

# Approach to Undifferentiated Chest Pain in the Emergency Department:

## A Review of Recent Medical Literature and Published Practice Guidelines

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### Abstract

Chest pain is the presenting complaint in over 6 million emergency department visits each year. Differentiating acute coronary syndrome (ACS) from other, noncardiac causes of chest pain is imperative in emergency practice. This article reviews the current medical evidence and published guidelines for the diagnosis of undifferentiated chest pain.

A MEDLINE database search was conducted for relevant English language articles discussing an approach to undifferentiated chest pain. The published guidelines of the American College of Emergency Physicians, the American Heart Association, and the American College of Cardiology were also reviewed.

The data surveyed suggest that, for all adult patients complaining of nontraumatic chest pain, a cardiac etiology for their presentation should be considered. History, physical examination, electrocardiogram, chest radiography, and to a lesser extent laboratory results can help differentiate ACS from other emergent diagnoses, e.g., aortic dissection, esophageal rupture, pulmonary embolus, pneumothorax, pneumonia, and pericarditis.

No single feature of a patient's history, physical examination, or diagnostic test results can diagnose ACS to the exclusion of other causes of chest pain. Consequently, patients presenting with a complaint of chest pain frequently require serial evaluations, and admission to an observation unit or the hospital.

**Key Words:** Angina pectoris, chest pain, differential diagnosis, electrocardiography, medical history taking, physical examination, practice guidelines, symptoms.

### Introduction

THE COMPLAINT OF acute nontraumatic chest pain presents one of the most difficult diagnostic challenges in emergency medicine (EM). Patients with this chief complaint account for approximately 5% of all emergency department (ED) visits (1). Given that coronary artery disease is the leading cause of death in the United States (2), rapid identification of an acute myocardial infarction is the foremost consideration in the emergency physician's differential. Despite scientific advances in both understanding and detecting acute myocardial infarctions, an estimated 2.1–5.3% of patients presenting with an acute coronary syndrome (ACS) are sent home from the ED (3, 4).

Patients with ACS often have symptoms indistinct from those of other emergent conditions. Afferent somatic and visceral nerve fibers of the heart, lungs, aorta and esophagus all synapse at the

same thoracic dorsal ganglia. Therefore, pain felt in any location from the jaw to the epigastrium can have origins in any of these anatomic structures. An apprehensive appearance and complaint of chest pain can be observed in patients with an aortic dissection, pulmonary embolism, pneumothorax, pericarditis or esophageal rupture. Delay in treatment and diagnosis of any of these conditions leads to an increase in morbidity and mortality. In addition, failure to diagnose myocardial infarction accounts for 25% of all malpractice dollars paid against emergency physicians (5). Yet an exhaustive cardiac work-up of patients with a psychiatric, gastrointestinal, or musculoskeletal cause of chest discomfort is both stressful to the individual and a drain on limited health care resources. The objective of this article is to review the current medical literature and practice guidelines recommendations with regard to the diagnosis of undifferentiated chest pain in the adult emergency department patient, to help determine which method or combination of methods may provide the quickest, most reliable differential diagnosis.

### General Approach

Upon arrival in the ED, patients with abnormal vital signs and complaining of chest pain or who

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appear to be ill should be triaged to a critical care area. Intravenous access should be established and abnormalities in oxygen saturation treated with supplemental oxygen. To meet the goal of a less than 30-minute door-to-intervention time, all patients suspected of an acute myocardial ischemic event require a 12-lead electrocardiogram (ECG) obtained within 10 minutes of arrival in the emergency department. Furthermore, recently published ACC/AHA guidelines recommend 12-lead ECG performance by EMS personnel prior to arrival in the ED, if possible, to expedite care (6).

Key elements of the history consist of a description of the pain (quality, severity, duration, activity at onset, radiation, worsening and alleviating factors, and previous occurrence), pertinent medical conditions, medications, allergies, and treatment thus far. Initially, the skin and cardiopulmonary, vascular and neurological systems are briefly examined for pallor, diaphoresis, jugular venous distension, tracheal deviation, new murmurs, abnormal breath sounds, pulse and gross motor deficits. Together with the ECG and chest radiography, this approach can help distinguish an acute coronary syndrome from aortic dissection, pulmonary embolism, pneumothorax, pericarditis, or esophageal rupture. Further patient stabilization and treatment should occur in accord with a more detailed medical history and physical examination and in conjunction with laboratory testing and further diagnostic imaging. The physician should also remain aware of other (nonemergent) causes of non-cardiac chest discomfort. The basic data for differential diagnosis of the most common emergent and nonemergent causes of chest pain follow.

### Emergent Causes of Chest Pain

**Aortic dissection.** More than 14,000 people die each year in the United States from aortic dissections (2). Most of these individuals are males (75%) in the seventh decade of life (7). A tear in the intimal layer of the thoracic or abdominal aortic wall can result from either longstanding hypertension or a structural abnormality. Stanford Type A dissections involve the ascending aorta with or without involvement of the descending portion. Stanford Type B dissections are located in the descending aorta beyond the junction with the subclavian artery. Type A dissections are usually treated surgically and Type B with medical control of blood pressure. Risk factors for this disease include arteriosclerosis, advanced age, Marfan's syndrome, connective tissue disease, Turner's syndrome, and hypertension (7–10). Elevated blood pressure may drive the initial tear to expand into a

false lumen. Impending rupture leads to a myriad of symptoms and signs in the supplied organs: brain, heart, kidneys and intestines. The medical literature abounds with atypical cases of aortic dissections presenting as a stroke, syncope, congestive heart failure, isolated limb ischemia or numbness, abdominal discomfort, flank pain, acute renal failure or gastrointestinal bleeding.

A patient who complains of chest pain that is maximal at onset with an accompanying neurological or pulse deficit should immediately be suspected of having an aortic dissection. Failure to take an adequate pain history on initial clinical evaluation has been found to delay diagnosis (10). A 2002 review of 274 MEDLINE articles found a history of sudden pain with a maximal intensity at onset to have a pooled sensitivity of 90% in detecting thoracic aortic dissection (9). The pain is frequently described as "tearing" or "ripping," with radiation to the back, interscapular, or abdominal region. Physical examination may reveal jugular venous distension from cardiac tamponade, blood pressure differential of greater than 20 mm Hg between extremities, mediastinal air or aortic regurgitation. Classic findings such as pulse quality difference between limbs (15–38%) (7, 11) and gross motor defect (17%) occur more commonly in Type A dissections. Their presence increases the positive likelihood of disease, from 5.7 for a pulse or blood pressure differential to 6.6–30 with a neurological deficit (7). Chest radiography usually reveals a widened mediastinum, loss of the aortic contour, displacement of the aorta, or pleural effusion. Since as many as 10% of patients will have a normal initial radiograph, this radiograph cannot be used to exclude disease (7). ECG findings can show left ventricular hypertrophy of longstanding hypertension or, for dissections occurring retrograde into the coronary arteries, an acute myocardial infarction.

Clinicians must quickly distinguish aortic dissection from an ACS before the administration of antiplatelets and antithrombin agents. No single finding is sufficient to exclude the diagnosis of aortic dissection, but a constellation of clinical variables (immediate, maximal tearing or ripping pain; pulse or blood pressure differential; mediastinal widening) can identify up to 96% of cases (11). Patients thus identified will require medical control of hypertension, surgical consultation, and further imaging, e.g., transesophageal echocardiography, computed tomography, magnetic resonance imaging. Overall in-hospital mortality for aortic dissection, from the International Registry of Acute Aortic Dissection (IRAD), is reported at 27% (7).

**Pulmonary embolism.** Pulmonary embolism (PE) represents a common, life-threatening and frequently missed diagnosis in the ED. An estimated 187,000 cases of first-time venous thromboembolism occur in American adults over the age of 45 years (12). These patients can present with chest pain of pleuritic nature, fatigue, dyspnea, syncope, hemoptysis and/or cardiac arrest (13, 14). Risk factors for PE include increasing age, immobilization, recent surgery, malignancy, pregnancy, trauma, and previous thromboembolic disease (12, 14, 15). Physical findings on examination can be minimal. Normal oxygen saturation or presence of a fever cannot exclude the diagnosis (14, 16, 17). Increased respiratory rate is the most common sign associated with PE (14, 17). An electrocardiogram can show acute pulmonary hypertension and a right heart strain pattern, or T wave inversions (17). Chest radiography may reveal atelectasis, pulmonary parenchymal disease or pleural effusions, or it may be entirely normal (14, 17). Patients should be stratified into low, intermediate and high-risk categories (18) (see article on “Pulmonary Embolism” in this issue of the *Journal*). The advent of rapid, enzyme-linked immunosorbent assay (ELISA)-based d-dimer testing has proven useful in excluding the presence of PE in low-risk patients (19–21).

**Esophageal perforation.** Spontaneous esophageal rupture (Boerhaave’s syndrome) is a rare but potentially lethal cause of chest pain. As with aortic dissection, if this condition is misdiagnosed as ACS, the unintentional administration of thrombolytics may lead to rapid clinical deterioration (22). Given its relative rarity, there are no well-designed studies to help guide evidence-based decision making regarding the diagnosis and management of the condition. A classic history of vomiting followed by severe chest pain, shortness of breath, subcutaneous emphysema and rapid circulatory collapse is not always present. Median age of occurrence is from 63–71 years (23, 24), with isolated cases reported in younger adults (25). Depending on the case series, 12–50% of patients have no history of prior vomiting (23, 24, 26). Patients with esophageal perforation generally appear ill and may complain of dyspnea, cough, fever and abdominal pain. Patients presenting more than 12 hours after the onset of symptoms may show signs of sepsis (26). Physical examination may reveal diminished breath sounds, heart sounds with audible crepitus (Hamman’s crunch), or subcutaneous air in thorax or neck. The majority of patients (71–100%) will have abnormalities on chest radiography that include pneumomediastinum, hydro-pneumothorax, pleural effusion or mediasti-

nal widening (23, 24, 27). Confirmatory studies include esophageal contrast radiography, computed tomography (CT) scans, or endoscopy. Studies present mortality rates varying from 14–64% (23, 24, 26, 28); they are higher with a delay in diagnosis beyond 24 hours. All ill-appearing patients with undifferentiated chest pain should be questioned about antecedent vomiting and have their chest radiographs reviewed before medical treatment is initiated.

**Pneumothorax.** Patients with a spontaneous pneumothorax generally present with pain and complaints of shortness of breath. Risk factors for occurrence include smoking, previous pneumothorax, chronic obstructive pulmonary disease, underlying pulmonary pathologies, and abrupt changes in barometric pressure. Pain is described as sudden, sharp and pleuritic in nature. Associated respiratory distress can be severe. If a tension pneumothorax develops, the trachea may be deviated away from the collapsed lung, and jugular venous distension may be present. Absence of breath sounds and hyper-resonance to percussion may be seen on the effected side. An upright chest radiograph is typically diagnostic. According to an American College of Chest Physicians (ACCP) consensus statement, patients with small, non-expanding pneumothoraces can be safely discharged from the ED after 6 hours of observation with follow-up in two days (29). Patients with large pneumothoraces or unstable vital signs require placement of a chest tube and hospital admission.

**Acute pericarditis.** Approximately 800 deaths per year in the United States are attributed to diseases of the pericardium and myocardium (2). In a majority of patients, acute pericarditis is of either viral or idiopathic etiology (30–32). More than half of the patients will present complaining of chest pain (31, 33) that may radiate to the back, neck or shoulders. In contrast to acute coronary syndromes, pericardial pain worsens with inspiration and is improved while sitting up and leaning forward. Approximately 25–40% of patients will complain of dyspnea and 17% of fever (31, 33). At some point during their disease, 85% of patients without a severe pericardial effusion will have a pericardial friction rub (32). Individuals with associated cardiac tamponade may show jugular venous distension, tachycardia, hypotension, and/or pulsus paradoxus. Published guidelines of the European Society of Cardiology (ESC) suggest an ECG, chest radiography, laboratory testing (ESR, C-reactive protein, lactic dehydrogenase [LDH], WBC, cardiac markers) and echocardiography, with Level B evidence for the diagnostic pathway (34). Classical ECG findings include concave ST

segment elevation, T-wave inversions, and PR-segment depression. ECG changes occur throughout the precordium and, unlike ACS, are not distributed in distinct anatomic regions. Low QRS voltage throughout the limbs leads is suggestive of cardiac tamponade (35). A chest radiograph may demonstrate an enlarged cardiac silhouette or be entirely normal. ED ultrasonography has emerged as the preferred diagnostic test in these cases. Younger patients and those with recent infection may have elevations of troponin I, unrelated to symptom intensity or disease severity (30, 36). Management consists of pericardiocentesis for severe cardiac tamponade, treatment of the underlying cause, and nonsteroidal anti-inflammatory drug administration.

**Pneumonia.** Pneumonia is a potentially life-threatening condition in the immunocompromised elderly or in individuals with significant comorbidities. Approximately 65,000 people in the United States die each year from pneumonia (2). Patients may complain of chest pain that ranges from sharp and pleuritic to dull and substernal. Physical examination may reveal fever, rales, decreased breath sounds or bronchial breath sounds and varying degrees of respiratory distress. Elderly patients notoriously present with few symptoms or signs and may have only an alteration in mental status. Diagnosis is usually confirmed on chest radiograph, with few cases requiring a computed axial tomography (CAT) scan or bronchoscopy. Decisions to admit or discharge should be based on risk stratification via published guidelines or the pneumonia severity index (37, 38). Antibiotic selection is based on the patient and local bacterial sensitivities to various drugs (39, 40). Clinicians should be aware of reports of increasing resistance of pneumococcal pneumonia to fluoroquinolones (41, 42). One recent retrospective review of 18,209 patients found antibiotic administration within 4 hours of hospital arrival to be associated with a decrease in in-hospital mortality [adjusted odds-ratio = 0.85 (CI 0.74–0.98)] and 30-day mortality [AOR 0.85 (CI 0.76–0.95)] (43, 44).

**Acute coronary syndrome.** Acute coronary syndromes can be divided into ST-segment elevation acute myocardial infarction (STEMI), non-ST segment elevation acute myocardial infarction (NSTEMI) and unstable angina (UA). All three have similar clinical features and are difficult to distinguish from other cases of chest pain. A standard 12 lead electrocardiogram is the most valuable tool in the investigative armamentarium (45). Chest radiography is useful in excluding other disease process and assessing for the presence of congestive heart failure. Cardiac biomarkers are im-

portant in distinguishing between the three entities and form the basis of the new definition of acute myocardial infarction. ACS is discussed in detail in other articles in this issue of the *Journal*.

### Nonemergent Causes of Chest Pain

**Panic disorder.** Anxiety disorders and isolated panic attacks occur in 2–13% of the adult population (46, 47). As per the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) definition, attacks are accompanied by any four of the following symptoms: palpitations, diaphoresis, tremor, dyspnea, choking, chest pain or discomfort, nausea, dizziness, derealization or depersonalization, fear of losing control or dying, paresthesias, chills or hot flushes (48). An estimated one million panic disorder patients present to EDs each year with complaints of chest pain (49, 50). The vast majority of these patients (98%) are discharged without a definitive diagnosis of their condition (49). Recently published studies have found a correlation between panic disorder and lack of pre-existing coronary artery disease (CAD), atypical quality to the pain, female sex, younger age, and a high self-reported anxiety level (51–53). However, panic disorder and CAD frequently co-exist, which can lead to exacerbation of both disease states. Some success has been reported in both screening for panic disorder and starting anxiety medications in the ED chest pain unit (54).

**Gastrointestinal diseases.** Several disorders of the gastrointestinal tract, including gastroesophageal reflux, esophageal spasm, peptic ulcers, pancreatitis, biliary colic and cholangitis, can all present with chest pain. Indeed, up to 40% of chest pain patients seen in the ED and not diagnosed with ACS may have gastroesophageal disease (55). Discriminating these disorders from ACS can be difficult based solely on history and physical examination. Pitfalls abound, from early closure of diagnoses to missing concomitant presentations. Chest pain from gastroesophageal reflux (GERD) is usually described as a burning in the mid-epigastrium or in the lower chest. However, chest pain described as being of this nature does not exclude the presence of cardiac ischemia (56, 57).

Moreover, given the prevalence of GERD in the adult population, previous history of the disease does not exclude an ACS event. Gastroesophageal reflux may provoke myocardial ischemia in patients with underlying coronary artery disease (58). Diagnosing GERD in chest pain patients by antacid administration is not acceptable medical practice. Similarly, esophageal spasm pain and other non-cardiac disorders can improve with

### Key Concepts

1. Undiagnosed myocardial infarction is a major cause of morbidity and mortality for chest pain patients.
2. History, physical examination and chest radiography are often useful in identifying non-ACS etiologies of chest pain.
3. Aortic dissection and acute myocardial infarction can coexist in the same patient.
4. A significant percentage (25%) of patients with acute coronary syndrome (ACS) do not have a primary complaint of chest pain
5. Gastroesophageal symptoms are non-specific for gastrointestinal etiology and can be seen in ACS.

nitroglycerin administration (59). Peptic ulcer disease can wake individuals from sleep and is usually located in the mid-epigastrium. A perforated duodenal ulcer can present with severe chest pain, vital sign abnormalities, and free air on upright chest radiography. Diagnoses of acute pancreatitis and biliary tract disease can be achieved from history, physical examination, bedside ultrasonography and supporting laboratory studies. Patients presenting with acute chest pain suspected of having a gastrointestinal etiology should nonetheless have their cardiac risk factors assessed and ACS considered in the differential diagnosis.

**Chest wall syndromes and nerve root compression.** Approximately 28% of undifferentiated non-cardiac chest pain patients may have chest-wall syndromes (55). Costochondritis is an inflammation of the costal cartilages that can result in an acute, well-localized, sharp chest pain. Patients, who appear otherwise well, may feel increased discomfort with deep respiration or movement. Pain is reproducible upon palpation of the involved cartilage. Pain that is positional, pleuritic, or reproduced with palpation gives a likelihood ratio of 0.2–0.3 for myocardial infarction (60). Interpretation of this finding should be balanced with the overall clinical picture, for patients with an ACS event can have a tender chest wall.

Compression of the cervical or thoracic ventral nerve roots can produce a dull chest pain that mimics angina. The discomfort is worsened with neck movement, coughing, or sneezing. On physical examination, application of steady pressure to the head increases axial loading on the nerve root, which can reproduce symptoms (Spurling's maneuver). Further diagnostic testing in the absence of other neurological findings is not indicated in the emergency department setting. Patients can be safely discharged with follow-up arrangements.

### Conclusions

Adult patients presenting to the emergency department with a chief complaint of chest pain can

have a myriad of conditions. Emergent conditions such as aortic dissection, pulmonary embolism, pneumothorax, pericarditis, esophageal rupture and ACS require rapid diagnosis and treatment. Once the patient is stabilized, other diagnoses, such as anxiety disorder, gastritis, gall bladder disease, and musculoskeletal pain can be considered. An individual may have more than one cause for a clinical presentation. In the evaluation of patients with acute chest pain, it is critical that all potential causes be considered and premature closure of the diagnosis be avoided.

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