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Review Article

Subsegmental pulmonary embolism: A narrative review☆

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ABSTRACT

Through the introduction of computed tomography pulmonary angiography (CTPA) for diagnosis of the pulmonary embolism (PE), the high sensitivity of this diagnostic tool led to detecting peripheral filling defects as small as 2–3 mm, termed as subsegmental pulmonary embolism (SSPE). However, despite these substantial increases in diagnosis of small pulmonary embolism, there are minimal changes in mortality. Moreover, SSPE patients generally are hemodynamically stable with mild clinical presentation, lower serum level of biomarkers, lower incidence of associated proximal DVTs and less frequent echocardiographic changes compared to the patients with emboli located in more central pulmonary arteries. However, the pros and cons of anticoagulant therapy versus non-treating, monitoring protocol and exact long term outcome of these patients are still unclear. In this article we review existing evidence and provide an overview of what is known about the diagnosis and management of subsegmental pulmonary embolism.

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1. Introduction

Acute Pulmonary embolism (PE) is a relatively common and potentially life-threatening disease with yearly incidence of ~2% and 30-day mortality rate of near 10% [1,2]. Nevertheless, despite the traditional fear from acute PE and along with advances in computed tomography pulmonary angiography as the main diagnostic tool for PE, there is also increasing concern about overdiagnosis and overtreatment [3–5]. Since the introduction of computed tomography pulmonary angiography(CTPA) in late 1990s, there has been a revolution in diagnostic approach to patient with suspected PE. Along with significant(81%)increase in incidence of PE [6],the high sensitivity of CTPA has led to the detection of filling defected in arteries as small as 2–3 mm in diameter, termed as subsegmental pulmonary arteries [4,7]. The rate of subsegmental pulmonary embolism (SSPE) diagnosis varies among positive CTPAs from 4.7% (95% Confidence interval [CI]: 2.5–7.6) by single-detector CTPA (SDCT), to 15.0% (95% CI: 7.7–24.1) by 64 slice multi-detector CTPA (MDCT) [8]. However despite these substantial increases in diagnosis, there are

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minimal changes in mortality [6]. Considering that treatment of PE is not risk-free and could even have fatal complications, there is increasing concern about the practical significance of detecting isolated SSPE by CTPA. Being a modality of too high sensitivity does not always imply that the modality is so good. We have encountered a few patients with over-diagnosis of acute pulmonary embolism following availability and excessive use of multidetector CT angiography in our center (Fig. 1). If the consequence and the burden of over-diagnosis is considerable, the elected modality should present high accuracy [4]. In this article we review the existing evidence about the diagnosis and management of subsegmental pulmonary embolism.

2. Anatomy

Pulmonary artery divides repetitively alongside the bronchial divisions from the main pulmonary artery which is the first order down to branches to form the alveolar capillaries. The second order is the lobular artery and then the segmental arteries. Each segmental artery divides into at least two smaller arteries, the subsegmental arteries (fourth order) with diameter of about 3 mm, which branch into fifth order subsubsegmental arteries. Almost all of the subsegmental and the majority of the subsubsegmental arteries are visible in the current CTPAs. Nevertheless, relatively poor inter-observer agreement has been reported for subsegmental and/or small pulmonary artery defects [9,10]. Scanning time for 4-row, 16-row, or 64-row scanner is about 10–12 s, during which the patient should tolerate holding her breath while 0.5–1 mm continuous slices are imaged throughout the lung fields [11]. For the imaging of PE in small pulmonary arteries, accurate timing between the imaging and injection is crucial something that is not always achievable.

3. Clinical characteristics

Although the most common presenting symptom of central pulmonary emboli is dyspnea, pain is the most common symptom in subsegmental and segmental pulmonary embolism [12,13]. In SSPE, incidental CT findings (with no clinical presentation attributed to PE) are more prevalent and proximal DVTs are less common as compared to the emboli located in more central pulmonary arteries [13]. Moreover, patients with subsegmental and segmental pulmonary emboli have lower serum levels of biomarkers, less frequent electrocardiographic change and higher PaO_2 and O_2 saturation [13]. Generally, patients with SSPE are hemodynamically stable and the echocardiography does not show RV dysfunction.

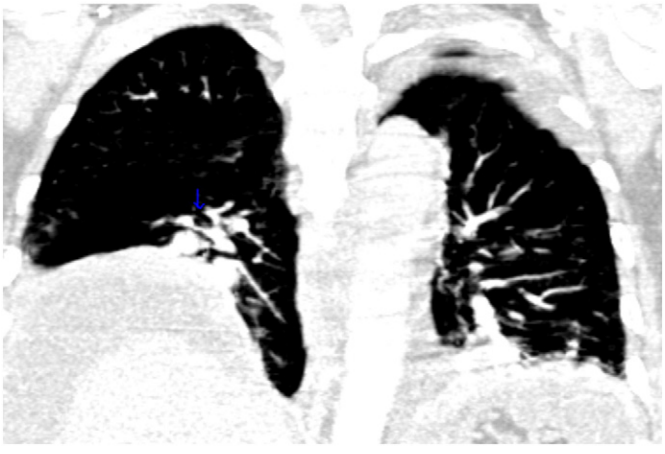

Fig. 1. Coronal reconstruction of the CT angiography of a patient aged 54 case of ovarian cancer with metastases to the liver and peritoneal seeding. She experienced dyspnea and CT angiography illustrated clot a subsegment of posterior basal segmental artery of the right lower lobe (blue arrow). Lung perfusion scan was reported "negative for acute PTE based on PISAPED criteria" and the symptoms relived after supportive treatment and peritoneal paracentesis without anti-coagulation. She is now on close medical follow-up.

4. Advances in the computed tomography and improvement in diagnosis

CTPA virtually replaced ventilation–perfusion scan(V/Q scan) [14] after rather poor diagnostic performance presentation of the employed interpretation criteria in the original PIOPED study [15] and the fascinating results of the PIOPED II study [16], illustrating the superior performance of CTPA as well as the possibility to detect alternative diagnosis [2]. However, after the improvement of imaging techniques, new clinical challenges arise. The main concerns here are the high radiation dose to the patient and the side effects of contrast use [3,17]. Alternatively, it was shown in selected suspected PEs that V/Q scan and CTPA demonstrated equal false negative rate at 3 months with almost thrice PE diagnoses with CTPA suggesting over-diagnosis [18]. Such concerns brought the V/Q scan back into the diagnostic algorithms, endorsing V/Q scintigraphy as being as accurate a diagnostic tool as CTPA [19].More sensitive detectors, delicate computer systems and SPECT imaging were added into the diagnostic yield of the perfusion scan and reducing the need for ventilation scan [20,21]. Furthermore, the hybrid SPECT/CT imaging overcame the major drawback of the perfusion scan that is lack of parenchymal data to assess alternative diagnoses [22]. As a result of routine use of CTPA, the detection of SSPE is increasing but the clinical relevance is uncertain [23]. The rate of SSPE is twice as high for MDCT as compared to previously used SDCT pulmonary angiography [3,6].The 3-month incidence of VTE was similar for patients without anticoagulant with either normal single-detector or multi-detector CT scan results [24].

The safety of discontinuing anticoagulant in patients in whom pulmonary emboli was excluded by CTPA has been assessed in some studies [25,26]. In a meta-analysis, among 3089 patients in which PE was excluded by CTPA with or without lower extremities Doppler Ultrasonography(DUS), 3-month VTE rate was 1.2% (95% CI: 0.8–1.8)and 1.1% (95% CI: 0.6-2.0) respectively [27].

Excessive fear from PE together with more availability of CTPA lead to another concern about the overuse of this imaging modality. Adams et al. [28] found that among 3500 requested CTPA, only 1592 (45.5%) followed the recommendations of PIOPED II investigators. Loyalty to pretest clinical prediction rules and D-dimer testing decrease the overutilization of this imaging modality and probably prevents discovering clinically in significant small PE [29,30].

Multi detector CTPA has improved the sensitivity for detection of the pulmonary embolism and the detection of SSPE has undoubtedly been increased [7,31]. Despite the increase in PE detection, mortality rates remained unchanged [6]. This evidence suggests that the additional cases of PE detected by newer CT generations might be associated with a much more favorable outcome [3,32].

5. SSPE and deep vein thrombosis

There is existing evidence that the presence of concomitant DVT is an independent prognostic factor in patients with PE [33–35]. In a study of 707 patients with a first episode symptomatic acute PE, all-cause mortality was significantly higher in patients with concomitant DVT (hazard ratio [HR]: 2.05; 95% CI, 1.24 to 3.38; $P = 0.005$). PE-specific mortality was also higher in this group (HR: 4.25; 95% CI, 1.61 to 11.25; $P = 0.04$) [34]. Meanwhile in another study [36], concomitant proximal DVT in patients with SSPE was lower than those with more central PE (7.1%; 95% CI, 1.2–31.5% vs. 41.8%; 95% CI, 34.5–49.1%). Accordingly, the lower incidence of DVT in patients with SSPE possibly will point to a more favorable outcome with fewer upcoming thromboembolic recurrence. So it is prudent to exclude