REVIEW

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Diagnostic value of computed tomography (CT) angiography in patients with acute pulmonary embolism

Małgorzata Olga Zamecka, Ewa Kurys-Denis, Witold Krupski

II Department of Radiology, Medical University, Lublin, Poland

Abstract: Computed tomography angiography (CTA) is an accurate test for the detection of pulmonary embolism (PE) and is gaining increased acceptance as a first-line study for diagnosing acute pulmonary embolism. Prompt and accurate diagnosis of PE is of great importance because treatment reduces mortality from 30% to < 10%. Recent advances in single-detector row helical CT pulmonary angiography include improvements in x-ray tube technology and faster gantry rotation, which allow for increased body coverage by using narrower collimation. These advances have been associated with an improved sensitivity and specificity of the technique, from more than 80% to more than 90% in recent series. The most important advantage of CT over other imaging modalities is that both madiastinal and parenchymal structures can be evaluated, and thrombus can be directly visualized. Investigators have reported that subsegmental emboli can be missed; however, visualization of smaller arterial branches, and therefore detection of small emboli, have improved with the availability of multidetector scanners. PE being a pathologic condition causes both partial and complete intarluminal filling defects, which should have a sharp interfece with intravascular contrast material. In acute pulmonary embolism that manifestes as complete arterial occlusion, the affected artery may be enlarged. Partial filling defects due to acute pulmonary embolism are often centrally located, but when eccentrically located they form acute angles with the vessel wall. Some factors that cause misdiagnosis of pulmonary embolism may be patient-related, technical, anatomical or pathological. The radiologist needs to determine the quality of a CT pulmonary angiography study and whether pulmonary embolism is present. If the quality of the study is poor, the radiologist should identify which pulmonary arteries have been rendered indeterminate, and whether additional imaging is necessary. The aim of this study was to introduce the current views for diagnosing PE in CTA.

Key words: pulmonary embolism, computed tomography, embolic pulmonary index

INTRODUCTION

Pulmonary embolism is a serious and potentially fatal condition associated with significant morbidity and mortality. It is the third most-common cause of cardiovascular death after myocardial ischemia and stroke [1]. Diagnosis of pulmonary embolism continues to pose a challenge to both clinicians and radiologists because the clinical signs and symptoms of PE are non-specific. They might include: dyspnea with or without associated anxiety, pleuritic chest pain, hemoptysis, pneumonia, exacerbation of chronic obstructive pulmonary disease (COPD), congestive heart failure, lung cancer, lightheadedness, syncope, tachycardia, tachypnoe, fever or pleuritic rub [2, 3].

Objective diagnostic testing is therefore mandatory, but imaging of the pulmonary arteries is preferably not carried out in every patient because of costs and potential harmfulness [4].

In the original Prospective Embolism Diagnosis (PIOPED) study, only one-third of the 755 patients who underwent computed tomography pulmonary angiography (CTPA) had the diagnosis of PE confirmed. In many patients, the first diagnosis of PE is made in acute cardiac decompensation or, worse yet, postmortem [5].

Corresponding author: Witold Krupski, MD, PhD, II Department of Radiology, Medical University, Staszica 16, 20-081 Lublin, Poland.
E-mail: krupskiw@wp.pl

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The incidence of PE in the last decades has decreased substantially by 45%, whereas that of deep-vein thrombosis (DVT) remains unchanged [6]. This change is probably due to a number of factors which involve a decreased incidence of PE, decreased case fatality rate, venous thromboembolism (VTE) prophylaxis, and also improvement of diagnostic means [7].

The consequences of thromboembolism in the lung depend largely on the size of the occluded pulmonary artery, reflecting the size of the embolus, and on the cardiopulmonary status of the patient [3]. Most commonly, a thrombus forms in the deep veins of the legs, typically in the popliteal vein and larger veins above it, and subsequently migrates into the pulmonary arterial circulation [3, 8].

Prompt and accurate diagnosis of PE is of a great importance because treatment reduces mortality from 30% to < 10% [3, 8].

Many methods and different algorithms have been used for diagnosing patients suspected with having PE. These involve electrocardiogram, chest radiography, echocardiography, ventilation-perfusion scintigraphy, catheter pulmonary angiography, lower extremity vein evaluation with venography, sonography, CT venography(CTV) and MR angiography [8].

In recent years, laboratory tests such as D-dimer have played an increasing role in the accurate diagnosis of patients with suspected pulmonary embolism, but for most practical purposes computed tomography has practically become the first-line imaging test in daily clinical routine. The most

important advantage of CT over other imaging modalities is that both madiastinal and parenchymal structures can be evaluated, and thrombus can be directly visualized. CT may not only be used for evaluating thoracic anatomy in cases where PE is suspected, but also allows the derivation of physiologic parameters on lung perfusion at single-detector row electron-beam and multi-detector row CT. It is also now possible to scan the entire chest faster at the peak of contrast material opacification during a single breath-hold [9].

Direct signs of acute and chronic PE. The direct radiological signs, shown on angiography, are required to make a diagnosis of acute or chronic pulmonary thromboembolic disease. Even though CT angiography and conventional angiography have complementary roles in the accurate diagnosis of acute and chronic thromboembolic disease, the CT angiography should be preferred as a non-invasive method, leaving conventional angiography as a reference method to be used only in doubtful cases.

Complete obstruction (Fig. 1). On pulmonary angiograms, the diagnostic sign of acute PE with complete obstruction is a concave filling defect or 'trailing edge' observed without the contrast material at the level of obstruction [10, 11]. CT is superior to the conventional angiography in showing a thrombus located distally to the obstruction. At the site of the thrombus, the diameter of the pulmonary artery may be increased because of impaction of the thrombus by pulsatile flow [12].

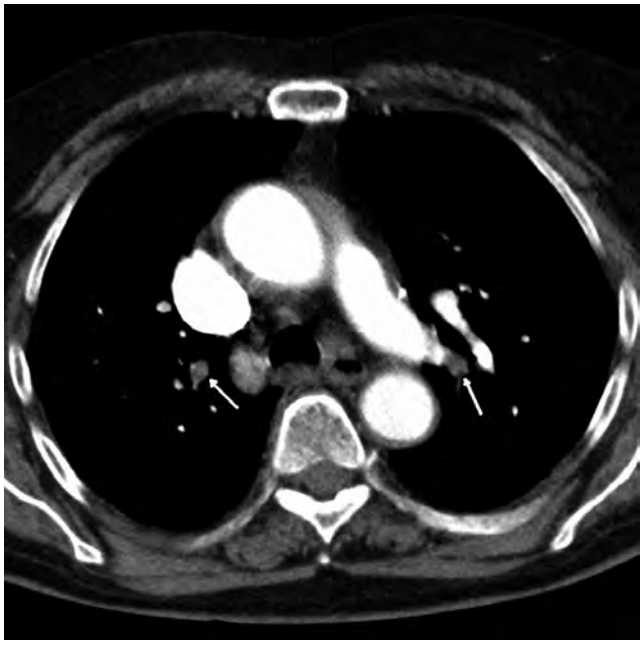

Figure 1 Acute pulmonary embolism. Complete obstruction of both right and left lower lobes arteries (arrows) with expension of vessel diameters – Qanadli Score 20.

Nonobstructive filling defect (Fig. 2, 3). A non-obstructive filling defect can be central or eccentric in location. On angiography, a central filling defect is completely surrounded by contrast material [10, 11], whereas on CT it is seen as a well-defined central filling defect in either an axial or longituidinal plane with respect to the vessel [12]. Such a non-obstructive central filling defect cannot float within the centre of the lumen without being attached to either a non-obstructive eccentric filling defect or a complete obstruction thrombus. In acute PE, a non-obstructing eccentric filling defect forms acute angles with respect to the vessel wall which can be observed on angiography or CT [12].

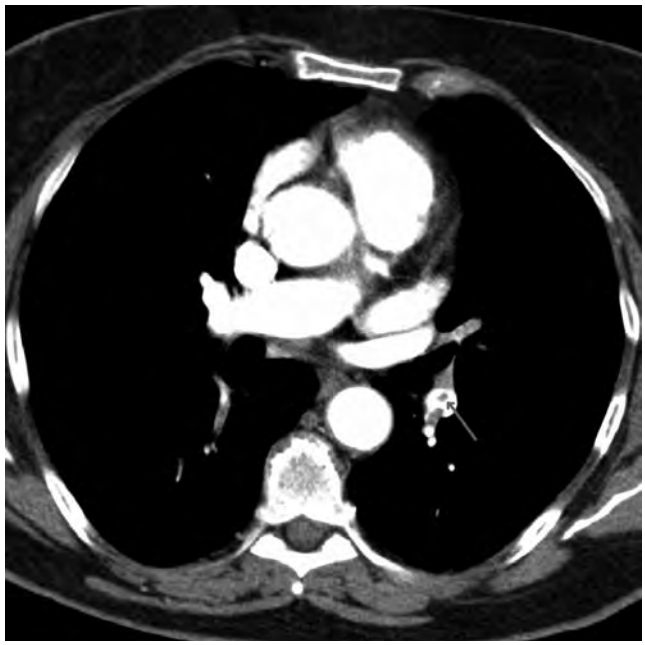

Figure 2 Axial CT image shows a central filling defect in the left lower lobe artery, a well-defined central thrombus is completely surrounded by contrast material (arrow) – Miller Score 3.

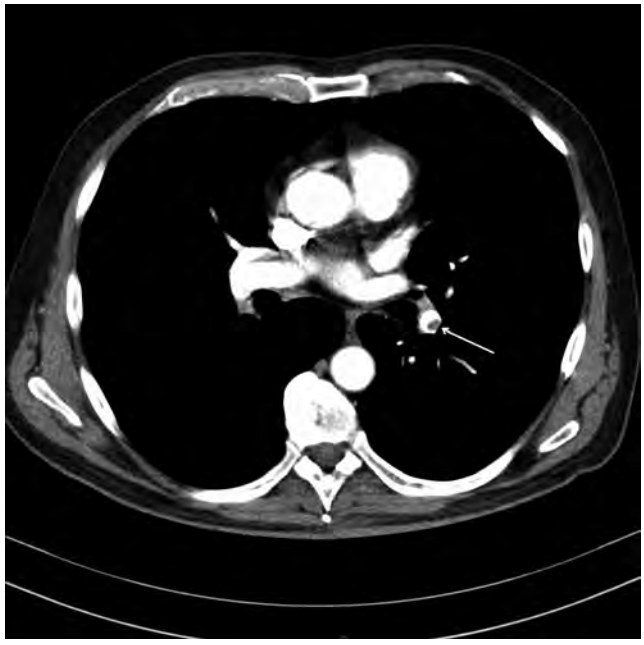

Figure 3 Eccentric filling defect within the left lower lobe artery visualized on an axial CT image – Qanadli Score 5.

PA Clot Load Scores. There are 4 different scoring systems, proposed by Miller et al. [13], Walsh et al. [14], Qanadli et al. [15] and Mastora et al. [16], which assess the presence, location, and degree of obstruction of arterial clots.

Miller Score. The right PA has 9 major segmental branches (3 to the upper lobe, 2 to the middle lobe, and 4 to the lower lobe), and the left PA has 7 major branches (2 to the upper

lobe, 2 to the lingula, and 3 to the lower lobe).The presence of the filling defect or obstruction in any one of these branches scorse 1 point. A filling defect proximal to segmental branches scorses a value equal to the number of segmental branches arising distally (Fig. 1). The maximum score is therefore 9 for the right lung and 7 for the left lung, with the maximum possible CT obstruction score of 16 for both lungs. In addition, the score originally evaluated the effect of embolism on PA flow, which currently cannot be assessed with CT pulmonary angiography [13].

Walsh Score. This score has a maximum of 18 for both lungs. Different scores are given for filling defects and obstructions and for their anatomic locations. The following guidelines apply to embolic abnormalities:

(a) filling defects in a single segmental PA receive a total score that does not exceed 1, regardless of the type or number abnormalities;
(b) the total maximum score is 3 for abnormalities in a single upper lobar region, 2 for abnormalities in the middle lobe or lingula, and 4 for abnormalities in the lower lobes;
(c) obstructions in central anatomic regions receive scores according to the vessel involved;
(d) if the total score for one lung is greater than 4 without considering filling defects in central regions, the central filling defects are ignored. All filling defects in a single central region, whether single or multiple, receive a score of 3;
(e) if a single vessel contains both a filling defect and obstruction, only the obstruction is scored;
(f) the sum of scores for all abnormalities in one lung may not exceed a value of 9, and the maximum CT obstruction score is 18 [14].

Qanadli Score. The arterial tree of each lung is regarded as having 10 segmental PAs (3 to the upper lobes, 2 to the middle lobe or lingula, and 5 to the lower lobes). Similar to the Walsh score, the embolism of a segmental PA is scored as 1 point, and emboli at the more proximal arterial level are scored at a value equal to the number of segmental PAs arising distally. To provide additional information on the residual perfusion distal to the embolus, a weighting factor is used for each value (0 = no defect, 1 = partial occlusion, and 2 = complete occlusion) (Fig. 2, 3). An isolated subsegmental embolus is considered as a partially occluded segmental PA and is given a value of 1.The maximum CT obstruction index is 40 [15].

Mastora Score. This scoring applies to 5 mediastinal PAs (PA trunk, right and left PAs, and right and left interlobar PAs), 6 lobar PAs, and 20 segmental PAs (3 in the upper lobes, 2 in the middle lobe or lingula, and 5 in the lower lobes). The CT severity score is based on the percentage of obstructed surface of each central and peripheral PA section, and uses a 5-point scale (1 = < 25%, 2 = 25-49%, 3 = 50%-74%, 4 = 75%-99%, 5 = 100%.) A central score (mediastinal and lobar PAs), a peripheral score (segemental PAs), and a global score (central and peripheral PAs) can be calculated. The maximum CT obstruction score is 155 [16].

All the above-mentioned indexes enable a quantitative assessment of the severity of pulmonary embolism. For comparison between each of them, the scores can be expressed as a percentage of vascular obstruction, and calculated by dividing the patient's score by the maximum total score and multiplying the results by 100 (range 0%-100%).

Computed Tomography. In 1978, Sinner [17] first reported a case of pulmonary embolism on CT, and soon afterwards, in 1982, he reported a series of 21 consecutive patients with pulmonary embolism seen on CT. Subsequently, in 1980, Godwin et al. [18] reported embolism on CT in the central pulmonary arteries, and in 1984 Breatnach and Stanley [19] in the segmental pulmonary arteries. CT began to be used to evaluate the extent of pulmonary embolism in patients with known diagnosis of pulmonary embolism, but was not specifically used as a diagnostic test for pulmonary embolism until the advent of helical CT.

In 1992, Remy-Jardin at al. [20] reported the first prospective study comparing single-detector helical CT at 5-mm collimation with selective pulmonary angiography as the reference test in 42 patients with central pulmonary embolism. Their results – 100% sensitivity and 96% specificity – showed promise for the use of CT. Later, Teigen et al. [21,22] reported similar results on electron beam CT for the detection of central pulmonary embolism.

For single detector helical CT, sensitivity and specificity in the detection of PE have been reported from 53%-91% and from 78%-97%, respectively [23]. On the basis of another small prospective patient study by Goodman et al. [24], with separate analysis of 20 different arterial territories, 3-mm collimated helical CTA provided good interobserver agreement for the main, lobar and segmental level. However, dedicated analysis of the subsegmental territories had a high incidence of nonvaluable and poor interobserver agreement

Radiation exposure of helical CT is lower than that of classical pulmonary angiography [25]. Resten et al. [26] performed measurements of radiation dose using a predefined standardized CTA acquisition protocol, and compared the results with a standard selective pulmonary arteriogram using an anthropomorphic phantom and thermoluminescent dosimetry. An average dose was 4.375 times lower for CT (6.4+- 1.5 mGy vs 28+-7.6 mGy).

Multidetector CT (MDCT). MDCT scanners with 4, 8, 16, 32 and 64-detector-rows are now several years old. The collimation or slice thickness used today is commonly close to 1-mm, with subsecond gantry rotation speeds of 0.3 - 0.5 seconds, resulting in improved spatial and temporal resolution. The increased number of detectors also means faster scanning. Volume acquisition in MDCT scanner allows even imaging of the entire thorax in a single gantry rotation. Scan times range from 18-28 seconds on 4-MDCT, 8-13 seconds on 16-row MDCT, and 4-6 seconds on 64-MDCT [27].

Compared with single-slice CT, MDCT can more precisely delineate clots down to the subsegmental level: third subsegmental branches can be assessed with 4 × 2.5 mm collimation, and delineation of arteries down to the 5th and 6th order can be performed with 4 × 1 mm collimation [28]. Using thin sections (approx 1 mm) significantly improves interobserver agreement in detection of PE. Further combining such a dedicated examination protocol with additional 3D shaded-surface display reconstruction images allows precise anatomical analysis of peripheral pulmonary arteries [29].

Further advantages of CT include the ability to depict other conditions that clinically mimic PE: acute pneumonia, lung abscess, pneumothorax, pneumomediastinum, pleural or pericardial effusion, aortic dissection, cardiovascular disease, mediastinitis, mediastinal abscess, esophageal rupture,

malignancy and interstitial pulmonary fibrosis. In this respect, CT is better than V/Q scintigraphy, pulmonary angiography, and MR angiography. In addition, 64-detector scanners have the additional ability to detect coronary artery disease during the same study if the appropriate parameters are set. In 11%-70% of CT examinations performed for patients suspected of having acute PE [30-32], the other above conditions are found.

With multidetector CT, the reported sensitivity and specificity range from 83%-100% and 89%-97%, respectively [33-35]. In 2 studies each of fewer than 100 patients, sensitivities for the detection of PE with 4-slice CTPA have been reported to be 96% and 100%, with respective specificities of 98% and 89% [35-36]. PIOPED II was the largest and most significant study assessing the use of MDCT in the diagnosis of PE. In PIOPED II, the sensitivity of CTPA for PE was 83% and specificity 96%. In subjects in whom CTV was also performed, the combined sensitivity for PE and CTV was 90% and the specificity 95%.

In most protocols for helical CT of PE, the effective dose is between 3-5mSv, equivalent to 1-2 years exposure to background radiation. The cancer risk associated with this exposure would be approximately 150 excess cancer deaths per million people exposed to a single spiral CT examination for PE [37]. In a study by Kuiper et al., the average effective dose for 4-row multidetector CTPA was 4.2 mSv. In PIOPED II, the radiation dose to the chest using 16 and 64 detector CT scanners was estimated to be 3.8 mSv. More recently, Hurvitz et al. [38] reported the radiation dose from a 64-detector CTPA protocol with an anthropomorphic female phantom to be 19.9+1,38 mSv. They also estimated that the lifetime attributable risk (LAR) of lung cancer ranged from 38 excess casses per 100,000 in 55-year-old men, or 51 excess cases per 100,000 in 25-year-old-men, to 86 excess cases per 100,000 in 55-year-old women, or 118 excess cases per 100,000 in 25-year-postparum women. In addition, the LAR of breast cancer ranged from 20 excess cases per 100,000 in 55-year-old-women, or 503 excess cases per 100,000 in 25-year-old postpartum women [38]. Although radiation exposure is greater with the use of MDCT, the benefit is improved visualization of the segmental and subsegmental pulmonary arteries and greater accuracy for PE diagnosis.

Table 1 Evolution of CT Protocol Pulmonary angiography with Increasing Detector Rows.

CT Parameter	Single-Detector CT	4-MDCT	8-MDCT	16-MDCT
Reconstruction	3	1.25	1.25	1.25
Table speed (mm/rotation)	1.6	7.5	13.5	13.75
Pitch	1.3-1,6	1.5	01:35:01	1.375:1
Peak voltage(kVp)	120	120	140	140
Current(mA)	240	400	Maximum	Maximum
Time per rotation (sec)	1	0.8	0.5	0.5
Volume of contarst material injection	150	135	135	135
Injection rate(ml/sec)	4	4	4	4
Scan coverage	12 cm	Entire chest	Entire chest	Entire chest

Table 2 Sensitivity and specificity of individual investigations.

First author (Ref)	Detectors	Collimation (mm)	Sensitivity n/N(%)	Specificity N/N (%)
Blachere(15)	1	2 or 3	64/68(94)	104/111(94)
Coche(25)	4	1	27/28(96)	65/66(98)
Garg(17)*	1	3	4/7(57)	18/18(100)
Goodman(13)	1	5	7/11(64)	8/9(89)
Kim(18)	1	3	23/25(92)	75/78(96)
Mayo(19)	1	3	40/46(87)	88/93(95)
Otmani(20)	1	5	41/50(82)	22/22(100)
Pruszczyk(21)	1	5	17/17(100)	6/6(100)
Sostman(22)	1	5	10/13(77)	13/15(87)
Van Rossum(24)	1	5	64/68(94)	78/81(96)
Van Strijen(27)	**1,2**	**3**	**117/135(87)**	**106/117(91)**
Velmahos(14)	1	3	6/15(40)	20/22(91)
Winer-Muram(26)	4	2,5	18/18(100)	67/75(89)

* Garg had only patients with intermediate V-Q

Indirect CTV. In 90% of patients with PE the source of the emboli are the lower-extremity veins (i.e. DVT). Combined CTPA and CT venography (CTV) is a single examination without requiring any additional intravenous contrast material that combines multidetector CTPA and CTV of the abdomen, pelvis and lower extremities. It adds only a few additional minutes to the scanning time [39, 40]. Performing CTPA combined with CTV was first described by Loud et al. in 1998. Some investigators have reported a high degree of accuracy (sensitivity varies between 71-97% and specificity between 93-100%) when CTV is compared to venous US [41, 42]. Combined CTPA and CTV will save time and inconvenience to patients as they do not have to go through different time-consuming examinations.

However, combined CTPA and CTV increase the radiation exposure and associated risks of late stochastic effects. It exposes the patients' gonads to a radiation dose of the order of 2.1-10.7 mSv, with variation between individuals and sex. [33]. The addition of indirect CTV increases the gonad radiation dose by 500-2,000-fold compared to CTPA alone.

Several studies have shown that the addition of CTV to the CTPA examination increases the percentage of patients requiring anticoagulation by 5-27% [43, 44]. A further advantage of CTV is the ability to evaluate the pelvic and abdominal veins not always assessable to ultrasound, specifically the inferior vena cava and iliac veins. Indirect CT venography may be performed as contiguous helical imaging or discontinuous CT imaging of the lower extremities for the detection of DVT.

Interobserver agreement for DVT on CT venography is moderate to almost perfect with kappa values of 0.56-0.88. When the use of CT is compared with sonography or coonventional venography, there is moderately good to almost perfect interobserver agreement, with reported kappa values of 0.59-0.88 [45, 46].

Table 3 Sensitivity, specificity, PPV, NPV the computed tomography venography (CTV) alone and CTV combined with sonography or conventional venography.

		CTV	CTV with sonography or conventional venography
1	Sensitivity	71-100%	94.50%
2	Specificity	94-100%	98.20%
3	PPV	67-100%	-
4	NPV	97-100%	-

Table 4 Concordantly and discordantly high, low and intermediate probability on clinical assessment in CTPA with CTV and in CTPA without CTV.

		CTPA with CTV	CTPA without CTV
1	Concordantly high probability on clinical assessment or NPVs	96.00%	96.00%
2	Intermediate probability on clinical assessment	89.00%	92.00%
3	Concordantly low probability on clinical assessment	96.00%	97.00%
4	Discordantly high probability on clinical assessment	60.00%	82.00%
5	Intermediate probability on clinical assessment	92.00%	90.00%
6	Discordantly low probability on clinical assessment	58.00%	57.00%

As CTV has the limitation of additional radiation dose, Doppler ultrasound should be considered in younger patients. Estimates of pelvic radiation vary considerably according to the specific CTV protocol used. In PIOPED II, the calculated radiation doses to the pelvis, and thighs were 6.0, and 3.2 mSv, respectively [33]. Kava et al. showed that the effective radiation dose for CTV was 5.2 mSv+ 0.5 SD for the pelvis, and 0.6 mSv + 0.2 SD for the lower extremities, and suggested that CTV should be limited to the lower extremities to reduce overall radiation dose.

Goodman et al., using data from 150 PIOPED II subjects, compared whether discontinuous incremental CT of the lower extremities, with skip areas between images, is as accurate as contiguous helical scanning for the detection of DVT. They found that there was agreement for the presence of DVT in at least one leg (same leg), or for the absence of DVT in both legs in 133 of the 150 study patients (89%). The authors concluded that although there was good agreement between continuous helical and discontinuous axial imaging for the detection of DVT, given the interobserver and intraobserver variation, there appeared to be little difference between the 2 approaches, supporting the use of adopting discontinuous imaging as a dose-reduction strategy.

Preference. In a recent survey among physicians practicing in the United States of imaging practices for diagnosing acute PE that explored factors associated with practice decisions, Weiss and co-workers surveyed 855 physicians selected at random from membership lists of 3 professional organizations (general internists, pulmonologists, and emergency medicine specialists) by mail. Completed questionnaires were received from 29.8% participants practicing in 44 States. The authors found that 86.7% of respondents believed that CTPA was the most useful imaging procedure for patients with acute PE, compared with 8.3% for V/Q lung scintigraphy, and 2.5% for conventional pulmonary angiography [46]. After chest radiography, CTPA was the first imaging test requested 71.4% of the time, compared with 19.7% for V/Q scintigraphy and 5.8% for lower-limb venous ultrasound. The respondents reported that they received indeterminante or inconclusive results 46.4% of the time for V/Q scintigraphy, 10.6% of the time for CTPA , and 2.2% of the time for conventional pulmonary angiography. With respect to availability, 88.3% of respondents reported that CTPA was available around the clock versus 53.8% for V/Q scintigraphy and 42.5% for conventional pulmonary angiography. 68,6% of respondents reported that they received CTPA results in 2 hours or less versus 37.5% for V/Q scintigraphy and 22.9% for conventional pulmonary angiography. CTPA was also reported to provide an alternate diagnosis to PE or showed other significant abnormalities 28.5% of the time, and these findings frequently altered management. The authors of this study concluded that US clinicians unequivocally prefer CTPA in patients with suspected acute PE. The reasons for this preference included availability and timely reporting, a lower rate of inconclusive results, and the additional diagnostic capabilities that CTPA can provide.

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