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Abbreviations:
CTE = chronic thromboembolism
ROC = receiver operating characteristic

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Identifying the Cause of Unilateral Hypoperfusion in Patients Suspected to Have Chronic Pulmonary Thromboembolism: Diagnostic Accuracy of Helical CT and Conventional Angiography[1]

PURPOSE: To determine the prevalence of unilateral hypoperfusion in patients suspected to have chronic thromboembolism (CTE), to identify the most common cause of hypoperfusion, and to compare the accuracy of helical computed tomographic (CT) angiography with that of conventional angiography in helping to determine the cause.

MATERIALS AND METHODS: Radionuclide lung scan reports showed asymmetric hypoperfusion in 47 of 410 consecutive patients referred because of suspected CTE. Twenty-seven patients had unilateral or predominantly unilateral perfusion abnormalities. Each pulmonary angiogram and CT angiogram in these patients was interpreted independently by two readers blinded to clinical information and surgical outcome. Surgical confirmation of the diagnosis was available in 39 of the 47 patients with asymmetric hypoperfusion.

RESULTS: Unilateral ($n = 11$) or predominantly unilateral hypoperfusion ($n = 16$) was found in 6.6% (27 of 410 patients) of patients referred, and CTE was the most common cause. The accuracies of CT angiogram readers (reader 1, 83%; reader 2, 89%) were greater than those of conventional angiogram readers (reader 1, 73%; reader 2, 65%) for distinguishing CTE from other causes.

CONCLUSION: Unilateral hypoperfusion occurred in 6.6% of our study population, most frequently because of CTE. CT angiography is an excellent diagnostic alternative to conventional angiography for distinguishing patients with CTE from those with other causes.

Chronic pulmonary thromboembolism is a relatively uncommon cause of unilateral hypoperfusion (1,2). Other causes include bronchogenic carcinoma, fibrosing mediastinitis, postsurgical vascular occlusion, congenital anomaly, pulmonary arteritis, and angiosarcoma (3–13).

Chest radiographs can help in recognizing bronchogenic carcinoma, but to diagnose other causes of vascular occlusion, additional imaging is usually necessary. At this institution, unilateral hypoperfusion, recognized at scintigraphy, is frequently followed with conventional pulmonary angiography to determine the cause. The angiographic appearance of the various diseases that cause unilateral hypoperfusion can be confusing, however. Computed tomographic (CT) angiography may indicate intravascular, intramural, or extravascular mediastinal abnormalities and therefore may be a good alternative for determining the cause of unilateral hypoperfusion.

The purpose of our study was to determine the prevalence of unilateral and predominantly unilateral hypoperfusion identified on radionuclide scans in patients referred because of suspected chronic thromboembolism (CTE), to identify the most common cause of unilateral hypoperfusion in this population, and to compare the diagnostic accuracy of helical computed tomographic (CT) angiography with that of conventional angiography in determining the cause.

MATERIALS AND METHODS

Patients

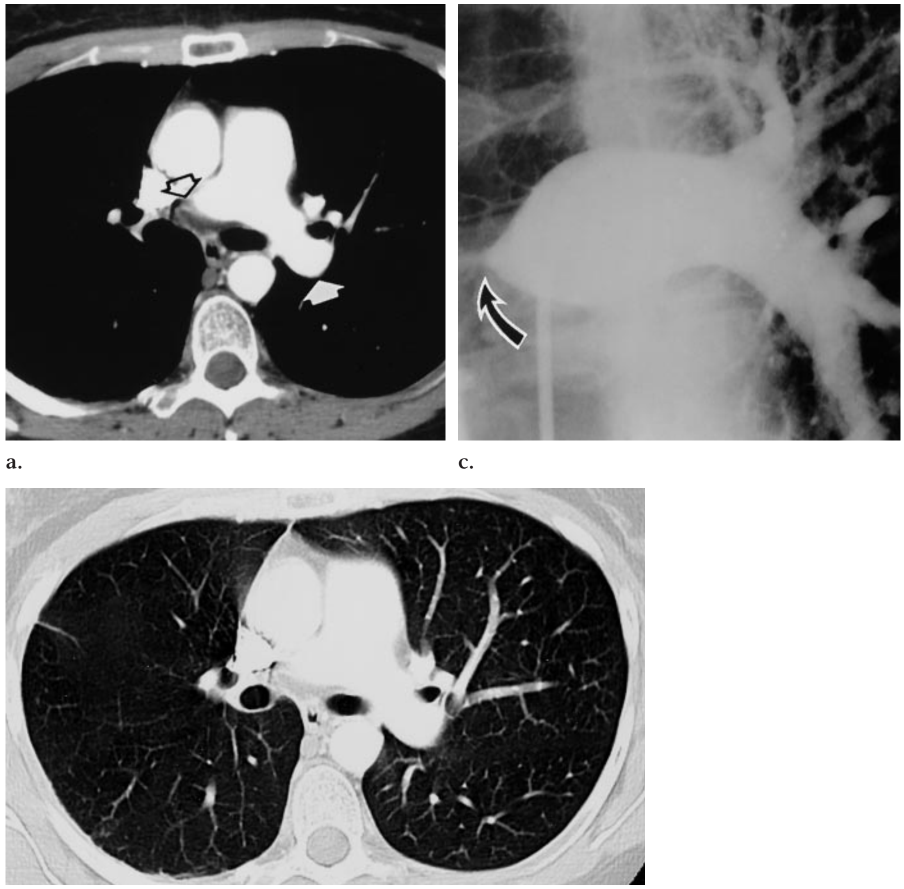
This retrospective study was approved by the institutional review board. The initial ventilation-perfusion scan reports (n = 410) obtained in all patients referred because of suspected CTE between January 1994 and October 1996 were reviewed. Forty-seven reports suggested asymmetric perfusion abnormalities; the scans (n = 47) referred to in these reports were reanalyzed.

Unilateral hypoperfusion was defined as total absence of perfusion on one side with normal perfusion on the other. Predominantly unilateral hypoperfusion was defined as either complete occlusion on one side and a segmental or subsegmental defect on the other side or near-total occlusion on one side and normal perfusion or subsegmental defects on the other side. Pulmonary angiograms were obtained in all patients, and helical CT angiograms were available in 18.

Ventilation-Perfusion Scanning

Technique.—With a protocol used routinely for examination of patients referred for suspected CTE who may be candidates for thromboendarterectomy, posterior ventilation images were obtained with 20-mCi (740-MBq) xenon 133 (Medinuclear, Baldwin Park, Calif) during wash-in, equilibrium, and washout phases. Four-millicurie (148-MBq) technetium 99m macroaggregates of human serum albumin (Du Pont, Billerica, Mass) was then injected intravenously with the patient in the supine position, and posterior, anterior, right and left anterior oblique, and both lateral projections were obtained.

Interpretation.—Forty-seven scans were selected for further analysis on the basis of reports that suggested asymmetric hypoperfusion. Images were interpreted by a nuclear medicine physician by using the modified Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria (14), without other diagnostic information except for a chest radiograph, if available. Scans were divided into three groups: Group I included scans indicating unilateral hypoperfusion, defined as normal perfusion on one side and complete occlusion on the other; group II included scans indicating predominantly unilateral hypoperfusion, defined as either total occlusion on one side and one segmental or subsegmental defect on the other or near-total occlusion on one side and normal perfusion or segmental defects on the other; and group III included scans indicating asymmetric disease, defined as less severe disease in which there was neither total nor near-total occlusion of either side.



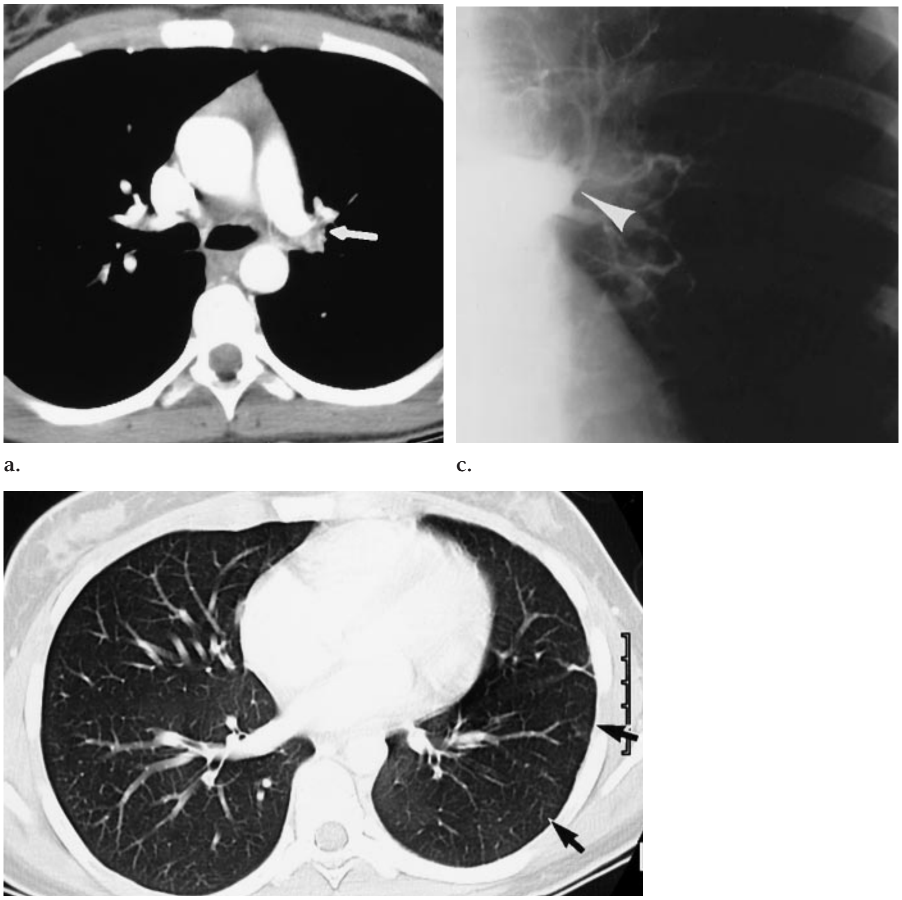
a. c. b.

Figure 1. Pulmonary arteritis in a 43-year-old woman. **(a)** Transverse CT angiogram shows tapering of the right pulmonary artery (open arrow) and a normal left pulmonary artery (solid arrow). **(b)** Transverse CT angiogram obtained with lung windows shows decreased size of vessels in the right middle and right upper lobes. Vessel size and perfusion on the left are normal. **(c)** Anteroposterior conventional angiogram shows abrupt tapering of the right pulmonary artery (arrow) and normal arteries in the left lung.

CT Angiography

Technique.—Helical CT angiography was performed with a HiSpeed Advantage helical scanner (GE Medical Systems, Milwaukee, Wis). Transverse angiograms were obtained with 5-mm collimation and 5 mm/sec table speed, and images were reconstructed at 5-mm intervals. Additional images reconstructed at 2-mm intervals were viewed on the monitor to aid in diagnostically challenging cases. Delayed images were also obtained in one patient suspected to have pulmonary angiosarcoma. In most patients, two breath-held helical examinations were necessary for coverage from the pulmonary apex to the level of the diaphragm.

Contrast material (125 mL of ioversol [Optiray 320; Mallinckrodt, St Louis, Mo]) was injected intravenously through peripheral 18- or 20-gauge catheters at 3–4 mL/sec with a Liebel-Flarsheim (Cincinnati, Ohio) power injector. Scanning delays of 10–20 seconds were chosen on the basis of cardiac function and the diameter and location of the intravenous access catheter.



a. c. b.

Figure 2. CTE in an 18-year-old woman. **(a)** Transverse CT angiogram shows abrupt occlusion of the left pulmonary artery (arrow). No flow was identified on images obtained at lower levels. **(b)** Transverse CT angiogram obtained with lung windows demonstrates decreased perfusion to the left lung (arrows), with decreased size of segmental vessels. **(c)** Anteroposterior conventional angiogram shows abrupt tapering of left pulmonary artery (arrowhead).

Interpretation.—CT angiograms were interpreted by an experienced thoracic radiologist (C.J.B.) and a CT fellow (J.P.H.) independently, neither of whom had knowledge of clinical data or other imaging results. CT angiograms were assessed for evidence of CTE on the basis of previously published data (15,16). They were also evaluated for evidence of mediastinal abnormalities suggestive of fibrosing mediastinitis; for masslike abnormalities suggestive of malignancy; and for unilateral narrowing of the main pulmonary arteries suggestive of arteritis, in which there was no mass effect or other evidence of thromboembolism.

CT angiograms were assessed with a four-point level-of-confidence scale: 1 indicated the CT angiogram was diagnostic of CTE; 2, suggestive of CTE but not diagnostic; 3, indeterminate; and 4, diagnostic of a nonthromboembolic cause. CT angiographic features used to increase reader confidence in diagnosing CTE included evidence of intraluminal material of soft-tissue attenuation, asymmetric sizes of segmental vessels, and mosaic perfusion in the lung parenchyma.

Features suggesting alternative diagnoses included a solitary mass that obstructed a pulmonary artery, particularly if the mass enhanced with contrast material or extended outside the contour of the vessel. Evidence of mediastinal or hilar lymphadenopathy that obstructed central vessels suggested fibrosing mediastinitis. CT angiograms were likely to be interpreted as suggesting arteritis if the contour of the narrowed pulmonary artery tapered smoothly and if there were no features suggestive of other specific diseases.

Conventional Angiography

Technique.—All patients underwent pulmonary angiography. Standard techniques were used, with separate injections of 55–60 mL of iohexol 300 (Omnipaque; Nycomed, Princeton, NJ) into the right and left main pulmonary arteries. Biplanar, rapid-sequence angiograms were obtained in the anteroposterior and lateral projections.

Interpretation.—Pulmonary angiograms were reviewed independently by two of the readers (R.N.C., P.F.F.) who interpret all pulmonary angiograms obtained in patients suspected to have CTE at this institution. These readers were not the same as those interpreting the CT angiograms. At the time of review, both readers were blinded to patient identity and were unaware of other imaging findings.

Conventional pulmonary angiograms were graded with a four-point confidence-level scale: 1 indicated the angiogram was diagnostic of CTE; 2, suggestive of CTE; 3, indeterminate; and 4, diagnostic of a cause other than CTE. Diagnostic criteria for CTE were based on previously published data (17).

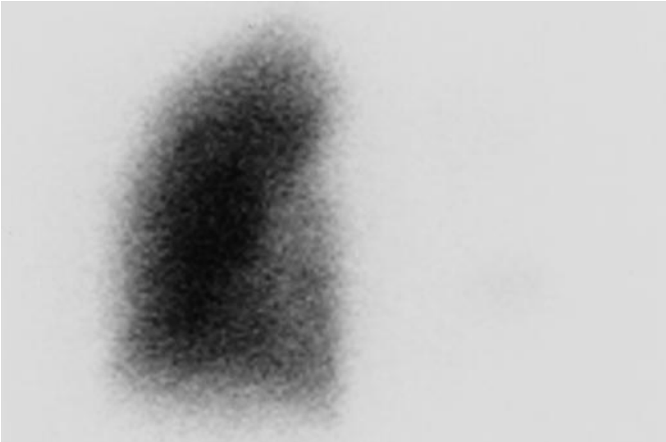
Statistical Analysis

We compared the frequencies of CTE among each of the three perfusion patterns: unilateral, predominantly unilateral, and asymmetric. Conventional pulmonary angiographic and CT angiographic findings were compared only for the groups with unilateral or predominantly unilateral hypoperfusion (groups I and II).

With NCSS statistical software (NCSS Statistical Software, Kaysville, Utah), data were plotted on receiver operating characteristic (ROC) axes, and areas under the curves were determined for each reader and each modality in patients with unilateral or predominantly unilateral hypoperfusion. Curve fitting was not performed because of the small number of data points. The sensitivities, specificities, and relative accuracies for detecting CTE were determined for each reader, with confidence levels 1 and 2 considered to be positive readings.

Accuracies were compared between readers and between imaging modalities with the χ^2 test. Data from both readers were pooled to compare imaging modalities. Groups I, II, and III were analyzed for disease distribution within each radionuclide pattern.

In the Table, interobserver agreement is given as the number of concordant cases divided by the number of total cases. The κ statistic also was used to determine interobserver agreement. Only exact agreement on diagnosis and certainty level was considered as agreement between readers.



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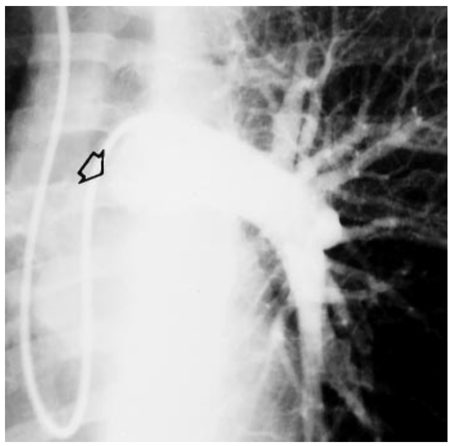

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Figure 3. CTE in a 27-year-old woman. **(a)** Posterior projection of a radionuclide scan shows normal perfusion in the left lung and near-total occlusion in the right lung. **(b)** Transverse CT angiogram shows tapering of the right pulmonary artery (arrow) and a normal left pulmonary artery; it was interpreted as indeterminate for the presence of CTE by both readers. **(c)** Transverse CT angiogram obtained with lung windows shows unilateral hypoperfusion, with decreased size of segmental arteries in the right lung compared with those in the left lung. **(d)** Anteroposterior conventional angiogram shows minimal irregularity in the contour of segmental vessels of the left pulmonary artery and abrupt cutoff (arrow) of the right pulmonary artery. It was interpreted as suggestive of CTE by one reader and diagnostic of tumor by the other.

RESULTS

Forty-seven of the 410 patients had radionuclide scan reports that suggested asymmetric perfusion abnormalities. After reviewing the scans of these 47 patients, readers found that 27 patients had unilateral (group I, n = 11) or predominantly unilateral (group II, n = 16) hypoperfusion. One patient with predominantly unilateral hypoperfusion was suspected to have angiosarcoma according to angiographic criteria but was excluded from further analysis because he refused surgery. Twenty patients had asymmetric disease that did not cause unilateral hypoperfusion (group III).

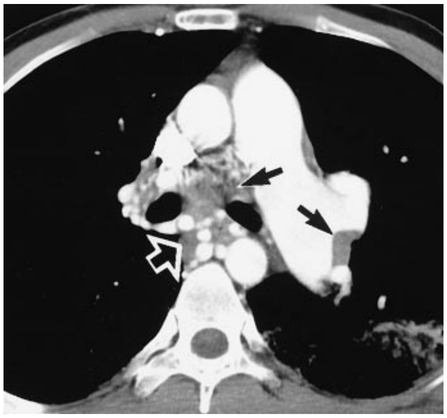
Sensitivities, Specificities, and Accuracies of Independent Readers in Identifying CTE with Conventional Angiography and with CT Angiography

	Angiography			
	Conventional		CT	
Statistic	Reader 1	Reader 2	Reader 1	Reader 2
Sensitivity (%)	67 (12/18)	61 (11/18)	73 (8/11)	82 (9/11)
Specificity (%)	88 (7/8)	75 (6/8)	100 (7/7)	100 (7/7)
Accuracy (%)	73 (19/26)	65 (17/26)	83 (15/18)	89 (16/18)
Interobserver agreement (%)	58 (15/26)		78 (14/18)	

Note.—Numbers in parentheses represent the data used to calculate the percentages. Per the four-point confidence-level scale, a cutoff between 2 and 3 was used.

Patients with unilateral hypoperfusion (group I) included seven patients with CTE, one with angiosarcoma, and three with arteritis. In the group with predominantly unilateral hypoperfusion (group II), there were 11 patients with CTE, two with fibrosing mediastinitis, one with arteritis, and one with angiosarcoma. Fifteen of the 20 patients with asymmetric disease (group III) had CTE, three were presumed to have fibrosing mediastinitis on the basis of the CT angiographic appearance, one had angiosarcoma, and one had interstitial fibrosis.

Surgical confirmation of the diagnosis was available in 39 patients, 33 of whom had CTE and underwent thromboendarterectomy, three of whom had arteritis, and three of whom had angiosarcoma. In the remaining seven patients, surgery was not performed, and diagnosis was based on the combined clinical and imaging findings, including angioscopic, CT angiographic, and conventional pulmonary angiographic findings. These seven patients included five patients with fibrosing mediastinitis, one with arteritis in whom the diagnosis was based on the angiographic appearance and a nega-



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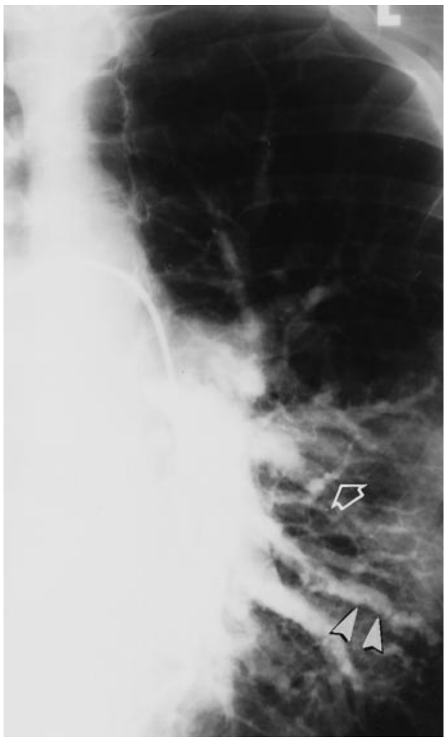

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Figure 4. CTE that was initially diagnosed as fibrosing mediastinitis in a 37-year-old man. **(a)** Transverse CT angiogram shows left hilar nodes and mediastinal soft-tissue attenuation (solid arrows) initially misinterpreted as lymph nodes by one reader. There are extensive collateral vessels (open arrow) in the mediastinum. **(b)** Transverse CT angiogram obtained with lung windows shows diminutive upper-lobe segmental vessels (open arrow) in the right lung compared with those (solid arrow) in the left lung. Parenchymal opacity in the left lung was attributed to incidental infection, since it cleared on a subsequent CT scan. **(c)** Anteroposterior conventional angiogram shows few vessels in the upper lobe of the lung. In the lower lobe, the vessels are tortuous (arrow), with intimal irregularity (arrowheads) interpreted by one reader as indeterminate and by the other as suggestive of CTE.

tive angioscopic result, and one with interstitial lung disease.

Conventional pulmonary angiograms and CT angiograms were reviewed only in patients with either unilateral or predominantly unilateral hypoperfusion (groups I and II). On the basis of the pulmonary angiographic appearances of the lung contralateral to the side with severely diminished perfusion and on the basis of the appearance of the obstructed proximal pulmonary artery, both conventional angiogram readers identified studies reasonably well in patients in whom unilateral hypoperfusion was due to CTE (reader 1: sensitivity, 67%; specificity, 88%; reader 2: sensitivity, 61%; specificity, 75%) (Table).

Reader 1 also accurately identified conventional angiograms in four patients with arteritis (Fig 1), but reader 2 misinterpreted one as suggestive of CTE. The conventional angiogram in one patient with angiosarcoma was correctly identified; however, the angiogram in another patient was interpreted as indeterminate by both readers. The angiogram in only one of the two patients with fibrosing mediastinitis was correctly identified by one of the readers. Reader 1 considered the angiogram in one patient with fibrosing mediastinitis to be diagnostic of CTE and the angiogram in another to be indeterminate; reader 2 interpreted the angiogram in one patient as suggestive of fibrosing mediastinitis and the angiogram in another as suggestive of CTE.

Helical CT angiograms were available in 18 patients, nine of whom had total unilateral hypoperfusion (group I) and nine of whom had predominantly unilateral hypoperfusion (group II). Of the 11 patients with CTE in whom CT angiograms were available, eight had CT angiograms that were correctly identified by reader 1 (sensitivity, 73%, specificity, 100%), and nine had CT angiograms that were correctly identified by reader 2 (sensitivity, 82%; specificity, 100%) (Table) (Fig 2). Three had CT angiograms read as indeterminate by reader 1, and one had a CT angiogram read as indeterminate by reader 2 (Fig 3). The condition of one patient with CTE was misdiagnosed as fibrosing mediastinitis by reader 2 because of the presence of hilar and mediastinal lymph nodes. The conventional angiogram of this patient was interpreted as suggestive of CTE by one reader and as indeterminate by the other (Fig 4).

The diagnoses in both patients with angiosarcoma and in the three with arteritis in whom CT angiograms were available were made correctly. One of the patients with angiosarcoma correctly diagnosed at CT angiography had a conventional angiogram interpreted as indeterminate by both readers (Fig 5). In both patients with fibrosing mediastinitis, the condition was recognized from the CT angiographic appearances by both readers because of extensive mediastinal lymphadenopathy. By using pooled data from both readers and a cutoff between 2 and 3 on the confidence scale, the difference in accuracies between CT angiographic and conventional angiographic interpretations was not statistically significant. Interobserver agreement was higher for CT angiography (κ = 0.70) than for conventional angiography (κ = 0.41).

The ROC-configured data for CT angiography and conventional angiography are shown in Figure 6. Areas under the curves were greater for CT angiographic interpretation (reader 1: mean, 0.96 ± 0.28 [SD]; reader 2: mean, 0.93 ± 0.27) than for conventional angiographic interpretation (reader 1: mean, 0.73 ± 0.19; reader 2: mean, 0.76 ± 0.19).

DISCUSSION

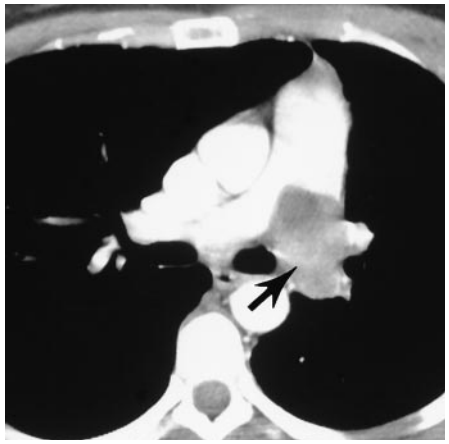
Unilateral pulmonary hypoperfusion is uncommon and is caused by a variety of diseases (1–11). Discussion of this entity has been limited to case reports and small series, in the largest of which (1) researchers identified unilateral hypoperfusion in approximately 3% of patients referred for radionuclide scans. Unilateral hypoperfusion due to CTE has been associated with younger patients who are predominantly female and who have lower pulmonary arterial pressures and pulmonary vascular resistance (12). Accurate recognition of this entity is important not only for appropriate management but also for recognizing potential complications if the cause is CTE.

We found complete unilateral hypoperfusion (group I) in 11 of 410 (2.7%) patients referred for evaluation of CTE, a proportion similar to that found in a previous study (1) in which patient selection was not based on the suspicion of CTE. Predominantly unilateral hypoperfusion (group II) occurred in 16 (3.9%) patients, and less severe asymmetric hypoperfusion was identified in an additional 20 (4.9%). The prevalences of CTE in each of the three patterns of perfusion abnormality—unilateral, predominantly unilateral, and asymmetric— were similar. Thus, the degree of asymmetry in the pattern of perfusion abnormality on radionuclide scans did not distinguish CTE from other causes of hypoperfusion.

Although pulmonary angiography is commonly used for examining patients with unilateral hypoperfusion, our results suggest that CT angiography may be more appropriate. Our angiogram interpreters had extensive experience in identifying patients with CTE, but in this group of patients with markedly asymmetric perfusion abnormalities, we found that interpretation of CT angiograms tended to be more accurate than that of conventional angiograms for identifying patients with CTE. Furthermore, CT angiography was more accurate in distinguishing between patients with CTE, fibrosing mediastinitis, arteritis, or angiosarcoma.

Both CT angiogram readers reliably diagnosed the conditions of all patients with nonthromboembolic causes of unilateral and predominantly unilateral hypoperfusion. It is not surprising that conventional angiographic interpretation in patients with unilateral pulmonary artery obstruction is fraught with difficulty. Technically, conventional angiography is more challenging because of the rapid transit time for contrast material when only one lung is perfused. In addition, the angiographic criteria for diagnosing CTE pulmonary artery obstruction, which include pouching defects, pulmonary artery webs and bands, intimal irregularity, abrupt narrowing of pulmonary vessels, and obstruction of vessels at their point of origin (17), typically are more easily recognized at the lobar and segmental levels. Lack of perfusion to one lung limits the number of segmental vessels available for interpretation and thereby compromises the specificity of the angiographic findings.

Overall accuracies in this study are biased in favor of CT angiography, since depiction of extensive mediastinal lymphadenopathy, together with the absence of thromboembolism at pulmonary angioscopy, was used to diagnose fibrosing mediastinitis; therefore, these patients with fibrosing mediastinitis did not undergo surgery. One patient had CT angiographic features of both fibrosing mediastinitis and CTE, and at surgery was found to have thromboembolism amenable to thromboendarterectomy. This patient's example serves as a warning against excluding CTE as a diagnosis because of the presence of enlarged mediastinal or hilar lymph nodes.



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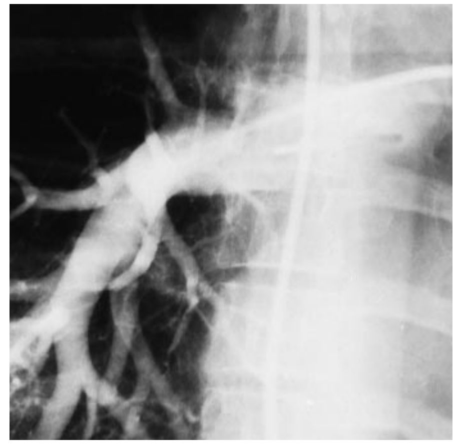

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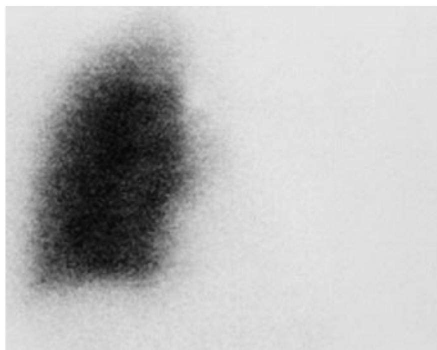

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Figure 5. Angiosarcoma in a 32-year-old man. **(a)** Transverse CT angiogram shows contrast material enhancement within the tumor (arrow) that occluded the left pulmonary artery. **(b)** Anteroposterior conventional angiogram shows a normal right pulmonary artery, but there is insufficient flow to the left pulmonary artery to diagnose the central tumor. **(c)** Anterior projection of radionuclide scan shows absent perfusion to the left lung and near-normal perfusion to the right lung.

It is important to recognize how difficult it can be to distinguish CTE from fibrosing mediastinitis, particularly in patients with unilateral disease. The clinical, conventional angiographic, and CT angiographic features of these diseases can be similar. Dyspnea is common to both conditions, and pulmonary arterial hypertension, a common sequela of CTE, may also occur in fibrosing mediastinitis because of obstruction of central pulmonary arteries and veins. Reviewers of conventional angiograms frequently cannot distinguish vascular distortion and occlusion caused by extrinsic nodal masses from that due to CTE. Since only intraluminal irregularities are depicted, the spatial relationship between enlarged nodes and pulmonary vessels cannot be appreciated on conventional angiograms.

It is also important to recognize that the CT angiographic appearance of fibrosing mediastinitis that causes vascular disruption is not always definitive, since mediastinal lymph nodes are common in the general population, particularly in areas in which tuberculosis, histoplasmosis, and other granulomatous diseases are endemic. Obstruction of central vessels in patients with fibrosing mediastinitis can also cause the sizes of segmental vessels and mosaic perfusion in the lung parenchyma to be asymmetric, similar to that depicted on CT angiograms of patients with CTE (15,16).

Furthermore, the CT angiographic appearance of the thromboembolic material lining the central vessels is not always readily distinguished from the appearance of vessels narrowed by mediastinal nodal tissue. Thus, determining the relative effect of vascular occlusion caused by lymphadenopathy versus that due to CTE can be challenging with either modality.

However, CT angiography enables clearer depiction of the spatial relationships between nodes and pulmonary arteries and veins than does conventional angiography. These relationships help to determine the functional effect of enlarged lymph nodes. Angioscopy can also help in making diagnoses in patients with more confusing symptoms because it en-

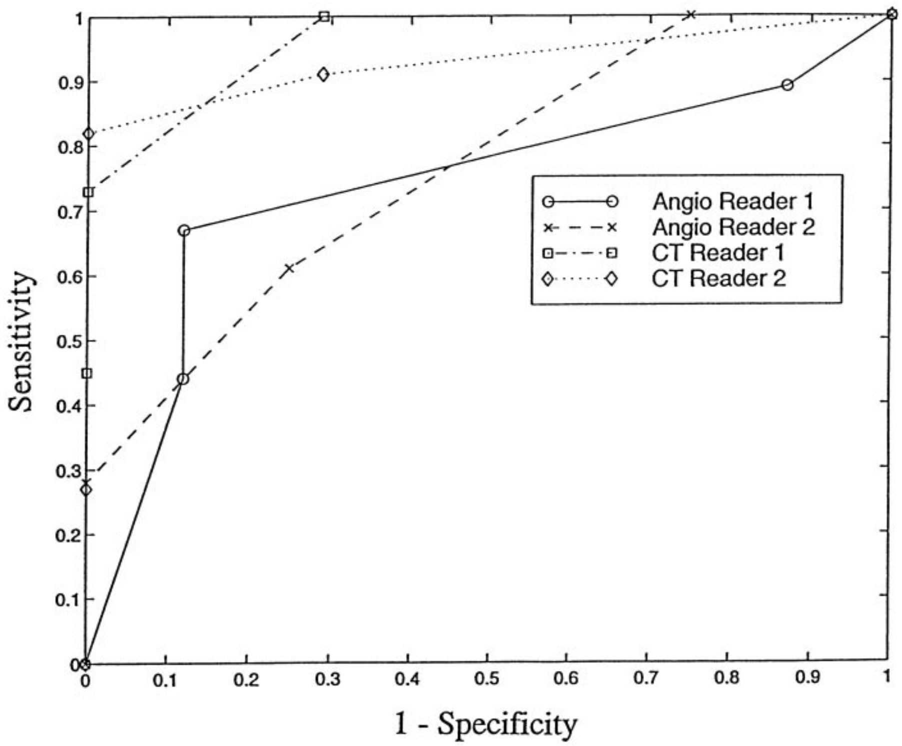

Figure 6. Graph shows data configured to ROC axes for readers of CT angiograms and conventional angiograms (*Angio*). The areas under the CT angiogram curves are greater than the areas under the conventional angiogram curves.

ables direct visualization of the thromboembolic material within the vessels.

CT angiography also has advantages over conventional angiography in depicting tumors of the pulmonary arteries. CT angiograms can demonstrate contrast material enhancement within the tumor, tumor mass extending beyond the contour of pulmonary arteries, and distant pulmonary metastases. CTE, on the other hand, is distinguished by the contour of material that conforms to the arterial wall and by the lack of contrast material enhancement within the organizing thromboembolic material.

Although pulmonary involvement has been reported in up to 50% of patients with Takayasu arteritis (18), it is probably underrecognized as a cause of unilateral hypoperfusion. Signs and symptoms of systemic arteritis are useful in establishing the diagnosis but are not always present (13). To our knowledge, the CT angiographic appearance of this condition has not previously been described. Both conventional angiograms and CT angiograms demonstrated unilateral, smooth tapering of the pulmonary artery in patients with arteritis; abrupt tapering is more characteristic of congenital absence of the pulmonary artery.

Arteritis cannot be distinguished reliably from CTE on the basis of CT angiography or conventional angiography. The conventional angiographic appearance can be similar in CTE and arteritis (13), although arteritis was far less common in our study population. At CT, the finding of smoothly tapering arteries without visible intraluminal thrombus may suggest the diagnosis of arteritis rather than of CTE. Surgical confirmation was available in three of four patients with conditions diagnosed as arteritis in this series. One had known Takayasu arteritis and systemic symptoms, one had histologic evidence of chronic perivascular inflammation, and one had a graft for bypass of the focal narrowing in the pulmonary artery that is characteristic of arteritis.

The population we studied was not representative of all patients with unilateral hypoperfusion, since it included many more patients with CTE than would present with symptoms to most institutions. In other geographic locations, fibrosing mediastinitis may be more common. It is important to recognize the diagnostic challenge that distinguishing patients with CTE from those with fibrosing mediastinitis, pulmonary angiosarcoma, and arteritis poses to the clinician and to understand how CT angiographic features can help.

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