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REVIEW

Pulmonary Embolism: Clinical Features and Diagnosis

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ABSTRACT

Pulmonary embolism is a lethal yet treatable disease. Given the significant overlap of symptoms and signs between the presentation of pulmonary embolism and acute coronary syndromes, it becomes clear that emergency room physicians must be familiar with the diagnosis of pulmonary embolism. A critical issue is always to consider pulmonary embolism in the differential diagnosis of chest pain. However, the clinical diagnosis of pulmonary embolism remains problematic due to the nonspecific presenting symptoms, signs, electrocardiographic abnormalities, arterial blood gas and chest X-ray findings. D-dimers are becoming a widely available useful laboratory tool in the diagnosis of suspected pulmonary embolism. In this concise overview, the diagnostic value of clinical assessment in patients with possible pulmonary embolism will be explored.

KEY WORDS: *Pulmonary embolism, chest pain, d-dimer, deep venous thrombosis, thromboembolism*

Pulmonary embolism is responsible for 5-10% of all in-hospital deaths. Pulmonary embolism is an important diagnosis to establish, given that undiagnosed pulmonary embolism has a hospital mortality rate as high as 30%, which falls to nearly 8% if diagnosed and treated appropriately [1-3]. Unfortunately, however, the diagnosis of pulmonary embolism remains one of the most difficult problems. The main reason for this is that the clinical manifestations of pulmonary thromboembolism (Table 1) are non-specific, condition difficult to diagnose [2]. Indeed, pulmonary embolism is considered in the differential diagnosis of many clinical presentations including chest pain, hemoptysis and dyspnea. Less than 35% of patients suspected of having pulmonary embolism actually have the diagnosis confirmed. Therefore, many patients without pulmonary embolism are needlessly hospitalized and anticoagulated while awaiting confirmatory testing [4-6]. Given the high mortality of untreated pulmonary embolism, timely diagnostic testing must be performed to enable the initiation of antithrombotic therapy for patients proven to have this condition while at the same time avoiding the risks of anticoagulation for patients in whom this diagnosis is excluded [4,7].

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CLINICAL PARAMETERS AND SYMPTOMS

It is believed that diagnosis of pulmonary embolism is more difficult than treatment. Additionally, for patients with pulmonary embolism the most treacherous period is that preceding the establishment of diagnosis. Clinical suspicion of this disease is of paramount importance in guiding diagnostic testing. Firstly, the patient's age is

TABLE 1. Symptoms and signs of pulmonary embolism

	Frequency
Symptoms	
Dyspnea	80%
Chest pain (pleuritic)	52%
Chest pain (substernal)	12%
Cough	20%
Hemoptysis	11%
Syncope	19%
Signs	
Tachypnea (>20/min)	70%
Tachycardia (>100/min)	26%
Signs of deep venous thrombosis	15%
Fever (>38.5 °C)	7%
Cyanosis	11%

TABLE 2. Risk factors for venous thromboembolism

Primary	
Factor V Leiden	Antithrombin III deficiency
Resistance to activated protein C	Hyperhomocysteinemia
Prothrombin 20210 mutation	Antiphospholipid antibodies
Protein C deficiency	Protein S deficiency
Secondary	
Surgery/Immobilization/Trauma	Advanced age
Stroke/Spinal cord injury	Obesity
Malignancy/Chemotherapy	Diabetes mellitus
Heart failure	Smoking
Pregnacy/puerperium	Hypertension
Central venous catheters	Oral contraceptives
Chronic venous insufficiency	Long distance air travel

consistently a statistically significant univariate predictor for pulmonary embolism. Furthermore, the frequency of pulmonary embolism among patients with a malignant neoplasm at necropsy is highly increased in elderly patients [3]. On the other hand, the patient's gender does not appear to be predictive. Dyspnea, syncope or cyanosis indicate massive pulmonary embolism [8]. The lack of clinical manifestations of massive pulmonary embolism might be related to the insidious onset and progressive development of thromboembolism. However, the patient gradually adapts to and/or compensates for hemodynamic changes [9]. Contrariwise, pleuritic chest pain often signifies that the embolism is small and located in the distal pulmonary arterial system, near the pleural lining. In any event, individual presenting symptoms do not reliably differentiate between patients with and without pulmonary embolism. The exceptions in individual studies include pleuritic chest pain and sudden dyspnea [10,11]. Leg symptoms are consistently more likely in patients who have pulmonary embolism. Hemoptysis is a rare presenting symptom in suspected pulmonary embolism [11].

RISK FACTORS

Risk factors for venous thromboembolic disease (Table 2) are well characterized in the literature [8]. In patients treated for confirmed venous thromboembolic disease, one or more risk factors were present in over 96% of patients. Additionally, the presence of one or more risk factors was more common in patients with pulmonary embolism as opposed to those without pulmonary embolism. In patients with suspected pulmonary embolism the only risk factors, which are consistently present more often in patients who are ultimately confirmed to have pulmonary embolism, are thromboembolic disease, malignancy, recent surgery and immobilization. However, only the last two factors reach statistical significance [6]. It is interesting to note that Medina et al [12] observed that in patients with primary antiphospholipid syndrome, the most frequent clinical manifestations were venous thrombosis, thrombocytopenia, and pulmonary thromboembolism.

CLINICAL SIGNS

Patients with pulmonary embolism are more likely to be tachypneic and tachycardic than patients without pulmonary embolism. In the study of Hull et al6 there appears to be no difference in blood pressure, the presence of a pleural rub on auscultation or temperature in patients with confirmed and suspected pulmonary embolism. A commonly held misconception is that the presence of chest wall tenderness in patients with pleuritic chest pain excludes pulmonary embolism. In one study the presence of a fourth heart sound, loud second pulmonary heart sound and inspiratory crackles on chest auscultation were more common in patients with pulmonary embolism than in patients without pulmonary embolism [13].

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of pulmonary embolism remains extensive and covers a broad spectrum of life-threatening and other diseases (Table 3). Some patients have concomitant pulmonary embolism and other diseases. Hence, we must, for example, take into account that if pneumonia or heart failure does not respond to appropriate therapy, the possibility of coexisting pulmonary embolism should be considered. Discerning between pulmonary embolism and primary pulmonary hypertension is of critical importance. Although both diseases warrant anticoagulation, other advances in management require differentiation between these two diseases [14].

Differential diagnosis in patients with massive pulmonary

TABLE 3. Differential diagnosis of pulmonary embolism

Myocardial infarction/myocardial ischemia/angina
Acute heart failure
Pneumonia/atelectasis
Asthma/chronic obstructive pulmonary disease
Pericarditis/myocarditis
Pleuritis/pleurodynia
Pneumothorax/pneumomediastinum
Primary pulmonary hypertension
Rib fracture
Costochondritis (Tietze's syndrome) – Musculoskeletal pain
Intrathoracic cancer
(Early) Herpes zoster
DaCosta syndrome (psychogenic pain)/Hyperventilation
Acute cholecystitis
Shock (cardiogenic, septic, hypovolemic)
Cardiac tamponade

embolism includes acute myocardial infarction, cardiac tamponade and septic or other shock. On occasion, in patients without pulmonary infarction, presenting symptoms and signs may be attributed to anxiety with hyperventilation because of the paucity of objective pulmonary findings. When pulmonary infarction occurs, the differential diagnosis may include pneumonia, atelectasis, pericarditis, and heart failure.

ELECTROCARDIOGRAPHIC FINDINGS

A variety of electrocardiographic changes have been suggested in several studies as having diagnostic value in patients with suspected pulmonary embolism [11,13,15,16]. However, these studies have one disadvantage relating to the fact that the investigators have only studied patients with confirmed pulmonary embolism. Rodger et al [16] found that tachycardia and incomplete right bundle branch block were significantly more frequent in patients with pulmonary embolism than in patients without pulmonary embolism. More recently, Sinha N et al [15] reported that sinus tachycardia, an S1/Q3/T3 pattern, atrial tachyarrhythmias, a Q wave in lead III, and a Q3/T3 pattern were findings significantly associated with pulmonary embolism. These investigators [15] concluded that standard 12-lead electrocardiographic changes can increase the pretest probability of pulmonary embolism before performing computed tomography (CT) pulmonary angiography, and that these electrocardiographic findings have relatively low likelihood to be of clinical use.

CHEST X-RAY

Stein et al13 found that the most sensitive chest X-ray finding was atelectasis or parenchymal abnormality having a sensitivity of 68%. It is a fact, however, that one cannot depend on chest x-ray for the diagnosis of pulmonary embolism [15]. In one study, chest x-rays of patients with suspected pulmonary embolism were interpreted by radiologists who agreed on the presence of pulmonary embolism in only 33% of patients and among them in only 33% of patients was the diagnosis correct [17].

ARTERIAL BLOOD GAS ANALYSIS

One commonly held misconception is that a normal arterial-alveolar gradient excludes pulmonary embolism [18], despite reports to the contrary [19]. Stein et al [19] have proposed prediction rules based on arterial blood gas but these rules could not be validated in subsequent studies [20].

D-DIMER

An abnormally elevated level of Elisa-determined plasma D-dimer has more than 90% sensitivity for identifying patients with pulmonary embolism proven by lung scan or by angiogram [21,22]. In the study of Hammond and Hassan [23], retrospective analysis of a sequential series of 376 patients revealed that no patient with D-dimer of <275 ng/ml was diagnosed with pulmonary embolism, irrespective of clinical probability. Egermayer et al [24] showed that a negative D-dimer, a paO_2 of ≥80 mmHg and a respiratory rate less than 20, also had a negative predictive value of 100% in patients with suspected pulmonary embolism. Rodger et al [25] were able to demonstrate a negative predictive value of 95% with this rule.

CLINICAL PREDICTORS

Despite the limitations of the individual clinical predictors described by the PIOPED investigators [4], it has been demonstrated that the overall clinical assessment should guide diagnostic management. They were able to separate a cohort of patients with suspected pulmonary embolism into high-, moderate- and low-probability groups using clinical assessment alone [25]. Perier et al [26] were also able to stratify patients into different risk categories using clinical assessment alone. In both of these studies patients were stratified into risk categories using the clinical judgment of the individual clinicians based on overall diagnostic impression alone. Additionally, Wells et al [27] included in their study 1200 patients with suspected pulmonary embolism. These patients were separated based on clinical criteria, into low-, moderate-, and high-probability subgroups using the explicit clinical

model. The prevalence of pulmonary embolism in the low-, moderate- and high-probability subgroups was 3%, 28%, and 78%, respectively. In an attempt to simplify the explicit clinical model, they subsequently performed a logistic regression analysis on clinical data collected in the aforementioned study. Their preliminary results have demonstrated that the simplified clinical model can separate patients into low-, moderate- and high-risk subgroups, although it appears that the emergency room physicians have a lower threshold for suspecting pulmonary embolism, so the overall pulmonary embolism rate was low in the validation study. Also, Miniati et al [28] reported the benefits of clinical assessment. Their combination of clinical predictors had a negative predictive value of 94% and pulmonary embolism could be excluded in 42% of patients in their validation set.

DIAGNOSTIC ALGORITHM

The diagnosis of acute pulmonary embolism is based on the assessment of factors, consistent symptoms and signs, and the lack of an alternative clinical explanation for the condition of the patient. If the probability of pulmonary embolism is low or intermediate, the diagnosis can be reliably excluded by a negative D-dimer test (Figure 1). A positive D-dimer test requires further evaluation with (perfusion and/or ventilation) lung scan or spiral computer tomography (CT) technique to confirm or rule out pulmonary embolism [29].

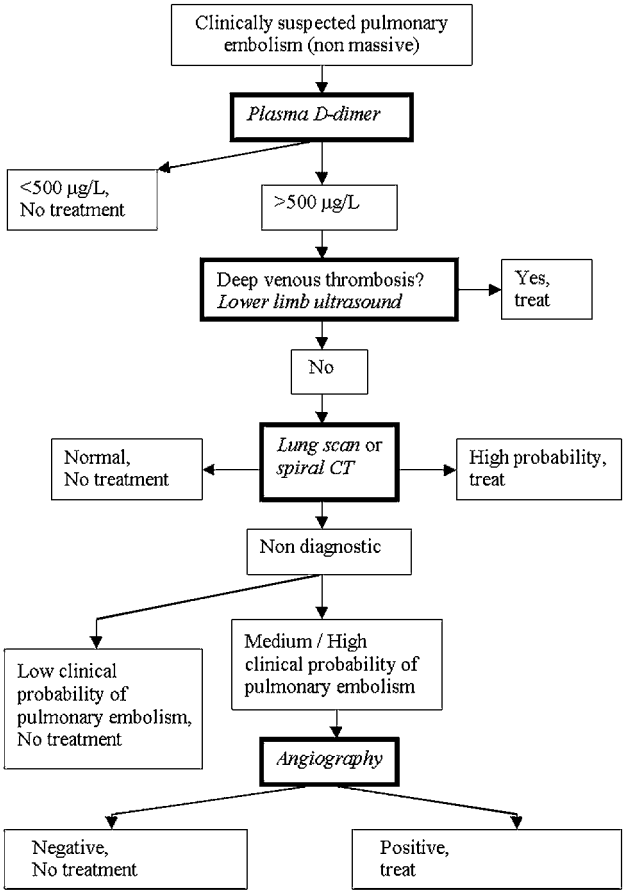

FIGURE 1. Diagnostic algorithm for suspected non-massive pulmonary embolism. CT indicates computed tomography.

IMAGING MODALITIES

Imaging modalities have a significant role, beyond standard clinical assessment, in the diagnosis of pulmonary embolism and decision making thereafter. Spiral chest CT is currently preferred over pulmonary radionuclide perfusion (and/or ventilation) scintigraphy as the initial imaging test. First generation CT scanners had a sensitivity of 70% compared to pulmonary angiography [30]. However, latest generation multidetector-row CT scanners have excellent resolution and are likely to supplant pulmonary angiography as the gold standard imaging study. Pulmonary radionuclide perfusion (and/or ventilation) scintigraphy is at present a second choice test, reserved for patients with contrast allergy, renal insufficiency or pregnant women (lower radiation dose for fetus compared to spiral chest CT). Echocardiography is a useful, rapid, bedside modality with a major role to detect right ventricular dysfunction or dilation, and thus guide therapy, particularly in the case of massive pulmonary embolism when in need for thrombolytic treatment. It is, therefore, not a routine diagnostic test but it contributes to risk stratification, prognosis and therapeutic decision making [31]. Magnetic resonance imaging is sensitive and specific for segmental or larger pulmonary embolism, while it provides valuable information about right ventricular function [32]. However, it is not widely available and experience is limited concerning diagnosis of pulmonary embolism. Venous ultrasonography is useful in detecting proximal deep venous thrombosis which is a surrogate for pulmonary embolism. However, since a negative study can not rule out pulmonary embolism, its role is supplementary. Finally, standard pulmonary angiography has been considered the gold standard for the diagnosis of pulmonary embolism, but it is rarely performed since the advent of spiral chest CT scanning. At present, it is used when catheter-based interventions are planned, such as catheter-directed thrombolysis or suction embolectomy.

Diagnostic procedures for pulmonary embolism continue to be refined and modalities such as spiral computer tomography or magnetic resonance imaging have the potential to further increase the possibility of diagnosis of pulmonary embolism and thus obviate the need for pulmonary angiography.

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