The clinical diagnosis of pulmonary embolism (PE) is difficult in coronary care units (CCUs) because many findings of PE are similar to those of acute coronary syndromes and heart failure. Immobilization of only 1 or 2 days may predispose to PE. Heart failure and acute myocardial infarction add to the risk. Dyspnea may be absent or occur only with exertion. The onset of dyspnea may occur over seconds to days. Orthopnea occurs with PE as well as heart failure. When the clinical probability and results of objective testing are discordant, the posttest probability of PE may be neither sufficiently high nor sufficiently low to permit therapeutic decisions. Objective scoring systems for clinical assessment have not been developed for patients in a CCU. D-dimer is likely to be of little value for the exclusion of PE in CCUs, because elevations occur with heart failure, unstable angina, and myocardial infarction. Computed tomographic pulmonary angiography with venous phase imaging of the low pelvic and proximal leg veins (computed tomographic venography) is recommended for imaging. Scintigraphy in women aged <50 years with normal or nearly normal results on chest x-ray may be the preferred imaging test to reduce the risk for radiation. Echocardiography with leg ultrasonography is a rapidly obtainable combination of bedside tests that may be useful for young patients and patients in extremis. In conclusion, the choice of diagnostic test depends on the clinical probability of PE, the condition of the patient, the availability of diagnostic tests, the risks of iodinated contrast material, radiation exposure, and cost. © 2009 Elsevier Inc. (Am J Cardiol 2009;103: 881–886)

Pulmonary embolism (PE) is a major cause of morbidity and mortality in hospitalized patients with heart disease. Among 198 patients with severe congestive heart failure in a coronary care unit (CCU), 9.1% developed PE during the hospitalization, although most had received thromboprophylaxis. Among 1,032 hospitalized cardiac patients who died and underwent autopsy, 24.4% had PE and 9.7% had massive PE. Among those with massive PE, the diagnosis was unsuspected before death in 82%. The clinical diagnosis of pulmonary embolism (PE) is particularly difficult in CCUs because many findings of acute PE are similar to those of acute coronary syndrome or heart failure. A need for increased vigilance of the possibility of PE is critical. Occasion ally, patients with acute PE have chest pain and electrocardiographic changes suggestive of acute coronary syndromes. In patients with such findings in whom coronary angiographic results are normal, PE would be a diagnostic possibility.

Predisposing Factors

Immobilization of only 1 or 2 days may predispose to PE. Among patients in whom immobilization was a predisposing factor, 65% were immobilized ≤2 weeks. The risk for PE in patients hospitalized with heart failure is twice that of hospitalized patients who do not have heart failure. The lower the ejection fraction, the greater the risk for venous thromboembolism.

Symptoms of Acute Pulmonary Embolism

Clinical findings such as unexplained dyspnea, tachypnea, and chest pain are useful for the selection of patients for further diagnostic testing. Dyspnea is not a universal finding. It occurred in 73% of patients with PE and no previous cardiopulmonary disease. Dyspnea may occur only with exertion. The onset of dyspnea occurred over seconds or minutes in 72% of patients with no previous cardiopulmonary disease and over seconds, minutes, or hours in 83%. In some, however, the onset of dyspnea occurred over days. Orthopnea is a symptom of PE as well as heart failure and may occur in those who have dyspnea at rest or only on
exertion. Pleuritic chest pain occurs more frequently than hemoptysis in patients with PE. Nonpleuritic chest pain may occur in a minority of patients with PE, and the characteristics are highly variable. It has been described as substernal, left anterior, right anterior, left posterior, right posterior, left lateral and right lateral. The pain usually does not radiate. It may, however, radiate to the back, neck, and rarely left or right arm. Cough may be a symptom of PE. It is usually nonproductive, but it may be productive of clear, purulent, blood-streaked, or less frequently completely bloody sputum. Calf pain occurred in 39% of patients with PE, and 17% had calf pain and thigh pain, but thigh pain alone was uncommon.

**Signs of Acute Pulmonary Embolism**

Tachypnea (respiratory rate ≥ 20 breaths/min) occurred in 54% to 70% of patients who did not have previous cardiopulmonary disease. Tachycardia (heart rate > 100 beats/min) occurred less frequently (24% to 30%). One of the signs of right atrial, right ventricular, or pulmonary artery pressure elevation (neck vein distension, right ventricular lift, accentuated pulmonary component of the second sound) was documented in only 21% of patients who did not have previous cardiopulmonary disease.

Lung examination showed abnormalities in 30% of patients with PE. Rales (crackles) and decreased breath sounds were the most frequently detected abnormalities. Wheezes and rhonchi were heard occasionally. A pleural friction rub was rare. Fever can be the presenting physical finding in patients with venous thromboembolism, especially in intensive care units. Fever occurred with similar frequency in those with pulmonary hemorrhage or infarction and those with PE who did not have pulmonary hemorrhage or infarction. The fever was usually of low grade. Signs of deep venous thrombosis were observed in 15% to 47% of patients with acute PE.

**Combinations of Signs and Symptoms**

Either dyspnea or tachypnea was shown in > 80% of patients with acute PE. However, even in patients with circulatory collapse, the most severe presentation of acute PE, both dyspnea and tachypnea may be absent. Dyspnea or tachypnea or pleuritic pain was shown in > 90%. One of these findings or signs of deep venous thrombosis was found in 96% of patients with PE.

Unexplained changes on chest x-ray or unexplained shock or loss of consciousness may suggest PE. Initial a priori assessment of the probability of acute PE is strongly recommended. Guidelines for diagnosis recommend that before any diagnostic tests are performed, the clinical probability of acute PE should be assessed. When the clinical probability and results of objective testing are discordant, the posttest probability of PE may be neither sufficiently high nor sufficiently low to permit therapeutic decisions. Under these circumstances, further objective testing is mandatory. Objective scoring systems for clinical assessment, although generally preferable to intuitive assessment, have not been developed for patients in CCUs.

In non-CCU patients, physicians with experience in PE showed similar results with empirical assessment and assessment with objective scoring systems.

**Partial Pressure of Oxygen in Arterial Blood and Alveolar-Arterial Oxygen Difference**

The partial pressure of oxygen in arterial blood, when low in patients with suspected acute PE, is a helpful adjunct in the diagnostic assessment. However, patients with acute PE may have normal partial pressure. A normal alveolar-arterial oxygen difference (alveolar-arterial oxygen gradient) also does not exclude acute PE. Alveolar-arterial oxygen gradients were normal in 14% of patients with PE.

**Electrocardiography**

In patients with mild to massive PE, normal results on electrocardiography were shown in 30%. Atrial flutter or atrial fibrillation in patients with acute PE is infrequent in patients with no previous heart disease. Abnormalities of the ST segment and T wave are the most frequent electrocardiographic manifestations of PE.

Electrocardiographic manifestations of acute cor pulmonale (S1Q3T3, complete right bundle branch block, P pulmonale, or right-axis deviation) occurred in 26% to 32% of patients with submassive or massive acute PE who did not have associated cardiac or pulmonary disease.

The problem of distinguishing the prominent Q waves known to occur with PE from those of myocardial infarction has been recognized for many years. Electrocardiographic results may simulate infarction in any region of the heart.

Leftward shifts of the frontal plane axis in PE are frequent in acute PE and were observed more frequently than rightward shifts. Low-voltage frontal plane QRS complexes may be a sign of acute PE, although they are uncommon.

**Chest X-Ray**

Some of the nonspecific x-ray abnormalities combined with symptoms and electrocardiographic abnormalities may suggest that PE is present. The chest x-ray, in addition, is useful for the exclusion of conditions that mimic acute PE (pneumonia, pneumothorax, pleurisy) or to evaluate comorbid or predisposing conditions (heart failure), as well as to aid in the diagnostic interpretation of some imaging tests (pulmonary scintigraphy).

Most patients with acute PE and no previous cardiopulmonary disease have an abnormal findings on plain chest x-rays, although normal findings were observed in 24%. An elevated hemidiaphragm is readily observed and occurs in 28% to 41% of patients with acute PE. An elevated hemidiaphragm, consolidation, pleural effusion, or atelectasis occurred in about 2/3 of patients with acute PE. A pleural-based density or costophrenic density suggests pulmonary infarction (Hampton’s hump). In patients with pleural effusions, only blunting of the costophrenic angle was shown in 86% of patients with PE. No patients with PE and
no previous cardiopulmonary disease had pleural effusions that occupied >1/3 of a hemithorax.4

Either focal oligemia or distension of the proximal portion of the pulmonary artery or both (Westermark’s sign) occurred more frequently in patients with massive PE than submassive PE (42% vs 26%).24 Alveolar pulmonary edema may occur, but it is rare (1%), and interstitial edema is uncommon (3%).4

Cardiac Troponin

It has been thought for many years that some of the electrocardiographic changes in acute PE reflect myocardial ischemia.25 Myocardial infarction has been shown at autopsy of patients who died of PE and had normal coronary arteries.25 Coronary artery spasm does not occur in experimentally induced PE in animals. In fact, experimentally induced PE in dogs26 and pigs27 showed that left and right coronary artery blood flow increased concordantly with increasing pulmonary artery pressure and decreasing partial pressure of oxygen in arterial blood. This suggests that right ventricular strain in combination with hypoxemia may cause myocardial damage and the release of chemical markers. In a CCU, if acute coronary syndromes are excluded, elevated chemical markers of ischemia may suggest acute PE.28,29 Pooled data in patients with PE and elevated troponin I showed in-hospital all-cause mortality of 22%, compared with 6% in patients with normal troponin I.30 In patients with PE with elevated troponin T, in-hospital all-cause mortality was 17%, compared with 3%31 in patients with normal troponin T.

Myoglobin

In 21 patients with PE who had right ventricular distension and elevated myoglobin levels, in-hospital all-cause mortality was 35%, compared with no deaths in 25 such patients who had normal myoglobin levels.32

Natriuretic Peptides

Elevations in brain natriuretic peptides33 and N-terminal–pro-brain natriuretic peptide34 are associated with right ventricular dysfunction in acute PE. Natriuretic peptide levels are also increased in patients with right ventricular pressure overload due to causes other than PE, including primary pulmonary hypertension, chronic thromboembolic hypertension, congenital heart disease, and chronic lung disease.35 Brain natriuretic peptides in patients with PE, when low, predict a benign clinical outcome, with few in-hospital deaths from PE.35

D-Dimer: Negative results on a d-dimer test, measured by any method, in combination with a low-probability clinical assessment, provide reasonable certainty for excluding PE.36 Intermediate clinical probability would also exclude PE with reasonable certainty if d-dimer were measured by rapid enzyme linked immunosorbent assay36,37 or, in the opinion of some, a quantitative latex agglutination test.37 If clinical assessment is high probability, negative results on a d-dimer test do not exclude PE,11 and further diagnostic tests are indicated.

Unfortunately, hospitalized patients often have disorders that cause positive d-dimer test results,38 and d-dimer is particularly likely to be elevated in patients in CCUs. The exclusion of PE on the basis of negative d-dimer results and clinical assessment would be cost effective. The charge for a d-dimer test is about 1% the charge (including physician fees) for computed tomographic (CT) angiography, 3% the charge for a ventilation-perfusion (V-Q) scan and about 4% the charge for bilateral venous ultrasound.11

D-Dimer may be elevated in patients with unstable angina.39 Some have observed elevations of d-dimer in patients with myocardial infarction,40 although others have observed elevations of d-dimer infrequently in conventionally treated patients.41 Congestive heart failure also causes elevations of d-dimer.42

Role of Computed Tomographic Angiography and Computed Tomographic Venography

Contrast-enhanced CT angiography has become the reference standard for the diagnosis of acute PE13,14 and in most circumstances is the imaging test of choice. The combination of contrast-enhanced multidetector CT pulmonary angiography (CT angiography) and venous phase imaging of the low pelvic and proximal leg veins (CT venography) is recommended for patients in CCU.43 Although the diagnostic yield of CT venography was small (1.3%) in patients with negative results on 64-detector CT angiography, the proportion of diagnoses of venous thromboembolism was 10.3%.44

On the basis of data with mostly 4-slice computed tomography, if PE was shown in a main or lobar pulmonary artery, the positive predictive value was 97%.45 Because the rate of false-positive diagnoses increases with decreasing vessel size, it is important to ascertain the radiologist’s degree of certainty for a diagnosis of PE in segmental or subsegmental pulmonary artery branches. If the diagnosis is not unequivocal, further testing may be necessary. Positive CT angiographic findings may be relied on if the clinical impression indicates a high probability of PE (96% had PE).45 If results of CT angiography and CT venography are negative in a patient with a high-probability clinical assessment, the false-negative rate is 18%, and further evaluation is recommended by V-Q scan, serial ultrasound, or conventional angiography.11

If the clinical assessment indicates an intermediate probability of PE, most patients with positive CT angiographic results (92%) have PE, and treatment is indicated.13 If the apparent PE is only in a segmental or subsegmental branch, further testing is optional. Negative results on combination CT angiography and CT venography excluded PE in 92% of patients with a moderate probability clinical assessment, and no treatment is necessary in such patients.11

If clinical assessment indicates a low probability of PE, CT angiography can be considered diagnostic if the PE is shown in a main or lobar pulmonary artery, but if the apparent PE is in a segmental or subsegmental branch, the confidence in the CT diagnosis must be reassessed, and further evaluation may be necessary.11 If the results of combination CT angiography and CT venography are negative in a patient with a low-probability clinical assessment,
PE was excluded in 97% of patients, and treatment is not indicated.11

**Optional Pathways**

Venous ultrasound before imaging with CT angiography or CT angiography combined with CT venography is optional and may guide treatment if the results are positive. Venous ultrasound detected deep venous thrombosis in 15% of patients with suspected PE46 and in 29% with proved PE, thereby allowing treatment with no further obligatory testing.

**Patients With Allergy to Iodinated Contrast Material**

With severe iodine allergy, pulmonary scintigraphy may be a useful alternative. A low-probability V-Q lung scan combined with a low-probability clinical assessment showed PE in only 4% of patients.16 A high-probability V-Q scan in a patient with a high-probability clinical assessment showed PE in 96%.16 With other combinations, PE was present in 16% to 88%, and further evaluation is needed. Further evaluation may include serial venous ultrasound.11

**Patients With Impaired Renal Function**

For patients with impaired renal function, venous ultrasound is recommended, and if the results are positive, treatment is indicated. Pulmonary scintigraphy is recommended if the results of venous ultrasound are negative. Serial venous ultrasound is an option if the results of scintigraphy are equivocal.

**Digital Subtraction Pulmonary Angiography**

Conventional pulmonary angiography is rarely considered necessary today, but it continues to have the advantage of a radiologist’s being with the patient during the entire procedure to assess the need for additional injections and/or views or superselective injections when initial results are nondiagnostic.

**Ventilation-Perfusion Lung Scans**

In patients who lost consciousness on the day of study entry, V-Q lung scans were interpreted as showing high probability for PE in 4 of 5 (80%).10 Although this is a small number of patients, it is clear that the lung scan may not show high-probability interpretations in patients with severe PE. Most patients on ventilatory support, 41 of 46 (89%), showed nondiagnostic (intermediate- or low-probability) V-Q scan results.47 Scintigraphy in patients with normal or nearly normal results on chest x-ray may be the imaging test of choice in women aged <50 years because of the risk for radiation with CT angiography, particularly radiation to the breasts. Breast radiation with V-Q scintigraphy is approximately 0.28 to 0.9 mGy,48 which is not more than 0.5% to 5% the radiation dose to the breasts caused by CT angiography.15 Although in the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED), V-Q scans gave definitive diagnoses in only 28% of patients,16 in a more recent investigation, 46% had definitive diagnoses by V-Q scans.49 Retrospective analysis of data from PIOPED II (75% of patients) showed definitive V-Q scan results in 74% of patients.50 If the results of chest x-rays were normal or nearly normal, definitive readings of the V-Q scan were shown in 91% of patients.51 A very low probability interpretation of the V-Q scan is as reliable as CT angiography in excluding PE when the clinical probability is low or moderate.52

Normal results on a perfusion lung scan exclude PE with a negative predictive value close to 100%.16 The ventilation scan can be eliminated when the perfusion scan results are normal in most patients without reducing diagnostic accuracy.53 It is arguable that the benefits of more comprehensive imaging with CT angiography would outweigh the smaller risks of radiation in an older population, and in men of all ages.

**Echocardiography**

Right ventricular distention on the echocardiogram may suggest acute PE if unexplained by other findings. Right ventricular dysfunction in a patient with PE and normal systolic blood pressure has been classified as “impending hemodynamic instability.”54 The in-hospital prognosis is good, however, in patients with PE and right ventricular enlargement (on the basis of data from CT angiography) if not in shock, acutely ill, on ventilatory support, or having had recent myocardial infarction or life-threatening arrhythmia.55 Right ventricular enlargement alone in patients with PE, therefore, does not appear to indicate a poor prognosis or an indication for thrombolytic therapy.

Transesophageal echocardiography may be useful in patients with suspected massive PE who require immediate and aggressive therapy.56 Because of the high prevalence of bilateral central thromboemboli in such patients, transesophageal echocardiography allowed definitive diagnoses in 92%.56 Other than in patients with massive PE, transesophageal echocardiography had limited accuracy in comparison with CT.57

**Role of Magnetic Resonance Angiography**

Investigations in a few patients showed sensitivity for the detection of PE with gadolinium-enhanced magnetic resonance angiography of 77% to 100% and specificity of 95% to 98%.58 There is concern about nephrogenic systemic fibrosis or nephrogenic fibrosing dermopathy, which occurs rarely in patients with poor renal function who receive gadolinium-containing contrast material (215 patients reported worldwide).59 Among the reports that included information about renal status, all patients had acute or chronic severe renal insufficiency (glomerular filtration rate <30 ml/min/1.73 m²), renal dysfunction due to the hepato-renal syndrome, or renal dysfunction in the perioperative liver transplantation period.60 Most patients were receiving hemodialysis.60 To date, there has not been a report of nephrogenic systemic fibrosis or nephrogenic fibrosing dermopathy in a patient with normal renal function or mild to moderate renal insufficiency after exposure to gadolinium-containing contrast agents.60 The length of magnetic reso-
nance angiographic examinations, the difficulties with close monitoring, and the need for nonmagnetic support equipment make this modality of limited use for CCU patients.

**Recommendations for Patients in Extremis**

Echocardiography and leg ultrasonography are recommended as rapidly obtainable bedside tests. Right ventricular enlargement or poor right ventricular function, in a proper clinical setting, can be interpreted as being caused by PE. Positive results on venous ultrasound in the appropriate clinical setting also indicate PE. If echocardiographic and compression ultrasound results are negative, appropriate imaging studies should be performed when the patient stabilizes. A portable perfusion scan may give diagnostic information at the bedside. Some recommend immediate transfer to an interventional catheterization laboratory.

**Acknowledgment:** We thank Fadi Matta, MD, and Abdo Y. Yackoub, MD, for their assistance in the preparation of this report.

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