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CLINICAL UTILITY OF COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF PULMONARY EMBOLISM

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This prospective clinical pilot study describes the clinical utility and cost effectiveness of computed tomography (CT) with contrast in the diagnosis and management of pulmonary embolism. The setting is a university teaching hospital, and the 20 patients, 26 to 81 years old, were found to have CT findings consistent with pulmonary embolism. Intraluminal pulmonary artery clots were observed on CT and contributed to clinical management, often obviating pulmonary arteriography. CT, particularly spiral CT, may demonstrate pulmonary embolism and offers advantages over ventilation-perfusion lung scanning and pulmonary arteriography in making the diagnosis of pulmonary embolism in high-risk patients or patients with preexisting parenchymal lung disease.

KEY WORDS:
Pulmonary embolism; Computed tomography; Helical computed tomography

INTRODUCTION

Pulmonary embolism affects approximately 630,000 individuals in the United States each year but is discovered antemortem in only a third (1, 2). In two-thirds of patients, clinical assessment combined with ventilation-perfusion lung scans is unable to establish or exclude the diagnosis of pulmonary embolism (3). Despite the development of impedance plethysmography and Doppler sonographic studies of the lower extremities to detect deep vein thrombosis (4), pulmonary arteriography is not infrequently necessary to establish the diagnosis of pulmonary embolism. Because pulmonary arteriography is invasive, costly, and associated with morbidity and mortality (5–7), a definitive noninvasive, cost-effective test for the diagnosis of pulmonary embolism has been sought.

Remy-Jardin et al. (8) and Goodman et al. (9) studied consecutive patients with helical computed tomography (CT) who had angiographic confirmation of pulmonary embolism and found CT to have a high sensitivity and specificity. We performed a prospective pilot study utilizing computed tomography to assess the clinical utility of CT in the diagnosis of pulmonary embolism.

METHODS

From July 1993 to January 1995, 20 patients in whom CT diagnosed pulmonary embolism by demonstrating intraluminal clot in the pulmonary arterial system were encountered. Some patients underwent subsequent CT, which documented resolution of emboli after treatment.

CT was performed on the GE advantage scanner using contrast injection. If pulmonary embolism was not suspected prior to CT, we performed our standard protocol of administering up to 150 cc of nonionic contrast (Omnipaque, Winthrop Pharmaceuticals) via an automatic injector pump. If pulmonary embolism was suspected, 50 cc of contrast was injected (1 cc/s), and scans were obtained, after a 40-s delay, from the aortic arch to the inferior hilar struc-

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tures using 5-mm collimation during a single breath hold. Images were reconstructed by 1-mm intervals with a field of view concentrating on the central pulmonary arteries. The diagnosis of pulmonary embolism was made after a radiologist without knowledge of the results of other diagnostic studies reviewed the reconstructed CT images.

RESULTS

Among the 20 patients, 10 were female, and the average age was 63 (see Table 1). Thirteen patients had preexisting lung disease, 7 had underlying malignancies, and 4 had clinically evident cardiovascular disease. All but 3 presented with dyspnea or chest pain. CT contributed to both the diagnosis and management of pulmonary embolism in our patients and offered advantages over pulmonary arteriography and ventilation-perfusion lung scanning in selected patients. Prior to CT, 11 patients had undergone a ventilation-perfusion scan, 6 of which were interpreted as "high probability" for pulmonary embolism, 4 were "indeterminate," and 1 was "low probability" for pulmonary embolism. In 19 of 20 patients, CT established the definitive diagnosis of pulmonary embolism. In only 1 patient was pulmonary arteriography required, and in this patient, in confirmed the CT diagnosis. CT was then repeated to document clot resolution 2 months later. CT avoided the risks of cessation of anticoagulation and catheter insertion for pulmonary arteriography in patients who had recurrent emboli while anticoagulated. Pulmonary arteriography was also avoided in high-risk patients who were septic (patient 11), had advanced emphysema (patients 2, 3), or who had severe pulmonary hypertension (patients 4, 6, 19, 20). In one individual (patient 13), the CT finding of right ventricular clot explained the lack of improvement after inferior vena cava filter insertion. Serial CT studies demonstrated improvement or lack of improvement of pulmonary emboli while on anticoagulation. In one individual with severe pulmonary hypertension (patient 6) where repeated pulmonary arteriography would have entailed unacceptable risk, serial CT studies led to the recommendation of pulmonary angioscopy and possible thromboendarterectomy. CT permitted the differentiation of clot from tumor compression of the pulmonary artery (patient 7). It revealed unsuspected pulmonary embolism in five patients (patients 3, 4, 14, 15, 17). In three patients who were unstable due to severe gas exchange abnormalities associated with preexisting parenchymal lung disease and systemic hypotension, CT circumvented the risks of pulmonary arteriography and the likely nonspecificity and delay of ventilation-perfusion lung scanning (patients 8, 13, 19).

Representative case reports and CT images (Figures 1–4) follow.

Patient 4

This 67-year-old female with a history of rheumatic mitral and tricuspid regurgitation and chronic atrial fibrillation presented with shortness of breath, fever of 102°F, and chest soreness. Chest X ray revealed cardiomegaly and a moderate right pleural effusion. Thoracentesis revealed a transudate. Tracheoesophageal echocardiography showed a vegetation on the atrial side of the mitral valve and 4+ mitral regurgitation. CT revealed unsuspected pulmonary emboli in the right and left interlobar pulmonary arteries and a small pericardial effusion (Figure 1). Doppler studies of the lower extremities were negative for deep venous thrombosis. The patient was treated with intravenous heparin followed by Coumadin and empiric antibodies for culture-negative endocarditis. After cardiac catheterization, she underwent mitral valve replacement.

Patient 6

This 68-year-old female developed pleuritic chest pain 2 years prior to this admission, and a diagnosis of pulmonary embolism was made at another institution by ventilation-perfusion lung scan. She was treated with heparin followed by Coumadin for 3 months. She then experienced progressive dyspnea and weight loss over the next year. The physical exam upon admission showed jugular venous distension, accentuation of the pulmonic component of the second heart sound, clear lung fields, and lower extremity venous varicosities. Chest X ray showed enlargement of the main right and left pulmonary arteries. Arterial blood gases breathing room air showed $p0_2$ 64-mm Hg, $pC0_2$ 26-mm Hg, pH 7.47. Two-dimensional echocardiography with doppler showed normal left ventricular function, dilated right-sided chambers, and flattening of the interventricular septum consistent with right ventricular pressure overload. There was severe tricuspid regurgitation with a tricuspid regurgitant jet velocity of 4.9 m/s corresponding to a peak systolic tricuspid valve gradient of 95-mm Hg and a right ventricular systolic pressure of 105-mm Hg. Due to severe pulmonary hypertension, pulmonary arteriography was deferred. CT revealed central clot in intralobar pulmonary arteries (Figure 2). After 9 months of treatment with Coumadin, repeat CT showed little change. The patient is being evaluated for pulmonary angioscopy and thromboendarterectomy.

TABLE 1. Patient Characteristics

Patient	Age/Sex	Underlying disease	Preexisting lung disease	Presenting symptoms physical exam	Ventilation perfusion scan finding (probability for PE)	Pulmonary angiog. finding	Relative contraindication to pulmonary arteriography	Clinical advantage of CT Dx of pulmonary emboli
1	67 F	Recent CABG	None	Dyspnea, tachypnea, rales	Indeterminate	ND	Anticoagulated; recent heart surgery	Avoided PAgram; IVC filter placed
2	65 M	Ischemic cardiomyopathy	Severe COPD	Pleuritic chest pain, dyspnea and tachypnea	Indeterminate	ND	Severe COPD	Avoided PAgram; RA clot detected
3	66 M	Lung CA	COPD	Dyspnea, tachypnea	ND	ND	Severe COPD, hypoxemia	Unsuspected PE
4	67 M	RHD mitral disease	Congestive heart failure	Fever, chest pain	ND	ND	Passive pulmonary hypertension	Unsuspected PE
5	81 M	Prostate CA, atrial fibrillation	None	Dyspnea, pleuritic chest pain, hemoptysis	Low	Positive for clot	None, serial studies needed	Serial studies needed; avoided PAgram
6	68 F	None	Pulmonary hypertension; PE in past	Dyspnea, weight loss, RV failure	High	ND	Severe pulmonary hypertension by Echo-Dopplers	Avoided PAgram
7	26 F	Colon CA	None	Dyspnea	High	ND	None	Differentiated tumor compression from clot
8	67 F	Total knee replacement	Adult respiratory distress syndrome	Dyspnea, chest pain, hypotension	ND	ND	Severe respiratory failure on respirator	Avoided PAgram; IVC filter placed
9	72 F	Gastric ulcer	None	Dyspnea, syncope	High	ND	None	Avoided PAgram
10	74 M	Recurrent benign pleural mesothelioma	None	Leg edema, dyspnea, hypotension	Indeterminate	ND	Severe respiratory failure	Avoided PAgram
11	60 F	Metastatic breast cancer, sepsis	Lung metastases	Chills, rigors, dyspnea	High	ND	Sepsis	Avoided PAgram; confirmed PE
12	61 M	Ischemic cardiomyopathy	None	Dyspnea, hemoptysis, rales	Indeterminate	ND	None	Avoided PAgram
13	65 F	Metastatic rectal CA	Lung metastases	Dyspnea, tachypnea	ND	ND	Terminal condition	Avoided PAgram; clot in RV detected
14	69 M	None	Sarcoidosis	Fever, cough, mental status changes	ND	ND	None	Unsuspected PE
15	56 M	Lymphoma	None	Leg edema	ND	ND	None	Unsuspected PE
16	40 M	AIDS; DVT	Lung CA	Pleuritic chest pain; dyspnea	ND	ND	Anticoagulated	Avoided PAgram
17	79 M	CVA	Lung nodule	Cough	ND	ND	Anticoagulated	Unsuspected PE; clot in LV detected
18	28 F	Breast CA	Lung metastases	Dyspnea	High	ND	None	Source of clot in SVC
19	78 F	None	IPF	Fever; dyspnea	ND	ND	Pulm hypertension; hypoxemia	Avoided V/Q scan and PAgram
20	75 F	None	PE 10 years prior	Dyspnea; tachypnea	High	ND	Severe pulm. hypertension; RV dysfunction	Avoided PAgram; demonstrated extent of clot

Abbreviations: CA = cancer; CABG = coronary artery bypass graft surgery; COPD = chronic obstructive pulmonary disease; CVA = cerebrovascular accident; DVT = deep venous thrombosis; F = female; IPF = idiopathic pulmonary fibrosis; IVC = inferior vena cava; LV = left ventricle; M = male; ND = not done; PAgram = pulmonary arteriogram; PE = pulmonary embolus; RA = right atrium; RHD = rheumatic heart disease; V/Q = ventilation perfusion.

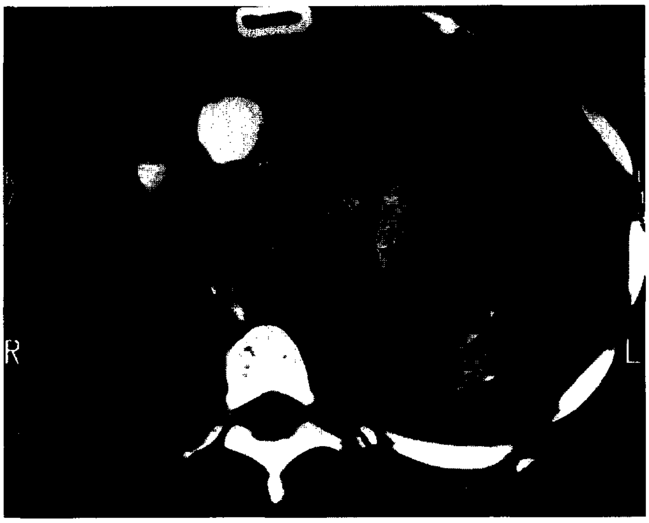


FIGURE 1. CT with contrast on patient 4 demonstrating filling defects (*arrows*) in the right and left intralobar pulmonary arteries. There is also a small pericardial effusion.

Patient 11

This 60-year-old woman was admitted to The New York Hospital with fever to 103°F, chills, rigors, cough, and dyspnea. Her past history was notable for metastatic adenocarcinoma of the breast treated since 1988 with mastectomy, systemic chemotherapy, and tamoxifen. In 1993 she developed a left hilar mass that at bronchoscopy, was found to be metastatic breast carcinoma. She was subsequently treated with radiation therapy to the mass and further chemotherapy. A Broviac catheter had been placed in January 1994. Blood cultures from the Broviac catheter on admission grew *Streptococcus fecalis.* Chest radiography showed subsegmental atelectasis at the left lung base and a widened mediastinum. A ventilation-perfusion lung scan was interpreted as "high probability" for pulmonary embolism. CT showed regression of the hilar mass and also confirmed pulmonary emboli in the lobar branches to the right lower and middle lobes (Fig. 3). The patient improved and was discharged after treatment with intravenous antibiotics, removal of the Broviac catheter, and anticoagulation with heparin followed by Coumadin.

Patient 13

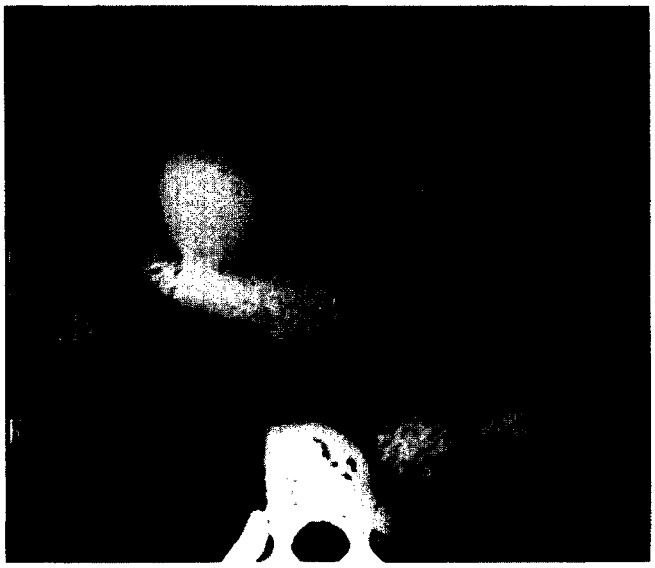
This 65-year-old female with a history of metastatic rectal carcinoma to the liver and lungs presented with acute shortness of breath. Physical examination showed tachypnea and hepatomegaly. CT was performed to assess the known metastatic disease to the lung; it revealed unsuspected extensive intraluminal filling defects in the lobar pulmonary arteries of the left upper and lower lobes as well as clot in the right ventricle (Fig. 4). Two-dimensional echocardiography with Doppler confirmed the right ventricular clot and also showed 3+ tricuspid regurgitation, elevated pulmonary arterial pressures, and dilated right-sided structures. The patient was treated with intravenous heparin, and, after persistent rectal bleeding, an inferior vena cava umbrella filter. She has failed to improve and was not considered a candidate for further intervention.

DISCUSSION

Pulmonary embolism often occurs in patients with serious concomitant medical conditions, particularly right ventricular dysfunction and pulmonary hypertension. Although usually considered a low-risk procedure, in these circumstances pulmonary arteriography, considered the definitive diagnostic procedure for pulmonary embolism, is more hazardous, (5–7) and a less invasive study would be desirable. We have found contrast-enhanced CT to be useful in the diagnosis and management of pulmonary embolism in such patients. This study, however, was not designed to assess the sensitivity and specificity of CT compared to pulmonary arteriography and ventilation-perfusion lung scans.

The diagnosis of pulmonary embolism by CT was initially described in 1978 (10). Prior to the introduction of spiral or helical CT scanning, visualization of the pulmonary vasculature by CT was limited by the prolonged scanning time, which resulted in respiratory and cardiac motion artifact. In addition, prior scanners had other technical limitations resulting from beam collimation and computer software. Limitations of conventional CT compared to pulmonary arteriography included the less accurate visualization of small vessels due to motion and partial volume averaging making it difficult to differentiate between intraluminal filling defects and imaging artifacts in lobar pulmonary arteries (8, 11–14). Spiral or helical CT permits better visualization of the central pulmonary artery and its proximal branches. During a single breath hold of 20 s, the entire CT scan of these vessels can be obtained. Usual doses of contrast with spiral CT are between 50 and 100 cc compared to the typical pulmonary arteriogram which utilizes 250–300 cc. Overlapping 1-mm spiral CT images may be reconstructed to increase the ability to resolve questions about intraluminal filling defects.

Clinically silent or unsuspected pulmonary embolism is a recognized but troublesome medical condition (15). In a retrospective study of 4500 con-



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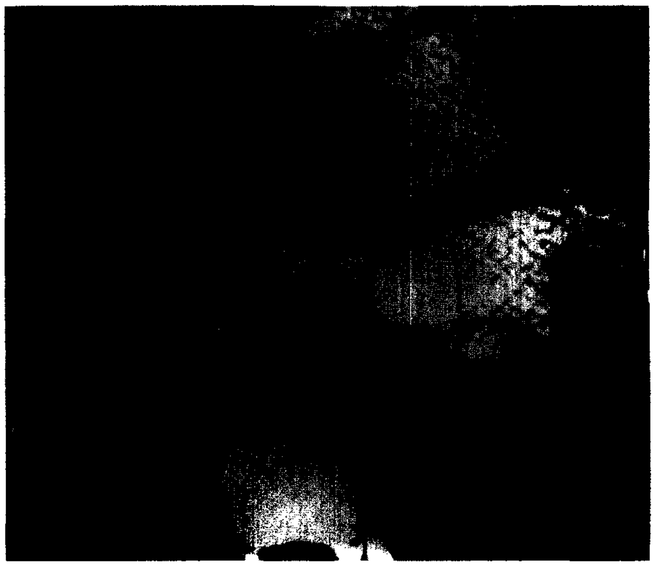

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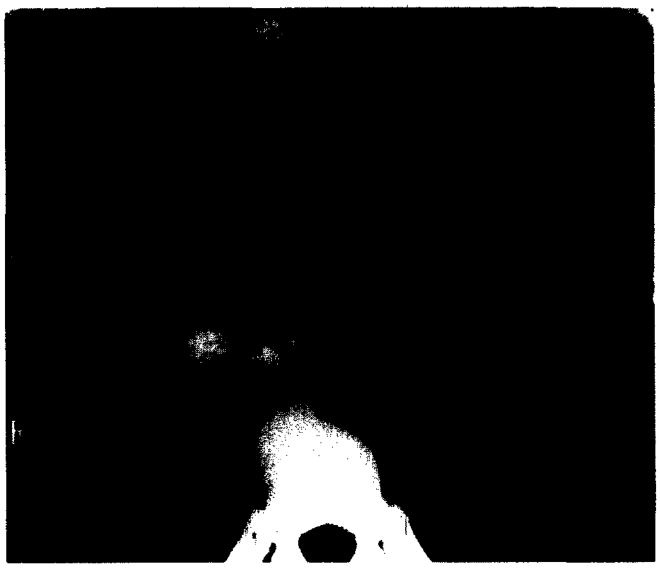

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FIGURE 2. Spiral CT scan with contrast of patient 6 showing the dilated main right and left pulmonary arteries. Clots *(arrows)* are seen in the right intralobar artery **(A)**, right lower lobe pulmonary artery **(B)**, and left lobar artery **(C)**.

secutive conventional CTs, pulmonary emboli were observed in 25 (11). In 13 of 25, pulmonary emboli were clinically unsuspected or "silent." In 5 of our 20 patients, pulmonary embolism was also unsuspected.

Spiral CT has been prospectively compared to pulmonary arteriography. In a study (8) of 42 consecutive patients, 18 found to have pulmonary embolism by arteriography had an abnormal CT, yielding 100% sensitivity. All patients with normal pulmonary arteriograms had a normal CT, a 100% negative predictive value. One false-positive CT was encountered, yielding 96% specificity. The finding of central emboli in the main, lobar, and segmental pulmonary arteries by CT correlated precisely with the arteriographic findings. CT reliably depicted emboli in second- to fourth-generation pulmonary vessels. An intersegmental lymph node misinterpreted as a filling defect was the cause of the single false-positive spiral CT. In a more recent prospective study, CT had a sensitivity of 86% and a specificity of 92% in the detection of central vessel pulmonary emboli, but a lower sensitivity and specificity (63 and 89%, respectively) in smaller vessels (9).

While the negative predictive value of pulmonary arteriography has been established, it has not been confirmed as conclusively for CT. In one study of 147 patients with normal pulmonary arteriograms, no patient experienced pulmonary emboli when left untreated for 6 months (16). A comparable study of CT has not been performed.

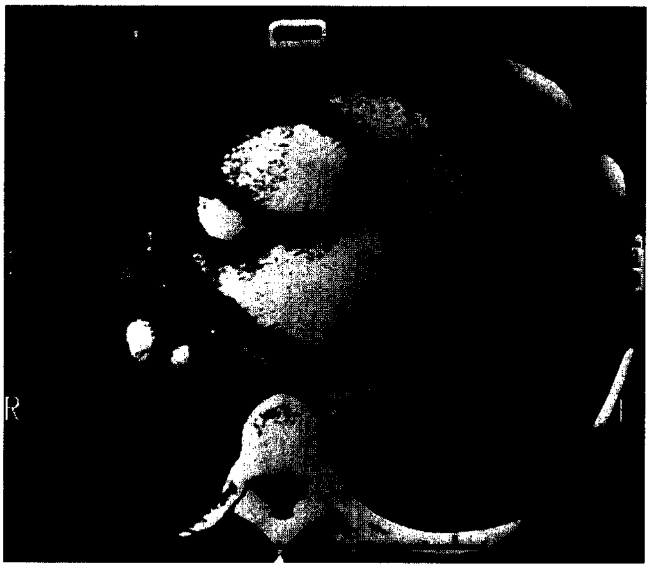
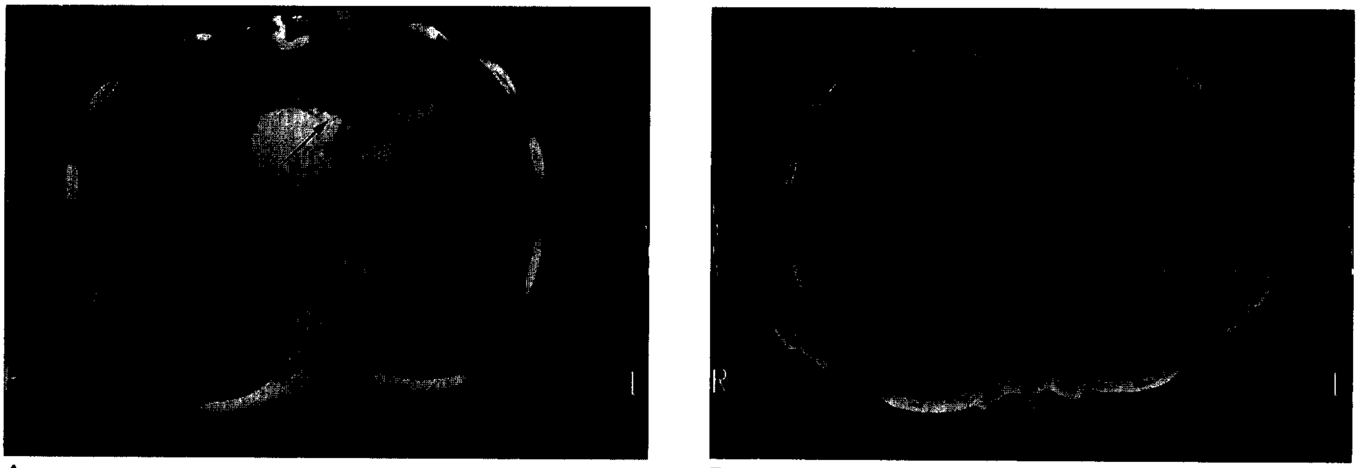


FIGURE 3. CT scan with contrast in patient 11 showing filling defect (*arrow*) in the right middle lobar pulmonary artery.

Relative advantages, risks, and financial cost of CT, pulmonary arteriography, and ventilation-perfusion lung scanning are depicted in Table 2. In our institution, the financial cost of CT or ventilation-perfusion lung scan is 15–20% of the cost of pulmonary arteriography. The dye load for CT is considerably less than that for pulmonary arteriography, and CT avoids the risk of catheter insertion. Given the lower financial cost and lower medical risk of CT compared to pulmonary arteriography, and assuming comparable sensitivity and specificity of CT and pulmonary arteriography for detecting central emboli (8, 9) and a higher sensitivity and specificity of CT compared to ventilation-perfusion scanning (3), CT might assume a prominent place in a clinical diagnostic algorithm. The actual selection of the test(s) depends on a variety of clinical variables including the likelihood of pulmonary embolism in a given patient population.

To help select the most appropriate diagnostic test, the cost effectiveness of CT for pulmonary embolism should be compared to the standard algorithm for the diagnosis of pulmonary embolism which usually recommends a ventilation-perfusion lung scan followed by pulmonary arteriography. Estimates of cost effectiveness should consider not only the costs, sensitivity, and specificity detailed in Table 2 but also the risk of contrast reactions, other morbidity and mortality risks of each of the tests and the results of subsequent treatment or lack of treatment. The mortality and morbidity of the diagnostic test increases its "effective cost" (17, 18). The cost of mortality may be estimated to be $100,000 and cost of morbidity to be $10,000 as additional hospitalization and treatment may be required. For CT, the likelihood of mortality and morbidity, respectively, are estimated to be 0.001 and 4%. The effective cost of CT increases from $759 to $1106. Similarly, the cost of the pulmonary arteriogram increases from $4653 to $5253 assuming the probability of mortality to be 0.04% and the probability of morbidity to be 2%. The cost of the ventilation-perfusion scan does not change as there is no morbidity or mortality associated with this test. The final test comparison should also consider the sensitivity and specificity of the test. However, even using conservative values of



A B

FIGURE 4. CT scan with contrast in patient 13 demonstrating previously unsuspected large clot (*black arrow*) in the right ventricle (**A**) as well as clot (*white arrows*) in the lobar pulmonary arteries to the left lower and right lower lobes (**B**).

TABLE 2. Comparison of CT, Pulmonary Arteriography, and Ventilation-Perfusion Lung Scan in the Diagnosis and Management of Pulmonary Embolism

	CT	Pulmonary arteriography	Ventilation-perfusion scan
Risk to patient	Low	Relatively high (5)	Negligible
Charge[a]	$758.50	$4653.00	$862.00
Serial studies to evaluate therapy	Ideal, easy to perform	Only under special circumstances	Easy to perform
May reveal intracardiac clot	Yes	No	No
Disclose unsuspected pathology in parenchyma and mediastinum	Yes	Unlikely	No
Dye load	<100 cc	200–300 cc	None
Utility in central or massive embolism	Good	Uncertain	Uncertain
Physician and technician time	Low	High	Intermediate
Visualization of small emboli	Uncertain	Good	Uncertain
Risk with pulmonary hypertension and RV dysfunction, coagulopathies, respiratory failure, cardiac disease or sepsis	Low	High	Low
Sensitivity	100% (8)	90–100 (3)	33–95% (3)
Specificity	96% (8)	100% (3, 16)	25% (3)

[a] Charged at The New York Hospital–Cornell Medical Center July 1, 1995. Includes charges for both physician interpretation and technical components. References appear in parentheses.

85% for the sensitivity and specificity of CT, this test has a lower effective cost than the standard algorithm (18, 19).

In conclusion, in light of the improved visualization of the pulmonary arterial system with advances in imaging technology, CT may prove to be an attractive alternative to pulmonary arteriography and ventilation-perfusion lung scanning for the diagnosis of pulmonary embolism. We have found it to be most useful for those patients who are too ill to undergo pulmonary arteriography due to serious general medial conditions, severe pulmonary parenchymal disease, or severe pulmonary hypertension with right ventricular dysfunction. Preexisting parenchymal lung disease often results in nonspecific ventilation and perfusion abnormalities, rendering radionuclide lung scans nonspecific, costly, and time-consuming studies. There may be situations where spiral CT should be the initial study to diagnose pulmonary embolism. When the clinical suspicion for pulmonary embolism is high, the effective cost of ventilation-perfusion lung scanning followed by pulmonary angiogram, if necessary, may far exceed that of CT (17, 18). As risk-free studies such as pulmonary magnetic resonance angiography are perfected, their effective cost in some circumstances may become equal to or lower than other diagnostic modalities including CT and pulmonary arteriography (19). Both a prospective study examining clinical outcome in patients without evidence for pulmonary embolism on CT and a study of the sensitivity and specificity of CT compared to pulmonary arteriography and ventilation-perfusion lung scanning need to be done to clarify the indications for CT in the diagnosis and management of pulmonary embolism.

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