# Differential Diagnosis and Overlap of Acute Chest Discomfort and Dyspnea in the Emergency Department

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*Acute chest discomfort and dyspnea are 2 of the most common nontraumatic symptoms that prompt emergency department evaluations in the United States. The overlap between these presenting symptoms is considerable. In addition, each symptom calls for a broad differential diagnosis that requires rapid refinement according to details in the history, physical examination, blood biomarkers, and radiographic evaluation. This article highlights the epidemiology and the evidence supporting critical decision making, which makes judicious use of the clinical laboratory and diagnostic radiology in the evaluation of the acutely ill patient with chest discomfort and dyspnea.*
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**Key words:** Chest pain • Dyspnea • Emergency department • Differential diagnosis • Biomarkers • CT angiography

Dyspnea and chest discomfort are common chief complaints among patients who present to the emergency department (ED). A chief complaint of dyspnea, or shortness of breath, made up 3.5% of the more than 115 million visits to US EDs in 2003.[1] Chest pain is the chief complaint in about 1% to 2% of outpatient visits as well.[2] The priority in patients presenting with chest pain and dyspnea is to quickly identify or rule out the occurrence of life-threatening causes such as acute coronary syndromes (ACS), heart failure (HF), pulmonary embolus (PE), and aortic dissection. Though a presentation with dyspnea is thought to be associated with a HF presentation it can be a dominant symptom in patients with ACS, just as patients with HF can present with chest pain. This can be explained by the fact that ischemic events can precipitate

an HF exacerbation and HF can lead to an exacerbation of ischemic heart disease. In the Global Registry of Acute Coronary Events (GRACE), over the period of July 1999 to June 2002, 20,881 patients were admitted to the hospital with ACS, of whom 1763 (8.4%) presented with atypical symptoms. The dominant presenting symptom in these patients was dyspnea (in 49.3%).[3] Ischemia and ACS play a primary role in 15% of HF presentations.[4]

The epidemiology of chest pain and dyspnea differs markedly between outpatient and emergency settings. Cardiovascular conditions such as myocardial infarction (MI), angina, PE, and HF are found in more than 50% of patients presenting to the ED with chest pain. The most common causes of chest pain seen in outpatient primary care are musculoskeletal conditions, gastrointestinal disease, stable coronary artery disease (CAD), panic disorder or other psychiatric conditions, and pulmonary disease.[5,6]

## Differential Diagnosis

Over 1.5 million patients are admitted annually with a diagnosis of ACS.[7] Patients who present with ACS represent a heterogeneous population, ranging from those with new onset or progression of anginal symptoms who are biomarker negative, to those who have progressive symptoms such as protracted rest angina who are biomarker positive without ST elevation on electrocardiogram (ECG), and those who have chest discomfort and present with ST-segment elevation myocardial infarction (STEMI). PE is the second most common cause of sudden death after sudden cardiac death. It is often a difficult diagnosis to make as it can masquerade as a benign condition such as an upper respiratory illness or as a serious condition such as cardiogenic shock. Thoracic aortic dissection is not nearly as common as other causes of chest pain and dyspnea. It occurs once per 10,000 patients admitted to the hospital; approximately 2000 new cases are reported each year in the United States.[8] Cardiovascular manifestations can mimic those of ACS, HF, or PE, including symptoms and signs suggestive of congestive HF, secondary to acute severe aortic regurgitation or dyspnea, orthopnea, bibasilar crackles, or elevated jugular venous pressure.[9] Anterior chest pain is a manifestation of ascending aortic dissection. Neck or jaw pain is a manifestation of aortic arch dissection. Interscapular tearing or ripping pain is a manifestation of descending aortic dissection.[10]

Despite the availability of diagnostic aids, including a stethoscope, chest radiograph, pulmonary function testing, ECG, and echocardiography, defining the root cause of acute dyspnea and chest discomfort often remains a challenge. Patients with comorbidities such as chronic obstructive pulmonary disease (COPD), CAD, valvular and hypertensive heart disease, HF, pulmonary hypertension, diabetes, and anemia can make identifying the primary etiology of symptomatic exacerbation difficult. It is estimated that as many as 20% of patients presenting with dyspnea due to HF are misdiagnosed and up to 13% of patients with MIs are missed in the ED.

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## Diagnostic Evaluation

When the history and physical findings are nondiagnostic, biomarkers (natriuretic peptides [NPs], troponin [Tn], myoglobin, D-dimer) enhance our diagnostic accuracy. Diagnostic challenges can remain for those patients with biomarkers in the intermediate or nondiagnostic range. The availability of advanced imaging such as 64-slice cardiac computed tomography (CT) allows for the rapid and accurate assessment of the coronary arteries for obstructive disease, pulmonary arteries for emboli, and the aorta for dissection and aneurysm formation.

The initial stage of evaluation of the patient with dyspnea and/or chest discomfort is patient observation. This includes obtaining a complete history from the patient, family members, and other caregivers, and performing a comprehensive physical examination concentrating on the assessment of the chest and cardiovascular system. As a part of the initial clinical assessment a metabolic survey including electrolytes, blood urea nitrogen, serum creatinine, blood counts, and biomarkers (including Tn and NP), and in certain cases D-dimer values should be obtained. A 12-lead ECG and chest radiograph should also be performed (Figures 1 and 2).

The clinical history and physical examination have only modest positive and negative predictive abilities to diagnose the root cause of the dyspnea/chest pain presentation. In the case of HF, the positive and negative likelihood ratios of the history, physical examination findings, and radiologic assessment fall short of what is experienced with NP levels (Table 1).

The lack of sensitivity and specificity of different aspects of the history, physical examination, and radiologic assessment can lead to diagnostic uncertainty among ED physicians and other treating physicians. This

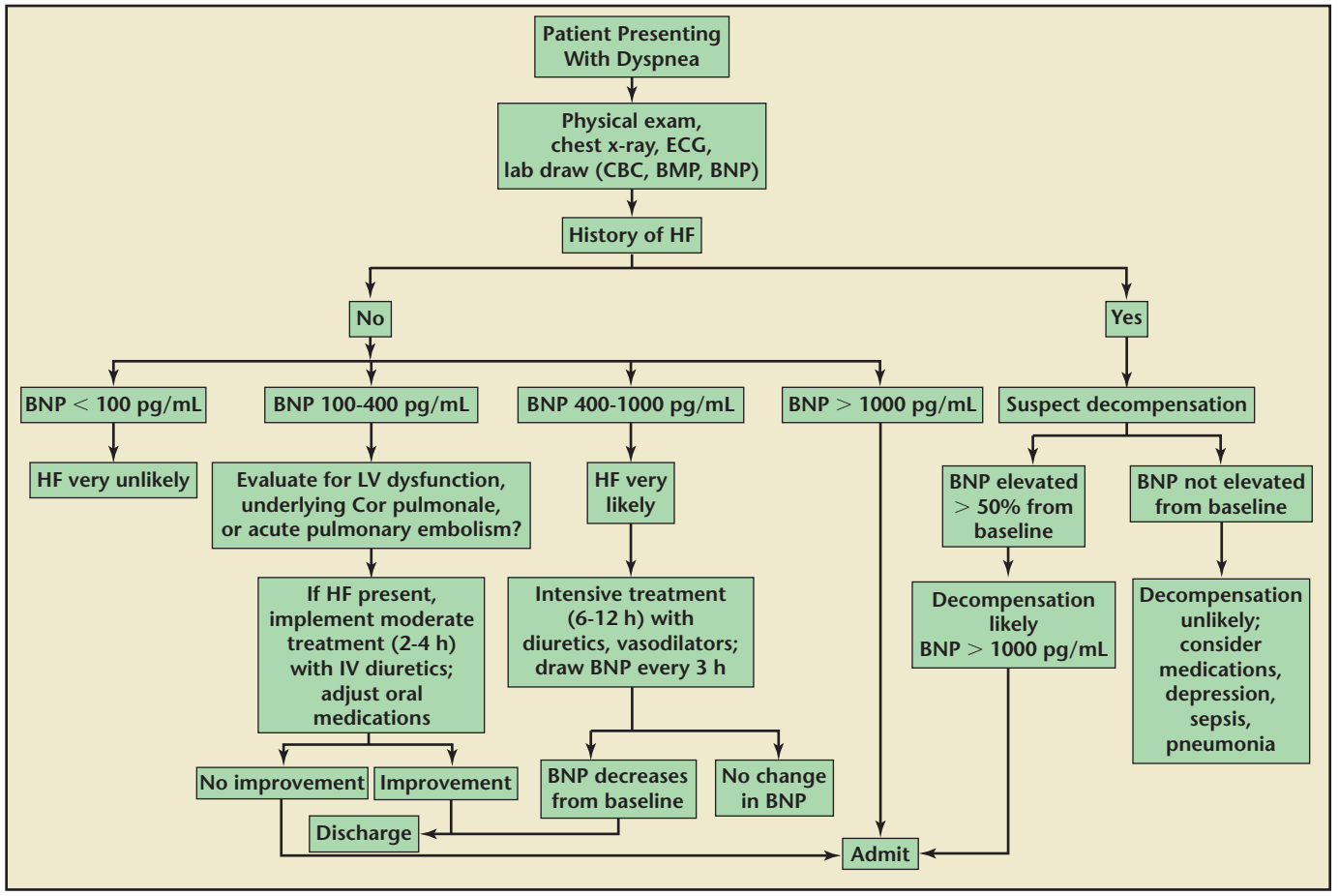


**Figure 1.** *Proposed algorithm for assessing dyspnea. BMP, bone morphogenic protein; BNP, B-type natriuretic peptide; CBC, complete blood count; ECG, electrocardiogram; HF, heart failure; IV, intravenous; LV, left ventricular. Reprinted with permission from Maisel A.*[40]

inevitably leads to delays in initiating optimal directed therapy. The treatment strategy for HF is aimed at reversing a volume overload state with diuretics and the use of vasodilators after load reduction, whereas the treatment of a COPD exacerbation commonly includes the use of bronchodilators that can actually have deleterious proarrhythmic effects. These effects can actually exacerbate the condition of a patient who presents with HF. Debates still occur in the ED and on the clinic ward between cardiologists and pulmonologists when trying to attribute a cardiac or pulmonary cause of the patient's presentation with acute dyspnea. The use of biomarkers such as NPs can often settle this debate. In a study by Rutten and colleagues,[11] ED physicians determined the impact of the N-terminal prohormone B-type NP (NT-proBNP) assay on their clinical assessment of the acutely dyspneic patient that included a history, physical examination, chest radiograph, and ECG. In patients who were classified as low likelihood for HF, 22% had high NP levels consistent with a HF diagnosis and another 33% had intermediate levels. NT-proBNP confirmed the HF diagnosis in only 45% of these patients. In patients who were felt to have a high likelihood for HF, only 3% had low levels of NT-proBNP. The use of NPs does not completely eliminate the debate that often occurs in defining the cause of dyspnea, but certainly adds significant clarity (Table 2).

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## Acute Coronary Syndromes

Attributing the diagnosis of an acute chest pain syndrome to ACS is often

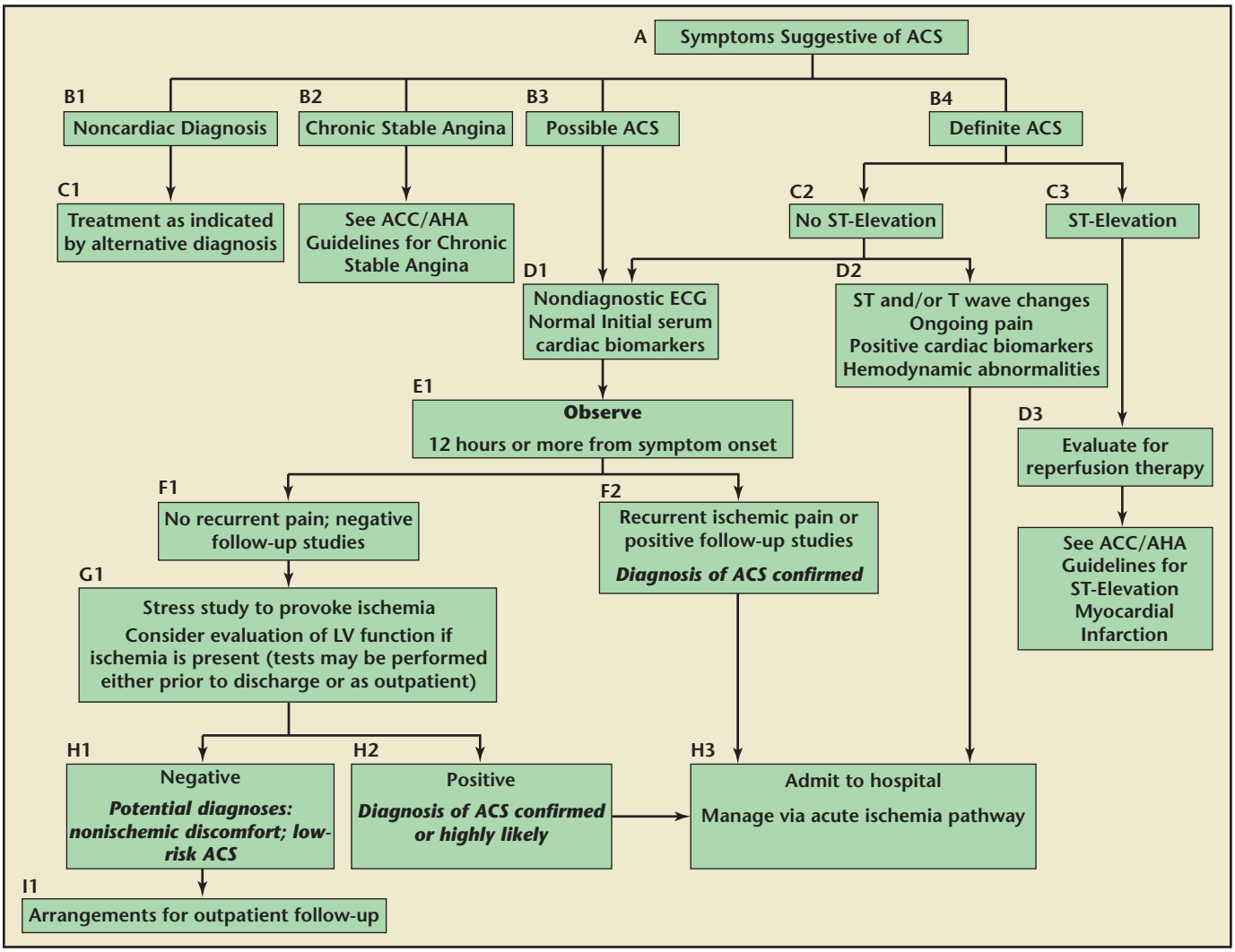


**Figure 2.** *Algorithm for assessing patient with suspicion of acute coronary syndrome (ACS). ACC/AHA, American College of Cardiology/American Heart Association; ACS, acute coronary syndromes; ECG, electrocardiogram; LV, left ventricular; STEMI, ST-elevation myocardial infarction. Reprinted from* Journal of the American College of Cardiology, *Vol. 50, Anderson JL et al, "ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-STElevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction) developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine," pp E1-E157, Copyright 2007, with permission from Elsevier.*[16]

a major challenge, especially in patients who are biomarker negative, as there is no gold standard for the clinical diagnosis. Because of the frequent inability to determine whether symptoms are related to ACS during the initial ED visit, further evaluation is often needed, resulting in an estimated 5 million admissions per year. Three-fourths of patients evaluated in the ED for suspected ACS will be found not to have acute ischemia.[12]

The major tools at the disposal of clinicians for making an early and accurate diagnosis on presentation include a comprehensive history, ECG, and biomarkers such as Tn. A detailed history remains the cornerstone for the diagnosis of ACS and in compelling cases can be sufficient for the diagnosis. The most important factors on the initial history, in order of importance, are the nature of the angina symptoms, prior history of CAD, male sex, older age, and an increasing number of traditional risk factors.[13,14] Symptoms of ACS can include chest pain, referred pain, nausea, vomiting, dyspnea, diaphoresis, and light-headedness. Some patients may present without chest pain; in a review by McCarthy and colleagues, it was found that sudden dyspnea was the sole presenting feature in 4% to 14% of patients with acute MI.[15]

The results of physical examination in patients with ACS are frequently normal as there are no physical findings specific for an ACS presentation. Ominous physical findings include a new mitral regurgitation murmur, hypotension,

**Table 1**
**The Predictive Likelihood of Various Aspects of the Heart Failure Assessment**

| Variable | Sensitivity | Specificity | Positive Likelihood Ratio | Negative Likelihood Ratio | Odds Ratio | 95% Confidence Interval |
|---|---|---|---|---|---|---|
| Chest radiographic findings | | | | | | |
| Cardiomegaly | 79% | 80% | 3.98 | 0.26 | 15.4 | 11.1-21.3 |
| Cephalization | 41% | 96% | 9.41 | 0.61 | 15.4 | 9.4-25.3 |
| Interstitial edema | 27% | 98% | 12.67 | 0.72 | 17.1 | 8.6-34.2 |
| Alveolar edema | 6% | 99% | 7.00 | 0.95 | 7.1 | 2.5-20.6 |
| Pleural effusion | 25% | 92% | 3.30 | 0.81 | 4.1 | 2.7-6.1 |
| No hyperinflation | 3% | 92% | 0.39 | 1.05 | 2.6 | 1.4-5.0 |
| No pneumonia | 4% | 92% | 0.51 | 1.05 | 2.1 | 1.2-3.7 |
| Medical history | | | | | | |
| Chronic heart failure | 62% | 87% | 4.71 | 0.44 | 10.9 | 7.7-15.2 |
| Myocardial infarction | 43% | 87% | 3.21 | 0.66 | 4.9 | 3.5-6.8 |
| Hypertension | 72% | 48% | 5.36 | 0.59 | 2.3 | 1.8-3.1 |
| Clinical findings | | | | | | |
| Orthopnea | 66% | 57% | 1.55 | 0.59 | 2.6 | 2.0-3.4 |
| Jugular vein distention | 38% | 90% | 3.80 | 0.69 | 5.5 | 3.8-7.9 |
| $S_3$ gallop | 13% | 98% | 8.13 | 0.88 | 9.1 | 4.1-20.0 |
| Rales | 59% | 77% | 2.57 | 0.53 | 4.8 | 3.6-6.5 |
| Lower extremity edema | 64% | 74% | 2.41 | 0.50 | 4.9 | 3.7-6.5 |
| Abnormal electrocardiogram | 58% | 78% | 2.66 | 0.54 | 4.9 | 3.7-6.6 |
| B-type natriuretic peptide (pg/mL.) | | | | | | |
| ≥100 | 90% | 75% | 3.66 | 0.14 | 26.2 | 18.0-38.2 |
| ≥200 | 80% | 87% | 6.08 | 0.23 | 26.9 | 18.7-38.7 |
| ≥300 | 71% | 90% | 7.18 | 0.32 | 22.4 | 15.4-32.6 |
| ≥400 | 64% | 92% | 8.10 | 0.39 | 20.9 | 14.0-31.1 |

**Table 2**
**Clinical Assessment and NT-proBNP in the ED Patient With Dyspnea**

| | Likelihood of Heart Failure Based on NT-proBNP Level | | |
|---|---|---|---|
| Physician's Score | Low, < 93 pg/mL (men), < 144 pg/mL (women) | No Definite Diagnosis | High, > 1017 pg/mL |
| No heart failure VAS score 0%-25%, no. of patients (%) | 128 (45) | 93 (33) | 61 (22) |
| No definite diagnosis, VAS score 26%-75%, no. of patients (%) | 22 (20) | 24 (23) | 59 (56) |
| Heart failure VAS score 76%-100%, no. of patients (%) | 2 (3) | 8 (11) | 60 (86) |

ED, emergency department; NT-proBNP, N-terminal prohormone B-type natriuretic peptide; VAS, Visual Analog Scale.
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**Table 3**
**Likelihood That Signs and Symptoms Represent ACS**

| Feature | High Likelihood—Any of the Following: | Intermediate Likelihood—Absence of High-Likelihood Features and Presence of Any of the Following: | Low Likelihood—Absence of High- or Intermediate-Likelihood Features but May Have: |
|---|---|---|---|
| History | Chest or left arm pain or discomfort as chief symptom reproducing prior documented angina<br>Known history of CAD, including MI | Chest or left arm pain or discomfort as chief symptom<br>Age > 70 y<br>Male<br>Diabetes mellitus | Probable ischemic symptoms in absence of any of the intermediate-likelihood characteristics<br>Recent cocaine use |
| Examination | Transient MR murmur, hypotension, diaphoresis, pulmonary edema, or rales | Extracardiac vascular disease | Chest discomfort reproduced by palpation |
| ECG | New, or presumably new, transient ST-segment deviation (≥ 1 mm) or T-wave inversion in multiple precordial leads | Fixed Q waves<br>ST depression 0.5 to 1 mm or T-wave inversion > 1 mm | T-wave flattening or inversion < 1 mm in leads with dominant R waves<br>Normal ECG |
| Cardiac markers | Elevated cardiac TnI, TnT, or CK-MB | Normal | Normal |

ACS, acute coronary syndromes; CAD, coronary artery disease; CK-MB, creatine kinase-myocardial band; ECG, electrocardiogram; MI, myocardial infarction; MR, mitral regurgitation; TnI, troponin 1; TnT, troponin T.

pulmonary rales, a new third heart sound ($S_3$ gallop), and new jugular venous distention. The finding of unequal pulses can indicate the presence of aortic dissection and a friction rub supporting the diagnosis of acute pericarditis (Table 3).[16]

In the ED, the ECG is initially used to help identify patients with chest discomfort due to an ACS and is the most important diagnostic tool. ST-segment elevation is the most specific tool for the diagnosis of MI and to distinguish a STEMI from those with non-STEMI (NSTEMI) and other ACS. Up to 20% of patients presenting with ACS have a normal ECG reading on presentation[17]; therefore, a normal ECG result cannot be depended on to reliably rule out the diagnosis of ACS. Conversely, among those with chest discomfort and a normal ECG, only 7% will go on to rule in for an acute MI.[18]

Biomarkers of cardiac necrosis have assumed great importance for identifying patients with ACS. The cardiac Tns (cTnT, cTnI) have become the standard for defining the diagnosis of MI (elevation of Tn above the 99th percentile of normal) along with the presence of at least 1 of the following criteria: ischemic ST- and T-wave changes, new left bundle branch block, new Q waves, percutaneous coronary intervention–related marker elevation, or imaging showing a new loss of myocardium.[19] Although Tns can be detected in blood as early as 2 to 4 hours after the onset of symptoms, elevation can be delayed for up to 8 to 12 hours (Figure 3).[16,20]

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Although cardiac Tns accurately identify myocardial necrosis, they do not inform as to the cause of necrosis because they are specific for cardiac injury but not for an ACS. The increasingly widespread use of cardiac Tns for a variety of clinical presentations such as sepsis, hypertensive crisis, and the finding of elevated levels can create confusion as they usually represent "type 2" or secondary MI rather than an ACS.[21] Therefore, in making the diagnosis of NSTEMI, cardiac Tns should be used in conjunction with other clinical criteria mentioned above (Table 4).

NPs are also of use in the early assessment of patients with confirmed ACS. NPs are released from the ventricles into the systemic circulation in response to cardiac stresses such as HF, ischemia, pulmonary hypertension,

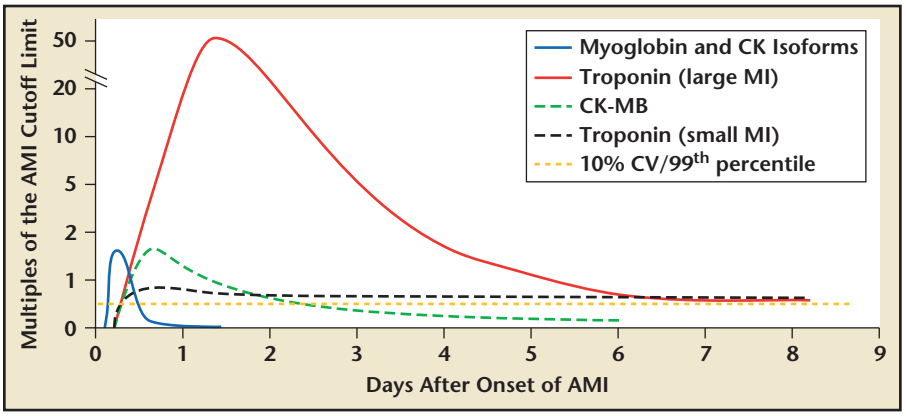


**Figure 3.** *Timing of release of various biomarkers after acute myocardial infarction. CK, creatine kinase; CK-MB, creatine kinase-myocardial band. Reprinted with permission from Anderson JL et al.*[16]

PE, and cardiac arrhythmias. NPs lack the specificity to play a key role in the diagnosis of ACS but they are potent predictors of both long- and short-term mortality in patients with ACS.[22] Measurement of BNP or NT-proBNP has a class IIb indication for use to supplement the assessment of global risk in patients with suspected ACS.[20]

Currently, a variety of imaging modalities can be used as adjuncts to the clinical evaluation, ECG, and biomarkers, including echocardiography, resting myocardial perfusion imaging (MPI), cardiac computerized tomographic angiography (CCTA), and cardiac magnetic resonance (cMR). Resting regional myocardial function as assessed by 2-dimensional echocardiography and resting coronary perfusion as assessed by MPI have been reported to provide a sensitivity and a negative predictive value of > 90% in patients with acute chest pain for ischemia detection.[23] Echocardiography, particularly with contrast, can effectively identify wall motion abnormalities in patients with persistent chest discomfort and nondiagnostic ECGs. Echocardiography for the evaluation of acute chest pain with suspected myocardial ischemia in patients with nondiagnostic laboratory markers and ECG results, and in whom a resting echocardiogram can be performed during pain, receives an appropriate recommendation from the 2007 ACCF/ASE/ACEP/ASNC/SCAI/SCCT/SCMR Echocardiography Appropriateness Criteria.[24]

Resting MPI enables clinicians to safely triage low-risk patients to delayed stress testing or discharge. However, MPI has limitations, including an increased incidence of equivocal findings in obese patients, lower sensitivity in patients without ongoing symptoms, inability to distinguish between older and newer perfusion defects, therefore being unsuitable in patients with previous myocardial damage. Perhaps most importantly, alternative diagnoses such as aortic dissection or PE cannot be evaluated with MPI. MPI is considered appropriate in patients with suspected ACS irrespective of Thrombolysis In Myocardial Infarction risk score or whether the Tn levels were elevated.[25]

CCTA has been shown to be a robust technique in the clinical setting of acute chest pain. A comparison of CCTA versus a standard diagnostic evaluation in lower-risk patients presenting with acute chest pain in the ED was performed by Goldstein and colleagues.[26] CCTA was found to have the same diagnostic accuracy as "standard procedures" but was able to provide a diagnosis in a shorter time or at a lower cost. In the more recently published Rule Out Myocardial Infarction Using Computer Assisted Tomography (ROMICAT) trial,[27] early CCTA was able to enhance the management of ACS patients with normal Tns and either normal or nondiagnostic ECG results in the ED. They found that 50% of patients with low- to intermediate-risk ACS had no ACS and were able to be managed as outpatients. The negative and positive predictive accuracy was 98% and 35%, respectively.

**Table 4**
**Non-CAD Causes of Troponin Elevation**

| | |
|---|---|
| Tachyarrhythmia | Pulmonary emboli |
| Hypertension | Subarachnoid hemorrhage |
| Myocarditis | Sepsis |
| Myocardial Contusion | Hypothyroidism |
| Acute and chronic HF | Shock |
| Renal Failure | Rhabdomyolysis |
| Drug toxicity (anthracyclines) | Burns |
| Acute neurological diseases | Cardiac infiltrative diseases |

CAD, coronary artery disease; HF, heart failure.
Adapted from *Journal of the American College of Cardiology,* Vol. 48, "Biomarkers in acute cardiac disease: the present and the future," pp. 1-11, copyright 2006, with permission from Elsevier.[21]

CCTA seems to have a place in assessing low- to intermediate-risk patients, particularly those with normal, nondiagnostic, or borderline ECGs and Tns. CCTA has a class IIa recommendation as an alternative to stress testing in patients with suspected ACS with a low to intermediate probability of CAD in patients with normal ECGs and cardiac biomarkers. CT of the chest is currently considered the gold standard for evaluation of the 2 most common serious alternative chest pain diagnoses: aortic dissection and PE. A single, rapid comprehensive imaging study that could reliably diagnose or exclude CAD, aortic dissection, and PE would allow quicker and more appropriate triage of this acutely ill population.

Cardiac MR has also been evaluated in the setting of ACS and has been found to be quite useful, as it provides information regarding ventricular function, early and late regions of infarction, and proximal coronary anatomy. In a study of 161 patients with ACS with nondiagnostic ECGs and biomarkers, cardiac MRI was found to have a sensitivity and specificity of 84% and 85%, respectively.[28]

## Pulmonary Embolism

It is estimated that 600,000 episodes of PEs occur each year in the United States, resulting in 100,000 to 200,000 deaths.[29] PE remains a challenging diagnostic dilemma due to the lack of specific signs and symptoms and the suboptimal accuracy of first-line tests, such as chest radiography, venous ultrasound, and ventilation perfusion imaging. The clinical presentation and routinely available laboratory data such as results on electrocardiography, chest radiography, and analysis of arterial blood gases cannot be relied upon to confirm or rule out PE. Although symptoms and signs such as dyspnea, pleuritic chest pain, tachypnea, and tachycardia can raise the suspicion of embolism and indicate a need for further evaluation, these findings are inconsistent in patients with embolism and are nonspecific (Table 5).[30]

One-third of patients with deep venous thrombosis (DVT) have no symptoms and lower extremity venous imaging has a high false-negative rate in the presence of nonocclusive thrombi. In two-thirds of patients with PE, no DVT was identified. Over 50% of patients who undergo ventilation perfusion imaging have a "nondiagnostic" scan result. As in the case of ACS, biomarkers and advanced imaging modalities have enhanced our ability to make the diagnosis correctly and more rapidly. The D-dimer assay has a high negative predictive accuracy when the levels are less than 500 with sensitivity of 95%.[31] D-dimer is the terminal product of the fibrin degradation process. The presence of elevated D-dimer values is proof that a fibrin clot is present and the fibrinolytic system is active. The sensitivity and specificity of the D-dimer test in one evaluation was 100.0% (95% confidence interval [CI], 91.6-100.0) and 27.7% (95% CI, 21.2-34.9), respectively.[32] Brain NPs and Tns add prognostic information. CT scanning has substantial diagnostic value when it is used in conjunction with a tool for assessing the clinical probability of embolism, ultrasonography of the legs, D-dimer testing, or some combination of these techniques. CT has become the first-line modality for imaging in patients suspected of having PE; the negative predictive value of a normal CT study is high, approaching 98%.[33]

*PE remains a challenging diagnostic dilemma due to the lack of specific signs and symptoms and the suboptimal accuracy of first-line tests such as chest radiography, venous ultrasound, and ventilation perfusion imaging.*

## Aortic Dissection

Acute aortic dissection (AoD) has an incidence of 2.9 to 3.5 cases per

**Table 5**
**Rules for Predicting the Probability of PE**

| Variable | No. of Points |
|---|---|
| **Risk factors** | |
| Clinical signs and symptoms of DVT | 3.0 |
| An alternative diagnosis deemed less likely than PE | 3.0 |
| Heart rate >100 beats/min | 1.5 |
| Immobilization or surgery in the previous 4 wk | 1.5 |
| Previous DVT or PE | 1.5 |
| Hemoptysis | 1.0 |
| Cancer (receiving treatment, treated in the past 6 mo, or palliative care) | 1.0 |
| **Clinical probability** | |
| Low | < 2.0 |
| Intermediate | 2.0-6.0 |
| High | > 6.0 |

DVT, deep venous thrombosis; PE, pulmonary embolism.
Adapted with permission from 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;83:416-420.[30]

100,000 patient years, much lower then the incidence of STEMI. During the initial evaluation of acute chest pain syndromes a correct diagnosis of acute AoD in patients initially known to have the disease occurred in only 15% to 43% of cases.[34] Historical information that needs to be obtained in patients presenting with the sudden onset of chest, back, or abdominal pain where there may be a suspicion of AoD includes a history of aortic pathology in an immediate family member and history of aortic valve disease. High-risk pain characteristics include an abrupt onset of severe pain and one that has a ripping, tearing, stabbing, or sharp quality. Patients under the age of 40 years with this type of clinical presentation need to be questioned and examined for features of Marfan syndrome, Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome, Turner syndrome, and other connective tissue disorders associated with thoracic aortic disease (Figure 4).[35] Several biomarkers, including plasma smooth muscle myosin heavy-chain protein, D-dimer, and high-sensitivity C-reactive protein are under investigation for use in patients with AoD.[36-39]

Definitive identification or exclusion of thoracic aortic disease or one of its anatomic variants requires dedicated aortic imaging. Selection of the most appropriate imaging study depends on patient-related factors such as hemodynamic stability and renal function and institutional capabilities. Routine chest radiograph may occasionally detect abnormalities of aortic contour or size that require definitive aortic imaging and should be performed in low- and intermediate-risk patients. Chest radiograph may establish an alternative diagnosis for the acute chest pain syndrome. Urgent and definitive imaging of the aorta using transesophageal echocardiogram, CT imaging, or MR imaging is recommended to identify or exclude thoracic AoD in patients at high risk for the disease. CT has the ability to image the entire aorta, including lumen and wall, and to distinguish among types of acute aortic syndromes (intramural hematoma, penetrating atherosclerotic ulcer, and acute AoD) with short acquisition times. CT imaging has been shown to have sensitivities up to 100% and specificities of 98% to 99% for the diagnosis of AoD.

## Conclusions

The differential diagnosis of acute chest pain and dyspnea includes life-threatening conditions such as ACS, HF, AoD, and PE. Making the correct diagnosis in the shortest period of time will lead to more rapid initiation of optimal therapies which have the best opportunity to improve outcomes. A comprehensive history, careful physical examination, ECG, biomarkers (including cardiac Tn and NPs), and adjunctive cardiovascular imaging are the necessary steps in an integrated, accurate, and rapid diagnostic evaluation of the acutely ill patient with chest discomfort and dyspnea. ■

## Main Points

- Acute chest discomfort and dyspnea are 2 of the most common nontraumatic symptoms that prompt emergency department evaluations in the United States. The overlap between these presenting symptoms is considerable. The priority in patients presenting with chest pain and dyspnea is to quickly identify or rule out the occurrence of life-threatening causes such as acute coronary syndromes (ACS), heart failure, pulmonary embolus, and aortic dissection.
- When the history and physical findings are nondiagnostic, biomarkers (natriuretic peptides [NPs], troponin [Tn], myoglobin, D-dimer) enhance our diagnostic accuracy. Diagnostic challenges can remain for those patients with biomarkers in the intermediate or nondiagnostic range.
- The initial stage of evaluation of the patient with dyspnea and/or chest discomfort is observation. A complete history from the patient, family members, and other caregivers should be obtained, and a comprehensive physical examination concentrating on the assessment of the chest and cardiovascular system must be performed. The lack of sensitivity and specificity of different aspects of this initial evaluation can lead to diagnostic uncertainty among treating physicians, and inevitably leads to delays in initiating optimal directed therapy.
- Biomarkers of cardiac necrosis have assumed great importance for identifying patients with ACS. The cardiac Tns have become the standard for defining the diagnosis of myocardial infarction. NPs lack the specificity to play a key role in the diagnosis of ACS but they are potent predictors of both long- and short-term mortality in patients with ACS.
- Cardiac computed tomography angiography has been shown to be a robust technique in the clinical setting of acute chest pain. Cardiac magnetic resonance in the setting of ACS is also quite useful, as it provides information regarding ventricular function, early and late regions of infarction, and proximal coronary anatomy.

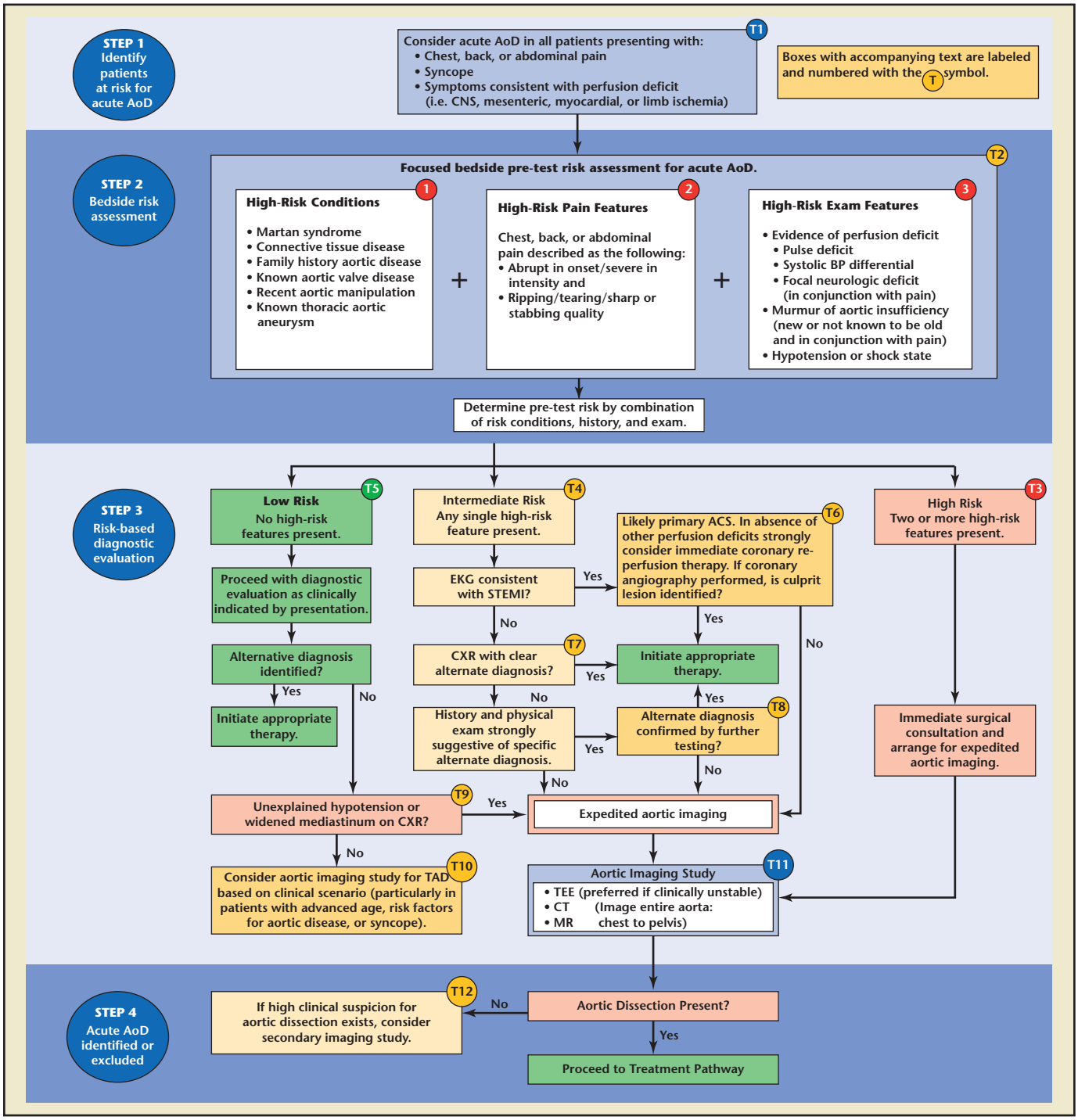


**Figure 4.** *Aortic dissection (AoD) evaluation algorithm pathway. ACS, acute coronary syndromes; BP, blood pressure; CNS, central nervous system; CT, computed tomography; CXR, chest X-ray; EKG, electrocardiogram; MR, magnetic resonance; TAD, thoracic aortic dissection; TEE, transesophageal echocardiogram; STEMI, ST-segment elevation myocardial infarction. Reprinted from* Journal of the American College of Cardiology, *Vol. 55, "2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease," pp. e27-e129, copyright 2010, with permission from Elsevier.*[35]

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## References


1. American College of Emergency Physicians Web site. www.acep.org/webportal/Newsroom/NewsMediaResources/StatisticsData/default.htm. Accessed February 4, 2006.
2. Cherry DK, Woodwell DA. National Ambulatory Medical Care Survey: 2000 summary. *Adv Data*. 2002;328:1-32.
3. Brieger D, Eagle KA, Goodman SG, et al; GRACE Investigators. Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: insights from the Global Registry of Acute Coronary Events. *Chest*. 2004;126:461-469.
4. Ang DS, Welsh P, Watt P, et al. Serial changes in adiponectin and BNP in ACS patients: paradoxical associations with each other and with prognosis. *Clin Sci (Lond)*. 2009;117:41-48.
5. Buntinx F, Knockaert D, Bruyninckx R, et al. Chest pain in general practice or in the hospital emergency department: is it the same? *Fam Pract*. 2001;18:586-589.
6. Klinkman MS, Stevens D, Gorenflo DW. Episodes of care for chest pain: a preliminary report from MIRNET. Michigan Research Network. *J Fam Pract*. 1994;38:345-352.
7. Rosamond W, Flegal K, Friday G, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2007;115:e69-e171.
8. Longe JL, ed. *The Gale Encyclopedia of Medicine*. 3rd ed. Detroit, MI: Gale Group; 2006.
9. Spittell PC, Spittell JA Jr, Joyce JW, et al. Clinical features and differential diagnosis of aortic dissection: experience with 236 cases (1980 through 1990). *Mayo Clin Proc*. 1993;68:642-651.
10. Rosman HS, Patel S, Borzak S, et al. Quality of history taking in patients with aortic dissection. *Chest*. 1998;114:793-795.
11. Rutten JH, Steyerberg EW, Boomsma F, et al. N-terminal pro-brain natriuretic peptide testing in the emergency department: beneficial effects on hospitalization, costs, and outcome. *Am Heart J*. 2008;156:71-77.
12. Selker HP, Beshansky JR, Griffith JL, et al. Use of the acute cardiac ischemia time-insensitive predictive instrument (ACI-TIPI) to assist with triage of patients with chest pain or other symptoms suggestive of acute cardiac ischemia: a multicenter, controlled clinical trial. *Ann Intern Med*. 1998;129:845-855.
13. Morise AP, Haddad WJ, Beckner D. Development and validation of a clinical score to estimate the probability of coronary artery disease in men and women presenting with suspected coronary disease. *Am J Med*. 1997;102:350-356.
14. Ho KT, Miller TD, Hodge DO, et al. Use of a simple clinical score to predict prognosis of patients with normal or mildly abnormal resting electrocardiographic findings undergoing evaluation for coronary artery disease. *Mayo Clin Proc*. 2002;77:515-521.
15. McCarthy BD, Wong JB, Selker HP. Detecting acute cardiac ischemia in the emergency department: a review of the literature. *J Gen Intern Med*. 1990;5:365-373.
16. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-Elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction) developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. *J Am Coll Cardiol*. 2007;50:e1-e157.
17. Turnipseed SD, Trythall WS, Diercks DB, et al. Frequency of acute coronary syndrome in patients with normal electrocardiogram performed during presence or absence of chest pain. *Acad Emerg Med*. 2009;16:495-499.
18. McCullough PA, Ayad O, O'Neill WW, Goldstein JA. Costs and outcomes of patients admitted with chest pain and essentially normal electrocardiograms. *Clin Cardiol*. 1998;21:22-26.
19. Thygesen K, Alpert JS, White HD, et al. Universal definition of myocardial infarction. *Circulation*. 2007;116:2634-2653.
20. Shapiro BP, Babuin L, Jaffe AS. Cardiac biomarkers. In: Murphy JG, Lloyd MA, eds. *Mayo Clinic Cardiology: Concise Textbook*. 3rd ed. Rochester, MN: Mayo Clinic Scientific Press; 2007:773-780.
21. Jaffe AS, Babuin L, Apple FS. Biomarkers in acute cardiac disease: the present and the future. *J Am Coll Cardiol*. 2006;48:1-11.
22. de Lemos JA, Morrow DA, Bentley JH, et al. The prognostic value of B-type natriuretic peptide in patients with acute coronary syndrome. *N Engl J Med*. 2001;345:1014-1021.
23. Jesse RL, Kontos MC, Roberts CS. Diagnostic strategies for the evaluation of the patient presenting with chest pain. *Prog Cardiovasc Dis*. 2004;46:417-437.
24. Douglas PS, Khandheria B, Stainback RF, Weissman NJ. ACCF/ASE/ACEP/ASNC/SCAI/SCCT/SCMR 2007 appropriateness criteria for transthoracic and transesophageal echocardiography: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American Society of Echocardiography, American College of Emergency Physicians, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and the Society for Cardiovascular Magnetic Resonance endorsed by the American College of Chest Physicians and the Society of Critical Care Medicine. *J Am Coll Cardiol*. 2007;50:187-204.
25. Hendel RC, Berman DS, Di Carli MF, et al. ACCF/ASNC/ACR/AHA/ASE/SCCT/SCMR/SNM 2009 Appropriate Use Criteria for Cardiac Radionuclide Imaging: A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the American Society of Nuclear Cardiology, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the Society of Cardiovascular Computed Tomography, the Society for Cardiovascular Magnetic Resonance, and the Society of Nuclear Medicine. *J Am Coll Cardiol*. 2009;53:2201-2229.
26. Goldstein JA, Gallagher MJ, O'Neill WW, et al. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. *J Am Coll Cardiol*. 2007;49:863-871.
27. Hoffmann U, Bamberg F, Chae CU, et al. Coronary computed tomography angiography for early triage of patients with acute chest pain: the ROMICAT (Rule Out Myocardial Infarction using Computer Assisted Tomography) trial. *J Am Coll Cardiol*. 2009;53:1642-1650.
28. Kwong RY, Schussheim AE, Rekhraj S, et al. Detecting acute coronary syndrome in the emergency department with cardiac magnetic resonance imaging. *Circulation*. 2003;107:531-537.
29. Dalen JE, Alpert JS. Natural history of pulmonary embolism. *Prog Cardiovasc Dis*. 1975;17:259-270.
30. 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;83:416-420.
31. 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;144:165-171.
32. Eng CW, Wansaicheong G, Goh SK, et al. Exclusion of acute pulmonary embolism: computed pulmonary angiography or D-dimer. *Singapore Med J*. 2009;50:403-406.
33. Remy-Jardin M, Tillie-Leblond I, Szapiro D, et al. CT angiography of pulmonary embolism in patients with underlying respiratory disease: impact of multislice CT on image quality and negative predictive value. *Eur Radiol*. 2002;12:1971-1978.
34. Mészáros I, Mórocz J, Szlávi J, et al. Epidemiology and clinicopathology of aortic dissection. *Chest*. 2000;117:1271-1278.
35. 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. *J Am Coll Cardiol*. 2010;55:e27-e129.
36. Weber T, Högler S, Auer J, et al. D-dimer in acute aortic dissection. *Chest*. 2003;123:1375-1378.
37. Eggebrecht H, Naber CK, Bruch C, et al. Value of plasma fibrin D-dimers for detection of acute aortic dissection. *J Am Coll Cardiol*. 2004;44:804-809.
38. Suzuki T, Katoh H, Watanabe M, et al. Novel biochemical diagnostic method for aortic dissection. Results of a prospective study using an immunoassay of smooth muscle myosin heavy chain. *Circulation*. 1996;93:1244-1249.
39. Suzuki T, Katoh H, Tsuchio Y, et al. Diagnostic implications of elevated levels of smooth-muscle myosin heavy-chain protein in acute aortic dissection. The Smooth Muscle Myosin Heavy Chain Study. *Ann Intern Med*. 2000;133:537-541.
40. Maisel A. Algorithms for using B-type natriuretic peptide levels in the diagnosis and management of congestive heart failure. *Crit Pathways in Cardiol*. 2002;1:67-73.