Spiral Computed Tomography for Acute Pulmonary Embolism

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There is still considerable debate about the optimal diagnostic imaging modality for acute pulmonary embolism. If imaging is deemed necessary from an initial clinical evaluation such as d-dimer testing, options include nuclear medicine scanning, catheter pulmonary angiography, and spiral CT. In many institutions, spiral CT is becoming established as the first-line imaging test in daily clinical practice. With spiral CT, thrombus is directly visualized, and both mediastinal and parenchymal structures are evaluated, which may provide important alternative or additional diagnoses. However, limitations for the accurate diagnosis of small peripheral emboli, with a reported miss rate of up to 30% with single-slice spiral CT so far, have prevented the unanimous embrace of spiral CT as the new standard of reference for imaging pulmonary embolism. The clinical significance of the detection and treatment of isolated peripheral pulmonary emboli is uncertain. Evidence is accumulating that it is safe practice to withhold anticoagulation in patients with suspected pulmonary embolism on the basis of a negative spiral CT study. Remaining concerns about the accuracy of spiral CT for pulmonary embolism detection may be overcome by the introduction of multidetector-row spiral CT. This widely available technology has improved visualization of peripheral pulmonary arteries and detection of small emboli. The most recent generation of multidetector-row spiral CT scanners appears to outperform competing imaging modalities for the accurate detection of central and peripheral pulmonary embolism. In this review, we assess the current role and future potential of CT in the diagnostic algorithm of acute pulmonary embolism. (Circulation. 2004;109:2160-2167.)

Key Words: diagnosis • embolism • imaging • thrombosis

Pulmonary embolism (PE) is protean in nature, continues to masquerade as other illnesses, and is frequently overlooked and misdiagnosed, at times even by experienced clinicians. Noninvasive imaging tests for PE are increasingly sophisticated and provide previously unimaginable fine resolution of peripheral pulmonary arteries. Despite technical progress, imaging the pulmonary arteries has remained costly and potentially harmful, even with noninvasive approaches. Therefore, imaging tests cannot be ordered on every patient who presents with a remote possibility of PE. Accordingly, diagnostic algorithms have been developed to rationalize the use of noninvasive imaging tests.

Ideally, there is a progression from clinical assessment to fundamental nonimaging tests before imaging of the pulmonary arteries ensues (Table 1). The diagnostic process can identify other important illnesses (such as myocardial infarction on ECG or pneumonia or pneumothorax on chest radiograph). Bedside tests have been refined to assess the clinical likelihood of PE. The test developed by Wells and colleagues,1 for example, is a simple questionnaire for patients with possible PE. With 7 basic questions, the test can rapidly assess the clinical probability of PE.

Arterial blood gas analysis2 and calculation of alveolar-arterial oxygen tension difference3 are not reliable tools to detect patients who have PE. The principal blood-screening test has become the d-dimer assay. d-dimer testing is highly sensitive and has a very high negative predictive value, so it is an excellent screening test for emergency department patients. At Brigham and Women’s Hospital’s Emergency Department, with 1106 consecutive assays for suspected PE, the sensitivity was 97% and the negative predictive value was 99.6%.4 Similar results have been obtained in other emergency departments.5 Initial evaluation and testing should be completed within several hours in the emergency department setting. At that point, the decision to proceed with direct chest imaging for PE must ensue. d-dimer is less useful for patients who are already hospitalized because the levels are elevated in many illnesses that mimic PE, such as pneumonia and myocardial infarction. d-dimer levels are also elevated in patients with cancer and sepsis, those who are pregnant, and those in the postoperative state. To increase the precision of the diagnostic workup, the standardized clinical assessment and d-dimer test result can be used together to help decide which patients warrant further workup.6–8

Ordinarily, the workup for PE can stop if the d-dimer ELISA is normal. While awaiting results of the d-dimer, most patients should undergo ECG and chest radiography. The ECG may be normal in patients with massive PE. Sometimes, there are signs of right-side heart strain such as negative T waves in the precordial leads,9 right bundle-branch block, the classic S1Q3T3 pattern,10 and the recently described Qr in lead V1.11 The chest radiograph may be normal, even in...
patients with massive PE. The most common radiographic
abnormality is cardiomegaly.\textsuperscript{12}

The utility of venous ultrasonographic screening of pa-
tients without leg symptoms who have suspected PE is
controversial.\textsuperscript{13–16} If a diagnosis of deep venous thrombosis
(DVT) can be established in a patient with symptoms of PE,
the course of therapy is most often predetermined. However,
this approach may miss more than half of patients with PE,\textsuperscript{15}
probably because the DVT has often completely embolized to
the lungs. Also, venous ultrasonography is notoriously insen-
tive for diagnosing DVT in asymptomatic patients.\textsuperscript{13,14,16} If
CT is used as the primary imaging test for suspected PE, the
feasibility of combining CT angiography of the pulmonary
arteries with CT venography of the deep venous system for a
comprehensive evaluation for venous thromboembolism has
been demonstrated.\textsuperscript{17,18}

Finally, echocardiography is not recommended as a routine
imaging test to diagnose suspected acute PE. Instead, echo-

\begin{table}
\centering
\caption{Diagnostic Approaches to Acute PE: Strengths and Weaknesses}
\begin{tabular}{|l|l|l|}
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\textbf{Test} & \textbf{Strengths} & \textbf{Weaknesses} \\
\hline
Wells questionnaire\textsuperscript{1} & Rapid bedside stratification of likelihood of PE & Influenced by one subjective question: whether
alternative diagnoses are more likely than PE \\
Arterial blood gases: hypoxemia\textsuperscript{2} & Rapid; widely available & Does not discriminate well between patients with
and without PE \\
Arterial blood gases: A-A gradient\textsuperscript{3} & Rapid; widely available & Normal gradient present in as many as 20% of
patients with PE \\
d-dimer\textsuperscript{4,5} & Rapid; widely available; high negative predictive value & Not specific; low positive predictive value \\
Electrocardiogram\textsuperscript{9–11} & Universally available; may indicate right heart strain & Not specific; may be normal despite PE \\
Chest x-ray\textsuperscript{12} & May identify mimics of PE: pneumonia, pneumothorax, congestive
heart failure & May be normal despite PE; patients may have concomitant PE and pneumonia or PE and
congestive heart failure \\
Venous ultrasound\textsuperscript{13–16} & May identify DVT, thus establishing the presence of venous thrombosis & May be normal despite PE (because DVT embolized) \\
CT venography\textsuperscript{17,18} & May obviate venous ultrasonography if DVT is detected & Low sensitivity for calf DVT; radiation exposure \\
Echocardiography\textsuperscript{20} & Identifies patients at high risk if right ventricular dysfunction is
detected; on rare occasions will visualize the PE & Usually normal despite PE \\
Lung scanning\textsuperscript{30,31} & Avoids contrast injection; useful if normal or high probability & Often nondiagnostic \\
Pulmonary angiography\textsuperscript{23–25} & Classically considered the “gold standard”; detailed display of
pulmonary vascular morphology, oligemic areas of perfusion,
manifestations of antecedent, chronic emboli (webs, pouches,
laminated clot, vessel fenestrations), and venous drainage & Invasive; labor intensive; costly; high interobserver
variability for detection of subsegmental emboli \\
Spiral CT\textsuperscript{29,33,37,38,40,51–60} & De facto first line imaging test in clinical practice; widely available;
direct visualization of thrombus and of alternative or additional
diagnoses; cost effective; high negative predictive value for
clinically relevant PE & Requires use of iodinated contrast material; radiation exposure \\
\hline
\end{tabular}
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Figure 1. Contrast-enhanced 16-slice CT examination of 72-year-old man with extensive, acute central PE with “saddle embolus”
(arrows) extending into both central pulmonary arteries. Colored volume-rendering technique seen from an anterior (A) and anterocra-
nial (B) perspective allows intuitive visualization of location and extent of embolism.
cardiography is most useful for risk stratification and prognostication after the diagnosis of PE has been established.\textsuperscript{19,20}

**Imaging Acute PE**

**Pulmonary Angiography, Nuclear Medicine Lung Scanning, and MRA**

Catheter pulmonary angiography has been hailed as the “gold standard” technique for PE diagnosis and has the advantage of providing simultaneous hemodynamic information that may be useful for patient management. In reality, however, this test is infrequently performed.\textsuperscript{21,22} The morbidity and mortality rates for this invasive test are reported to range from 3.5\% to 6\% and 0.2\% to 0.5\%, respectively.\textsuperscript{23–25}

Use of nuclear medicine imaging, once the first imaging study for suspected PE, is in decline\textsuperscript{26,27} because of the high
Spiral CT for Imaging Acute PE

In many institutions, spiral CT is becoming the first-line imaging test for the assessment of patients with suspected acute PE in daily clinical practice. Both mediastinal and parenchymal structures are evaluated, and thrombus is distinctly visualized (Figure 1). Many patients with an initial suspicion of PE receive other diagnoses, and spiral CT can decrease the proportion of indeterminate scintigraphic studies but cannot offset the limitations inherent to a functional imaging test. Different from other imaging tests, ventilation-perfusion scintigraphy is an indirect test for PE based on assessment of pulmonary perfusion. This differs from imaging modalities that allow direct visualization (Figure 1) of PE and other thoracic pathology.

Contrast-enhanced MRA has acquisition protocols that lack sufficient spatial resolution for reliable evaluation of peripheral pulmonary arteries. More important, this modality has not seen widespread use in the acutely ill patient with suspected PE because of a lack of general availability, relatively long examination times, and difficulties in patient monitoring.

Spiral CT Limitations for Imaging Peripheral Pulmonary Emboli

The main impediment for spiral CT has been limitations of this modality for the accurate detection of small peripheral emboli. Early studies comparing conventional single-slice spiral CT with selective pulmonary angiography demonstrated the high accuracy of spiral CT for detecting PE from the main pulmonary artery to the segmental arterial level but suggested that subsegmental pulmonary emboli may be overlooked by spiral CT scanning. With older generations of conventional single-slice spiral CT scanners, false-negative rates of up to 30% were reported.

Detection and Treatment of Isolated Peripheral Pulmonary Emboli: Clinical Significance

Limitations for the accurate diagnosis of isolated peripheral emboli with single-slice spiral CT so far have prevented the unanimous embrace of spiral CT as the new standard of reference for imaging PE. The clinical significance of such isolated peripheral emboli, however, in subsegmental or smaller pulmonary arteries in the absence of central emboli is uncertain. It has been shown that 6% to 30% of patients with documented PE present with clots only in subsegmental or smaller pulmonary arteries in the absence of central emboli.

It is speculated that one important function of the lung is to prevent small emboli from entering the pulmonary circulation. Such emboli may form even in healthy individuals, although this notion has never been substantiated. Controversy also exists about the treatment of small emboli and whether this will result in improved clinical outcome. It is assumed that the presence of such emboli may indicate current DVT that potentially heralds more severe embolic events. A burden of small peripheral emboli is also thought to have prognostic relevance in individuals with cardiopulmonary disease and for the most cost-effective modality in the diagnostic algorithm of PE compared with algorithms that do not include spiral CT.
development of chronic pulmonary hypertension in patients with thromboembolic disease.

Although the accuracy of conventional single-slice spiral CT for the detection of isolated peripheral emboli may be limited, encouraging data are accumulating on the high negative predictive value of a normal spiral CT study (Table 2). According to these retrospective and prospective studies, patient outcome is not adversely affected if anticoagulation is withheld on the basis of a negative spiral CT study. The negative predictive value of a normal spiral CT study is high, compares very favorably with catheter pulmonary angiography, and approaches 98%, regardless of whether underlying lung disease is present. The frequency of a subsequent clinical diagnosis of PE or DVT after a negative spiral CT pulmonary angiogram is low, lower than that after a negative or low-probability V-Q scan. Thus,
even single-slice spiral CT appears to be a reliable imaging tool for excluding clinically relevant PE, so it appears that anticoagulation can be safely withheld when the spiral CT scan is normal and of good diagnostic quality.\textsuperscript{53,57,59,60}

**Advantages of Multidetector-Row Spiral CT for PE Imaging**

Remaining concerns about the accuracy of spiral CT for PE detection may be overcome by the introduction of multidetector-row spiral CT. Multidetector-row spiral CT, with simultaneous acquisition of 4 sections per scanner rotation instead of a single section, first became available in 1998.\textsuperscript{62,63} The advantages of fast, high-resolution image acquisition with multidetector-row spiral CT led to the widespread embrace of this modality, with close to 3000 installed units in the United States. The current generation of 4-, 6-, 8-, 10-, and 16-slice multidetector-row spiral CT scanners now allows acquisition of the entire chest with 1-mm or submillimeter resolution within a short single breath-hold (<10 seconds in the case of the 16-slice CT) (Figure 5). Covering substantial parts of the human anatomy with ever-finer spatial resolution has obvious advantages for imaging PE. Shorter breath-hold times benefit patients with underlying lung disease and reduce the percentage of nondiagnostic CT scans.\textsuperscript{64} High-resolution multidetector-row spiral CT data can be transformed easily for 2D and 3D visualization. This may, in some instances, improve PE diagnosis but is generally of greater importance for conveying information on localization and extent of embolic disease in a more intuitive display format (Figure 1).

Probably the most important advantage of multidetector-row spiral CT is improved diagnosis of small peripheral emboli (Figure 6). The degree of accuracy that could be achieved for the visualization of subsegmental pulmonary arteries and for the detection of emboli in these vessels with previously available modalities (single-slice, dual-slice, and electron-beam CT) was found to range between 61% and 79%.\textsuperscript{41,65–67} The high spatial resolution (ie, 0.6 x 0.6 x 0.6 mm in the x, y, and z extensions) of multidetector-row spiral CT data sets now allows evaluation of pulmonary vessels down to 6th-order branches and significantly increases the detection rate of segmental and subsegmental pulmonary emboli.\textsuperscript{68–70} This improved detection rate is likely due to the accurate analysis of progressively smaller vessels by use of thinner sections. Animal experiments that use artificial emboli as an independent gold standard indicate that high-resolution 4-slice multidetector-row spiral CT is at least as accurate as invasive pulmonary angiography for the detection of small peripheral emboli. The interobserver correlation for confident diagnosis of subsegmental emboli with high-resolution multidetector-row spiral CT exceeds the reproducibility of selective pulmonary angiography.\textsuperscript{69,71,72}

The true accuracy of multidetector-row spiral CT for the detection of small peripheral emboli in patients with suspected PE will be difficult to determine. As a direct result of high-resolution imaging capabilities, small peripheral clots that may have gone unnoticed in the past are now frequently seen, often in patients with minor symptoms (Figure 6). It appears highly unlikely that pulmonary angiography will be performed on a patient merely to prove the presence of a small (2 to 3 mm) isolated embolus.

The efficacy of multidetector-row spiral CT in patients suspected of having acute PE is currently being assessed by the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) II\textsuperscript{73} study. This prospective multicenter study began recruiting patients in 2001 and is expected to complete recruitment in 2004. In contrast to the original PIOPED\textsuperscript{28} study, which used contrast pulmonary angiography as the primary reference test for PE, PIOPED II uses a composite reference test for venous thromboembolism that is based on the ventilation/perfusion lung scan, venous compression ultrasound of the lower extremities, digital subtraction pulmonary angiography, and contrast venography in various combinations to establish the PE status of the patient.\textsuperscript{73}

**Conclusions**

CT has become an attractive means for a safe, highly accurate, cost-effective diagnosis of acute PE and may provide alternative diagnoses and explanations for symptoms in the absence of PE. Multidetector-row spiral CT technology has overcome past limitations of CT and is emerging as a preferred modality for imaging patients with suspected acute PE. New-generation multidetector-row spiral CT scanners now challenge catheter pulmonary angiography, once the standard of reference, for the accurate detection of PE.

**References**

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