REVIEW ARTICLE

The Role of Spiral Volumetric Computed Tomography in the Diagnosis of Pulmonary Embolism

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To evaluate the evidence for the use of spiral volumetric computed tomography (SVCT) in the diagnosis of acute pulmonary embolism (PE), the 11 English-language studies published through July 1998 that compared SVCT with a reference standard for PE were systematically reviewed. Among the reviewed studies, methodological problems were common. Only 5 of these studies fulfilled 5 of 11 basic standards addressing important issues in diagnostic test research. The reported sensitivities of SVCT compared with pulmonary angiography varied widely (64%-93%), which was likely the result of differences in study populations. Spiral volumetric computed tomography may be relatively sensitive and specific for diagnosing central pulmonary artery PEs, but it is insensitive for diagnosing subsegmental clots. Spiral volumetric computed tomography may have a role as a "rule-in" test for large central emboli, but additional research is required to establish its place in clinical practice. *Arch Intern Med. 2000;160:293-298*

Spiral volumetric computed tomography (SVCT) has been recognized as a test with potential for use in the diagnosis of pulmonary embolism (PE) since 1992, at which time Remy-Jardin et al[1] employed it in the evaluation of 42 patients. Initial results were promising, with sensitivity and specificity reported as 100% and 96%, respectively. Subsequent studies have reported similar impressive results, but it is not yet clear what role this new imaging technique should play in the evaluation of patients with suspected PE. Because enthusiasm for new diagnostic tests sometimes precedes the scientific determination of their value,[2,3] we have critically reviewed the evidence for the use of SVCT in the diagnosis of acute PE.

METHODS

SELECTION OF CLINICAL STUDIES

Using the MEDLINE database (1966-1998) and *Current Contents* (January-July 1998), we sought all articles published in the English language that evaluated the role of SVCT in the diagnosis of PE. All pertinent references from this group of articles were also reviewed. Studies selected for detailed review were those that established the diagnosis of PE by pulmonary arteriogram or another clinical reference standard (eg, high-probability ventilation-perfusion [V̇/Q̇] scan combined with high clinical suspicion). Fourteen articles were considered, and 11 met our criteria for inclusion in this review.[1,4-13]

CRITICAL REVIEW OF SELECTED STUDIES

We performed a detailed evaluation of each study to determine how well it satisfied 11 basic methodological standards addressing important issues in diagnostic test research. These standards, adapted from Ransohoff and Feinstein[3] and Philbrick et al,[14] are described below.

Standard 1: Did the Authors Provide a Clear Description of the SVCT Technique So That Others Could Perform Similar Studies?

The first step in examining a new diagnostic test is to study the details of performing and interpreting the test. To allow test interpretation, replication, and application, this standard required an explicit description of pertinent radiographic parameters, including collimation (slice thickness), table

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feed, and anatomic sites at which scanning began and ended.

Standard 2: Did the Authors Provide Clear Criteria for a Positive or Negative Result So That Others Reading the Studies Would Make Similar Interpretations?

The next logical step in evaluating a diagnostic test is to define what constitutes a positive and a negative result. Satisfaction of this standard required clear guidelines with respect to radiographic signs considered diagnostic for pulmonary embolism.

Standard 3: Did the Authors Assess the Reliability of the Interpretation by Comparing Independent (Blinded) Readings?

Reliability is the extent to which repeated measurements of the same relatively stable phenomenon are reproducible. To ensure an assessment of the reliability of radiologists' interpretation of SVCT results, this standard required separate blinded readings by more than one radiologist of the same SVCT films, with a calculation of the variability between those readings.

Standard 4: Did the Authors Assess the Reliability of SVCT by Having Some Patients Undergo Repeated Testing With Comparisons of Both Tests?

This standard required repeated SVCT of some of the patients by at least one additional examiner and blinding of the examiners to each other's findings when interpreting the test results.

Standard 5: Was the Selection Process Described in Sufficient Detail So That a Similar Group of Patients Could Be Assembled if the Study Were Repeated?

Patients with suspected PE constitute a heterogeneous population, varying widely from those with severe underlying cardiopulmonary disease to otherwise healthy outpatients. In addition, investigators often use different means for seeking patients and different criteria for admitting patients to their studies. Consequently, patients ultimately admitted to the studies can vary widely in their clinical characteristics, and this variation can have an important influence on the results. This standard required that the authors walk the reader through the process of assembling the study group and that the method of selecting patients be described in sufficient detail to allow a similar group of patients to be selected if the study were repeated. For example, a study that enrolled "75 consecutive patients . . . referred for pulmonary angiography because of clinical suspicion of acute PE"[7] fulfilled this standard.

Standard 6: Were the Patients Described Sufficiently for the Reader to Compare Them With His or Her Patients?

To clarify the clinical spectrum of patients tested, we required that the age and sex of the patients be reported along with a brief summary of the major clinical characteristics of the patients tested.

Standard 7: Were the Eligible Patients Who Were Not Enrolled Described Sufficiently?

Studies that investigated SVCT were required by this standard to give a summary of the age, sex, and clinical setting of the eligible patients who did not undergo further investigation. This standard is designed to give the reader a sense of how the selection process shaped the patient population of a given study.

Standard 8: Was the Extent of Disease Described in Sufficient Detail to Allow Stratification of Results by Location or Severity of PE?

Since PE varies widely in extent and prognosis, diagnostic tests for PE should be evaluated across the full spectrum of anatomic diseases. For example, it is important to know if the sensitivity and specificity of SVCT is the same for central and subsegmental PE. To satisfy this standard, we required either a detailed angiographic description of the number and size of the affected pulmonary arteries down to the segmental level or a cataloging of the number of patients found to have subsegmental PE.

Standard 9: Were Non-PE Diagnoses Reported So That the Discriminative Ability of SVCT for Patients Without PE Could Be Inferred?

One of the purported benefits of SVCT is its ability to detect intrathoracic pathologic characteristics that may mimic PE. Patients who undergo evaluation for PE often have a number of alternative intrathoracic differential diagnoses. The reader is better able to determine the utility of SVCT in these patients if an explicit description is provided of those disease processes that SVCT detected in the course of evaluation for PE.

Standard 10: Were Patients Referred for SVCT and the Reference Standard Regardless of the Results of Either?

Workup bias occurs if the results of SVCT influence the chance that a patient underwent testing with the reference standard (eg, pulmonary angiogram). For example, if the SVCT result is positive, a patient may be less likely to undergo the discomfort and risk of an angiogram. Consequently, a disproportionate number of patients with negative SVCT results may be enrolled in a study. This bias could cause a relative increase of both false-negative and true-negative test results and would result in a spuriously low sensitivity and high specificity for SVCT. To avoid workup bias, this standard required a study design that committed patients to both SVCT and the reference standard before SVCT was performed.

Standard 11: Were Results of SVCT and Reference Standard Studies Interpreted Independently?

Diagnostic review bias occurs when the result of one test influences the interpretation of another standard. For example, if the angiogram result is known to the reader of a given

Table 1. Summary of Studies and Results of Methodological Review*

Source	Country	Standards Satisfied†	No. of Patients: SVCT	No. of Patients: SVCT Compared With Any Reference Standard	No. of Patients: SVCT Compared With PA	Selection Criteria for PA‡
Remy-Jardin et al,[1] 1992	France	1, 2, 6, 8, 10	42	42	42	Clinical suspicion of PE
Blum,[11] 1994	France	1, 6, 8, 11	10	10	10	Clinical suspicion of acute massive PE
Goodman et al,[5] 1995	United States	1-3, 5, 6, 8, 10, 11	20	20	20	Unresolved clinical and scintigraphic diagnosis of PE§
Remy-Jardin et al,[7] 1996	France	1, 2, 5, 8, 10	75	75	75	Clinical suspicion of PE
Sostman et al,[8] 1996	United States	1, 3, 11	28	28	. . .	. . .
van Rossum et al,[9] 1996	The Netherlands	1-3, 8, 11	185	149	56	Indeterminate or discordant V̇/Q̇ scan and SVCT results
van Rossum et al,[10] 1996	The Netherlands	1, 2, 5, 9	77	77	45	Nondiagnostic or discordant V̇/Q̇ scan and SVCT results‖
Christiansen,[4] 1997	Sweden	2, 8, 10, 11	70	70	70	High clinical likelihood of PE
Mayo et al,[6] 1997	Canada	1-3, 8	142	139	41	Indeterminate or nondiagnostic SVCT or V̇/Q̇ scan results, or high clinical suspicion and negative or nondiagnostic SVCT and/or V̇/Q̇ scan results¶
Cross et al,[12] 1998	Great Britain	1, 9	59	50	2#	. . .
Garg et al,[13] 1998	United States	1, 2, 6-9	54	54	26	. . .

*SVCT indicates spiral volumetric computed tomography; PA, pulmonary angiography; PE, pulmonary embolism; V̇/Q̇, ventilation/perfusion; and ellipses, could not be determined from available data.

†See "Methods" section for description of standards.

‡All patients who underwent PA had either discordant clinical and V̇/Q̇ scan findings or an indeterminate V̇/Q̇ scan. Not all patients with these characteristics underwent PA.

§Patients with normal V̇/Q̇ scans with both V̇/Q̇ scan and clinical findings suggesting a low probability of PE or with both suggesting a high probability of PE were excluded; patients with positive duplex ultrasonography results of the lower extremities were also excluded.

‖Patients selected for PA had either high-probability V̇/Q̇ scan and negative SVCT results or non-normal or non–high-probability V̇/Q̇ scan results.

¶Patients selected for PA had discordant SVCT and V̇/Q̇ scan results, indeterminate V̇/Q̇ scan or SVCT results, or high clinical suspicion for PE with negative or nondiagnostic SVCT and/or V̇/Q̇ scan results.

#Obtained in 2 of 5 patients with indeterminate SVCT and V̇/Q̇ scans and normal lower-extremity ultrasonography results.

Table 2. Comparison of Spiral Volumetric Computed Tomography (SVCT) and Pulmonary Angiography (PA) Results in All Vascular Zones*

Source	No. of Patients: SVCT+/PA+	SVCT+/PA–	SVCT–/PA+	SVCT–/PA–
Goodman et al,[5] 1995	7	1	4	8
Remy-Jardin et al,[7] 1996	41	0	3	21
van Rossum et al,[9] 1996	11†	0	4†	41
Christiansen,[4] 1997	19	4	3	44
Mayo et al,[6] 1997	11	2	3	21
Garg et al,[13] 1998	4	0	2	18
Total	**89**	**7**	**19**	**153**

*SVCT+ indicates positive SVCT results; SVCT–, negative SVCT results; PA+, positive PA results; and PA–, negative PA results.

†Average of readers 1 and 2.

SVCT scan, the interpretation of the scan may tend to be biased toward concordance with the angiogram. Conversely, an angiographer may be biased in his or her interpretation of the pulmonary arteriogram if the SVCT result is known beforehand. To address this form of bias, standard 11 required a statement that the determination of the SVCT result and the diagnostic standard were performed without knowledge of the other.

RESULTS

Table 1 lists the 11 studies that met our criteria for review and our ratings for compliance with the 11 standards for diagnostic test research. Since the ratings for each standard depended on the published text, some ratings might have been different if additional details of methods and results had been reported. In addition, Table 1 lists the number of patients in each study who underwent SVCT, the number of patients who had their SVCT scans compared with a reference standard, and the number of SVCT scans that were compared with our criterion standard, pulmonary angiography. **Table 2** summarizes the data from the 6 studies that provided data relating SVCT results to pulmonary angiography. Since these studies were not methodologically similar, we did not pool the results. The 11 studies were published recently (1992 through 1998), were undertaken in 6 different countries, and varied in the number of reported examinations (10-185). None of the studies adhered to all 11 standards, and only 5 studies met 5 or more standards.

There was general compliance with the first methodological stan-

dard, which was concerned with the description of the SVCT technique. Among the reviewed studies, the technique of SVCT was standardized with little technical variation. Collimation ranged from 3 to 5 mL, while table feed was typically 5 mm/s. Contrast consisted of 12% to 30% iodinated nonionic contrast agent that was power injected at a rate designed to achieve a maximal concentration in the pulmonary vasculature at the time of scanning. For example, 12% contrast was injected at 7 mL/s, while 30% contrast was injected at 5 mL/s.[1] As the scans must be initiated at the time the contrast agent passes through the pulmonary arteries, various techniques were employed to coordinate scanning during the peak enhancement phase after the initiation of contrast injection. This was achieved by setting a fixed scan delay time of 5 to 20 seconds, depending on the patient's hemodynamic status and the proximity of venous access to the central circulation. For example, Cross et al[12] used a 15-second scan delay time if the cannula was in an antecubital vein and a delay of 20 seconds if the cannula was placed at the wrist. Goodman et al[5] decreased the contrast agent injection rate for injections that were made through central venous catheters and increased the scan delay time for older patients. The amount of contrast injected was typically 120 cm^3, with a range of 90 to 180 cm^3. Most patients were able to hold their breath for the duration of the scans (typically 20 seconds). Patients who could not hold their breath performed either two 10- to 12-second breath holds interrupted by a 6-second pause[5] or, if that was not possible, employed shallow breathing.[10] Most scans were performed in the caudocranial direction from the diaphragm through the aortic arch for a total of 10 to 20 cm along the *z*-axis.

There was little variation in the major radiographic criteria for diagnosing PE. Criteria for a positive scan result included a partial filling defect (defined as central or marginal intraluminal areas of low attenuation surrounded by variable amounts of contrast medium with regular or irregular borders), a complete filling defect, the "railway track sign" (thromboembolic masses seen floating freely in the lumen, allowing the flow of blood between the wall of the vessel and the thrombus/embolus), and mural defects (found in peripheral areas of low attenuation with arterial sections). The 8 studies that gave criteria for positive or negative results[1,4-10,13] either explicitly stated them or referenced the 1992 study of Remy-Jardin et al.[1]

Only 4 of the 10 reviewed studies assessed the reliability of radiographic interpretations by comparing blinded readings.[5,6,8,9] None of the studies assessed the reproducibility of SVCT results by having patients undergo repeat testing with comparisons of both tests.

Three studies described the selection process in sufficient detail that a similar group of patients could be assembled if the study were repeated.[5,7,10] The principal cause of failure to meet this standard was the absence of consecutive patient selection.

Four studies described the patients sufficiently in terms of age, sex, and clinical setting to allow the reader to compare them with his or her patients.[1,5,11,13] None of the studies adequately described patients who were eligible but not enrolled.

Eight studies described the extent of disease rather than reporting results as simply positive or negative,[1,4-9,11,13] but only 6 of these reported the presence or absence of isolated subsegmental emboli.[4-7,9,13] Isolated subsegmental clot was identified by SVCT in only 5 of 17 cases reported in these studies.

Table 3 summarizes the data from the studies that provided data relating SVCT results to pulmonary angiography stratified by site, either central or subsegmental. Since these studies were not methodologically similar, we did not pool the results.

Despite the presumption that SVCT should be able to identify a number of non-PE intrathoracic diagnoses, only 4 studies reported on these.[5,10,12,13] The investigation by Cross et al[12] reported non-PE diagnoses detected by SVCT in 23 patients, including pleural effusion, focal areas of consolidation, enlarged mediastinal nodes, a pulmonary mass, and marked changes of emphysema. van Rossum et al[10] identified 24 patients with SVCT results negative for PE as having emphysema (n = 6), pneumonia

Table 3. Comparison of Spiral Volumetric Computed Tomography (SVCT) and Pulmonary Angiography (PA) Results: Central Vascular Zones and Subsegmental Vessels*

	Central Vascular Zones†				Subsegmental Vessels	
	SVCT+/PA+	SVCT+/PA–	SVCT–/PA+	SVCT–/PA–	SVCT+/PA+	SVCT–/PA+
Remy-Jardin et al,[1] 1992	18	1	0	23	. . .	. . .
Blum,[11] 1994	7	0	0	3	. . .	. . .
Goodman et al,[5] 1995	6	1	1	12	1	3
Remy-Jardin et al,[7] 1996	39	0	1	25	2	2
van Rossum et al,[9] 1996	11	0	1	44	0	3
van Rossum et al,[10] 1996	5	1	1	36	. . .	. . .
Christiansen,[4] 1997	17	2	2	49	2	1
Mayo et al,[6] 1997	11	2	1	23	0	2
Garg et al,[13] 1998	4	0	2	18	0	1
Total	**118**	**7**	**9**	**233**	**5**	**12**

**SVCT+ indicates positive SVCT results; SVCT–, negative SVCT results; PA+, positive PA results; PA–, negative PA results; and ellipses, data not available.*

†Central vascular zones included the pulmonary artery trunk, the right and left main pulmonary arteries, the anterior trunk, the right and left interlobar arteries, the left upper lobe trunk, and the right and left lower lobe arteries.

(n = 9), pleural effusion (n = 5), empyema (n = 1), lung fibrosis (n = 1), lymphadenopathy (n = 1), and diaphragmatic hernia (n = 1). Garg et al[13] described thromboembolic diagnoses detected in 9 patients, including esophageal cancer (n = 2), tumor that encased vessels (n = 2), bone metastases (n = 1), hypersensitivity pneumonitis (n = 1), interstitial lung disease with honeycombing (n = 2), and bronchiolitis (n = 1). **Table 4** lists the reported causes of false-positive and false-negative results along with the reasons for and numbers of indeterminate scans and technical failures.

Only 4 studies were free of workup bias,[1,4,5,7] and 5 studies were free of diagnostic review bias.[4,5,8,9,11]

COMMENT

Although the research base for the use of SVCT in the diagnosis of pulmonary embolism is small and still evolving, some preliminary conclusions can be derived from the available data. First, it is premature to assign to SVCT values of sensitivity and specificity for diagnosing PE. If we use only the data from Table 2, in which pulmonary angiography is used as the criterion standard, the reported sensitivity of SVCT ranges from 64% to 93%, and the reported specificity ranges from 89% to 100%. The patients described in each of the studies listed in Table 2 were highly selected, and enrollment criteria were inconsistent. Differences in study populations that were a result of disparate methods of enrolling subjects easily explain the variability of results. Because of this and other research design issues, clinicians should not attempt to rely on current published SVCT data to guide their evaluation of patients with suspected PE. A negative SVCT result may miss a clinically significant embolism, and a patient with a positive SVCT result may require further testing before a PE diagnosis is made.

A second conclusion suggested by the available data is that SVCT may be sensitive and specific for central pulmonary arteries but not for subsegmental arteries. For central pulmonary artery PE (ie, from the main pulmonary arteries down to the fourth-generation segmental arteries), the sensitivity and specificity ranged from 83% to 100% and 92% to 100%, respectively (Table 3). However, of 17 patients with angiographically confirmed subsegmental emboli mentioned in the reviewed studies, SVCT results were positive in only 5, for a sensitivity of 29% (Table 3). While SVCT may be useful in detecting the larger, more central PE, the smaller, more peripheral subsegmental emboli are likely to be overlooked. Unfortunately, small as well as large emboli can be clinically important.

What role should SVCT play in current clinical practice for the diagnosis of PE? There is not yet a clearly established place for SVCT. However, in patients with suspected massive PE who may not be able to undergo pulmonary arteriogram, SVCT could play a role in establishing the diagnosis of PE. In this situation, SCVT should be used as a "rule-in" test, a role supported by its generally high specificity for large central emboli. A negative SVCT result could not be relied upon to rule out PE. Additionally, patients in whom the differential diagnosis includes other intrathoracic pathologic characteristics in addition to PE, such as aortic dissection or tumor, could benefit from imaging with SVCT as the initial radiological test.

Future research may establish important roles for SVCT. If a high sensitivity and specificity of SVCT for central PE is confirmed, SVCT may replace the V̇/Q̇ scan as the initial test to evaluate suspected PE. However, unless the ability of the SCVT to detect subsegmental PE improves, diagnostic strategies will have to be developed to deal with small emboli that are missed. These strategies may include subsequent pulmonary arteriogram, bilateral lower-extremity ultrasonographic testing, or serial lower-extremity ultrasonography. Serial lower-extremity ultrasonography has been proposed by Hull et al[15,16] for patients with adequate cardiopulmonary reserve and indeterminate V̇/Q̇ scan results.

The clinical significance of isolated subsegmental emboli is not known. However, they are not rare, and it is not current practice to ignore them. The results of the Prospective Investigation of Pul-

Table 4. Reported Reasons for Unsatisfactory Results of Spiral Volumetric Computed Tomography

Causes of False-Positive Results (No. of Patients)
- Volume averaging of enhancing vessels with adjacent lymphadenopathy or atelectatic lung (2) (from Mayo et al[6])
- Hilar areas of hypoattenuation caused by hilar lymph nodes (1) (from Remy-Jardin et al[7])
- Breathing artifact (1) (from Goodman et al[5])
- Asymmetry in pulmonary vascular opacification secondary to chest trauma with effusion and consolidation (1) (from Remy-Jardin et al[1])
- Partial volume effects in obliquely oriented vessels, such as the lingula and right middle lobe arteries, suboptimal contrast, and/or intersegmental lymph nodes (3-6) (from van Rossum et al[9])

Causes of False-Negative Results (No. of Patients)
- Subsegmental clot (10) (from Christiansen[4]; Goodman et al[5]; Mayo et al[6]; Remy-Jardin et al[7]; van Rossum et al[9]; and Garg et al[13])
- Patient's large size (1) (from Mayo et al[6])
- Right middle lobectomy (1) (from Remy-Jardin et al[7])
- Embolus in anterior segmental artery of the right lower lobe (1) (from Garg et al[13])

Causes of Indeterminate Scans/Technical Failures (No. of Patients)
- Inadequate depiction of right middle lobe and/or lingular segmental arteries (4) (from Remy-Jardin et al[7])
- Breathing at the end of scanning (2) (from Remy-Jardin et al[7])
- Interruption of contrast injection before the end of data acquisition (1) (from Remy-Jardin et al[7])
- Limitation of breathing caused by pleuritic chest pain (1) (from Remy-Jardin et al[7])
- Severe dyspnea (2) (from Remy-Jardin et al[7])
- Patent foramen ovale (2) (from Remy-Jardin et al[7] and Garg et al[13])
- Technical difficulty with intravenous catheter connections (1) (from Remy-Jardin et al[1])
- Poor enhancement, poor signal-to-noise ratio, and/or excessive patient motion (4) (from Mayo et al[6])
- Moderate vascular opacification of the right lower lobe arteries (1) (from van Rossum et al[10])

monary Embolism Diagnosis (PIOPED)[17] reported subsegmental clot in only 5.6% of patients, but recent studies have reported prevalence figures ranging from 5% to 36%.[4-7,9,18] Furthermore, it appears that poorly compensated patients with isolated subsegmental emboli experience clinical improvement following appropriate therapy for PE.[7]

Although SVCT imaging for the diagnosis of PE is promising as a rapid, noninvasive test, much additional research is needed. At least one multicenter study is needed to provide the answers for SVCT that the PIOPED study provided for the V̇/Q̇ scan.[17] Since some of the controversy regarding SVCT surrounds its application for the detection of subsegmental emboli, future research should examine carefully the sensitivity of SVCT for these small clots. Also, the clinical utility of testing strategies employing SVCT must be determined and compared with currently employed algorithms, especially with regard to subsegmental emboli.

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