MDCT pulmonary angiography in patients with suspected pulmonary embolism in the emergency department: correlation of presence and distribution with D-dimer levels

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Pulmonary Embolism (PE) is reported as the third most frequent cause of cardiovascular disease [1] and it may be also lethal in the acute phase or lead to chronic disability. According to an epidemiological model, over 317'000 deaths were related to VTE (deep vein thrombosis/DVT and PE) in six countries of European Union in 2004, 34% of which presented with sudden fatal PE [2]. Otherwise, patients surviving the acute phase could develop Chronic Thromboembolic Pulmonary Hypertension (CTPH), a debilitating disease caused by chronic obstruction of major pulmonary vessels; it occurs in approximately five individuals per million population per year [3]. Overall annual incidence of PE has been reported of about 100-200 per 100000 inhabitants [1]; however, the real epidemiology is difficult to determine since a prompt diagnosis may be missed due to non-specific clinical signs and symptoms [4].

The combination of clinical evaluation and probability scores (Wells’ rule, PERC rule, revised Geneva score) [5-7], D-dimer measurements and imaging tests (echocardiography, chest X-ray, MDCT pulmonary angiography) have been widely proposed and then validated for PE diagnosis [8].

D-Dimer generally represents the first diagnostic step in patients with acute dyspnea and suspected PE in the Emergency Room because its concentrations are highly sensitive for thrombus formation. Actually, patients with a high clinical probability of PE do not require a D-dimer test and, therefore, imaging evaluation becomes warranted in order to rule out PE, regardless D-dimer results. Conversely, D-dimer test is useful to exclude venous thromboembolism (either as pulmonary embolism or DVT) in suspected cases in patients with a non-high clinical probability [9]. On the other hand, D-dimer specificity tends to steadily decrease with age (to almost 10% in patients of 80 years old) [10] and in a wide variety of clinical conditions such as cancer, trauma and recent surgery. Therefore, the role of D-dimer testing may be limited to some cases of suspected PE: above its elevated predictive negative value, D-dimer levels > 5000 ng/L represent a good predictor of central PE, according to recent studies.

MDCT pulmonary angiography (CT-PA) is the fundamental imaging test for PE diagnosis: it has high spatial and temporal resolution and allows obtaining proper vessels opacification, useful for adequate visualization of pulmonary arteries down at least to more distal branches [11]. It can also show the presence of right heart thrombi and detect any potential right ventricle enlargement, that might lead to right ventricular dysfunction, an独立的 predictor for adverse in-hospital outcome in patients with PE [12]. MDCT positive predictive value is lower in patients with a low clinical probability of PE, as compared to those with intermediate and high probability (58% vs 92% and 96%, respectively) [13]. Further testing may be considered, especially when thrombi are limited to segmental or sub-segmental arteries. Moreover, the definition of sub-segmental PE has yet to be standardized.
On these bases, the purpose of our study was to retrospectively evaluate any potential correlation between D-dimer levels and PE presence and distribution at CT-PA in patients with an intermediate-high pre-test probability of PE.
Methods and materials

We retrospectively evaluated a total of 94 patients (mean age 62.7±19.1 years; 52 females), who underwent between January and December 2015, in the Emergency Department, a CT-PA study on a 16-row scanner for suspected PE. The suspicion of PE was generally based on the acute onset of symptoms like dyspnea, chest pain and fatigue, especially in old-aged patients with clinical history of immobilization, DVT, recent surgery and cancer. Patients with no diagnostic CT-PA and/or no D-dimer results available on hospital records were excluded.

CT-PA was performed using a tube current time of 110 mAs, a pitch of 0.9, a collimation value of 1 mm and a reconstruction slice-thickness of 2-3 mm. Unenhanced examinations were generally not performed and the acquisition included a single post-contrast scan. About 60-90 mL of non-ionic iodinated contrast media (350 mg iodine/mL) were intravenously infused at a standard injection rate of 3.5-4 mL/sec (if a proper peripheral vein was available). Bolus tracking technique was employed, setting a threshold of 120-150 HU in a region of interest (ROI) placed in common pulmonary artery. Images acquisition proceeded with a cranio-caudal direction. Multiplanar (MPR) and, occasionally, maximum intensity projection (MIP) reconstructions were performed, providing a better visualization of distal pulmonary branches and also allowing to detect sub-segmental thrombi in some cases.

Negative and positive PE cases were distinguished. Positive CT-PA results were then recorded as PE distribution in pulmonary branches as follows: central, segmental and sub-segmental [14]. Then, for every patient we correlated the CT-PA results with D-dimer levels, setting as cut-off values < and > 5000 ng/L [15].

For every patient included, hospital records were also analyzed; clinical and anamnestic data at the time of Emergency Room visit were reported. Data collection included also demographics, clinical history (DVT, recent surgery or immobilization), chest X-ray main findings, sPESI (simplified Pulmonary Embolism Severity Index, a clinical score which defines a 30-days mortality risk) and Well's score (a clinical score stating the pre-test probability of PE).
Results

PE was present in 30/94 patients (32%). In 25/30 (83%) D-dimer was > 5000 ng/L: 17/25 (68%) patients had a central PE pattern (Figure 1) while 5/25 (20%) demonstrated a segmental involvement. As shown in Table 1, in 5/30 (17%) cases D-dimer was < 5000 ng/L: 3 patients had a D-dimer range of 3000-4000ng/L and segmental PE (Figure 2) while 2 with sub-segmental pattern presented a range of 1000-2000 ng/L (Figure 3). Moreover, in 7/25 patients with D-dimer > 5000 ng/L (5 central and 2 segmental PE) chest X-ray revealed cardiomegaly and prominent vascular marking (Table 2 and Figure 4).

In 12 patients both with D-dimer levels > 5000 ng/L and negative CT-PA, final alternative diagnoses were mainly related to cardio-aortic diseases and DVT, without known history of active/recents cancer or recent surgery. The majority of patients (90%) with D-dimer levels < 5000 ng/L had no signs of PE on CT-PA and the main diagnosis was acute heart failure.
Table 1: Table 1. D-dimer values ranges (<2000, 2000-5000, >5000 ng/L) and relation to specific distributions of pulmonary thrombi observed at CT scans (central, segmental, subsegmental). Central PE subtype is exclusive for D-dimer levels >5000 ng/L. PE: pulmonary embolism. [Faenza S. et al. Desio Hospital - Department of Diagnostic Radiology]

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Table 2: Chest X-ray findings and PE distribution (central, segmental/subsegmental) [14]. Cardiomegaly and prominent vascular marking, along with focal lung opacities, even if not specific, were frequently observed (up to 80%) in patients with central PE. More distal subtypes of pulmonary embolism tends to have normal findings or to be correlated with miscellaneous alterations (pleural effusion, atelectasia, bronchovascular bundles). PE: pulmonary embolism. [Faenza S. et al, Desio Hospital - Department of Diagnostic Radiology]

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A 31 years old woman was admitted at Emergency Room for sudden onset of dyspnea and thoracic pain. Chest X-ray (1-1 and 1-2) revealed focal left upper lobe opacity, suspicious for pneumonia (white arrows, 1-1 and 1-2). However, due to the very high level of D-dimer (>5000 ng/L), a CT-angiography of the lung was performed (1-3 and 1-4). Although pre-test probability (Wells' score) was about 0%, the exam revealed a thrombus in left main pulmonary artery as per central PE (white arrow, 1-3). Moreover, a concomitant air-filled parenchymal opacification was also detected (1-4); this was diagnosed as suspected tubercular cavern. PE: pulmonary embolism. [Faenza S. et al, Desio Hospital - Department of Diagnostic Radiology]

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**Fig. 2:** Figure 2. 40 years old man with dizziness and D-dimer of 3198 ng/L. MDCT angiography (axial 2-1, coronal 2-2) shows multiple clots in segmental branches of right pulmonary artery (white arrows, 2-1 and 2-2). [Faenza S. et al, Desio Hospital - Department of Diagnostic Radiology]

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**Fig. 3:** Figure 3. Axial images of a CT-PA study (3-1 and 3-2) that reveal multiple bilateral thrombi in sub-segmental arterial branches (white arrows, 3-1 and 3-2) in a patient with D-dimer level of 1048 ng/L. Axial MIP reconstruction (3-2) provides a better spatial resolution for distal pulmonary vessels. [Faenza S. et al, Desio Hospital - Department of Diagnostic Radiology]

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**Fig. 4:** Figure 4. A case of a 74 years old woman suffering dyspnea, with prominent vascular marking and cardiomegaly at chest X-ray film (4-1) and D-dimer value >5000 ng/L. Patient then underwent a pulmonary CT-angiography (4-2): a worm-shaped clot was observed in left main pulmonary artery as per central PE (white arrow, 4-2). [Faenza S. et al, Desio Hospital - Department of Diagnostic Radiology]

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Conclusion

D-dimer levels may correlate with the presence and the distribution of PE in pulmonary branches on CT-PA; particularly, central PE demonstrated to be correlated with D-dimer values > 5000 ng/L. Moreover, in this group of patients the prevalence of some findings on chest x-ray examination, such as cardiomegaly and prominent vascular marking or focal lung opacities, even if non-specific for PE, was increased.
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