Detection of Pulmonary Embolism in Patients with Unresolved Clinical and Scintigraphic Diagnosis: Helical CT Versus Angiography

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OBJECTIVE. This study was designed to prospectively compare helical CT with pulmonary angiography in the detection of pulmonary embolism in patients with an unresolved clinical and scintigraphic diagnosis.

SUBJECTS AND METHODS. Twenty patients with an unresolved suspicion of pulmonary embolism were evaluated with contrast-enhanced helical CT and with selective pulmonary angiography. An average of 11 hr separated the two studies. The CT scans were obtained during one 24-sec or two 12-sec breath-holds. CT scans were interpreted without knowledge of the results of scintigraphy or angiography. Selective pulmonary angiograms were obtained with knowledge of the findings on the ventilation/perfusion scan only. The sensitivity and specificity of CT were compared with those of angiography for central vessels (segmental and larger) only and for all vessels.

RESULTS. Eleven of the 20 patients had proved pulmonary embolism (seven in central vessels and four in subsegmental vessels only). When only central vessels were analyzed, CT sensitivity was 86%, specificity was 92%, and the likelihood ratio was 10.7. However, when subsegmental vessels were included, CT results were 63%, 89%, and 5.7, respectively.

CONCLUSION. In our subset of patients, helical CT was only 63% sensitive. Subsegmental emboli are difficult to diagnose. Pulmonary angiography remains the study of choice. CT has a limited role in the evaluation of acute pulmonary embolism.

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In patients with suspected pulmonary embolism, if both the clinical assessment before imaging and the findings on a ventilation perfusion (V/Q) scan suggest a high probability of pulmonary embolism, the diagnosis is confirmed by pulmonary angiography in more than 95% of patients. On the other hand, if results of both techniques suggest a low probability, the diagnosis of pulmonary embolism is correctly excluded in more than 90% of patients. In these situations, angiography is not usually done. Unfortunately, approximately two thirds of patients have indeterminate findings on the V/Q scan or have discordance between clinical and scintigraphic estimates of the likelihood of pulmonary embolism [1–4]. Although these patients present a diagnostic dilemma, some clinicians are reluctant to perform pulmonary angiography [5, 6]. The majority of patients do not have additional imaging studies, and a treatment decision is made on clinical grounds [7].

CT, both incidentally [8–10] and purposely [11, 12], has imaged pulmonary emboli and has potential for providing a reliable, noninvasive alternative to angiography. Remy-Jardin et al. [11], using helical CT scanning with volumetric acquisition and overlapping reconstruction, diagnosed pulmonary emboli in central pulmonary vessels with a sensitivity of 90% and a specificity of 96%. Subsegmental vessels were not analyzed. Teigen et al. [12], using electron-beam CT, found a similar sensitivity and specificity. These studies have generated much controversy regarding the role of CT. Gurney [13] editorialized that CT should replace scintigraphy and angiography, whereas Oudkerk [14] cautioned that CT is not a proven alternative. The following study was designed to prospectively compare helical CT with pulmonary angiography in patients with unresolved suspicion for pulmonary embolus. Both central and subsegmental vessels were studied.

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Subjects and Methods

Subjects

Patients sent for V/Q scanning for suspected acute pulmonary embolism were eligible for the study. Before the V/Q scan, the clinical service completed a 10-question survey and an independent overall estimate of the likelihood of a pulmonary embolism. Patients with normal findings on a V/Q scan, with both V/Q and clinical findings suggesting a low probability of pulmonary embolism, or with both suggesting a high probability of pulmonary embolism were not recruited. Those patients with a duplex Doppler study of the lower extremities that showed deep venous thrombosis were also excluded. All others were considered to have an unresolved suspicion for pulmonary embolism and were candidates for the study. Patients with a contraindication to IV contrast material (e.g., renal failure, heart failure, history of allergy) were not recruited. Informed consent for CT and pulmonary angiography was obtained in accordance with a protocol approved by the Human Research Review Committee.

Twenty-five patients were entered into the study. Of the 25, five were eventually excluded (one patient refused to have angiography after CT, one patient had a CT scan that revealed a large central tumor, and three patients had catheter or equipment problems before the CT study was completed). All patients with completed CT scans were included in the study. (During this period, pulmonary angiograms were obtained in 12 additional patients. Seven had medical conditions that precluded performing the additional CT, two refused to consent to CT, and three were not identified as potential candidates.)

All subsequent data refer to the 20 patients who had completed CT scans. The group included 12 men and eight women, with an average age of 53 years (range, 25–84 years). In 11 patients, the primary clinical diagnosis was pulmonary embolism; in three, heart disease; in two, respiratory insufficiency; and in four, miscellaneous conditions.

Clinical Questionnaire

The clinical survey was a 10-item questionnaire of signs and symptoms known to correlate with the presence or absence of pulmonary embolism [15], followed by a subjective clinical estimate of the likelihood of pulmonary embolism being present (high, >75%; medium, 25–75%; low, <25%).

Imaging Evaluation

For radionuclide lung imaging, technetium-99m macroaggregated albumin (^{99m}Tc-MAA) perfusion imaging was performed first, followed by ^{99m}Tc-pyrophosphate (^{99m}Tc-PYP) radioaerosol ventilation lung imaging. For the perfusion studies, 2–3 mCi of ^{99m}Tc-MAA was injected IV followed by 500,000-count eight-view planar perfusion imaging. The nuclear medicine physician supervising the study then chose the view for "wash-in" and subtraction technique ventilation imaging. The patient then inhaled ^{99m}Tc-PYP radioaerosol while 30 sequential wash-in images were obtained [16]. Before this radioaerosol wash-in imaging, a baseline ^{99m}Tc-MAA image was obtained and the count rate noted. The radioaerosol inhalation was terminated when the count rate had doubled (approximately 8–10 min). Using the initial baseline ^{99m}Tc-MAA image, a subtraction image was obtained, looking for evidence of significant ventilation at the site of any perfusion defects. Thereafter, up to eight-view ^{99m}Tc-PYP radioaerosol planar images were obtained for further comparison with the initial ^{99m}Tc-MAA eight-view perfusion study. Abnormalities in perfusion and ventilation, as shown with these radionuclide techniques, were graded in accordance with Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria [17].

CT scans were obtained on a General Electric High Speed Advantage Helical Scanner (17 patients) or on a Siemens Somatome VD30 Helical Scanner (three patients). Fourteen studies used a 24-sec breath-hold, and six used two 12-sec breath-holds with a 6-sec pause for breathing. Each scan used 5-mm collimation, 1:1 pitch, and covered 12 cm of the thorax. In the first 10 cases, scans were obtained in the craniocaudal direction starting at the aortic knob. Subsequent scans were obtained in the caudocranial direction starting at the diaphragm. Images were presented as overlapping 3-mm reconstructions and displayed at lung (–500/2000 H) and mediastinal (70/350 H) settings. Images were evaluated side by side with a 12-on-one film format.

One hundred forty milliliters of 30% iodinated contrast material was injected through a 20-gauge catheter placed in the antecubital fossa. The injection rate was 4.5 ml/sec with a 14-sec delay between injection and scanning. In older patients, a longer delay was used. (In four cases, injections were made through preexisting central venous catheters. This necessitated a slower, more prolonged injection and a longer delay before scanning.) Criteria for the presence of thrombi included one of two signs: (1) complete filling defect (abrupt absence of contrast material in a visible vessel) or (2) partial filling defect (visible central filling defect or contrast material tracking around a central filling defect). These criteria are modified from Remy-Jardin et al. [11].

For angiograms of the left or right main pulmonary artery, 40–50 ml of Omnipaque 350 was injected at 20–25 ml/sec by power injector through a 6.5-French Montefiore catheter (Cook, Bloomington, IN). Subselective studies used 10–15 ml by either hand or power injection at approximately 4–5 ml/sec through a 5-French curved tip catheter. Angiograms were recorded on conventional cut film in all 20 cases (Puck CM, Siemens Medical Instrumentation). In 12 cases, supplemental oblique angiograms were acquired on conventional film and in five cases on a high-resolution digital acquisition system (GE Medical AFM Advantx). The high-resolution digital system used a 1024 × 1024 matrix and a 12-cm field of view. Magnification images were not obtained.

The V/Q scan was used to plan each pulmonary angiogram. If the initial frontal and/or oblique angiogram showed pulmonary emboli, the opposite lung was not studied. If the first lung examined angiographically showed no emboli, a minimum of a single view of the contralateral lung was obtained. Thus, not every patient had bilateral angiograms. There were 13 bilateral studies and seven unilateral studies. Of the 20 patients, 17 had angiograms of the right pulmonary artery and 16 had angiograms of the left pulmonary artery. In addition, oblique views were obtained for 11 right lungs and nine left lungs. The diagnosis of pulmonary embolism required one of two findings: (1) vessel cutoff with meniscus or (2) contrast material tracking around an intraluminal thrombus.

In 10 cases, CT was done first; in 10 cases, angiography was done first. The decision to do one or the other study first was based on room and personnel availability rather than any patient-related factors. An average of 15.4 hr elapsed between the V/Q scan and the next study. In 18 of 20 cases, fewer than 24 hr elapsed. An average of 11 hr elapsed between pulmonary angiography and CT or between CT and pulmonary angiography. In 19 of 20 cases, fewer than 24 hr elapsed between studies.

Analysis

Both the CT scans and the angiograms were independently evaluated for clot in each generation of pulmonary artery. The right side included the right pulmonary artery; the anterior trunk; the interlobar trunk; the middle lobe artery; the basal artery; and the segmental and subsegmental arteries of the right upper lobe, right middle lobe, and right lower lobe. On the left, the evaluation included the left pulmonary artery; the interlobar trunk; the lingular artery; the basal artery; and the segmental and subsegmental arteries of the left upper lobe, lingula, and left lower lobe. (Early in the course of the study, it became clear that subsegmental vessels could not be reliably identified on CT scans, and attempts to grade these vessels on CT scans were abandoned. Clots identified in subsegmental vessels were scored.) If only a unilateral angiogram was obtained, only the CT scans of that lung were analyzed.

Each CT scan was scored independently by two of four radiologists experienced in chest CT. Discrepancies were resolved by consensus. The consensus was the final interpretation. Discrepancies were tabulated for later evaluation. CT scans were interpreted without knowledge of the findings on the V/Q scans or the angiograms. Pulmonary angiograms were scored independently by the contributing angiographer without knowledge of the CT findings.

Angiograms and CT scans were compared vessel for vessel. To simplify reporting, results were reported per patient and per lung, as not every patient had bilateral angiograms. CT findings were considered true-positive if the CT and the angiographic findings agreed on at least one embolus in that patient or in that lung. CT findings were considered true-negative if no clots were identified in either study. CT findings were considered false-positive if the CT scan showed an embolus in a given vessel and the angiogram did not but no true-positives were found elsewhere. CT findings were considered false-negative when the CT scan showed no embolus and the angiogram showed an embolus. (A CT scan that showed only an embolus in the right upper lobe and an angiogram that showed only an embolus in the right lower lobe would be considered a false-positive result in the right upper lobe, a false-negative result in the right lower lobe, and a false-negative result for that lung.) Sensitivity, specificity, and likelihood ratios (sensitivity/[1 − specificity]) were determined for each patient and for each lung. When the CT and angiographic interpretations were in disagreement, a joint interpretation session was held between the CT and the angiography reviewers.

TABLE 1: Scintigraphic Likelihood of Pulmonary Embolism

Embolism	Ventilation/Perfusion Scan Interpretation			
	Low	Mod/Ind	High	Total
Present	5	5	1	11
Absent	5	4	0	9
Total	10	9	1	20

Note.—Mod = moderate, Ind = indeterminate.

Results

Eleven patients had angiographically proved pulmonary embolism, and nine patients had normal pulmonary arteries. Ten of the V/Q scans were low probability; eight, moderate probability; one, indeterminate probability; and one, high probability. Only one of the 11 patients with pulmonary embolism had a high-probability scan, five patients had a moderate probability or indeterminate scan, and five patients had a low-probability scan (Table 1). Similarly, the clinical questionnaire and clinical likelihood estimates of pulmonary embolism were not predictive (Tables 2 and 3).

Of the 20 CT scans, 12 were thought to give good opacification of all vessels of interest, six were thought to be adequate, and two were thought to be poor in limited anatomic areas. The study included too few patients to objectively test whether the caudocranial scans were superior to the craniocaudad scans. It was our subjective impression that they were. Lingula and middle lobe vessels and segmental vessels in atelectatic lobes were the most difficult to evaluate. Subsegmental vessels were either difficult to evaluate or difficult to identify. In one patient, a breathing artifact on two contiguous slices led to a false-positive diagnosis of an embolus in the posterior basal artery of the left lower lobe.

Of the 20 patients, 11 had pulmonary emboli (Tables 4 and 5). Seven had emboli in major vessels (Fig. 1), and four had emboli in subsegmental vessels only. CT showed only one of the subsegmental emboli (Fig. 2). When all vessels were considered, CT had a sensitivity of 63%, a specificity of 89%, and a likelihood ratio of 5.7. When only the larger vessels were considered, the sensitivity was 86%, the specificity was 92%, and the likelihood ratio was 10.7.

Angiograms were obtained in 33 lungs. When only central vessels were analyzed, the CT sensitivity per lung was 70%, specificity per lung was 87%, and the likelihood ratio was 5.4. When all vessels were analyzed, the sensitivity was 54%, the specificity was 85%, and the likelihood ratio was 3.6.

TABLE 2: Clinical Estimates of Pulmonary Embolism

Clinical Estimate	Pulmonary Embolus			
	Present (n = 11)		Absent (n = 9)	
	Yes	No	Yes	No
Lower extremity orthopedic procedure	0	11	1	8
Diagnosis of cancer	0	11	1	8
Pelvic disease/surgery	1	10	2	7
Obesity	2	9	2	7
Congestive heart failure	1	10	3	6
Chest pain	4	7	5	4
Leg pain	2	9	2	7
Heart rate >90 beats per minute or increased by more than 20 beats per minute	7	4	6	3
Respiration rate >25/min or increased >10/min	7	4	7	2
Increased second heart sound	2	9	0	9
Total	26		29	
Average	2.4		3.2	

TABLE 3: Clinical Likelihood of Pulmonary Embolism

Embolism	Clinical Estimate			
	High (>75%)	Medium (25–75%)	Low (<25%)	Total
Present	4	4	3	11
Absent	3	4	2	9
Total	7	8	5	20

TABLE 4: Imaging of Central Vessels Only

CT	Pulmonary Angiography		
	Embolism Present	Embolism Absent	Total
Embolism present	6	1	7
Embolism absent	1	12	13
Total	7	13	20

Note.—$\chi^2 = 12.17$, df = 1, significant at $p \leq .005$.

TABLE 5: Imaging of All Vessels

CT	Pulmonary Angiography		
	Embolism Present	Embolism Absent	Total
Embolism present	7	1	8
Embolism absent	4	8	12
Total	11	9	20

Note.—$\chi^2 = 5.7$, df = 1, significant at $p = .025$.

There was modest agreement between the two CT reviewers for the presence or absence of thrombi for each specific site (main, lobar, and segmental vessels). The reviewers were in total agreement for right-sided vessels in 14 of 20 lungs, and for left-sided vessels in 16 of 20 lungs, giving a 75% overall concordance. Although disagreements were easily worked out for the final interpretation, the consensus interpretation did not necessarily result in a correct diagnosis. (Kappa statistics cannot be applied because the same two reviewers did not review every CT scan.)

Discussion

Our study looked at the most difficult cases to diagnose, those with unresolved clinical and scintigraphic signs and symptoms. This put CT to the ultimate test, but one likely to mimic clinical practice. A priori, CT should be shown most accurate in patients who have no pulmonary emboli (healthier patients, better quality CT scans, bias toward false-negative results) or in patients who have a high-probability V/Q scan (large central clots). Neither group was included in our sample by design. Nonetheless, for central vessels, our sensitivity (86%) and specificity (92%) were similar to the results of Remy-Jardin et al. [11] and Teigen et al. [12]. However, when all vessels were considered, sensitivity was a disappointing 63%. Three of the four false-negatives were in patients with subsegmental emboli only. In our study, four (36%) of 11 patients with pulmonary embolism had subsegmental clot only. The prevalence is similar to that in a recent report that found that 11 (33%) of 33 patients with pulmonary angiograms that showed an embolus had clots limited to the subsegmental vessels [18]. Thus, although our sample was small, the results were similar to those in published reports.

Although some subsegmental vessels are visualized on CT scans, they are not reliably visualized or easily interpreted. This is a major limitation of CT. Therefore, a CT scan with normal findings cannot be relied on to exclude small subsegmental emboli (Figs. 3 and 4). The significance of these small emboli remains controversial, but most physicians think that small emboli must be considered the harbinger of future larger emboli and therefore are clinically significant. A minority viewpoint is that tiny clots are from calf veins and do not require anticoagulation [4, 13, 19]. Until this controversy is resolved, all pulmonary emboli must be considered clinically important.

False-positive CT findings are also a concern because of the dangers of unnecessary anticoagulation. Only one of 20 patients had a false-positive CT scan. A breathing artifact on two contiguous scans caused a false-positive diagnosis of emboli in the left lower lobe, posterior basal segment. Among the 33 lungs with angiographic correlations, two additional scans were false-positive. Both were in segmental lower lobe vessels in patients with atelectasis or consolidation and pleural effusions. This caused slow flow through the basilar segmental vessels and the impression of emboli. Angiography showed slow but unobstructed flow through those vessels.

Interobserver agreement is another measure of the reliability of a test. In the PIOPED study, reviewers of V/Q scans agreed on 95% of high-probability interpretations, 92% of very low probability interpretations, and 94% of normal interpretations, but agreement decreased to 75% for indeterminate interpretations and to 70% for low-probability interpretations. In the same study for angiography, the gold standard, reviewers agreed on the presence of thrombi in 98% of lobar vessels and 90% of segmental vessels, but in only 66% of subsegmental vessels. Overall agreement between angiographers as to the presence or absence of pulmonary embolism in a given patient was only 81% [1, 20]. In our study, we found a 75% interobserver agreement as to the presence or absence of pulmonary embolism on the CT scan of a given lung.

Although CT scans were of good quality, several strategies might be used to improve the quality of both CT scans and the interpretation. (1) Scintigrams should be used in planning and interpreting CT scans, just as they are used in angiography. (2) Scanning in the caudocranial direction appears to improve visualization of the lower lobe vessel, where emboli are most common, and minimizes the artifact caused by dense contrast material in the superior vena cava. (3) A 20-ml preliminary bolus of contrast material with serial scans through the main pulmonary artery will show the time of maximal opacification and provide a guide for more precise timing of the final bolus. (4) Three-dimensional reconstruction of the pulmonary vessels is both labor- and time-intensive. Remy-Jardin et al. [21] report improved depiction of clot in the lobar and segmental

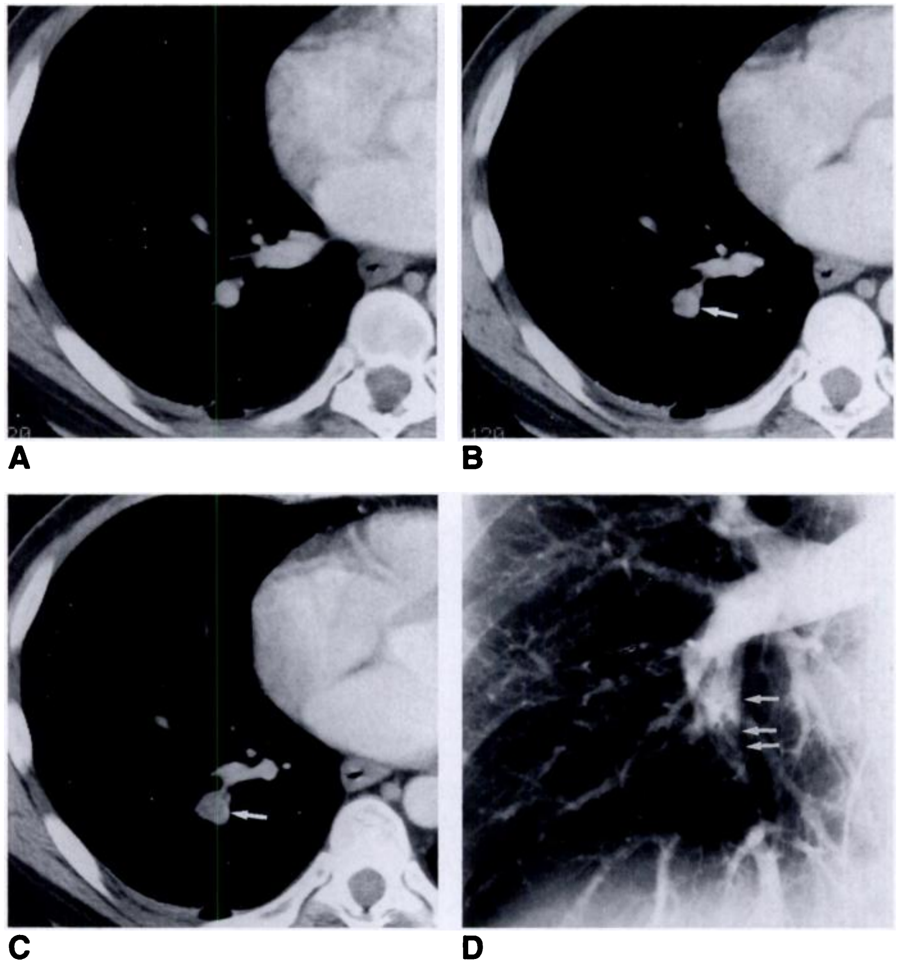


Fig. 1.—True-positive CT finding, segmental level. 47-year-old man with shortness of breath, low clinical suspicion for embolism, and high scintigraphic suspicion for embolism.

A, **CT scan through proximal posterior part of basal segmental artery shows IV contrast material filling lumen.**

B, **CT scan 12 mm farther caudad shows contrast material medial to a clot (*arrow*).**

C, **CT scan 3 mm farther caudad shows complete lack of opacification of vessel. Diameter of vessel here is larger than diameter of more proximal part of vessel.**

D, **Angiogram of right pulmonary artery shows clot in posterior basal segment. *Arrows* correspond to approximate levels of *A–C*.**

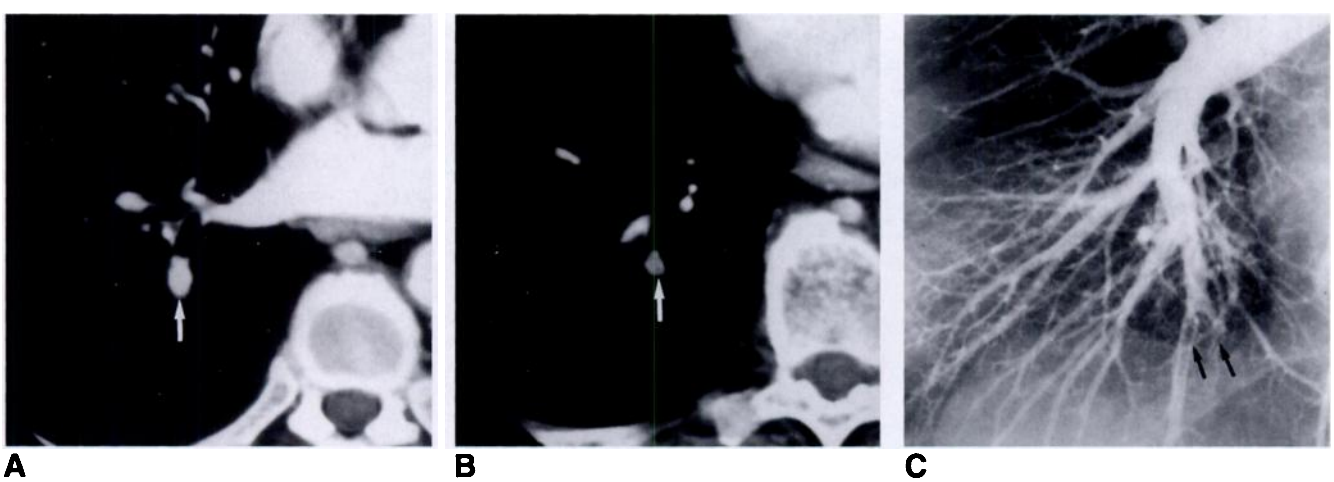


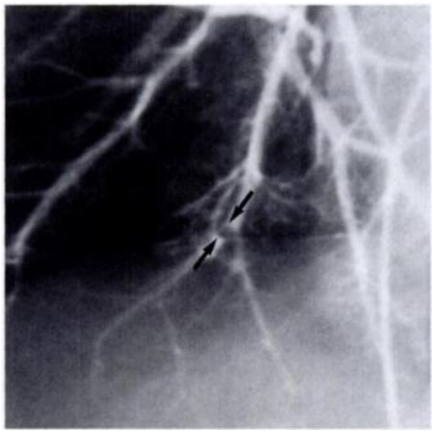
Fig. 2.—True-positive CT scan, subsegmental level. 72-year-old man with hypoxia and increased cardiac second sound. Clinical suspicion was moderate, and scintigraphic suspicion was low.

A, **CT scan shows normal posterior part of basilar segmental artery (*arrow*).**

B, **CT scan 9 mm farther caudad shows complete lack of opacification of vessel (*arrow*).**

C, **Selective angiogram of right pulmonary artery shows clot (*arrows*) limited to subsegmental vessels of posterior basilar segment.**

vessels but very limited value at the subsegmental level. (5) Scan interpretation requires detailed understanding of the segmental anatomy as well as considerable time and effort to evaluate both the lung and mediastinal windows [22, 23]. Consensus interpretations by two experienced reviewers, if feasible, appears to be very helpful.



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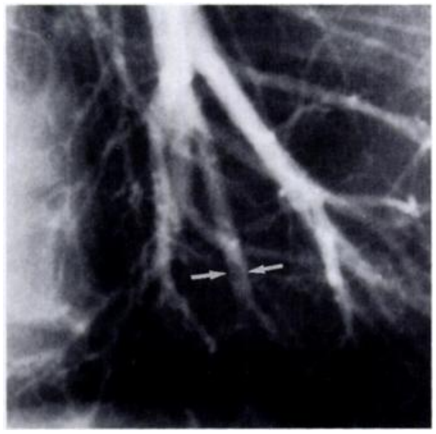

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Fig. 3.—False-negative CT, subsegmental clot only. 33-year-old woman with heart disease and shortness of breath. Clinical and scintigraphic findings were both moderately suggestive of pulmonary embolism. Oblique selective angiogram shows filling defect in subsegmental branch of posterior basal segmental artery. Clot is at level of diaphragm, probably 1 cm caudal to lowest CT section.

Fig. 4.—False-negative CT, subsegmental clot only. 50-year-old woman with chest pain and increased second heart sound. Both clinical and scintigraphic findings suggested low probability of pulmonary embolism. Selective angiogram shows filling defect (*arrows*) in subsegmental branch of left posterior basal segmental artery. At this level, subsegmental vessels were barely identifiable on CT scans.

In the ideal world, patients with normal findings on V/Q scans or low V/Q scan and clinical probability would not be studied further, patients with high-probability findings on V/Q scans and high clinical suspicion would be given anticoagulants, and all other patients would have pulmonary angiography. Schluger et al. [7] found, however, that 92% of patients with low-probability findings on V/Q scans and 78% of patients with indeterminate findings had no further imaging workup. Yet 20% of the former and 35% of the latter were given anticoagulants. Thus, most decisions were based on the "best clinical guess." We believe that in patients with unresolved clinical and scintigraphic evidence of pulmonary embolism, further imaging is indicated. Studies of the lower extremity veins are helpful when they show deep venous thrombosis; however, 50% of patients with a proved pulmonary embolism have normal findings on venous studies [3]. In our selected patient population, overall CT sensitivity was only 63% and specificity was 89%, better than the clinical estimate or V/Q scan estimate but inferior to angiography. We believe that pulmonary angiography is the procedure of choice and should be more widely used.

Perhaps with increased experience and some of the technique refinements just discussed, the sensitivity of CT can be improved. Detection of subsegmental emboli will remain a problem. Currently, the role of CT is limited. It can be used in patients who should not undergo or who refuse angiography, in patients in whom pulmonary embolism is one of several pulmonary diagnoses being considered clinically, for noninvasive follow-up of urokinase lysis of emboli [24], and to examine patients with chronic thromboemboli [25].

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