CHAPTER 1

Approach to Acute Chest Pain

Deborah B. Diercks and Nathan Parker

IN THIS CHAPTER

Initial approach
Acute coronary syndrome
Pulmonary embolism
Esophageal rupture
Tension pneumothorax
Aortic dissection
Cardiac tamponade
Ancillary tests
Advanced imaging
Clinical decision rules

More than 6 million Americans present to emergency departments every year with the chief complaint of acute chest pain.[1] The differential diagnosis is extremely broad (Table 1-1). Emergency physicians have the difficult task of differentiating life-threatening causes requiring immediate intervention from more benign causes. In this chapter, we focus on the presentation of the most common critical diagnoses, their initial workup, and the strategies employed to ensure a safe and successful disposition.

Initial Approach

All patients without an obviously benign cause of chest pain should have their vital signs assessed immediately, be connected to a monitor, and have intravenous access established. Ideally, an electrocardiogram (ECG) should be obtained in the prehospital setting. Recent data have shown that paramedics and nurses, given adequate training, can reliably diagnose ST-elevation myocardial infarction (STEMI) and subsequently alert destination hospitals.[2] Since it has been well established that early reperfusion reduces mortality and morbidity, a system should be in place to facilitate rapid percutaneous intervention or fibrinolysis once STEMI has been confirmed.[3] A focused history and physical examination should be performed promptly by the emergency care provider because successful management of conditions such as tension pneumothorax depends on the provider's acting within minutes of a patient's presentation.

KEY POINT

Patients with chest pain should have an ECG obtained on arrival.

Acute Coronary Syndrome

Of the common presenting causes of chest pain, acute coronary syndrome (ACS) presents a particular challenge to emergency physicians. Defined as the syndrome resulting from acute cardiac ischemia, ACS encompasses stable angina, unstable angina, STEMI, and non-STEMI (NSTEMI).

Missed acute myocardial infarctions (AMIs) are frequent causes of litigation against medical providers. Emergency physicians disagree over the acceptable rate of missed acute MI; most accept a rate between 0.01% and 2%.[4] Care providers in emergency departments with low patient volumes and limited resources face particularly difficult challenges in making the diagnosis; miss rates tend to be higher in these facilities.[5]

In the "classic" presentation of ACS, the patient usually describes the pain as pressure, squeezing, or crushing. The pain is located substernally or on the left, and it can radiate to the jaw,

neck, or arms. Associated symptoms usually include diaphoresis, nausea, vomiting, weakness, and syncope.[6] However, none of these signs and symptoms is sensitive or specific enough on its own to rule in or out ACS independent of an ECG, cardiac biomarkers, and other diagnostic tests.[7] Similarly, the presence of traditional risk factors such as hypertension, hyperlipidemia, diabetes mellitus, family history of coronary artery disease (CAD), and history of smoking, although positively correlating with adverse events within 6 months, does not correlate with the incidence of acute MI in the emergency department.[8] However, emergency care providers should be cautious about an initial impression of "noncardiac chest pain" if traditional risk factors are present because 3% of patients with those factors will experience an adverse cardiac event within 30 days.[9]

To further complicate the establishment of a diagnosis, many patients with an eventual diagnosis of acute MI present without chest pain at all.[10] This presentation is more common among women than men (42% and 31%, respectively), but the difference decreases with increasing age.[11] Atypical presentation of acute MI is also associated with diabetes, heart failure, advanced age, and nonwhite races.[12]

TABLE 1-1.

Causes of Chest Pain

Cardiovascular
Acute MI
Aortic dissection
Cardiac tamponade
Coronary spasm
Pericarditis
Stable angina
Unstable angina
Pulmonary
Bronchitis
Pneumonia
Pneumothorax
Pulmonary embolus
Gastrointestinal
Cholecystitis
Esophageal reflux
Esophageal rupture
Esophageal spasm
Esophageal tear
Gastritis
Hepatitis
Pancreatitis
Peptic ulcer disease
Musculoskeletal
Costochondritis
Muscle strain
Rib fracture

KEY POINT

Many patients with ACS present without chest pain.

Pulmonary Embolism

Pulmonary embolism (PE) accounts for up to 200,000 deaths in the United States annually.[13] Like ACS, PE represents a broad range of disease, from asymptomatic incidental findings to saddle embolus causing shock and sudden death. Among patients presenting in shock, the short-term mortality rate can reach as high as 50%.[14]

Reflecting this broad spectrum of disease, the clinical signs and symptoms are especially difficult to interpret. In a large, prospective study, the following symptoms were present in patients diagnosed with PE: dyspnea (79%), pleuritic pain (49%), cough (43%), wheezing (31%), calf or thigh swelling (39%), and calf or thigh pain (16%). On physical examination, the following signs were present: tachypnea (57%), tachycardia (26%), rales (21%), and signs of deep vein thrombosis (DVT) in the calf or thigh (47%).[15]

Risk factors for acute PE include recent surgery, trauma, immobility, cancer, neurologic disease with lower extremity paresis, oral contraceptive use, hormone therapy, and pregnancy.[12] Given the difficulty in diagnosing PE, multiple clinical decision rules have been devised to aid in the workup. These rules are discussed later in this chapter.

Esophageal Rupture

Esophageal rupture is a relatively rare cause of acute chest pain among emergency department patients. Although its true incidence is unknown, the diagnosis carries a high mortality rate—approximately 20% despite modern therapies.[16] The mean age of patients with esophageal rupture is the early 60s, and more than two thirds of patients are male.[17] Esophageal perforations are most commonly iatrogenic, usually caused by endoscopic procedures, with a minority of ruptures resulting spontaneously from increased intraabdominal pressures typically associated with vomiting (eg, Boerhaave syndrome).[18] Other causes include caustic ingestions and blunt or penetrating trauma.

The classic features of esophageal rupture include the sudden onset of chest pain precipitated by severe vomiting or retching. The Mackler triad of esophageal rupture—chest pain, vomiting, and subcutaneous emphysema—was first described in 1952; this triad is absent in most patients.[12] Associated symptoms include shortness of breath, dysphonia, dysphagia, abdominal pain, hematemesis, and melena. On physical exam-

ination, tachycardia is frequently noted, with fever presenting later. Crepitus in the neck or chest wall is indicative of subcutaneous emphysema. Rapidly progressing pleural effusions can be a late sign.[19]

Tension Pneumothorax

Nontraumatic spontaneous tension pneumothorax is also a relatively uncommon cause of acute chest pain. Approximately 1% to 2% of all spontaneous pneumothoraxes present under tension.[20] Clinically, a pneumothorax is considered to be under tension when it causes significant respiratory or hemodynamic compromise as a result of positive intrapleural pressure. In an awake patient being ventilated without positive pressure, this process can develop only if the intrapleural pressure is less than the atmospheric pressure during some period of the respiratory cycle. Therefore, the spectrum of tension pneumothorax can range from intrapleural pressure that is positive only at the end expiratory phase to pressure that is positive throughout the entire respiratory cycle.[21]

Spontaneous pneumothorax can be divided into the following two classifications: primary spontaneous pneumothorax, which occurs in the absence of apparent underlying lung disease, and secondary spontaneous pneumothorax, which develops as a result of underlying lung pathology. Risk factors for primary spontaneous pneumothorax include male sex (6:1 relative risk compared with females), tall stature, smoking, low body mass index, sudden changes in environmental pressure, genetic predisposition, inhalant use, and even exposure to loud music.[22,23] Risk factors for secondary spontaneous pneumothorax include chronic obstructive pulmonary disease, interstitial lung disease, infection, neoplasm, and connective tissue disease.[22]

Symptoms of tension pneumothorax typically include the rapid onset of pleuritic chest pain and shortness of breath. In addition to unilateral reduced breath sounds and hyperresonance, tension pneumothorax also can present with tachycardia, tachypnea, hypotension, and tracheal deviation away from the affected side.[24] If a tension pneumothorax is highly suspected based on the history and physical examination alone, steps should be taken immediately to relieve the pressure via needle or tube thoracostomy. A recent review showed tube thoracostomy to be superior to percutaneous aspiration; the reason was initially thought to be that the chest wall thickness exceeded the length of the catheter in percutaneous aspiration, but this does not appear to be the case.[25,26] Therefore, in patients with tension pneumothorax, immediate tube thoracostomy is indicated.

KEY POINT

Immediate decompression of a suspected tension pneumothorax with tube thoracostomy is indicated before confirmation with chest radiography.

Aortic Dissection

Few critical diagnoses are as feared by emergency care providers as acute aortic dissection, which is notoriously difficult to diagnose. Some studies suggest that up to one-third of all aortic dissections are initially misdiagnosed. The difficulty is compounded by its relatively low prevalence (1 case per every 10,000 emergency department visits).[27,28] Acute aortic dissection is often mistaken for myocardial infarction. The mortality rate associated with untreated dissection reaches 1% to 2% per hour during the first 48 hours.[29,30]

KEY POINT

Up to one-third of all aortic dissections are misdiagnosed.

Both the DeBakey and Stanford classifications systems have been widely used for describing aortic dissections. DeBakey type I begins in the ascending aorta and extends beyond the arch. Type II involves the ascending aorta only, while type III involves only the descending aorta. Stanford type A is any dissection that involves the ascending aorta, and type B dissections do not. Although both classifications can be used, it is most important to identify if the ascending arch is involved, as dissections involving the ascending arch usually require emergent surgical intervention.[31]

Recent guidelines published by the American Heart Association, in conjunction with other professional societies, describe important clinical risk factors for assessing the pretest probability of acute aortic dissection in patients with chest pain. These factors include Marfan or Ehlers-Danlos syndrome, a family history of aortic disease, aortic valve disease, recent aortic manipulation, thoracic aortic aneurysm, abrupt onset of pain, pain that is severe, pain that is ripping or tearing, pulse deficit in the upper limbs, focal neurologic deficit, hypotension or shock, and new aortic regurgitation murmur.[32] When these features were applied to the International Registry of Acute Aortic Dissection, over 95% of patients with confirmed aortic dissection had at least one of them.[28]

Research has been done to determine the factors that delay the time from presentation to diagnosis. Female patients, patients transferred from a non-tertiary care facility, and patients who have had previous cardiac surgery all had longer delays in diagnosis. The same is true for patients with mild or no pain, patients with atypical features such as fever, those with heart failure, and those with an initial ECG suggestive of myocardial ischemia.[33] A Japanese study suggested that patients who walk into the emergency department are also more likely to have a delay in diagnosis.[34] Given the high mortality rate associated with missed diagnosis and the relatively low incidence of this dangerous condition, high suspicion must be maintained to prevent complications.

Cardiac Tamponade

Cardiac tamponade, another relatively rare diagnosis, refers to hemodynamic compromise caused by increased pericardial pressure. The spectrum of this disease ranges from mild and asymptomatic (pericardial pressure <10 mm Hg) to severe, causing shock (pericardial pressure >20 mm Hg).[35] Other than trauma and recent cardiac surgery, medical causes of pericardial effusion include acute pericarditis, malignancy, acute MI causing wall rupture, aortic dissection, uremia, heart failure,

bacterial or viral infection, and collagen vascular disease.[12]

The Beck triad of low arterial blood pressure, distended neck veins, and muffled heart sounds has been used to describe the signs of cardiac tamponade, but these are probably late findings. Increased sympathetic drive usually causes hypertension before the physiologic reserve is exhausted.[36] A recent review of studies involving patients with pericardial effusion delineated the following signs and symptoms associated with the disease and their related sensitivities: dyspnea (87%–88%), pulsus paradoxus greater than 10 mm Hg (82%), tachycardia (77%), hypotension (26%), diminished heart sounds (28%), and elevated jugular venous pressure (76%).[37]

Ancillary Tests

Electrocardiography

The 12-lead ECG is one of the cornerstones in chest pain evaluation. This chapter reviews common ECG changes that, in general, suggest important diagnoses; subtleties of ECG interpretation are discussed in depth elsewhere in this book. ECGs provide a "snapshot" of the heart's electrophysiology. To fully capture a dynamic process, including an evolving myocardial infarction, serial ECGs repeated 30 to 60 minutes after the initial study are recommended when the initial tracing is nondiagnostic and suspicion remains for ongoing ischemia.[38] It is important to remember that a normal ECG does not rule out acute ischemia; more than 50% of patients with missed AMI had a normal initial ECG.[12]

ST-segment elevation has a variety of causes (Table 1-2). ST-segment elevation should raise suspicion for acute ischemia/infarct when it exists in two or more contiguous leads.[39] When reciprocal ST-segment depression is present, the diagnosis of STEMI becomes more likely.[40] When an inferior STEMI is suspected (elevation in lead II, III, or aVF), tracings from leads V_4R through V_6R can be obtained to evaluate for right ventricular infarction, as these patients are often preload dependent.[41]

Although diffuse ST elevation and PR depression (ST depression and PR elevation in aVR) constitute the classic ECG finding in acute pericarditis, once the condition has progressed to a significant pericardial effusion, electrical alternans can be seen.[42,43] For PE, the ECG is usually of little diagnostic utility. In PE, the classic finding of $S_1Q_3T_3$ is rarely seen. The most common ECG findings are sinus tachycardia or nonspecific ST-segment or T-wave changes.[44]

A recent study of 159 patients with type A aortic dissection showed that almost half of them had acute changes on the ECG. ST depression (34%) was the most common, but ST elevation (8%) was present as well. Finding these ST changes increases the risk of misdiagnosis.[45] ST elevation in acute dissection is also associated with involvement of the coronary ostia, the right coronary artery being most commonly involved.[46]

TABLE 1-2.

Causes of ST Elevation on ECG

Acute MI
Pericarditis
Left ventricular hypertrophy
Benign early repolarization
Prinzmetal angina
Brugada syndrome
Left ventricular aneurysm

Chest Radiograph

The chest radiograph (CXR) is another important diagnostic tool in patients with acute chest pain. Although the CXR rarely provides the diagnosis in isolation, it can rapidly change a treatment algorithm. For example, although a CXR can provide important information in a stable patient, delaying treatment for imaging in a patient with clinically suspected tension pneumothorax is not optimal. Still, tube thoracostomy is not indicated in other diagnoses such as diaphragm rupture, which can mimic the presentation of tension pneumothorax, so the decision to image or not must be individualized for each patient.

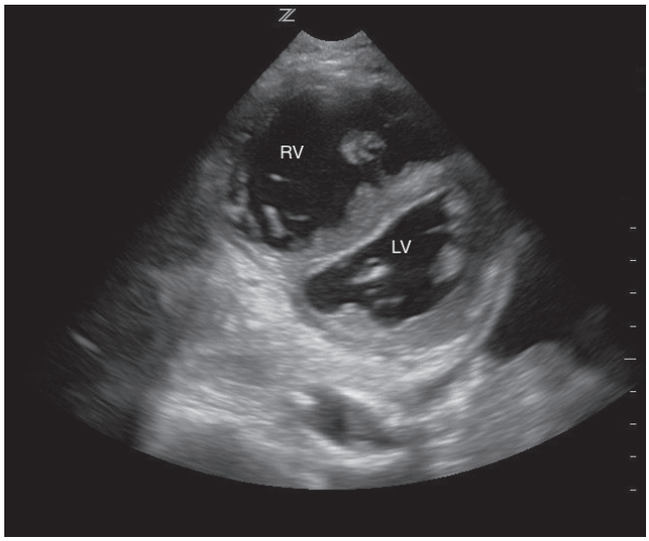
The CXR is commonly used to evaluate patients with suspected aortic dissection, but it is neither sensitive nor specific for this disease. In one study, only 73% of patients with known type A aortic dissection had signs suggesting dissection, most commonly widened mediastinum, while 16% of normal CXRs were thought to be suspicious for dissection.[47] Up to 90% of patients with esophageal rupture have abnormal findings on CXR, most commonly pneumomediastinum, hydropneumothorax, and isolated pleural effusion.[48] Interestingly, the esophagus ruptures most often on the left, with subsequent development of a pleural effusion on that side.[49]

KEY POINT

A normal chest radiograph does not rule out aortic dissection.

FIGURE 1-1.

Right heart strain; note dilated right ventricle. Photo courtesy of K. Kelley.



In one large study of patients known to have PE, cardiomegaly (27%) was the abnormality most frequently seen on CXR; 24% of patients had a normal CXR.[50] The classic Hampton hump is rarely seen. The CXR can provide useful information when the physician is deciding whether to perform ventilation-perfusion scintigraphy or CT angiography, as patients with known chronic lung disease have a higher incidence of nondiagnostic ventilation-perfusion scans.[51]

Ultrasonography

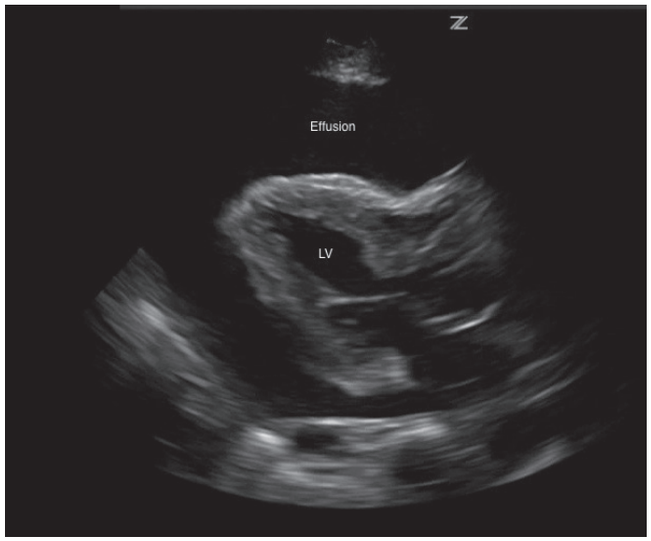
Ultrasonography has become an integral diagnostic tool in the provision of emergency care. In patients who come to the emergency department in shock, a two-dimensional transthoracic echocardiogram (2D-TTE) that shows no signs of right ventricular strain (Figure 1-1) can practically exclude PE as the cause of hypotension.[52] However, a negative ultrasound scan does not rule out PE as a cause of chest pain.[53] Two-dimensional transthoracic echocardiography is the gold standard for diagnosing pericardial effusion in the emergency department, and all patients with suspected pericarditis and any high-risk features should have bedside echocardiography to aid in diagnosis and rule out pericardial tamponade (Figure 1-2).[54]

When ACS is suspected, early 2D-TTE can contribute information to the prognosis by identifying wall motion abnormalities.[55] In a study of patients presenting to an emergency department with acute chest pain and a nondiagnostic ECG, those with a normal 2D-TTE (performed by a cardiologist) had no major cardiac events at 30 days.[56] Structural abnormalities that might change therapeutic management, such as papillary muscle rupture or ventricular septum rupture, can also be identified; images suggesting such abnormalities should be interpreted only by experienced cardiac sonographers.[57]

Limited data exist on the role of ultrasonography in the diagnosis of aortic dissection. In evaluating for an intimal flap, 2D-TTE can be combined with abdominal ultrasonography. The sensitivity of 2D-TTE in detecting acute aortic dissection has been reported to be 67% to 80%, while its specificity is 99% to 100%.[58] When dissection is identified in an unstable patient, emergent cardiothoracic surgery should be expedited.[59]

FIGURE 1-2.

Echocardiographic image of a patient with a pericardial effusion. Photo courtesy of K. Kelley.



Bedside ultrasonography performed by emergency physicians has a sensitivity approaching 100% for pneumothorax, compared with a 75% sensitivity for an upright CXR.[60] This degree of sensitivity, as well as ultrasound's portability, has fostered the use of ultrasonography in military operations and in remote locations where other imaging modalities are unavailable.[61] The detection of occult pneumothorax that was not seen on a CXR might not prove to be clinically significant, but it should prompt the care provider to monitor the patient closely for pneumothorax expansion.[62]

KEY POINT

Bedside emergency ultrasonography is a valuable tool in the workup of chest pain.

Troponins

Cardiac troponins (T and I) are the preferred markers of myocardial injury in patients presenting with chest pain. They are more sensitive and specific than the biomarkers used in the past.[63] It is important to remember, however, that myocardial necrosis can result from pathologies other than MI or ACS.[64] With the introduction of new highly sensitive troponin (hs-cTn) assays, which are 1,000- to 10,000-fold more sensitive than the original first-generation troponin assays, differentiating the causes of myocardial necrosis (including MI and ACS) will be more important as medical care providers are challenged with interpreting an increasing number of positive tests.[65]

Given our increased ability to measure very low concentrations of cardiac troponins, an upper limit of normal at the population-adjusted 99th percentile has been defined.[66] With the application of this newly defined cutoff, more patients with signs and symptoms suggesting acute MI have an elevated hs-cTn level when they come to the emergency department; a recent study showed an almost 200% increase in the number of hs-cTn–positive patients who were eventually diagnosed with chest pain unrelated to coronary occlusion. Troponin is released during tachyarrhythmia in young healthy people as well as in those undergoing sustained strenuous exercise.[67] However, even small increases in hs-cTn levels in patients presenting with chest pain have been associated with adverse short- and long-term prognoses.[68]

The definition of AMI, which includes the "rise and/or fall of cardiac biomarkers," may have to be refined with the advent of hs-cTn assays.[69] An acute change in the hs-cTn level of more than 20% has been suggested as representing either new or resolving myocardial injury. However, healthy study subjects have demonstrated a baseline variability of more than 50%.[70,71] It is important to note that simply changing the diagnostic criterion of AMI to include a hs-cTn change of more than 50% decreases the sensitivity of the test to less than 70%.[64]

It is likely that the introduction of hs-cTn assays will provide several benefits to emergency medicine practice, but its place in our diagnostic algorithm has not been fully defined. It has

been suggested that, given the fact that hs-cTn levels elevate earlier, the timing of our serial cardiac marker testing could be shortened to less than 3 hours after initial presentation.[72] The assay might take a role analogous to the D-dimer test, given its relatively high negative predictive value.[73] It will also be important to reevaluate our chest pain clinical decision rules, as most of them were developed before hs-cTn assays became available.

KEY POINT

The role of the new highly sensitive troponin assays remains unclear in the evaluation of patients with chest pain.

D-Dimer

The D-dimer assay has been used in the evaluation of patients for PE for more than 20 years. Although many assays exist, most used in emergency practice have a high sensitivity (typically in the mid 90% range) but low specificity for venous thromboembolism (VTE).[74] In the contemporary diagnostic algorithm, a highly sensitive D-dimer assay that is below the designated cutoff in a non–high-risk population can be used to exclude VTE because of its negative predictive value of more than 99% in this population.[75] In fact, the highly sensitive quantitative D-dimer test has one of the highest sensitivities of any test used in the screening of patients for VTE.

The D-dimer assay has been studied for both prognostic purposes and for evaluation of the burden of disease in PE. High D-dimer levels are associated with increased 15-day and 3-month mortality rates as well as a more central location of clots on CT angiogram.[76,77] High levels are also associated with a higher pulmonary artery obstruction index.[78]

KEY POINT

A negative D-dimer does not rule out pulmonary embolus in a population at high risk for the disease.

Recently, the use of the D-dimer assay was studied in the context of aortic dissection. A metaanalysis found a pooled sensitivity of 94%, but specificity remained poor.[79] Concern exists regarding the proposed use of the test to rule out aortic dissection in low-risk populations, as isolated intramural hematomas or thromboses have been associated with false-negative tests.[80] Given the low incidence of acute aortic dissection in the general population presenting with chest pain, it has been suggested that routine screening with D-dimer assays would increase CT scan utilization by approximately 40% and would not necessarily aid in timely diagnosis.[81]

Other Biomarkers

New research has focused on addressing methods for shortening the time needed to rule out MI in the emergency department. In low-risk populations, adding either N-terminal pro-B type natriuretic peptide (NT-proBNP) or copeptin to the initial troponin assessment at presentation significantly increased the sensitivity and the negative predictive value for MI.[82,83] Measuring unbound free fatty acids in addition to conventional or highly sensitive troponin also improves sensitivity and specificity in the detection of ACS.[84] Higher levels of NT-proBNP or ST2 (a novel biomarker of cardiac stress) in patients with chest pain have been associated with increased mortality.[85,86] Investigating the interesting concept that larger platelets are more active, researchers have found a correlation between mean platelet volume and ACS in patients with acute chest pain.[87]

Advanced Imaging

Computed Tomography Angiography

Computed tomography angiography (CTA) has become the gold standard as the initial imaging test in the workup of patients suspected of having aortic dissection or PE. The sensitivity and specificity of CTA in detecting acute aortic dissection have been reported as 100% and 98% to 99%, respectively.[88] The data associated with PE have shown larger variations in accuracy. The largest study to date, PIOPED II, reported sensitivity of 83% and specificity of 96%, but most of the scans were performed with four-slice CT.[89] It is possible that with the arrival of 64-slice multidetector CT the diagnostic accuracy will increase significantly, thereby allowing a negative CTA alone to be used to effectively rule out PE as the cause of chest pain in all risk groups.[88]

As diagnostic accuracy increases with improved technology, an increasing number of isolated subsegmental PEs are being diagnosed with CTA.[90] No consensus has been reached regarding the proper management of patients with isolated subsegmental PE because 3-month outcomes are generally favorable and the risk of hemorrhage with anticoagulation might outweigh the benefits.[91]

Coronary Computed Tomography Angiography

Coronary CTA (CCTA) has received much attention in recent years, with a flurry of data about its use coming out in a short time. Although the role of CCTA has not been established or extensively validated in the workup of chest pain in the emergency department, its proposed use has been hotly debated. A recent metaanalysis involving only prospective studies estimated the sensitivity and specificity of CCTA for ACS to be 95%

TABLE 1-3.

PERC Rule[101]

Age under 50 years
Heart rate less than 100 beats/min
Oxygen saturation of more than 94% on room air
No history of DVT/PE
No recent trauma/surgery
No hemoptysis
No exogenous estrogen
No clinical signs of DVT

If all eight criteria are met, patient has less than a 2% chance of having PE.

and 87%, respectively.[92]

Heralded for its high negative predictive value and its potential to rule out ACS with a negative scan, CCTA has been shown to decrease time to diagnosis and disposition.[93,94] Critics of CCTA point out its low positive predictive value—all patients with significant underlying CAD, stable or not, will likely have a positive scan and thus require additional testing.[95] The radiation exposure must also be considered, as well as the fact that the study cannot be performed in patients with renal failure, those unable to tolerate beta-blockers, and those with ectopic rhythms.[96] While not yet standard of care, CCTA will likely find a role in rapidly triaging patients who are at low to intermediate risk for ACS and who have initially normal cardiac markers and an ECG that does not raise concern.[97,98]

Triple-Rule-Out Computed Tomography Angiography

A recently developed protocol combines CCTA with imaging of the pulmonary arteries and thoracic aorta. Triple-rule-out CTA enables patients to be simultaneously evaluated for ACS, PE, and aortic dissection in less than 20 minutes. The protocol has significant limitations: it is technically difficult to perform, it delivers a 50% larger dose of radiation than CCTA, and its image quality varies.[99] However, because more than 20% of patients evaluated for ACS are simultaneously assessed for PE or aortic dissection, performing only one imaging study would decrease their overall radiation exposure.[100] As with CCTA, the use of triple-rule-out CTA has not yet been validated in large prospective trials, but it may still find a role in ruling out disease in low- to intermediate-risk patients.[1]

Clinical Decision Rules

Considering the difficulty in accurately diagnosing the cause of chest pain while performing an efficient and cost-effective workup, multiple clinical decision rules have been devised to assist emergency physicians. Many of these rules have been well validated in large prospective trials. These rules should never replace the physician's best judgment, but they can be helpful when the differential diagnosis remains large. In this section, we describe a few of the more recognized clinical decision rules, along with their limitations.

Pulmonary Embolism Rule-out Criteria

The pulmonary embolism rule-out criteria (PERC) rule (Table 1-3) was devised to avoid additional testing in patients with a low pretest probability for PE. If a patient meets all eight criteria, his or her probability of having PE is less than 2%, which is an appropriate cutoff to discontinue further testing.[101] The rule's sensitivity for detecting PE is 97%; however, caution is advised, because the rule applies only to patients for whom the clinical suspicion for PE is low (<15%).[102] In patients for whom the probability is high, the PERC rule does not safely exclude the condition.[103]

TABLE 1-4.

PE Risk Stratification[104,105]

Wells	
Criteria	**Score**
Clinical signs and symptoms of DVT	+3
PE is most likely diagnosis	+3
Heart rate above 100 beats/min	+1.5
Immobilization in past 3 days or surgery in the past 4 weeks	+1.5
Previous DVT/PE	+1.5
Hemoptysis	+1
Malignancy with treatment in past 6 months or palliative care	+1
Low risk (15%)	<2 points
Intermediate risk (29%)	2-6 points
High risk (59%)	>6 points

Revised Geneva	
Criteria	**Score**
Lower extremity tenderness and unilateral edema	+4
Unilateral leg pain	+3
Heart rate between 75 and 94 beats/min	+3
Heart rate above 95 beats/min	+5
Surgery or fracture within 1 month	+2
Previous DVT/PE	+3
Hemoptysis	+2
Active malignancy	+2
Patient older than 65 years	+1
Low risk (8%)	<4 points
Intermediate risk (28%)	4-10 points
High risk (74%)	>10 points

KEY POINT

In a low-risk population, a negative PERC score can preclude the need for further workup for pulmonary embolus.

Wells and Revised Geneva Scores

The Wells and revised Geneva scores (Table 1-4) were developed by assessing the clinical probability of PE and have been validated in large clinical trials.[104,105] Both scores successfully stratify patients into low-, intermediate-, and high-risk groups for PE, but the Wells score is superior for the identification of patients in the high-risk group.[106] Critics of the Wells score point to the subjective nature of the score. It asks care providers to determine if PE is the most likely diagnosis. In contrast, the revised Geneva score is based solely on objective data.[107] In patients with an "unlikely" probability in the Wells or revised Geneva score (≤4 or <4, respectively), a negative highly sensitive D-dimer assay may be used to exclude PE without additional testing.[108]

Thrombolysis In Myocardial Infarction Risk Score

The Thrombolysis In Myocardial Infarction (TIMI) risk score (Table 1-5) has been well validated as a method to stratify patients diagnosed with unstable angina/NSTEMI according to their risk for adverse events. The score is used to guide therapeutic and prognostic decision making.[109] The TIMI risk score also correlates with outcomes when applied to emergency department patients[110]; however, its sensitivity alone has been shown repeatedly to be inadequate at ruling out ACS in the unique population of emergency department patients.[110,111] Although attempts have been made to create a "modified TIMI score" with improved performance in risk stratification, the new decision rule was still unable to screen patients safely for adverse events in the emergency department.[112]

HEART Score and North American Chest Pain Rule

The HEART score and the North American Chest Pain Rule (NACPR) were devised to identify patients who experienced chest pain but are suitable for early discharge without stress testing or cardiac imaging.[113,114] Both tools have yet to be validated in large multicenter prospective trials, but they have been shown initially to have an acceptable miss rate (<1%) for adverse events when combined with serial troponin measurements.[115] It is unlikely that these rules will change clinical practice, as they generally describe the current standard of care for ACS evaluation in the emergency department.

TABLE 1-5.

TIMI Risk Score[109]

Age 65 years or older	+1
Three or more CAD risk factors (hypertension, diabetes, smoking, HDL below 40, family history of premature CAD)	+1
Known CAD (stenosis of 50% or more)	+1
Aspirin use in past 7 days	+1
Two or more anginal events in past 24 hours	+1
ST changes of 0.5 mm or more	+1
Positive serum cardiac marker	+1

Risk of adverse event: 1=4.7%; 2=8.3%; 3=13.2%; 4=19.9%; 5=26.2%; 6, 7=at least 40.9%

Conclusion

Chest pain is a common emergency department presentation and has multiple causes. Emergency providers should take a careful and systematic approach to evaluating patients with chest pain. As technology has improved and tests have become more sensitive, providers must navigate the increasingly complex workup and allocate resources appropriately. By using the strategies outlined in this chapter, emergency physicians should be able to diagnose the life-threatening causes of chest pain safely and successfully.

References

1. Halpern EJ. Triple-rule-out CT angiography for evaluation of acute chest pain and possible acute coronary syndrome. *Radiology*. 2009;252(2):332-345.
2. Feldman JA, Brinsfield K, Bernard S, et al. Real-time paramedic compared with blinded physician identification of ST-segment elevation myocardial infarction: results of an observational study. *Am J Emerg Med*. 2005;23(4):443-448.
3. O'Connor RE, Bossaert L, Arntz HR, et al. Part 9: Acute coronary syndromes: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Circulation*. 2010;122(16 Suppl 2):S422-S465.
4. Than M, Herbert M, Flaws D, et al. What is an acceptable risk of major adverse cardiac event in chest pain patients soon after discharge from the emergency department?: a clinical survey. *Int J Cardiol*. 2013;166(3):752-754.
5. Schull MJ, Vermeulen MJ, Stukel TA. The risk of missed diagnosis of acute myocardial infarction associated with emergency department volume. *Ann Emerg Med*. 2006;48(6):647-655.
6. Panju AA, Hemmelgarn BR, Guyatt GH, Simel DL. The rational clinical examination. Is this patient having a myocardial infarction? *JAMA*. 1998;280(14):1256-1263.
7. Goodacre SW, Angelini K, Arnold J, et al. Clinical predictors of acute coronary syndromes in patients with undifferentiated chest pain. *QJM*. 2003;96(12):893-898.
8. Body R, McDowell G, Carley S, Mackway-Jones K. Do risk factors for chronic coronary heart disease help diagnose acute myocardial infarction in the emergency department? *Resuscitation*. 2008;79(1):41-45.
9. Miller CD, Lindsell CJ, Khandelwal S, et al. Is the initial diagnostic impression of "noncardiac chest pain" adequate to exclude cardiac disease? *Ann Emerg Med*. 2004;44(6):565-574.
10. Canto JG, Shlipak MG, Rogers WJ, et al. Prevalence, clinical characteristics, and mortality among patients with myocardial infarction presenting without chest pain. *JAMA*. 2000;283(24):3223-3229.
11. Canto JG, Rogers WJ, Goldberg RJ, et al. Association of age and sex with myocardial infarction symptom presentation and in-hospital mortality. *JAMA*. 2012;307(8):813-822.
12. Woo KM, Schneider JI. High-risk chief complaints I: chest pain—the big three. *Emerg Med Clin North Am*. 2009;27(4):685-712.
13. Becattini C, Agnelli G. Acute pulmonary embolism: risk stratification in the emergency department. *Intern Emerg Med*. 2007;2(2):119-129.
14. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). *Lancet*. 1999;353(9162):1386-1389.
15. Stein PD, Beemath A, Matta F, et al. Clinical characteristics of patients with acute pulmonary embolism: data from PIOPED II. *Am J Med*. 2007;120(10):871-879.
16. Ryom P, Ravn JB, Penninga L, et al. Aetiology, treatment and mortality after oesophageal perforation in Denmark. *Dan Med Bull*. 2011;58(5):A4267.
17. Bhatia P, Fortin D, Inculet RI, Malthaner RA. Current concepts in the management of esophageal perforations: a twenty-seven year Canadian experience. *Ann Thorac Surg*. 2011;92(1):209-215.
18. Vidarsdottir H, Blondal S, Alfredsson H, et al. Oesophageal perforations in Iceland: a whole population study on incidence, aetiology and surgical outcome. *Thorac Cardiovasc Surg*. 2010;58(8):476-480.

19. Søreide JA, Viste A. Esophageal perforation: diagnostic work-up and clinical decision-making in the first 24 hours. *Scand J Trauma Resusc Emerg Med*. 2011;19:66.
20. Holloway VJ, Harris JK. Spontaneous pneumothorax: is it under tension? *J Accid Emerg Med*. 2000;17(3):222-223.
21. Leigh-Smith S, Harris T. Tension pneumothorax—time for a re-think? *Emerg Med J*. 2005;22(1):8-16.
22. Weldon E, Williams J. Pleural disease in the emergency department. *Emerg Med Clin North Am*. 2012;30(2):475-499.
23. Hassani B, Foote J, Borgundvaag B. Outpatient management of primary spontaneous pneumothorax in the emergency department of a community hospital using a small-bore catheter and a Heimlich valve. *Acad Emerg Med*. 2009;16(6):513-518.
24. Currie GP, Alluri R, Christie GL, Legge JS. Pneumothorax: an update. *Postgrad Med J*. 2007;83(981):461-465.
25. Aguinagalde B, Zabaleta J, Fuentes M, et al. Percutaneous aspiration versus tube drainage for spontaneous pneumothorax: systematic review and meta-analysis. *Eur J Cardiothorac Surg*. 2010;37(5):1129-1135.
26. McLean AR, Richards ME, Crandall CS, Marinaro JL. Ultrasound determination of chest wall thickness: implications for needle thoracostomy. *Am J Emerg Med*. 2011;29(9):1173-1177.
27. Asouhidou I, Asteri T. Acute aortic dissection: be aware of misdiagnosis. *BMC Res Notes*. 2009;2:25.
28. Rogers AM, Hermann LK, Booher AM, et al. Sensitivity of the aortic dissection detection risk score, a novel guideline-based tool for identification of acute aortic dissection at initial presentation: results from the international registry of acute aortic dissection. *Circulation*. 2011;123(20):2213-2218.
29. Zhan S, Hong S, Shan-Shan L, et al. Misdiagnosis of aortic dissection: experience of 361 patients. *J Clin Hypertens (Greenwich)*. 2012;14(4):256-260.
30. Imamura H, Sekiguchi Y, Iwashita T, et al. Painless acute aortic dissection - diagnostic, prognostic and clinical implications. *Circ J*. 2011;75(1):59-66.
31. Braverman AC. Aortic dissection: prompt diagnosis and emergency treatment are critical. *Cleve Clin J Med*. 2011;78(10):685-696.
32. Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease. *Circulation*. 2010;121(13):e266-e369.
33. Harris KM, Strauss CE, Eagle KA, et al. Correlates of delayed recognition and treatment of acute type A aortic dissection: the International Registry of Acute Aortic Dissection (IRAD). *Circulation*. 2011;124(18):1911-1918.
34. Kurabayashi M, Miwa N, Ueshima D, et al. Factors leading to failure to diagnose acute aortic dissection in the emergency room. *J Cardiol*. 2011;58(3):287-293.
35. Hoit BD. Pericardial disease and pericardial tamponade. *Criti Care Med*. 2007;35(8 Suppl):S355-S364.
36. Brown J, MacKinnon D, King A, Vanderbush E. Elevated arterial blood pressure in cardiac tamponade. *N Engl J Med*. 1992;327(7):463-466.
37. Roy CL, Minor MA, Brookhart MA, Choudhry NK. Does this patient with a pericardial effusion have a cardiac tamponade? *JAMA*. 2007;297(16):1810-1818.
38. Fesmire FM, Decker WW, Diercks DB, et al. Clinical policy: critical issues in the evaluation and management of adult patients with non–ST-segment elevation acute coronary syndromes. *Ann Emerg Med*. 2006;48(3):270-301.
39. Wagner GS, Macfarlane P, Wellens H, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part VI: acute ischemia/infarction: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol*. 2009;53(11):1003-1011.
40. Rowlandson I, Xue J, Farrell R. Computerized STEMI recognition: an example of the art and science of building ECG algorithms. *J Electrocardiol*. 2010;43(6):497-502.
41. Poh KK, Tan HC, Teo SG. ECG ST segment elevation in patients with chest pain. *Singapore Med J*. 2011;52(1):3-8.
42. Petrov DB. Sudden onset of chest pain associated with PR-segment depression in ECG. *Heart Lung*. 2009;38(5):440-443.
43. Lo E, Ren X, Hui PY. Electrical alternans and pulsus paradoxus. *J Hosp Med*. 2010;5(4):253-254.
44. Stein PD, Henry JW. Clinical characteristics of patients with acute pulmonary embolism stratified according to their presenting syndromes. *Chest*. 1997;112(4):974-979.
45. Hirata K, Wake M, Kyushima M, et al. Electrocardiographic changes in patients with type A acute aortic dissection. Incidence, patterns and underlying mechanisms in 159 cases. *J Cardiol*. 2010;56(2):147-153.
46. Ohtani H, Kiyokawa K, Asada H, Kawakami T. Stanford type A acute dissection developing acute myocardial infarction. *Jpn J Thorac Cardiovasc Surg*. 2000;48(1):69-72.
47. Gregorio MC, Baumgartner FJ, Omari BO. The presenting chest roentgenogram in acute type A aortic dissection: a multidisciplinary study. *Am Surg*. 2002;68(1):6-10.
48. Hegenbarth R, Birkenfeld P, Beyer R. Roentgen findings in spontaneous esophageal perforation (Boerhaave syndrome). *Aktuelle Radiol*. 1994;4(6):337-338.
49. Hingston CD, et al. Boerhaave's syndrome – rapidly evolving pleural effusion; a radiographic clue. *Minerva Anestesiol*. 2010;76(10):865-867.
50. Elliot CG, Goldhaber SZ, Visani L, DeRosa M. Chest radiographs in acute pulmonary embolism. *Chest*. 2000;118:33-38.
51. Daftary A, Gregory M, Daftary A, et al. Chest radiograph as a triage tool in the imaging-based diagnosis of pulmonary embolism. *AJR Am J Roentgenol*. 2005;185(1):132-134.
52. Torbicki A, Perrier A, Konstantinides S, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). *Eur Heart J*. 2008;29(18):2276-2315.
53. Roy PM, Colombet I, Durieux P, et al. Systematic review and meta-analysis of strategies for the diagnosis of suspected pulmonary embolism. *BMJ*. 2005;331(7511):259-267.
54. Spodick DH. Risk prediction in pericarditis: who to keep in the hospital? *Heart*. 2008;94(4):398-399.
55. Kontos MC, Arrowood JA, Paulsen WH, Nixon JV. Early echocardiography can predict cardiac events in emergency department patients with chest pain. *Ann Emerg Med*. 1998;31(5):550-557.
56. Muscholl MW, Oswald M, Mayer C, van Scheidt W. Prognostic value of 2D echocardiography in patients presenting with acute chest pain and non-diagnostic ECG for ST-elevation myocardial infarction. *Int J Cardiol*. 2002;84(2-3):217-225.
57. Shah BN, Ahmadvazir S, Pabla JS, et al. The role of urgent transthoracic echocardiography in the evaluation of patients presenting with acute chest pain. *Eur J Emerg Med*. 2012;19(5):277-283.
58. Perkins AM, Liteplo A, Noble VE. Ultrasound diagnosis of type a aortic dissection. *J Emerg Med*. 2010;38(4):490-493.
59. Barrett C, Stone MB. Emergency ultrasound diagnosis of type a aortic dissection and apical pleural cap. *Acad Emerg Med*. 2010;17(4):e23-e24.
60. Blaivas M, Lyon M, Duggal S. A prospective comparison of supine chest radiography and bedside ultrasound for the diagnosis of traumatic pneumothorax. *Acad Emerg Med*. 2005;12(9):844-849.
61. Monti JD, Younggren B, Blankenship R. Ultrasound detection of pneumothorax with minimally trained sonographers: a preliminary study. *J Spec Oper Med*. 2009;9(1):43-46.
62. Kirkpatrick AW, Sirois M, Laupland KB, et al. Hand-held thoracic sonography for detecting post-traumatic pneumothoraces: the Extended Focused Assessment with Sonography for Trauma (EFAST). *J Trauma*. 2004;57(2):288-295.
63. Bassand JP, Hamm CW, Ardissino D, et al. Guidelines for the diagnosis and treatment of non–ST-segment elevation acute coronary syndromes. *Eur Heart J*. 2007;28(13):1598-1660.
64. Christ M, Bertsch T, Popp S, et al. High-sensitivity troponin assays in the evaluation of patients with acute chest pain in the emergency department. *Clin Chem Lab Med*. 2011;49(12):1955-1963.
65. Baker JO, Reinhold J, Redwood S, Marber MS. Troponins: redefining their limits. *Heart*. 2011;97(6):447-452.
66. Thygesen K, Mair J, Katus H, et al. Recommendations for the use of cardiac troponin measurement in acute cardiac care. *Eur Heart J*. 2010;31(18):2197-2204.
67. Michielsen EC, Wodzig WK, Van Dieijen-Visser MP. Cardiac troponin T release after prolonged strenuous exercise. *Sports Med*. 2008;38(5):425-435.
68. Kavsak PA, Wang X, Ko DT, et al. Short- and long-term risk stratification using a next generation, high-sensitivity research cardiac troponin I (hs-cTnI) assay in emergency department chest pain population. *Clin Chem*. 2009;55(10):1809-1815.
69. Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. *Eur Heart* J. 2007;28(20):2525-2538.
70. NACB Writing Group, Wu AH, Jaffe AS, Apple FS, et al. National Academy of Clinical Biochemistry Laboratory medicine practive guidelines: use of cardiac troponins and B-type natriuretic peptide or N-terminal proB-type natriuretic peptide for etiologies other than acute coronary syndromes and heart failure. *Clin Chem*. 2007;53(12):2086-2096.
71. Vasile VC, Saenger AK, Kroning JM, Jaffe AS. Biological and analytical variability of a novel high-sensitivity cardiac troponin T assay. *Clin Chem*. 2010;56(7):1086-1090.
72. Scharnhorst V, Krasznai K, van't Veer M, Michels R. Rapid detection of myocardial infarction with a sensitive troponin test. *Am J Clin Pathol*. 2011;135(3):424-428.
73. Christ M, Popp S, Pohlman H, et al. Implementation of high sensitivity cardiac troponin T measurement in the emergency department. *Am J Med*. 2010;123(12):1134-1142.
74. Righini M, Perrier A, De Moerloose P, Bounameaux H. D-Dimer for venous thromboembolism diagnosis: 20 years later. *J Thromb Haemost*. 2008;6(7):1059-1071.
75. Schutgens RE, Ackermark P, Haas FJ, et al. Combination of a normal D-dimer concentration and a non-high pretest clinical probability score is a safe strategy to exclude deep venous thrombosis. *Circulation*. 2003;107(4):593-597.

76. Klok FA, Djurabi RK, Nijkeuter M, et al. High D-dimer level is associated with increased 15-d and 3 months mortality through a more central localization of pulmonary emboli and serious comorbidity. *Br J Haematol*. 2008;140(2):218-222.
77. Ghanima W, Abdelmoor M, Holmen LO, et al. D-dimer level is associated with the extent of pulmonary embolism. *Thromb Res*. 2007;120(2):281-288.
78. Jeebun V, Doe SJ, Singh L, et al. Are clinical parameters and biomarkers predictive of severity of acute pulmonary emboli on CTPA? *QJM*. 2010;103(2):91-97.
79. Marill KA. Serum D-dimer is a sensitive test for the detection of acute aortic dissection: a pooled meta-analysis. *J Emerg Med*. 2008;34(4):367-376.
80. Sutherland A, Escano J, Coon TP. D-dimer as the sole screening test for acute aortic dissection: a review of the literature. *Ann Emerg Med*. 2008;52(4):339-343.
81. Moysidis T, Lohmann M, Lutkewitz S, et al. Cost associated with D-dimer screening for acute aortic dissection. *Adv Ther*. 2011;28(11):1038-1044.
82. Reichlin T, Hochholzer W, Stelzig C, et al. Incremental value of copeptin for rapid rule out of acute myocardial infarction. *J Am Coll Cardiol*. 2009;54(1):60-68.
83. Truong QA, Bayley J, Hoffmann U, et al. Multi-marker strategy of natriuretic peptide with either conventional or high-sensitivity troponin-T for acute coronary syndrome diagnosis in emergency department patients with chest pain: from the "Rule Out Myocardial Infarction using Computer Assisted Tomography" (ROMICAT) trial. *Am Heart J*. 2012;163(6):972-979.
84. Bhardwaj A, Truong QA, Peacock WF, et al. A multicenter comparison of established and emerging cardiac biomarkers for the diagnostic evaluation of chest pain in the emergency department. *Am Heart J*. 2011;162(2):276-282.
85. Bassan R, Tura BR, Maisel AS. B-type natriuretic peptide: a strong predictor of early and late mortality in patients with acute chest pain without ST-segment elevation in the emergency department. *Coron Artery Dis*. 2009;20(2):143-149.
86. Aldous SJ, Richards AM, Troughton R, Than M. ST2 has diagnostic and prognostic utility for all-cause mortality and heart failure in patients presenting to the emergency department with chest pain. *J Card Fail*. 2012;18(4):304-310.
87. Chu H, Chen WL, Huang CC, et al. Diagnostic performance of mean platelet volume for patients with acute coronary syndrome visiting an emergency department with acute chest pain: the Chinese scenario. *Emerg Med J*. 2011;28(7):569-574.
88. Blanke P, Apfaltrer P, Ebersberger U, et al. CT detection of pulmonary embolism and aortic dissection. *Cardiol Clin*. 2012;30(1):103-116.
89. Stein PD, Fowler SE, Goodman LR, et al. Multidetector computed tomography for acute pulmonary embolism. *N Engl J Med*. 2006;354(22):2317-2327.
90. Auer RC, Schulman AR, Tuorto S, et al. Use of helical CT is associated with an increased incidence of postoperative pulmonary emboli in cancer patients with no change in the number of fatal pulmonary emboli. *J Am Coll Surg*. 2009;208(5):871-880.
91. Donato AA, Khoche S, Santora J, Wagner B. Clinical outcomes in patients with isolated subsegmental pulmonary emboli diagnosed by multidetector CT pulmonary angiography. *Thromb Res*. 2010;126(4):e266-e270.
92. Samad Z, Hakeem A, Mahmood SS, et al. A meta-analysis and systematic review of computed tomography angiography as a diagnostic triage tool for patients with chest pain presenting to the emergency department. *J Nucl Cardiol*. 2012;19(2):364-376.
93. Hoffmann U, Truong QA, Schoenfeld DA, et al. Coronary CT angiography versus standard evaluation in acute chest pain. *N Engl J Med*. 2012;367(4):299-308.
94. Goldstein JA, Chinnaiyan KM, Abidov A, et al. The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial. *J Am Coll Cardiol*. 2011;58(14):1414-1422.
95. Hendel RC. Is computed tomography coronary angiography the most accurate and effective noninvasive imaging tool to evaluate patients with acute chest pain in the emergency department? CT coronary angiography is the most accurate and effective noninvasive imaging tool for evaluating patients presenting with chest pain to the emergency department: antagonist viewpoint. *Circ Cardiovasc Imaging*. 2009;2(3):264-275.
96. Hendel R, Dahdah N. The potential role for the use of cardiac computed tomography angiography for the acute chest pain patient in the emergency department: a cautionary viewpoint. *J Nucl Cardiol*. 2011;18(1):163-167.
97. Nasis A, Meredith IT, Nerlekar N, et al. Acute chest pain investigation: utility of cardiac CT angiography in guiding troponin measurement. *Radiology*. 2011;260(2):381-389.
98. Hoffmann U, Bamberg F. Is computed tomography coronary angiography the most accurate and effective noninvasive imaging tool to evaluate patients with acute chest pain in the emergency department?: CT coronary angiography is the most accurate and effective noninvasive imaging tool for evaluating patients presenting with chest pain to the emergency department. *Circ Cardiovasc Imaging*. 2009;2(3):251-263.
99. Lee HY, Yoo SM, White CS. Coronary CT angiography in emergency department patients with acute chest pain: triple rule-out protocol versus dedicated coronary CT angiography. *Int J Cardiovasc Imaging*. 2009;25(3):319-326.
100. Rogg JG, De Neve JW, Huang C, et al. The triple work-up for emergency department patients with acute chest pain: how often does it occur? *J Emerg Med*. 2011;40(2):128-134.
101. Kline JA, Courtney DM, Kabrhel C, et al. Prospective multicenter evaluation of the pulmonary embolism rule-out criteria. *J Thromb Haemost*. 2008;6(5):772-780.
102. Singh B, Parsaik AK, Agarwal D, et al. Diagnostic accuracy of pulmonary embolism rule-out criteria: a systematic review and meta-analysis. *Ann Emerg Med*. 2012;59(6):517-520.
103. Hugli O, Righini M, Le Gal G, et al. The pulmonary embolism rule-out criteria (PERC) rule does not safely exclude pulmonary embolism. *J Thromb Haemostasis*. 2011;9(2):300-304.
104. Wells PS, Anderson DR, Rodger M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost*. 2000;83(3):416-420.
105. Le Gal G, Righini M, Roy PM, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. *Ann Intern Med*. 2006;144(3):165-171.
106. Penaloza A, Melot C, Motte S. Comparison of the Wells score with the simplified revised Geneva score for assessing pretest probability of pulmonary embolism. *Thromb Res*. 2011;127(2):81-84.
107. Klok FA, Kruisman E, Spaan J, et al. Comparison of the revised Geneva score with the Wells rule for assessing clinical probability of pulmonary embolism. *J Thromb Haemost*. 2008;6(1):40-44.
108. Lucassen W, Geersing GJ, Erkens PM, et al. Clinical decision rules for excluding pulmonary embolism: a meta-analysis. *Ann Intern Med*. 2011;155(7):448-460.
109. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. *JAMA*. 2000;284(7):835-842.
110. Chase M, Robey JL, Zogby KE, et al. Prospective validation of the Thrombolysis in Myocardial Infarction Risk Score in the emergency department chest pain population. *Ann Emerg Med*. 2006;48(3):252-259.
111. Lyon R, Morris AC, Caesar D, et al. Chest pain presenting to the Emergency Department—to stratify risk with GRACE or TIMI? *Resuscitation*. 2007;74(1):90-93.
112. Body R, Carley S, McDowell G, et al. Can a modified thrombolysis in myocardial infarction risk score outperform the original for risk stratifying emergency department patients with chest pain? *Emerg Med J*. 2009;26(2):95-99.
113. Backus BE, Six AJ, Kelder JC, et al. Chest pain in the emergency room: a multicenter validation of the HEART Score. *Crit Pathw Cardiol*. 2010;9(3):164-169.
114. Hess EP, Brison RJ, Perry JJ, Calder LA, et al. Development of a clinical prediction rule for 30-day cardiac events in emergency department patients with chest pain and possible acute coronary syndrome. *Ann Emerg Med*. 2012;59(2):115-125.e1.
115. Mahler SA, Miller CD, Hollander JE, et al. Identifying patients for early discharge: performance of decision rules among patients with acute chest pain. *Int J Cardiol*. 2013;168(2):795-802.