of complete heart block within the first 24 hours of the MI is similarly ominous.

Occasionally, one is called upon to assess for ischemia in the presence of a new or chronic LBBB. As noted, in a patient deemed highly likely to have an MI by history and physical, the presence of LBBB is an indication for thrombolytic therapy. However, the recognition of ischemia involving either the anterior or inferior walls can be challenging in the presence of LBBB. Indeed, there are no sensitive criteria for its detection. One sign, concordant changes, is helpful when it is present. Concordance can be appreciated by recognizing that LBBB is characterized by deep negative QRS complexes in leads V₁ through V₃ and tall positive QRS complexes in the lateral leads. Both the deeply negative QRS complexes and the tall positive ones are followed by ST segments that “overshoot” and are “discordant” with the prominent deflection of the antecedent QRS complex (Figure 6). Thus, slight ST elevations are commonly seen in leads V₁ through V₃ in association with the deeply negative QRS. If the ST segment is “concordant” with the prominent deflection of the QRS—elevated in a lead where the QRS is positive or vice versa—ischemia may be present. It has also been suggested that markedly positive ST elevations in leads...
V₁ through V₃ (> 5 mm) is also a sign of ischemia, but this criterion lacks specificity.²¹

**Mimics of Ischemic ST Elevations**

ST elevations of one form or another are not uncommon on routine ECGs. In the heat of the moment, when a patient is in front of one with active chest pain and “time is myocardium,” a rapid and accurate assessment of the nature of ST elevations can be challenging. It is therefore imperative that practicing clinicians be thoroughly familiar with the patterns of ischemia described above and also the various ischemia mimics that can masquerade as infarction-like patterns. This section describes some tips on how to distinguish ischemia from its pretenders and then reviews each of the more common “ischemia mimics” in detail.

The first step in ensuring one can correctly appreciate ischemic ST elevations is to memorize the patterns of infarction for the various anatomic regions of the heart described above and also the various ischemia mimics that can masquerade as infarction-like patterns. This section describes some tips on how to distinguish ischemia from its pretenders and then reviews each of the more common “ischemia mimics” in detail.

The ST elevation is generally small (1–2 mm but can be greater) and most prominent in leads V₁ to V₃ (where negative QRS complexes are most common). The ST segment is concave. Another common variant is the “early repolarization” abnormality frequently encountered in young men of African descent. It is similar to the normal variant ST elevation but is most prominent in the mid-precordial leads and often has “notching” at the J point in lead V₄.

LVH with repolarization abnormality is another common pattern seen on routine ECG (Figure 8). Patients will most often meet “voltage criteria” for LVH (ie, the sum of the largest S wave in lead V₁ or V₂ and the largest R wave in lead V₃ or V₆ is greater than 35) or the more specific criteria of the R wave in aVL being greater than 11 mm. Severe LVH with strain may manifest itself as ST depressions and T wave inversions laterally (V₄–V₆) and associated ST elevation in leads V₁ and V₂ (and V₃ to a lesser degree).

Patients with both acute pericarditis and focal
myocarditis can present with a clinical picture virtually indistinguishable from coronary ischemia. Both pericarditis and myocarditis can cause ST elevations, and focal myocarditis can cause both pain and CK elevations consistent with MI. Nevertheless, focal myocarditis is relatively uncommon, and the ECG features of pericarditis are usually sufficiently distinct to allow for easy clarification. The ST elevations of acute pericarditis are most commonly diffuse and do not exceed 5 mm. There are no reciprocal changes suggestive of MI. There is also associated PR depression, a feature not generally seen in MI (unless the MI causes pericarditis). The inferior ST elevations of pericarditis will also be associated with elevation in aVL, whereas with inferior wall MI there are reciprocal changes in aVL. Figure 9 illustrates some of the more common ST elevation “mimics” other than repolarization.

**ECG MANIFESTATIONS OF NSTEMI**

ST elevations are the most recognizable ECG manifestation of MI but not the most common. Indeed, the majority of patients with MI do not have ST elevations but rather have either ST depressions, T wave inversions, or no changes at all. When only these “nonspecific” changes are present, it is generally impossible to distinguish between UA and NSTEMI until cardiac biomarkers are measured. The following section discusses the ECG manifestations of NSTEMI and their prognostic significance.

**ST Depression**

ST depression has classically been described as representing ischemia to cardiac muscle but not overt infarction. For that reason, ST segment depression and its resolution are the criteria used to define ischemia in exercise stress testing. It is evident, however, that many patients with an ongoing MI will also manifest only ST depressions on the ECG. The changes can be subtle, with only a “flattening” of the ST segment without frank depression. ST depressions can be described as flattened (planar) or “horizontal,” the more classically ischemic pattern, or “downsloping,” which is less specific for ischemia (Figure 10). Patients with LVH and a “strain” pattern will have ST depressions in the lateral leads, but these are usually downsloping and occur in the setting of obvious LVH (Figure 8). Patients on digoxin can demonstrate more diffuse ST depressions.

In the appropriate setting and in the absence of a clear nonischemic cause, ST depressions should be considered a marker for a dynamic and potentially dangerous situation. Paradoxically, it has consistently been demonstrated that patients with coronary ischemia and

**T Wave Inversions**

T wave changes are the other ECG pattern known to be associated with ischemia and are the least specific. As noted, a hyperacute or peaked T wave is usually the earliest sign of an STEMI. There are other patterns of T wave changes that can be worrisome, however.
Inverted T waves are normally seen in leads III, aVR, and V₁ where there is also a negative QRS deflection. Deep and symmetrical T wave inversions, particularly in leads V₁ through V₃, are felt to be strongly associated with MI (Figure 11). Patients will frequently present with chest pain and flattened T waves that are not frankly inverted. These changes are very nonspecific but should not be ignored in the appropriate clinical setting.

**PRESUMPTIVE DIAGNOSIS**

Both the patient’s clinical presentation and her ECG are nonspecific. There is little to suggest pulmonary embolism, although one might consider ordering a D-dimer test, as a negative result would make this diagnosis very unlikely. Aortic dissection seems similarly improbable, though it cannot completely be discounted. Coronary ischemia is the leading diagnosis that must
be ruled out. Based on her ECG, we know that the patient is not experiencing an acute STEMI, but she still may be experiencing an ACS in the form of UA or NSTEMI.

• What is the role of cardiac biomarkers in patients at risk for ACS?

The distinction between UA and a NSTEMI cannot be made on the basis of the clinical presentation and ECG. It is the presence of cardiac biomarkers in the serum of patients experiencing a clinical syndrome suggestive of coronary ischemia that ultimately defines an MI.23 Because of their high sensitivity and specificity, cardiac troponins have now surpassed all other biomarkers in their importance in national guidelines and in overall clinical usefulness. CK-MB and myoglobin still have a niche role, but lactic dehydrogenase has been made redundant. The following section discusses these 3 cardiac biomarkers and suggests strategies for their use.

Cardiac Troponins

Cardiac troponins are now regarded as the standard biomarker for the detection of myocardial ischemic necrosis. The sensitivity of the test is such that any detectable amount of cardiac troponin is suggestive of myocardial damage and is a poor prognostic sign even in patients without symptoms of an ACS. Troponins are small molecules that form part of the troponin complex of cardiac myofibrils. With lysis of cells from ischemic necrosis, troponins are released into the circulation and can be measured by the use of monoclonal antibodies. Troponin T and I are unique to cardiac muscle. Assays for both have been developed and marketed and both have a similar sensitivity and specificity 6 hours after the onset of cardiac ischemia (Table 4). Physicians should make themselves aware of the troponin test used at their institution and its reference limits as these may vary, particularly with troponin T measurements.

Both troponin I and T, like CK, are poor indicators of infarction in the very early period (within 4 hours), and patients suspected of having ischemia should undergo serial testing every 6 to 8 hours. Once elevated, troponin reaches a peak within 12 to 48 hours of infarction and may remain elevated for up to 10 days. The degree of elevation reflects the size of the infarct (Figure 12). The fact that troponin remains elevated for more than a week after an ischemic event has obviated the need for lactic dehydrogenase measurement as troponin alone can diagnose remote infarcts.

Prior to the use of troponins, evidence from autopsy studies showed that CK did not detect all clinically significant myocardial necrosis.25 Indeed, the high sensitivity of troponins has led to the detection of approximately 30% more episodes of NSTEMI in patients who would otherwise have been considered to have UA.23 The increased sensitivity also led to questions

Table 4. Comparison of Troponin T and Troponin I

<table>
<thead>
<tr>
<th>Cardiac troponin T</th>
<th>Cardiac troponin I</th>
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<tbody>
<tr>
<td>All assays marketed by one manufacturer; good standardization</td>
<td>Assays manufactured by several companies</td>
</tr>
<tr>
<td>Earlier detection and longer permanence in blood after myocardial infarction</td>
<td>Lack of standardization between assays; impossible to compare results obtained by different assays</td>
</tr>
<tr>
<td>More clinical validation studies performed on the same assay</td>
<td>Analytical performance of different assays not comparable</td>
</tr>
<tr>
<td>Possibility of false-positive results in patients with myopathies</td>
<td>No increase observed in patients with skeletal muscle myopathy</td>
</tr>
<tr>
<td>May be falsely elevated in renal failure (17% to 53% of time)</td>
<td>Less false elevation in renal failure (7% of time)</td>
</tr>
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Figure 12. Biomarker elevations after acute myocardial infarction (AMI). CK = creatine kinase. (Adapted with permission from Panteghini M. Acute coronary syndromes: biochemical strategies in the troponin era. Chest 2002;122:1428–35.)
about whether all troponin elevations were prognostically meaningful. This concern has been put to rest by studies that have documented increased 30-day mortality in both STEMI and UA/NSTEMI patients who experience a troponin elevation. Troponin elevations have also served as a marker to identify “high-risk” ACS patients who have been shown to benefit from treatment with low-molecular-weight heparins, glycoprotein IIb/IIIa inhibitors, as well as an “early intervention” strategy consisting of angiography with percutaneous transluminal coronary angioplasty.

Cardiac troponins are more cardiospecific than any previously available biomarker, but there are conditions besides MI that can lead to an elevation. There is adequate evidence that troponins can be elevated in acute pericarditis, large pulmonary emboli, heart failure, myocarditis, sepsis, LVH with strain, and following the discharge of a cardiac defibrillator. Any form of myocardial damage that leads to cell lysis, such as blunt trauma, myocarditis, or myocardial drug toxicity, can also cause a troponin elevation.

Clinicians are frequently faced with small troponin elevations in patients with congestive heart failure or advanced LVH and elevated blood pressure. Early studies on this issue have documented that both entities can increase troponin in the absence of frank ischemia. Troponin elevations in heart failure are reflective of severity and may represent myocardial cell death with poor prognostic implications. As we await further studies on the issue, it is best to rely on sound clinical judgment and interpret troponin elevations in the overall clinical context.

Troponin elevations in patients with renal insufficiency can be particularly challenging as troponin values are frequently elevated even when there is no suspicion for ACS. The situation is made more complex by the fact that cardiovascular disease is exceedingly common in this population and is responsible for approximately 50% of all deaths. Three studies have documented that patients with renal failure and asymptomatic troponin elevations are at increased risk of death from all causes. As with troponin elevations in congestive heart failure, further research is needed in order to clarify the best management strategy for asymptomatic troponin elevations in renal failure.

**CK-MB**

In the past, CK-MB fraction was used as the primary biomarker for the detection of myocardial necrosis. While CK itself is present in all forms of muscle, the MB isoform is specific to cardiac muscle. Like troponin, CK levels begin to rise 4 to 6 hours after an infarction event, but unlike troponin, they will peak at 18 hours and return to baseline within 40 hours. This shortened period of elevation makes CK particularly useful in detecting recurrent infarction following an initial event. However, CK is overall less sensitive and specific than troponin for the detection of myocardial necrosis and its routine use may fade over time.

**Myoglobin**

The third most important cardiac biomarker is myoglobin. Myoglobin has poor specificity for cardiac muscle, but its high sensitivity and rapid rise following an infarction event makes it potentially useful in the early phase when troponin and CK levels are still low. Myoglobin becomes detectable in blood 2 to 3 hours after an event, peaks at 6 to 12 hours, and returns to baseline by 24 hours. Though it lacks specificity, its high sensitivity endows it with a high negative predictive value.

**Use of Biomarkers**

Various strategies for using biomarkers have been employed in the management of acute chest pain. The most common is to use the serial measurement CK and/or troponin alone for the diagnosis of myocardial ischemia. This strategy recognizes that the majority of patients will require a prolonged ED stay or short inpatient admission to definitively rule out active ischemia. A second strategy is to measure both myoglobin and troponin at presentation and, if both are negative, discharge the patient earlier if the pretest probability for ischemia is also low. This strategy has the potential advantage of avoiding unnecessary short stay admissions and identifying those at higher risk earlier.

**ADDITIONAL TESTING OF PATIENT**

Results of CK and troponin testing performed in the ED are both normal. The physician is also concerned about the possibility of pulmonary embolism after the patient’s chest radiograph is read as potentially having a hazy infiltrate at the periphery of her left lung. A D-dimer test is negative.

- What further assessment is indicated?
- What risk category does this patient fall into?

**Risk Assessment in UA/NSTEMI**

Various algorithms describing the risk assessment and early management strategy for patients with chest pain suggestive of UA/NSTEMI have been published. The 2000 ACC/AHA guidelines offered guidance...
for classifying patients presenting with UA into high-, intermediate-, and low-risk categories (Table 5). Patients considered at high risk should be admitted to an intensive care unit, closely monitored, and scheduled for cardiac catheterization. Patients at low risk can be admitted for a short stay or discharged with outpatient stress testing, depending on the physician’s level of concern. Intermediate-risk patients require admission and stress testing before discharge.

The creation and validation of the recently published TIMI risk score is anticipated to have an impact on clinical risk assessment. The TIMI risk score was derived from 2 large trials of low-molecular-weight heparin in patients with UA/NSTEMI. The score is calculated with 7 variables, each independently predictive of a poor outcome. These include age ≥ 65 years, ≥ 3 risk factors for CAD, ≥ 50% stenosis on angiography, ST segment changes > 0.5 mm, ≥ 2 anginal episodes in 24 hours before presentation, elevated serum concentration of cardiac markers, and use of aspirin in 7 days before presentation. Death rates at 14 days consistently increased with an increasing TIMI score, defined as the number of positive variables present. Based on the TIMI risk score, a 2-tiered algorithm (Figure 13) has been developed that dictates the management strategy.

**Patient Follow-up**

The patient’s clinical presentation, ECG, and troponin level put her in a low-risk category. The physician decides to admit her to the hospital overnight to complete the serial troponin measurements and plan for an exercise stress test in the morning.

**Conclusion**

The case presented in this manual is not unusual, as the majority of patients who present to acute care with chest pain will not be experiencing an ACS. However, those who are must be recognized promptly and given appropriate therapy.

**References**

3. Gibbons RJ. Nitroglycerin: should we still ask [editorial]?
Figure 13. Algorithm for unstable angina or non-ST segment elevation myocardial infarction. (Adapted from Grech ED, Ramsdale DR. Acute coronary syndrome: unstable angina and non-ST segment elevation in myocardial infarction. BMJ 2003;326:1259–61. Copyright © 2003, with permission from BMJ Publishing Group.)


