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Pulmonary embolism – diagnostic imaging algorithm and CTA evaluation

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Summary

Pulmonary embolism (PE) is one of the most undiagnosed cardiovascular diseases. Only up to 30% of PE cases are properly diagnosed antemortem. CT pulmonary angiography is a diagnostic tool considered as a standard of care for patients with suspected PE. This article reviews diagnostic tomographic criteria for acute and chronic PE and diagnostic imaging algorithm for PE, based on PIOPED II study guidelines.

Key words: computer tomography (CT) • CT angiography (CTA) technique • pulmonary angiography • acute pulmonary embolism • chronic pulmonary embolism • emergency radiology

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Background

Pulmonary embolism (PE) is a sudden blockage or narrowing of the pulmonary artery or its branches, usually by a deep venous thrombus or an intravascular pathologic or foreign body. The term "embolus" originates from the Greek "embolos" meaning plug. PE and deep vein thrombosis (DVT) are the main clinical manifestations of venous thromboembolic disease (VTE) – one of the most important problems in outpatient and hospital care.

Among cardiovascular diseaes, PE is the third leading cause of death in Europe and North America, surpassed only by myocardial infarction and stroke. The goal of the VITAE study (Venous Thrombo-Embolism Impact Assessment Group in Europe) was to estimate the total number of VTE within the European Union (EU) a year [1]. Based on this study, about 57,000 DVT cases and about 37,000 symptomatic PE events occur in Poland every year. Only up to 30% of PE cases are properly diagnosed antemortem.

PE has predilection to occur in the right lung and lower pulmonary areas. The typical location is the right lower lobe. In 90% of thromboembolic PE cases, embolism originates from vena cava inferior branches (deep veins of the lower extremity – 60%, deep veins of the pelvis – 40%). In 10% of cases, PE is caused by embolism from veins of the upper extremity or right heart chambers. Rarely, embolic matrial turns out to be nonthrombotic, such as intravascular metastases, septic, fat, air, hydatid or amniotic fluid embolism. The appearance at CT is often indistinguishable from pulmonary thromboembolism. Intravenous pulmonary talcosis and cotton embolism are specific for intravenous drug users. Iatrogenic PE can be caused by cyanoacrylate, lipiodol or sheared off fragment of intravenous catheters.

Diagnostic Imaging Algorithm for Pulmonary Embolism

The most frequent symptoms of PE include: shortness of breath (82%), tachypnea (60%), chest pain of a pleural or coronary nature (49%), tachycardia (49%), cough (20%), collapse or syncope (14%) and hemoptysis (7%) [2]. Although clinical manifestations of PE are highly insensitive and nonspecific, they are the only basis for suspecting the disease and performing further diagnostic tests.

According to PIOPED II study (Prospective Investigation On Pulmonary Embolism Diagnosis), the choice of diagnostic tests depends on the clinical probability of pulmonary embolism and the patient's condition [3]. Clinical probability assessment should be made with an objective method – Revised Geneva Score [4] (Table 1) or Wells' criteria [5] (Table 2).

Patients with low and moderate probability clinical assessment undergo a D-dimer rapid ELISA test (Figure 1). If D-dimer is normal, no further testing is required. Positive

Table 1. The revised Geneva Score.

Risk factors	Points
Age >65 years	1
Previous deep venous thrombosis or PE	3
Surgery (under general anesthesia) or fracture (of the lower limbs) within 1 month	2
Active malignant condition (solid or hematologic malignant condition, currently active or considered cured <1 year)	2
Symptoms	**Points**
Unilateral lower-limb pain	3
Hemoptysis	2
Clinical sign	**Points**
Heart rate: 75–94 beats/min ≥95 beats/min	 3 5
Pain on lower-limb deep venous palpation and unilateral edema	4
Clinical probability	**Points**
Low	0–3 total
Intermediate	4–10 total
High	≥11 total

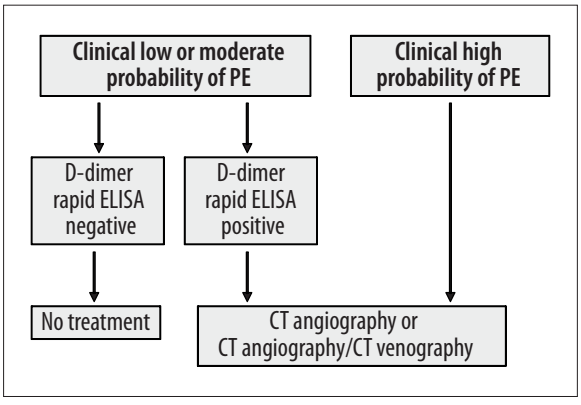

Figure 1. Diagnostic algorithm for patients with suspected PE (PIOPED II study).

D-dimer result (>500 μg/l) should be followed by CT angiography and venography. For patients with high probability clinical assessment, D-dimer testing is not necessary, because a negative result of the test in this group of patients may not exclude pulmonary embolism. PIOPED II study recommends CT angiography and venography as the first diagnostic test for patients with high probability of PE. In patients with segmental or subsegmental pulmonary emboli diagnosed by CT angiography only, the diagnosis should be reassessed using pulmonary scintigraphy, venous US or pulmonary digital subtraction angiography (DSA). Patients with shock or hypotonia (sRR <90 mmHg)

Table 2. Well's criteria.

Criteria	Points
Suspected deep venous thrombosis	3.0
An alternative diagnosis is less likely than PE	3.0
Heart rate >100 beats/min	1.5
Immobilization or surgery in the previous four weeks	1.5
Previous deep venous thrombosis or PE	1.5
Hemoptysis	1.0
Malignancy (on treatment, treated in the past six months or palliative)	1.0
Score range/Mean probability of PE	**Risk**
<2 points/3.6%	Low
2–6 points/20.5%	Moderate
>6 points/66.7%	High

are at high risk of death, so they undergo CT angiography instead of routine clinical probability assesment. If CT is not available immediately, echocardiography should be performed to exclude right ventricular strain or failure that can be caused by acute PE [6].

Patients with mild iodine allergies may be treated with steroids prior to CT angiography. Alternative diagnostic tests in patients with severe iodine allergy are venous ultrasonography (US) and pulmonary scintigraphy. Other options are serial venous US examinations and recently attempted gadolinium-enhanced angiography (0.3–0.4 mmol gadolinium per kilogram of body weight) [7].

In patients with impaired renal function, PIOPED II study recommends venous US or pulmonary scintigraphy (if venous US results are negative). Hydration with sodium bicarbonate 3 ml/kg/h for 1 hour before and 1 ml/kg/h for 6 hours after contrast injection is more effective than hydration with sodium chloride for prophylaxis of contrast-induced renal failure [8]. Nonsteroidal antiinflammatory drugs, dipyridamole and metformin should be discontinued before the administration of contrast material [9,10].

For women of reproductive age after positive D-dimer testing, investigators recommend CT angiography rather than pulmonary scintigraphy. Venous US is optional.

Pregnant women after positive D-dimer testing (results may be positive because of the pregnancy) should undergo venous US before imaging tests with ionizing radiation. The recommended test is pulmonary scintigraphy rather than CT angiography.

Chest Radiograph

While the chest radiograph (chest x-ray - CXR) is abnormal in the majority of PE cases, CXR alone cannot be used to either exclude or confirm the diagnosis of PE. Chest radio-

Table 3. CTA protocol for 16- and 64-section CT (normal-sized patients).

Parameter	16-section CT	64-section CT
Slice thickness (mm)	1.25	0.625
Reconstruction interval (mm)	1.25	0.625
Table movement (mm per rotation)	35	40
Pitch	1.75: 1	0.16: 1
Peak voltage (kVp)	120	120
Tube current (mAs)	100–320	320–800
Rotation time (sec)	0.5	0.35
Contrast material injection Rate (mL/sec)	3–4	4
Contrast material injection Volume (mL)	80	90

graphic findings can be used to diagnose diseases that have clinical manifestation similar to PE, such as pneumonia, pulmonary edema, or pneumothorax. CXR is also necessary for interpretation of the ventilation-perfusion lung scan.

Prevalence of chest radiographic signs in patients with PE versus those without PE is not significantly different [11]. The most common chest radiographic findings in patients with PE are atelectasis, parenchymal areas of increased opacity and pleural effusions. Hampton's hump appears as wedge-shaped area of increased opacity in the lung periphery with the base against the pleural surface. The Westermark sign results from oligemia in the arteries distal to the embolus, caused by mechanical obstruction to blood flow or by reflex vasoconstriction. The Fleischner sign (prominent central artery) is caused by pulmonary hypertension or by distention of the vessel by a large embolus. Other radiographic signs of PE are pleural effusion, elevated diaphragm, enlarged hilum and vascular redistribution.

CT Angiography

Imaging "gold standard" for PE – pulmonary angiography has been replaced by CT angiography (CTA) in the majority of cases. In a multicenter study [12], the prevalence of PE was 10% of 1,025 pulmonary CT angiograms. One of the major advantages of chest CTA is high accuracy for the detection of PE. Diagnostic studies give various results for the diagnostic accuracy of CTA. Hogg et al: [13] reviewed 24 diagnostic studies. The results showed sensitivity of CT pulmonary angiography ranging from 53% to 100%. Specificity was less variable – from 79 to 100%. False negative rate was 1.0 to 10.7%. It is more than certain that we will observe an increase in CT accuracy with the new technology.

High CTA resolution and post-processing methods make it possible to detect embolism up to subsegmental arteries. Data acquisition for CT imaging takes no more than one breath hold and has relatively low radiation dose. Another reason for its widespread use is the ability to detect non-vascular causes of acute chest pain (such as pneumonia, lung cancer, acute myocardial infarction, pericarditis, aortic dissection, pleural disease, including pneumothorax and pleuritis, esophagitis, esophageal rupture or chest wall abnormalities). Kim et al. [14] found the cause of chest pain in 67% of patients without PE on pulmonary CTA performed to rule out pulmonary embolism. On the other hand, PE is identified in 1.5% of contrast-enhanced CT scans performed for reasons other than suspected PE [15].

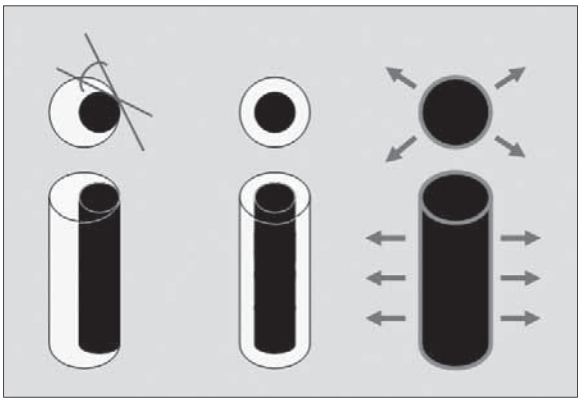

Figure 2. Acute pulmonary embolism.

Recent studies show that CT angiography with ECG gating can be successfully used for a complete assessment of the thoracic vessels to rule out PE, coronary artery disease and aortic aneurysm or dissection in a single exam. In these "triple rule out" protocols pulmonary, coronary arteries and aorta are simultaneously opacified [16].

CT Pulmonary Angiography Technique

At the moment, 16- and 64-MDCT scanners (GE Healthcare) with ECG-gated technique are used in our hospital to acquire the images of the thorax in a caudocranial direction. For IV access, the antecubital vein is preferred. We determine scanning delay after injecting of contrast material using the bolus-tracking technique. Images of a region of interest (the level of the main pulmonary artery) are acquired at 1 or 3 s intervals to detect the arrival of the contrast material bolus. The spiral scan is initiated manually if the density increases more than 50 HU with a delay of 3 s. The patient is instructed to hold his breath after inspiration. The parameters for the standard protocol are shown in the table (Table 3).

Images are viewed on a PACS using Advantage Workstation GE. The images are displayed with three different gray scales for interpretation of lung window (window width/level [HU] – 1500/600), mediastinal window (400/40), and pulmonary embolism-specific (700/100) settings. Pulmonary embolism can be missed when a case with very bright contrast is viewed only on mediastinal window settings.

Diagnostic Criteria for Acute Pulmonary Embolism in CT Angiography

At CTA, an embolus in pulmonary embolism appears as an intraluminal filling defect that has a sharp interface with the intravascular contrast material. There are three specific criteria of acute PE [17] (Figure 2).

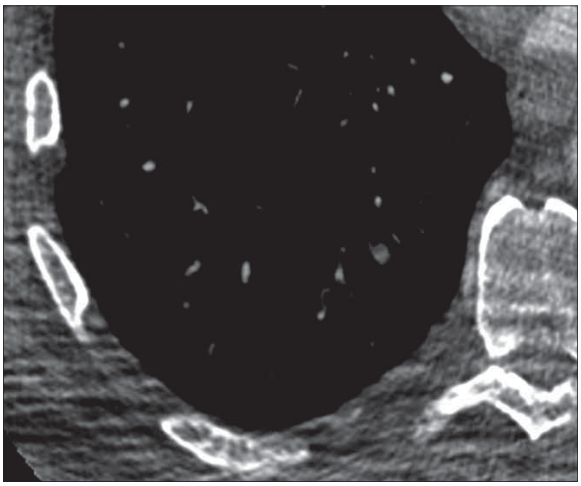

Figure 3. Artery lumen filled with embolic material, wider than adjacent patent arteries.

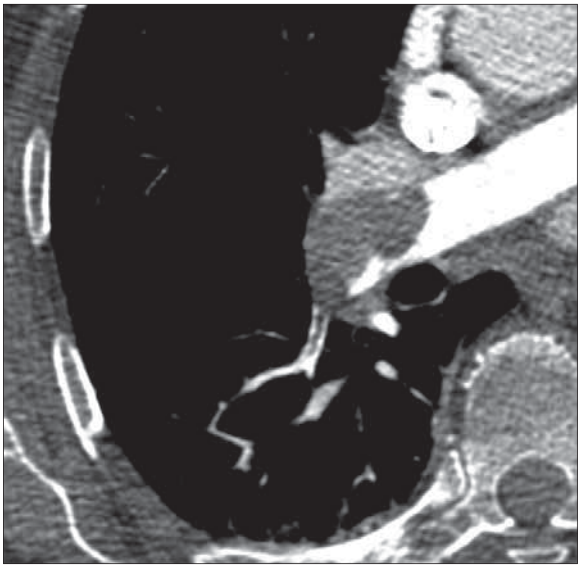

Figure 4. Embolic material in the center of the artery, surrounded by contrast agent - the "railway track" sign on images acquired longitudinally to the long axis of a vessel.

The first criterion – the arterial lumen is completely filled with embolic material that results in absence of vessel enhancement and widening of the vessel compared with adjacent patent arteries (Figure 3).

The second – embolic material is situated in the center of the artery, surrounded by contrast agent. On images acquired longitudinally to the long axis of a vessel, the embolus appears as the "railway track" sign (Figure 4). On perpendicular images of a vessel, the "polo mint" sign can be found (Figure 5).

The third specific sign – embolic material is located peripherally in the arterial lumen and forms acute angles with the arterial wall (Figure 6)

There are also other radiological features found at CTA that are ancillary but not specific for PE. They include: peripheral wedge-shaped opacity, linear bands and right ventricular strain or failure.

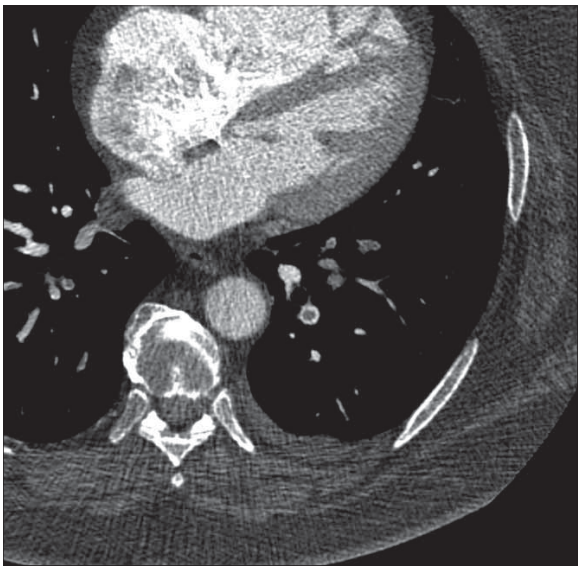

Figure 5. Embolic material in the center of the artery, surrounded by contrast agent – the "polo mint" sign on images acquired perpendicularly to the long axis of a vessel.

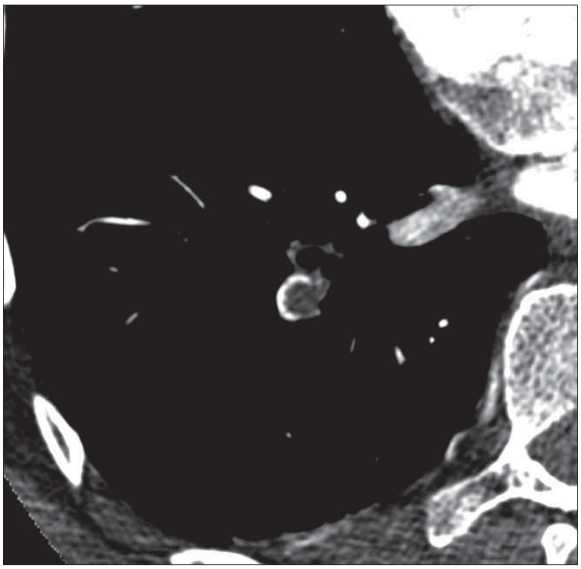

Figure 6. Embolic material located peripherally in the arterial lumen, forming acute angles with the arterial wall.

Peripheral wedge-shaped areas of hyperattenuation are the only parenchymal abnormality significantly associated with PE. This sign, observed in 25% of patients with PE, is caused by alveolar filling with blood and a peripheral inflammatory reaction around central necrosis (Figure 7). Although peripheral opacities are not specific for pulmonary infarction (they are seen for example in pneumonia, tumors or Wegener granulomatosis), it is possible to differentiate pulmonary infarction from other causes. The presence of central lucencies within a peripheral consolidation and the absence of air bronchograms strongly suggests pulmonary infarction [18].

PE is a risk factor for right-sided heart failure. CT findings may suggest the right ventricular strain or failure [19]. Right ventricular cavity wider than the left ventricular

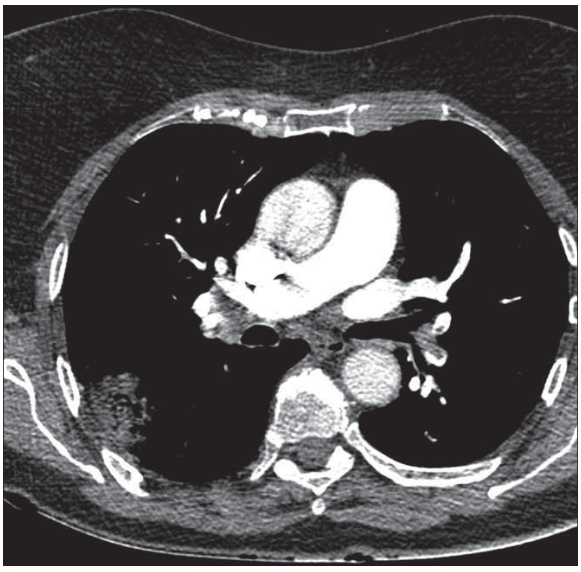

Figure 7. Pulmonary infarction – peripheral wedge-shaped areas of hyperattenuation with central lucencies.

cavity in the short axis is the sign of right ventricular dilatation (Figure 8). Deviation of the interventricular septum toward the left ventricle or backflow of the contrast agent into the hepatic veins may occur.

Elevation of right atrial pressure can result in the thrombus passing from the right to the left atrium via the patent foramen ovale (PFO), causing paradoxical embolism [20]. The prevalence of PFO reaches approximately 25%. A PFO remains physiologically closed as long as the pressure in the left atrium is higher than the pressure in the right atrium. Paradoxical embolisms represent two percent of arterial emboli.

If hyperattenuating filling defect located in main or lobar pulmonary arteries is identified at unenhanced CT, it suggests acute central pulmonary embolism and CTA should be performed [21] (Figure 9).

Diagnostic Criteria for Chronic Pulmonary Embolism in CT Angiography

It is important to differentiate acute from chronic pulmonary embolism. In chronic PE, radiological findings at CTA are different from the signs characteristic of acute disease [17] (Figure 10).

The arterial lumen can be completely filled with embolic material causing absence of vessel enhancement. In chronic PE, the occluded vessel is narrow compared with adjacent patent arteries.

If embolic material is located peripherally in the arterial lumen, it has shape of a crescent and forms obtuse angles with the arterial wall (Figure 11).

After recanalization of the occluded artery, the embolic material remains by the vessel wall. It results in contrast material flowing through thick-walled, often smaller arteries at CT scans (Figure 12).

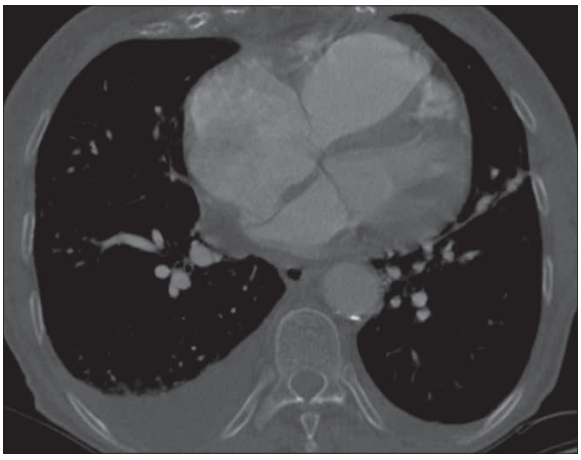

Figure 8. Right ventricular dilatation and deviation of the interventricular septum toward the left ventricle.

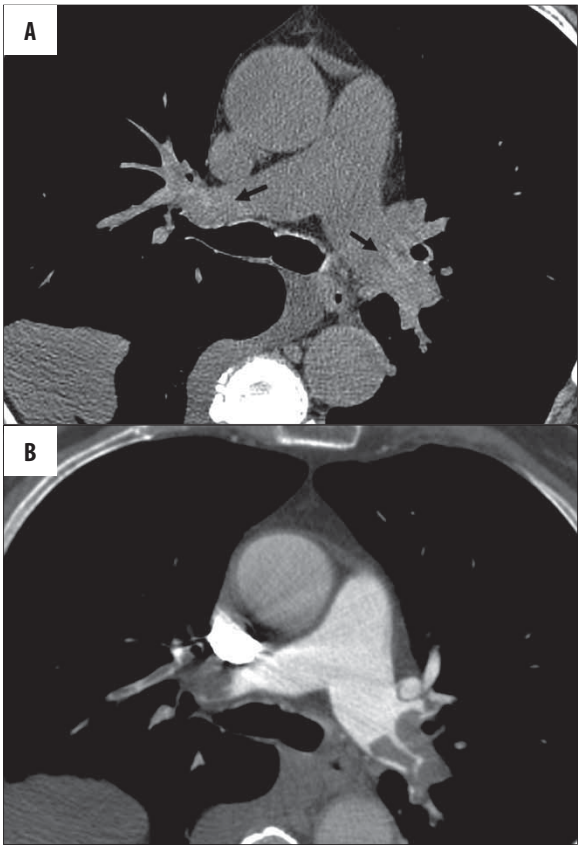

Figure 9. Hyperattenuating material located in right and left pulmonary arteries at unenhanced CT (A). CTA demonstrates acute pulmonary embolism (B).

Embolic material can also appear as a web or a flap in an artery filled with contrast agent.

Less characteristic signs of chronic PE include dilated bronchial, diaphragmatic or other collateral vessels and calcification of thickened arterial wall.

CTA can also reveal mosaic perfusion pattern. Areas of hypoattenuation represent underperfused lung due to

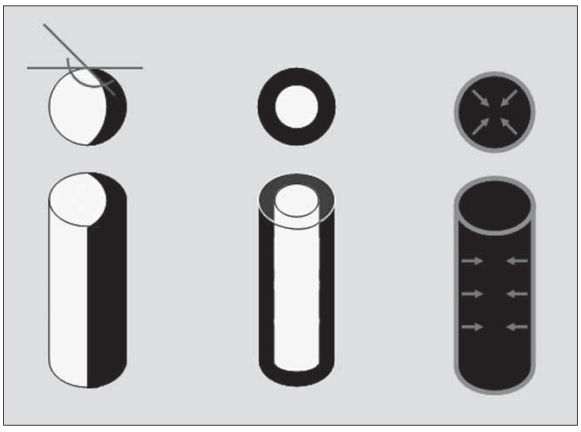

Figure 10. Chronic pulmonary embolism.

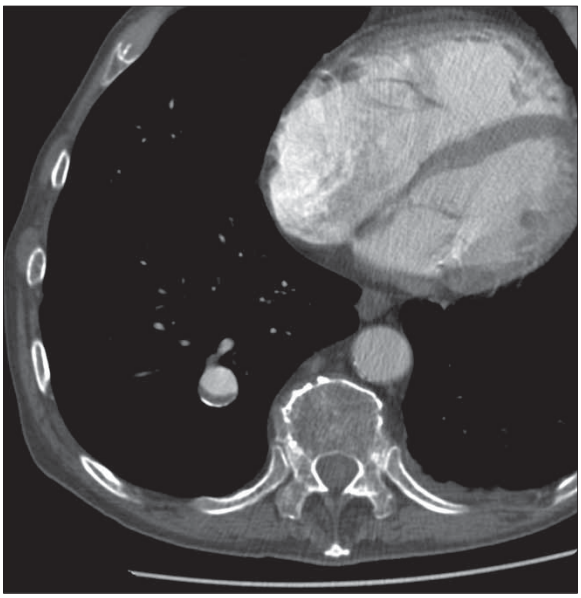

Figure 11. Embolic material located peripherally in the arterial lumen, forming obtuse angles with the arterial wall.

smaller arterial diameter. The normally perfused lung with patent vessels is seen as hyperattenuated areas (Figure 13).

One of the complications of chronic PE is pulmonary arterial hypertension (PAH). CT findings in PAH include pericardial fluid and main pulmonary artery diameter above than 33 mm (insensitive but highly specific for the presence of PAH [22]) (Figure 14).

Conclusions

PE incidence is underestimated – only up to 30% of PE cases are properly diagnosed antemortem. CT angiography is emerging as a diagnostic standard for patients with suspected PE.

The choice of diagnostic tests and imaging methods should depend on the clinical probability of PE and the patient's condition because of the great variability and lack of specificity of PE symptoms [3]. Patients with low and moderate probability clinical assessment should undergo a D-dimer rapid ELISA test. For patients with high probability clinical

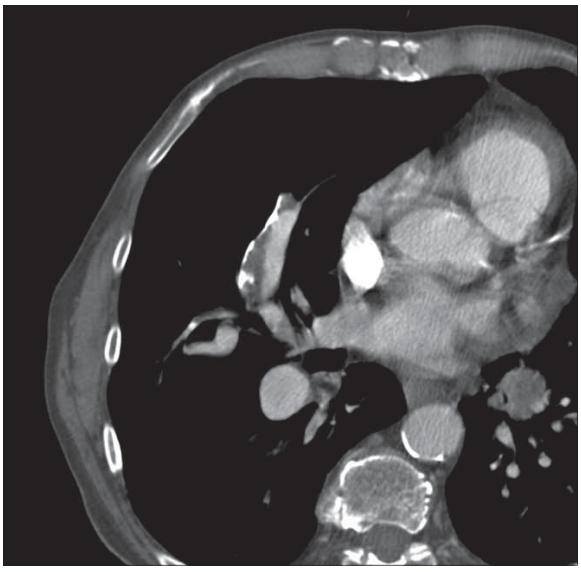

Figure 12. Occluded artery after recanalization.

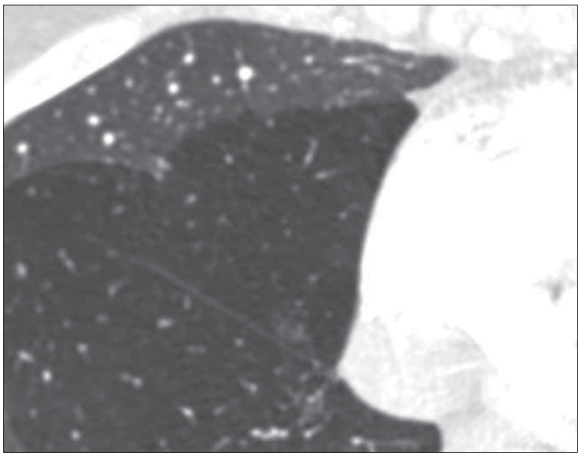

Figure 13. Mosaic perfusion pattern – areas of hypoattenuation represent underperfused lung.

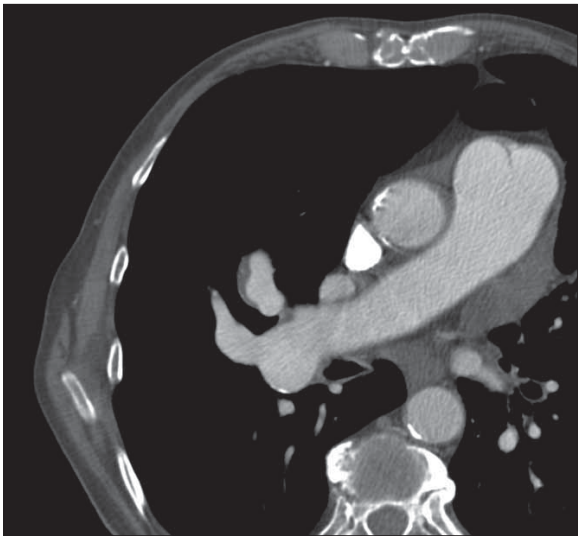

Figure 14. Main pulmonary artery diameter above 33 mm – insensitive but highly specific sign for the presence of pulmonary arterial hypertension

assessment CTA and venography are recommended as first diagnostic tests. Patients in shock or with hypotonia should undergo CTA instead of routine clinical probability assesment, becouse of high mortality rate. If CT is not available immediately, echocardiography should be performed in this group of patients.

The radiologist needs to determine whether radiological findings are caused by acute or chronic pulmonary embolism. If the results of CTA are indeterminate, the examination should be repeated or additional imaging using conventional pulmonary angiography is necessary. Alternatively, if lungs are clear, ventilation-perfusion scintigraphy can be performed.

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