Pulmonary embolism and computed tomography angiography: Characteristic findings and technical advices

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ABSTRACT

Pulmonary embolism (PE) is a condition due to blood clots obstructing pulmonary arteries, often related to deep venous thrombosis (DVT). PE can be responsible for acute and even life-threatening clinical situations and it may also lead to chronic sequelae such as chronic thromboembolic pulmonary hypertension (CTEPH). Signs and symptoms associated to PE may overlap those of many other diseases (e.g. chest pain, dyspnea, etc.), therefore an accurate clinical evaluation is mandatory before referring the patient to the most appropriate imaging technique. Pulmonary angiography (PA) has been traditionally considered the gold standard regarding the diagnosis of PE and it is also useful regarding the treatment of said condition. However, PA is an invasive technique, implying all the known risks concerning endovascular procedures. Nowadays, computed tomography angiography (CTA) is considered the imaging technique of choice regarding the diagnosis of PE. This technique is readily-available in most centers and it is able to provide high resolution images, although it implies the administration of ionizing radiations and iodinated contrast medium. Conventional CTA has further been improved with the use of ECG-gated protocols, aimed to reduce motion artifacts due to heartbeat and to evaluate other causes of sudden onset chest pain. Moreover, another interesting technique is dual energy computed tomography (DECT), which allows to elaborate iodine maps, allowing to detect areas of hypoperfusion due to the presence of emboli in pulmonary arteries. This review is aimed to describe the main findings related to PE with an emphasis on CTA, also discussing technical aspects concerning image acquisition protocol.

KEYWORDS
pulmonary embolism, computed tomography angiography, ECG-gated computed tomography, dual energy computed tomography, image acquisition protocol

Introduction

Definition, epidemiology and pathophysiology

Pulmonary embolism (PE) is due to blood clots obstructing pulmonary arteries [1] and is commonly due to venous thromboembolism (VTE) of lower limbs [1]. According to necropsy reports, PE is responsible for the death of about 5–10% of hospitalized patients [2] and VTE can have a mortality of 25%, which decreases between 1% and 5% with treatment. This represents a heavy economic burden, with an estimated cost of 7–10 billion every year in the United States [1, 2].
The pathophysiology of thromboembolism is based on Virchow’s triad, which includes hypercoagulability, stasis and endothelial injury. Therefore, any factor inducing one or more of these conditions increases the risk of VTE and subsequently PE. These risk factors can be categorized as patient-related (e.g. genetic mutations, sex, etc.) and setting-related risk factors (e.g. traumas, cancer, etc.). [1–3]

Clinical presentation

Patients affected by acute PE may show a wide variety of symptoms that are not specifically related to the disease, also ranging from completely asymptomatic to life-threatening clinical pictures. The most common symptoms are chest pain/discomfort and dyspnea (caused by ventilation/perfusion anomalies due to impaired blood flow in pulmonary arteries), and seldom hemoptysis. Syncope may also occur in patients with compromised hemodynamic reserve, in the most severe cases [3, 4]. Sometimes there are associated signs of DVT involving the lower limbs, such as unilateral lower leg pain, swelling and tenderness on physical examination [4].

Patients suspected of PE should undergo risk stratification beside clinical evaluation in order to guide the therapeutic management [5]. Therefore, different prediction rules have been developed, such as the Geneva rule [6], the Wells rule [7] and Pulmonary Embolism Rule-out Criteria (PERC) [8].

Long term sequelae

Chronic sequelae of PE affect up to 50% of patients, who develop the so-called “post-PE” syndrome. This condition includes disorders such as persistent impairment of respiratory function and physical exercise capacity, ultimately leading to a reduced quality of life [9]. More severe long-term complications of post-PE syndrome include chronic thromboembolic pulmonary hypertension (CTEPH), secondary to microvascular remodeling, flow redistribution within the pulmonary arterial system and increased pulmonary vascular resistance. These ultimately lead to severe pulmonary hypertension and right heart failure [3, 9].

Diagnosis

D-dimer test is the first step in diagnostic work-up of patients with a low suspicion of PE. If D-dimer values are in normal range, PE is reasonably excluded. Conversely, patients with high D-dimer values, along with patients characterized by moderate to high likelihood of PE, should be referred for cardiovascular imaging [3, 10].

Computed Tomography Angiography (CTA) is the imaging technique of choice for the diagnosis of PE. This technique is characterized by high sensitivity and specificity (both >90% in an optimal setting), and a short acquisition time. The main disadvantages of CTA are the administration of iodinated contrast medium and radiation exposure [3]. The acquisition of both CTA and Computed Tomography Venography (CTV), the latter aimed to detect DVT, significantly improves sensitivity of CTA alone, while maintaining similar values of specificity (Fig. 1) [11]. However, since CTV implies an increase in radiation exposure and larger volumes of contrast medium, venous compression ultrasonography (US) is currently the first line diagnostic technique for the detection of DVT, with similar diagnostic accuracy (Fig. 2) [12].

A valuable alternative to CTA is ventilation/perfusion scintillation, particularly useful in young patients, pregnant women and patients with chronic kidney insufficiency. This technique is characterized by high sensitivity and specificity (both >95%), lower radiation dose, and it is contrast medium sparing, although it is noticeably more expensive than CTA [3, 4].

Finally, other diagnostic techniques, included in the diagnostic pathway of PE are transthoracic echocardiography (TTE) and pulmonary angiography (PA), the latter being considered the gold standard [3]. TTE has proven useful to detect signs of right ventricle (RV) dysfunction due to PE, with a high specificity and a low sensitivity [13]. PA is an invasive imaging technique that is pivotal not only in diagnosis (demonstrating signs of pulmonary arteries filling defects), but also regarding the therapeutic management (i.e. catheter-directed thrombolysis) [14].

Computed tomography angiography for pulmonary embolism

Acquisition protocol

The acquisition protocol regarding conventional CTA consists in a scan covering the whole thorax performed at pulmonary arterial phase using a Computed Tomography (CT) [15]. Contrast medium (CM) transit can be monitored before scanning the patient by using bolus-tracking technique. The latter consists in placing a region of interest (ROI) on main pulmonary artery (MPA), secondary to microvascular remodeling, flow redistribution within the pulmonary arterial system and increased pulmonary vascular resistance. These ultimately lead to severe pulmonary hypertension and right heart failure [3, 9].

Acquisition protocol

The acquisition protocol and reconstruction parameters we advise are summarized in Table 1.

CTA scans performed to rule-out PE might be affected by cardiac motion artifacts [15]. Therefore, different authors explored the possibility to perform ECG-gated CTA to overcome this possible liability. They observed that ECG-gating significantly reduced cardiac motion artifacts, but without significant improvement of diagnostic performance [17].

Other authors evaluated the performance of ECG-gated CTA not only to detect PE but also coronary artery disease
Fig. 2. Ultrasonography and venous thrombosis. A, B Doppler Ultrasonography (US), axial and oblique plain respectively. Female patient (63yo) affected by lesser saphenous vein thrombosis. In A it is possible to detect the absence of flow regarding lesser saphenous vein (arrow), a superficial vein of the leg. Blood flow is detectable concerning popliteal vein (asterisk) and a gastrocnemius venous trunk. In B lesser saphenous vein appears as a non-compressible venous segment (arrowheads) with severely impaired blood flow and hyperechogenic intraluminal material, the latter likely being the thrombus.

Fig. 1. Computed tomography venography and deep venous thrombosis. A, B Computed tomography venography (CTV), axial and coronal plane, respectively. Male patient (57yo) affected by deep venous thrombosis (DVT) involving right popliteal vein (RPV). In both images it is possible to detect a thrombus which completely occludes RPV lumen and it appears as a hypo-attenuating intraluminal filling defect (arrow in A, arrowheads in B). As a side note, superficial veins appear engorged on the right side compared to the left side, another indirect sign of impaired venous drainage due to RPV occlusion. C, D CTV, axial and coronal plane, respectively. Female patient (27yo) affected by venous thrombosis involving right common iliac vein (RCIV). In both images it is possible to detect a thrombus which partially occludes RCIV lumen and it appears as a hypo-attenuating intraluminal filling defect (arrow in C, arrowheads in D) surrounded by a rim of hyper-attenuating blood. Both patients also showed CTA signs of pulmonary embolism.
Patient weight: 18-gauge needle is placed into right ante-cubital vein to avoid blooming artifact secondary to contrast medium (CM) flowing into brachiocephalic vein.

### Computed Tomography Angiography Single Source Acquisition Protocol

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Reconstruction</th>
<th>Pitch</th>
<th>Rotation Time</th>
<th>Tube voltage (kVp)</th>
<th>Tube charge (mAs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole chest</td>
<td>0.625 mm</td>
<td>&lt;1</td>
<td>0.5 s</td>
<td>80–120 kVp</td>
<td>Tube current modulation (from ~200 to maximum)</td>
</tr>
</tbody>
</table>

#### Contrast Medium Administration

<table>
<thead>
<tr>
<th>CM concentration</th>
<th>Patient weight</th>
<th>CM volume and flow rate</th>
<th>IDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>320 mgI/ml</td>
<td>350 mgI/ml</td>
<td>370 mgI/ml</td>
<td>400 mgI/ml</td>
</tr>
<tr>
<td>&lt;60 kg</td>
<td>70 ml, 5 ml s⁻¹</td>
<td>64 ml, 4.6 ml s⁻¹</td>
<td>60 ml, 4.3 ml s⁻¹</td>
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<tr>
<td>60–80 kg</td>
<td>78 ml, 5.6 ml s⁻¹</td>
<td>71 ml, 5.1 ml s⁻¹</td>
<td>67 ml, 4.9 ml s⁻¹</td>
</tr>
<tr>
<td>&gt;80 kg</td>
<td>87 ml, 6.2 ml s⁻¹</td>
<td>80 ml, 5.7 ml s⁻¹</td>
<td>76 ml, 5.4 ml s⁻¹</td>
</tr>
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#### Phase Acquisition

- **Arterial phase**: A scan is performed approximately 4s after reaching 100 HU within the Region of Interest placed on pulmonary trunk. The acquisition time is approximately 4s.
- **Venous phase (optional)**: A scan is performed 180s from CM administration, covering the abdomen and lower limbs, in order to rule-out deep venous thrombosis. It is of note that CTA it is not considered the first line diagnostic technique, the latter being venous compression ultrasonography.

and aortic disease, with a “triple-rule-out” (TRO) protocol. This protocol is aimed to simultaneously assess the three possible cause of acute chest pain with just one scan. It consists in an ECG-gated CTA scan performed to obtain optimal visualization and opacification of the pulmonary arteries, coronary arteries and thoracic aorta [18, 19].

We agree with the literature that ECG-gated acquisition does not have any added value concerning PE assessment only. When compared to a dedicated CTA, TRO uses higher contrast medium volumes and radiation dose. It is also more prone to image quality issues resulting in impaired diagnosis [20].

Another technique that can be possibly used in the diagnosis of PE is Dual Energy Computed Tomography (DECT). This consists in the acquisition of images at two different energy levels [21]. Tissues and contrast medium have different attenuations at different energy levels, therefore DECT provides a deeper insight on tissue characterization compared to conventional CT, the latter relying just on different densities [21]. DECT for pulmonary arterial vasculature evaluation should be performed using a high-concentration iodine CM, setting a higher scanning delay (compared to conventional CTA) to allow optimal contrast medium distribution throughout the lung parenchyma [21]. After the scan, distinct sets of images are reconstructed corresponding to different energy levels. Iodine maps are further elaborated, providing a thorough outlook regarding the distribution of contrast medium in pulmonary circulatory system, thus allowing detection of perfusion defects secondary to PE [22].

Among the main advantages of DECT is the possibility to use low-dose protocols concerning CM volume. This will improve image quality and aid in the detection of small peripheral emboli, easily missed on conventional CTA [23–25].

DECT may be also useful in the management of PE complications such as CTEPH, by proving able to correlate lung perfused blood volume with hemodynamics parameters [26].

### Acute pulmonary embolism findings in computed tomography angiography

The key finding of acute pulmonary embolism is an intraluminal filling defect involving a pulmonary arterial vessel. An acute embolus usually appears as a central filling defect with a surrounding rim of contrast medium, yielding a characteristic “polo mint” or “railway” appearances depending on whether the major axis of the vessel is orthogonal or parallel to the image plane [27]. Emboli can also be eccentrically located rather than centrally and can also be detected in right chambers. If the embolus is particularly large, lying across the pulmonary trunk bifurcation, it is defined as a “saddle embolus” (Fig. 3). As a consequence of obstruction, the MPA and involved pulmonary arteries may also appear dilated [27].

On iodine maps obtained by DECT, the characteristic finding of PE is a wedge-shaped perfusion defect corresponding to the vascular distribution of the obstructed pulmonary arterial vessel (Fig. 4) [21, 22].
**Fig. 3. Basic signs of pulmonary embolism and pulmonary infarction.** A, B, C, Computed Tomography Angiography (CTA), multiple oblique planes. Female patient (77yo) affected by massive pulmonary embolism. In A and B it is possible to detect an embolus (arrowhead) inside the lumen of right interlobar artery, yielding the characteristic appearance of “polo mint” in A and “railway” in B. In C it is possible to detect a “saddle embolus” (arrow) lying across the main pulmonary artery bifurcation. D, CTA, axial plane. Female patient (41yo) affected by massive pulmonary embolism complicated with pulmonary infarction. It is possible to detect a wedge-shaped consolidation area (asterisk) with a pleural basis and an apex directed towards the hilum. The finding described is suggestive for a pulmonary infarction due to obstruction of the pulmonary segmental artery feeding left lower lobe lateral segment. It is also possible to see a smaller infarction involving basal anteromedial segment, near the fissure.

**Fig. 4. Dual energy computed tomography and pulmonary embolism.** A, B Dual energy computed tomography (DECT) angiography, axial plane. Female patient (70yo) affected by right pulmonary artery thromboembolism. In A (DECT virtual monoenergetic reconstruction at 80 kV) it is possible to detect a thrombotic apposition (arrow) inside the lumen of right pulmonary artery (RPA). In B (iodine map) it is possible to detect a perfusion defect (asterisk), which is represented as a wedge-shaped area of reduced contrast medium distribution and it is the consequence of RPA partial occlusion due to said thrombotic material. Case courtesy of Dr. S. Dell'Aversana, University of Naples Federico II, Naples, Italy.
There are often ancillary signs associated to acute PE that can be useful to confirm the diagnosis. For example, this condition is related to pulmonary circulation anomalies that can ultimately lead to pulmonary infarction (PI). In patients affected by PE it is possible to visualize areas of lung parenchyma with different perfusion rates and thus attenuation, yielding the characteristic “mosaic perfusion” appearance, the latter being present also in other pathologies involving the airways and in chronic embolism [28]. If PI occurs, it is possible to detect a wedge-shaped area of altered attenuation with a pleural base and the apex being directed towards the hilum. The infarcted area can be seen as a consolidation, a ground-glass opacity or even as a ground-glass opacity surrounded by a rim of consolidated parenchyma (“reverse halo sign”). It can be associated with pleural effusion. As the PI evolves, it reduces in size from the periphery (“melting sign”) and becomes more nodular in appearance [29].

Acute PE may also lead to RV dysfunction, with characteristic CTA signs including increased ventricular cavity diameter, flattening or leftward deviation of the interventricular septum and reflux of contrast medium into the inferior vena cava and hepatic veins [30]. As a result of increased right atrial pressure, the superior vena cava and azygos vein may also appear dilated (if >20.9 mm and >10.4 mm in diameter, respectively) (Fig. 5) [31].

Beside thromboembolism, there are also other uncommon conditions that might be responsible for acute PE (e.g. fat embolism and cement embolism). Fat embolism is defined as the presence of fat globules in the pulmonary or peripheral circulation, most commonly secondary to trauma, and orthopedic procedures [32]. Cement embolism is a complication of vertebral cement augmentation procedures with the characteristic finding of hyperdense cement emboli in pulmonary arteries (Fig. 6) [33].

Chronic pulmonary embolism findings in computed tomography angiography

Chronic embolism may lead to pulmonary circulatory system remodeling with ensuing pulmonary hypertension and thus RV dysfunction, defining the CTEPH.

Chronic emboli may completely obliterate the pulmonary artery lumen or can manifest as webs, bands or irregular vessel wall thickening if they are partially occluding [34]. Pulmonary arterial vessel may also appear abruptly interrupted or decreased in caliber, as a consequence of chronic obstruction. Furthermore, the impairment of pulmonary arterial circulation may lead to compensatory enlargement and tortuous appearance of bronchial arteries and even of other thoracic arteries (internal mammary arteries, intercostal arteries, etc.) [34, 35].

CTEPH findings may include signs of RV dysfunction and increasing pulmonary arterial resistances. Among the most characteristic findings is MPA dilation, that can be secondary to a wide variety of pathologies. It can manifest both in acute and chronic PE due to thrombi load and fibrous stenosis, respectively. As showed by Raymond et al., a MPA diameter >33 mm or a Pulmonary artery/Aortic diameter ratio >1.1 have a specificity of 95% and 92% respectively, regarding the detection of pulmonary hypertension (Fig. 7) [36].

RV dysfunction findings secondary to CTEPH are similar to those described for acute PE, with the addition of signs chronic myocardial remodeling such as RV hypertrophy and dilation.

Finally, CTEPH findings can be associated to parenchymal scars derived from previous infarctions. These may vary in appearance, from wedge-shaped consolidation areas to peripheral ill-defined bands, often involving the lower lobes and associated to pleural thickening [34].

Fig. 5. Pulmonary Embolism with right ventricular strain and dysfunction. A, B, C. Computed Tomography Angiography (CTA), axial plane. Female patient (81yo) affected by massive pulmonary embolism. In A and B it is possible to detect main pulmonary artery (MPA) severe dilation (48 mm maximum diameter) with enlarged left and right pulmonary arteries. Thromboembolism are also detectable inside the lumen of right pulmonary artery (arrowhead). In B it is possible to detect mild dilation of superior vena cava (SVC, 25 mm maximum diameter) and azygos vein (AV, 12 mm maximum diameter). In C, it is possible to detect right ventricle (RV) dilation with leftward deviation of interventricular septum (arrowheads)
CTA and risk stratification

CTA can be also used to perform a quantitative evaluation concerning the impact of acute PE on pulmonary vasculature hemodynamics and provide instruments for risk stratification. For clot burden evaluation, one of the most used approach is the CT obstruction index (CTOI) described by Qanadli et al. [37]. This index is calculated by evaluating pulmonary arteries’ patency with a numerical score (0: no thrombus, 1: partial occlusion, 2: total occlusion), regarding the pulmonary arterial tree as constituted by 10 segmental arteries for each lung. CTOI’s primary aim is to evaluate the impact of impaired blood flow due to PE on pulmonary circulation and RV function, ultimately predicting the outcome. In a recent study by Rotzinger et al., CTOI was able to predict the outcome in a selected cohort of patients with nonmassive acute PE and without cardiopulmonary disease: patients with an increased CTOI values showed a statistically significant increase in 30-days and 3-months mortality when compared to patients with lower values [38].

Another useful imaging feature regarding outcome prediction is the increased ratio between RV and left ventricle diameters (RVD/LVD) measured on axial plane, that is an indirect sign of RV dysfunction. As showed by Shen et al., RVD/LVD has been able to reliably predict high-risk PE, with an area under the curve equal to 0.9 [39].

CTA can be also useful regarding the risk stratification and thus therapeutic management of patients affected by chronic PE. As said before, chronic PE may ultimately lead to CTEPH, which is potentially curable with pulmonary endoarterectomy (PEA), the latter being a surgical procedure aimed to improve long-term outcome. In particular, CTA is considered a pivotal imaging technique regarding the assessment of patient operability, together with imaging techniques such as PA and ventilation/perfusion scintillation [40]. Rodriguez Chaverri et al. in a recent study also evaluated a noninvasive operability evaluation approach based on CTA in patients affected by CTEPH, using PA as the reference standard. The authors obtained similar results concerning patients’ classification among the two imaging techniques [41]. Moreover, Leone et al. elaborated a CTA-based severity score for the evaluation of patients affected by CTEPH, including a variety of typical findings (e.g. MPA dilation, signs of chronic RV dysfunction, etc.). The study population included patients who were scanned at baseline and some of them were also scanned after PEA. Interestingly, the CTEPH severity score correlated with
functional parameters such as mean pulmonary artery pressure and pulmonary vascular resistance concerning the whole study population, including the patients who underwent PEA [42].

**Conclusion**

CTA is nowadays the pivotal imaging technique concerning not only diagnosis but also management of PE. It can also detect PE-related conditions such as right heart dysfunction and PI, providing additional valuable information concerning the severity of the disease. Beside image interpretation, emphasis should be also put on correct acquisition protocol, because an accurate diagnosis is strictly dependent on the latter. Therefore, it is of uttermost importance for all to gain the necessary know-how to properly manage the diagnostic pathway of this common condition.

**Authors’ contribution:** EM devised the main conceptual ideas and wrote the manuscript. AP and CP contributed to write the manuscript and to choose the most appropriate figures. MD, CD, GM and AL contributed to write the manuscript and supervised the project.

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