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ORIGINAL ARTICLE

Dots are not clots: the over-diagnosis and over-treatment of PE

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Abstract The purpose of this work is to question the conventional theory that all pulmonary emboli (PE) are abnormal, and to test the hypothesis that small peripheral PE are a function of life. Most radiologists report any filling defect, independent of size, as clinically significant PE when detected in the pulmonary arteries. We sought to reinforce the theory that small dots in the pulmonary arteries are not clinically significant clots in the conventional setting. The necessity for anticoagulation should be balanced against the risk of bleeding. This retrospective HIPAA-compliant study was approved by the institutional review board; informed consent was not required. All patients diagnosed with PE by 16-slice or 64-slice multidetector computed tomography (CT) over a 6-month period who also had a lower extremity venous ultrasound (US) performed within 7 days of CT were identified. The study group included 26 women and 24 men (mean, 56 years; range, 21–90 years). The locations of the PE were plotted on a pulmonary arterial diagram, and width of the most proximal clot for each patient was measured. Of 1,273 consecutive CT studies, 101 were positive (7.9%) and 50 patients underwent lower extremity US. Thirty-three (66%) patients had PE in the central pulmonary arteries, of which 19 (58%) had deep vein thrombosis (DVT). Seventeen (34%) patients had peripheral PE; DVT was detected in 0 (0%) patients. The peripheral clots measured 1.0–3.8 mm (mean, 2.5 mm). These clots appeared focal and rounded with a "dot-like" appearance. Peripheral, focal filling defects in the pulmonary arteries, which we termed "dots," are not traditional embolic clots, are not associated with detectable lower-extremity clot load, and may represent "normal" embolic activity originating from the lower extremity venous valves. We suggest that more in-depth understanding about small peripheral PE is needed. The necessity of conventional anticoagulation should be critically reviewed in patients with subsegmental PE and minimal clot burden.

Keywords DVT · Pulmonary embolus · CT pulmonary embolus

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Introduction

Pulmonary embolism (PE) is a common disorder with an annual incidence of 23–69 per 100,000 [1, 2]. The overall age- and gender-adjusted annual incidence of venous thromboembolism (deep vein thrombosis [DVT] and PE) is estimated to be 1.17 per 1,000 [1], and extrapolation to today's population suggests more than 350,000 adults are affected in the USA [3].

Multidetector computed tomography (CT) angiography is the imaging modality of choice for the detection of suspected PE. Recent studies have demonstrated high accuracy of multidetector CT in the detection of PE with sensitivity and specificity of 83–100% and 89–97%, respectively [4–6]. Multidetector CT offers significant improvements in spatial and temporal resolution, decreased section thicknesses, faster scan times, and shorter breath holds. These advancements allow routine visualization of segmental and even subsegmental pulmonary arteries [7–9]. In the Emergency Department setting, multidetector CT has replaced the ventilation–perfusion (V/Q) scan as the initial imaging study in the work up of suspected PE.

The increased use of CT in patients clinically suspected for PE has led to a marked increase in the diagnosis of PE without change in mortality [10]. Reports of incidental PE detected in 1.0–5.7% of patients

undergoing contrast-enhanced multidetector CT scanning of the chest for various clinical indications suggest we are diagnosing PE previously undetected by V/Q scintigraphy or single-detector helical CT [11–14].

Conventional teaching to medical students, Emergency Medicine, and Radiology residents states that all PE are abnormal. The purpose of this study was to question the old wisdom and test the hypothesis that it may be normal to find peripheral clots in pulmonary arteries—i.e., small peripheral PE are a function of life.

Materials and methods

This HIPAA-compliant study was approved by the institutional review board; informed patient consent was not required. We retrospectively identified all contrast-enhanced CT pulmonary angiographic studies performed for suspected PE at our institution between July 16, 2007, and December 31, 2007 (n=1,273). Of the 1,273 CT studies, 101 (7.9%) were positive for PE. For patients who underwent multiple CT examinations, only the first scan was included to ensure each patient appeared once in the study group. Studies initially considered positive for PE but concluded negative upon subsequent review were excluded from the study (n=2). In addition to the positive CT study, inclusion in the study required a lower-extremity venous ultrasound performed within 7 days of the CT (n=50). Fifty CT studies in 50 patients constituted the study group. Mean patient age was 56 years (age range, 21–90 years). There were 26 women (mean age, 61 years; age range, 21–90 years) and 24 men (mean age, 51 years; age range, 27–83 years) in the study.

All CT studies were obtained with a 16-slice CT scanner (Siemens Somatom Sensation 16, Siemens USA, Malvern, PA, USA; GE Lightspeed 16, GE Medical Systems, Milwaukee, WI, USA; GE Lightspeed Pro 16, GE Medical Systems) or 64-slice CT scanner (GE Lightspeed VCT, GE Medical Systems). The acquisition parameters on the 16-slice scanners were: 1.25–1.5 mm×16 collimation; 0.75–0.8 s rotation time; pitch of 1.25–1.75:1.0. The acquisition parameters on the 64-slice scanner were: 0.625 mm×64 collimation; 0.8 s rotation time; pitch of 1.375:1.0. A volume of 100 mL of low-osmolar contrast material was injected at a rate of 4 mL/s with a scan delay of 22 s. Images were reconstructed to 2–2.5-mm slices for interpretation on a picture archiving and communication system (PACS) workstation.

Images from each CT examination and venous ultrasound study were independently reviewed at a dedicated PACS workstation by two board-certified radiologists (J.J.C., T.T. H.), who were blinded to the original imaging report and clinical history. CT exams were assessed for the presence of PE, defined as a low-attenuation complete or partial defect within the pulmonary arterial vasculature. The locations of the clots were plotted on a diagram of the pulmonary arterial tree, as seen in Fig. 1 [15]. The width of the clot located at the most proximal level of the vessel was measured and recorded. Patients were divided into two groups (classic emboli and "dots") based on location, size, and quality of clots. Venous US exams were assessed for the presence of DVT, seen as complete or partial filling defects in the veins with lack of vessel compressibility.

Medical records were analyzed, and the following information was collected for each of the 50 patients: (a)

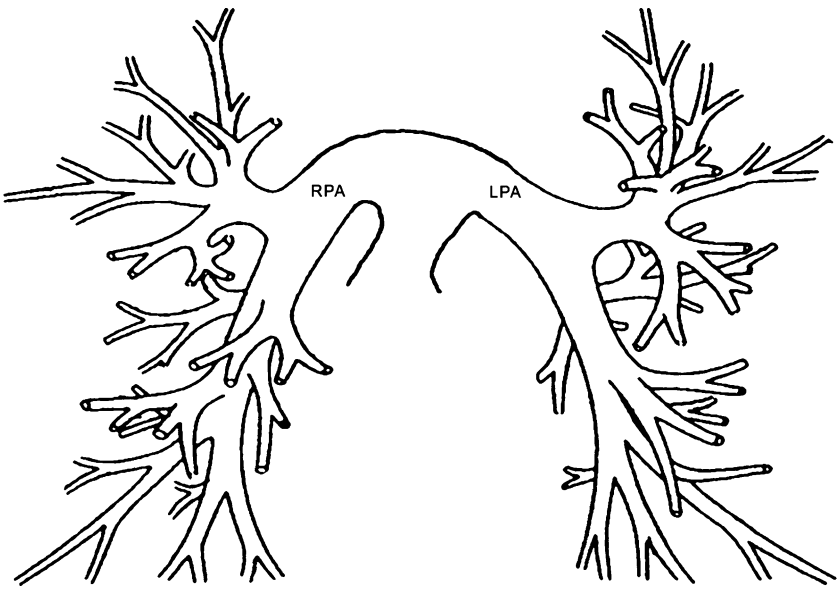

Fig. 1 Diagram of the pulmonary arterial tree. *RPA* right pulmonary artery, *LPA* left pulmonary artery

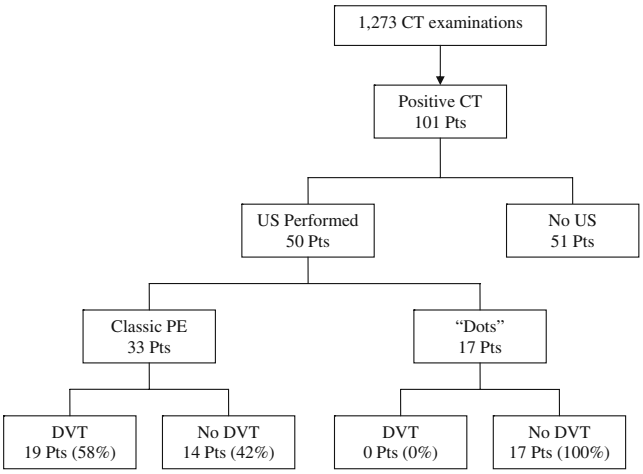

Fig. 2 Figure demonstrating prevalence of PE detected by multidetector CT and DVT assessed by lower extremity venous US

anticoagulation therapy received (yes or no) and (b) risk factors for venous thromboembolism (i.e., history of PE and/or DVT, cancer, recent surgery, trauma, hypercoagulable state, and prolonged immobilization). The rates of DVT in patients with classic PE and patients with "dots" were compared using the chi-square test.

Results

The results are summarized in Fig. 2 and Table 1. A total of 1,273 consecutive CT angiographic studies were performed at our institution during the 6-month study period. Of these studies, 101 (7.9%) were positive, and 50 patients underwent lower-extremity venous ultrasound examination within 7 days of the CT.

Table 1 Characteristics of 50 study patients with PE

Patient characteristic	Number of patients (%)
Sex	
Female	26 (52)
Male	24 (48)
Anticoagulation received	
Yes	48 (96)
No	2 (4)
Risk factors	
History of PE and/or DVT	10 (20)
Cancer	12 (24)
Recent surgery	11 (22)
Prolonged immobilization	9 (18)
Trauma	1 (2)
Hypercoagulable state	2 (4)
Other	5 (10)

The study population was divided into two groups according to the location, size, and quality of the most proximal PE in each patient. In 33 patients, an extensive clot load was detected in the central (main, lobar) pulmonary arteries, and termed classic PE. Among the 33 patients with classic PE, 19 (58%) were diagnosed with DVT at lower-extremity compression venous ultrasound. All thirty-three (100%) patients received anticoagulation treatment. Characteristics of the patients with classic PE are summarized in Table 2.

In 17 patients with diagnosed PE, small clots ("dots") were found in the peripheral pulmonary arteries (segmental, subsegmental, and distal fifth-order branches). None of these patients had DVT. Figure 3 illustrates the locations of the most proximal "dots." The average width of the most proximal PE in this group of 17 patients was 2.5 mm (range, 1.0–3.8 mm). These 17 patients had clots that were noted to have blood flowing around them and, except in the most terminal branches, were focal, rounded, and had a "dot-like" appearance. Fifteen (88%) patients received anticoagulation treatment. Characteristics of the patients with "dots" are summarized in Table 3.

The prevalence of DVT was 58% (19/33) in the patients with classic PE vs 0% (0/18) in the patients with "dots" ($P < 0.01$) (Table 4). One hundred percent (33/33) of the patients with classic PE received anticoagulation, vs 88% (15/17) of the patients with "dots" ($0.10 > P > 0.05$) (Table 5).

Discussion

This retrospective review demonstrated the prevalence of PE, lower-extremity DVT, and administration of

Table 2 Characteristics of 33 patients with classic PE

Patient characteristic	Number of patients (%)
Sex	
Female	16 (48)
Male	17 (52)
Anticoagulation received	
Yes	33 (100)
No	0 (0)
Risk factors	
History of PE and/or DVT	6 (18)
Cancer	8 (24)
Recent surgery	9 (27)
Prolonged immobilization	6 (18)
Trauma	0 (0)
Hypercoagulable state	2 (6)
Other	2 (6)

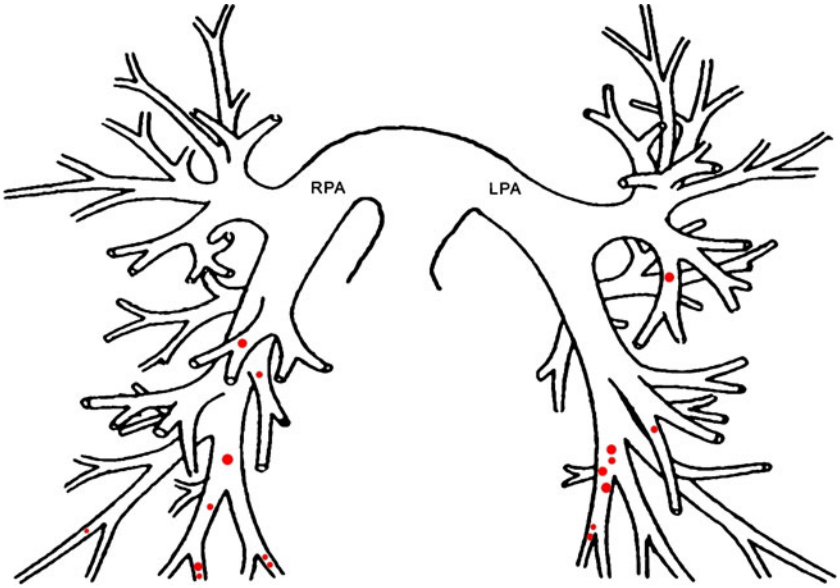

Fig. 3 Most proximal clot found in each of the 17 patients with "dots." *RPA* right pulmonary artery, *LPA* left pulmonary artery

anticoagulation treatment in a study population of 50 patients selected from 1,273 consecutive CT angiographic examinations performed over a 6-month period. From the clinical perspective, all these cases were treated similarly with anticoagulation.

Our results characterized a subset of patients with small peripheral PE, leading us to support the theory that small peripheral PE are "dots" rather than "clots" in the traditional sense. We propose that these account for the "incidental" PE reported by others.

None of the patients with "dots" in our study also had DVT, compared to 58% of patients with classic PE (large tubular-filling defects involving the proximal pulmonary vasculature). The difference in prevalence of DVT was statistically significant ($P<0.01$). Conventional theory says PE is essentially a consequence of DVT. In our study, "dots" (average clot width, 2.5 mm; range, 1.0–3.8 mm) were not associated with detectable clot load in the lower extremities. The absence of lower-extremity DVT suggests that the passing of small clots from the lower-extremity valves to the lungs is a physiologic process with the lung capillary beds trapping and dissolving the emboli by endogenous fibrinolysis, thereby protecting the systemic circulation. We believe that "dots" may represent "normal" embolic activity originating from the lower-extremity venous valves [16].

Advancements in CT technology have greatly impacted the ability to diagnose PE. Pulmonary angiography has traditionally been the gold standard, but multidetector CT now allows the visualization of the segmental and subsegmental arteries, leading to improved visualization and diagnosis of peripheral PE. Recent studies reported frequencies of isolated subsegmental PE ranging from 1.0% to 5.4% in study populations of patients clinically unsuspected for PE [11–14]. In contrast, our study reflected a prevalence of 34% in "dots." We believe the difference in prevalence may be attributable to differences in CT technology as those studies used single-, four-, eight-, and 16-slice CT scanners compared to the 16- and 64-slice CT scanners in our study. The higher prevalence of "dots" may be due to the improved image quality provided by these scanners. These "dots" may well be incidental and, with prior imaging such as V/Q scan and four-slice screening, have been too small to be visualized.

In 1993, Gurney asked, "If small emboli are missed at pulmonary angiography, what are the consequences for the patient?" [17]. Patient outcome studies at that time

Table 3 Characteristics of 17 patients with "dots"

Patient characteristic	Number of patients (%)
Sex	
Female	10 (59)
Male	7 (41)
Anticoagulation received	
Yes	15 (88)
No	2 (12)
Risk factors	
History of PE and/or DVT	4 (23)
Cancer	4 (23)
Recent surgery	2 (12)
Prolonged immobilization	3 (18)
Trauma	1 (6)
Hypercoagulable state	0 (0)
Other	3 (18)

Table 4 Prevalence of DVT in patients with classic PE and in patients with "dots"

	Classic PE	"Dots"
DVT	19 (58%)	0 (0%)
No DVT	14 (42%)	17 (100%)

demonstrated few adverse outcomes for patients with negative pulmonary angiograms [18, 19]. More recently, Goodman has stated that "[i]t is not always clear whether small PE, in the absence of demonstrable DVT, justify the expense, mortality, and serious morbidity associated with anticoagulation" [20]. The Fleischner Society also noted that "[t]he clinical relevance of small peripheral PE and the need to administer anticoagulants in such cases remain a subject of debate" [21].

The risks associated with anticoagulation, as well as the burden of carrying a diagnosis of prior PE may outweigh the benefits of treatment for these patients. A meta-analysis of 33 studies investigating patients with venous thromboembolism who received oral anticoagulant therapy for at least 3 months with a target international normalized ratio, 2.0 to 3.0, revealed a major bleeding rate of 13.4% per 100 patient-years of treatment [22]. In our study, there was no statistical difference ($0.10>P>0.05$) in the treatment between patients with classic PE and patients with "dots." We sense that referring physicians employ a binary evaluation and do not factor the size or position of clot into determining the need for treatment. The suggestion that small peripheral emboli may have little consequence continues to be worthy of discussion today in light of improving technology and questions regarding "dots."

Mainstream understanding by practicing radiologists and Emergency Medicine physicians suggests that all clots are equal and are treated the same with anticoagulation. Certainly, subspecialty studies in the thromboembolic literature suggest that some PE may be normal. We propose that these peripheral "dots" are clots, but not the clots we are significantly concerned about. At a minimum, a discussion between the radiologist and referring clinicians should ensue when "dots" are detected. Do the risks of anticoagulation justify its use when a "dot" is detected? Are we treating a normal development of the coagulation system?

One possible limitation to this study is its retrospective design. Our data reflected the prevalence of PE and DVT and characterized the clots in patients at a single urban acute care hospital and do not necessarily project to other clinical settings. A prospective study may be of use to confirm this data and further characterize patients with "dots."

Table 5 Frequency of anticoagulation treatment received by patients with classic PE and by patients with "dots"

	Classic PE	"Dots"
Anticoagulation	33 (100%)	15 (88%)
No Anticoagulation	0 (0%)	2 (12%)

In conclusion, there is clearly a spectrum of embolic disease in the lung—i.e., all PE are not equal. Of the 50 patients with positive CT at our institution over a 6-month period, 17 patients (34%) had "dots." The majority of these 17 patients (88%) received anticoagulation, although they were not found to have DVT at lower-extremity ultrasound. We learned that "dots" are far more common today due to advancements in CT technology, and we will need further studies to determine their significance.

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