Focus on pulmonary embolism imaging: where are we?

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ABSTRACT

Purpose: This paper aims to realize an analysis of available radio-imaging methods for outlining various forms of pulmonary embolism (acute or chronic) with highlights on the semiology and adequate medical indications.

Methods: There are several types of radiological examinations used in the evaluation of pulmonary embolism such as perfusion scintigraphy V/Q, digital subtraction angiography, computer tomography angiography, magnetic resonance angiography and cardio-pulmonary radiography.

Results: Based on existing studies to date and the informations accumulated in our Department of Radiology and Medical Imaging, we have outlined an imaging pathway in pulmonary embolism assessment.

Conclusions: Computer tomography angiography is actually considered the gold standard of diagnosis in suspected acute pulmonary embolism. Digital subtraction angiography plays a primary adjuvant therapeutic role or a diagnostic role in case of inconclusive computer tomography angiography examinations. In case of chronic thromboembolic pulmonary hypertension, computer tomography angiography serves as a confirmation tool for the thromboembolic etiology and in conjunction with digital subtraction angiography is mapping the emboli vital for curative thromboendarterectomy. Computer tomography angiography proves its role in the diagnosis of unsuspected pulmonary embolism in oncological patients, discovery that has a negative impact on patient prognosis. In cases where computer tomography angiography refute the diagnosis of pulmonary, the examination may reveal other causes that may explain the patient's symptoms with medical impact. Digital subtraction angiography maintains especially a therapeutic role. Magnetic resonance angiography starts to become of interest in the evaluation and follow-up of subacute or chronic pulmonary embolism. Chest X-ray has not changed over time its place in pulmonary embolism assessment and continues to be of secondary importance.

Key words: pulmonary embolism (PE), computer tomography angiography (CTA), angiography with digital subtraction, magnetic resonance angiography (MRA), cardio-pulmonary radiography (chest X-ray)

INTRODUCTION

Pulmonary embolism (PE) is considered to be the third cause of death after myocardial infarction and cerebral vascular accident. Risk of death in acute massive PE is approximately 15% and is considered to be lethal in up to 5% of

the cases within the first hour from the debut, having a greater impact than in acute myocardial infarction (1).

Awareness of its comorbid effect has placed PE in the area of major interest in medical world and the results are beginning to be seen through the development of - clinical probability scores for PE diagnosis and grading of the likelihood of serious early prognosis, - D dimer biochemical tests with increasingly performance and practical application and heart biomarkers, - radio-imaging diagnostic techniques readily available, CT angiography (CTA) being currently the method of choice and, - treatment protocols that continues to be improved (2).

Purposes

This article aims to present the place of medical imaging in PE diagnosis, and to discuss and illustrate the radio-imaging semiology, in acute and chronic PE.

Radio-imaging techniques

The milestone in the evolution of PE imaging were the multicenter PIOPED and PIOPED II (Prospective Investigation for Pulmonary Embolism Diagnosis) studies made possible based on the explosive evolution of radio-imaging technologies - digital subtraction angiography, multislice computer tomography and magnetic resonance imaging. (3)

Based on the findings of PIOPED study, perfusion scintigraphy V/Q considered a standard in PE diagnosis more than three decades has significantly reduced its role. According to PIOPED prospective study conducted in the 90s the scintigraphic interpretation was stratified into three degrees of probability, small, medium or high in terms of selection of patients with a high clinical probability of PE. A small percentage, 15% of patients had a high probability for thromboembolic disease and there was angiographic evidence of PE in cases scintigraphically stratified with small and medium probability. Corroborating the PIOPED study data with the evidence of reduced accessibility in daily medical practice for ventilation scintigraphy V/Q examination lead this method, in obscurity in PE diagnosis (4).

Digital subtraction angiography has proven over time accuracy in PE diagnosis. It is considered the method of choice to those who will benefit from the therapeutic interventional procedures, suction embolectomy, mechanical clot fragmentation and local thrombolysis or patients with CTA examination uninterpretable or uncertain. It is widely accepted its increased sensitivity in the PE diagnosis of approximately 98%. Specificity is reduced to 95% because PE may mimic other diseases, e.g. vascular obstructive tumor mass (5).

Angiographic criteria for acute PE were defined 40 years ago and their validity was confirmed and accepted so far.

Direct signs are completely stop of the vessel, the concave edge or filling defect. PE angiographic diagnosis accuracy decreases as the pulmonary artery diameter decreases, while reaching the level of sub-segmental arteries it becomes uncertain.

Indirect signs of PE are considered to be: a low flow of contrast, local hypoperfusion and delayed, decreased or absent venous flow. Angiography cannot establish the diagnosis of PE based only on indirect criteria.

Chronic PE can be diagnosed by angiography on the following signs: wall thrombi are adherent reason for not moving under the effect of contrast flow channeled stenotic areas and incomplete thrombus resolution visible as complete vascular obstruction or strip and internal contour irregularities and revascularization present by highlighting the collaterals.

There are also a number of limitations of the method, the well-known complications including risk of death, but the most important is its reduced availability especially in the emergency situations (6).

The introduction of multi-detector computer tomography, with multi-slice spiral acquisition with 4, 16, 64 and 128 rows has permitted the development of computer tomography angiography protocol (CTA), dedicated for pulmonary circulation respectively, in PE: the 0.625 mm or 1.25 mm thin sections have proven sensitivity and specificity higher than digital subtraction angiography, CT being currently widely accepted as the gold standard. As in the case of digital subtraction angiography, CTA loses sensitivity in the diagnosis of isolated subsegmental PE being about 63% (7). It remains to be determined what is the clinical impact of isolated subsegmental PE since a number of studies consider its incidence to be small, at most 4.7% and it is not very clear whether this form is a pathological or physiological process and if it requires anticoagulation (8).

Acute PE

Direct CTA signs: it highlights recent thrombus with hematic densities, hyperdense compared to vascular lumen, in rare cases. Most commonly, the thrombus is visualized after contrast injection surrounded by it, not adherent to the vascular wall. It can be viewed both axially and longitudinally as central or eccentric filling defect with sharp interface. Incongruity in diameter between the thrombus which is greater than that of the obstructed arterial vessel, may cause arterial consequent dilatation (9).

Depending on its location it can cover an arterial bifurcation with the appearance of the "saddle embolus" most often, located in the bifurcation of the pulmonary artery trunk but not exclusively. The "saddle embolus" generally has the diameter of the vein of origin. In case of a peripheral thrombus, complete occlusion of the artery occurs, with complete and sudden stop of the column of contrast material. For a better visualization of peripheral arrest, MPR (multi planar reconstruction) and MIP (maximum intensity projections) reconstructions are recommended along the longitudinal axis of the vessel (*figure 1*)

The "mosaic perfusion" pattern may be present especially, in situations where there is a peripheral vessel occlusion with associated thrombosis in situ. Generally in complete thromboembolic occlusion the affected parenchyma perfusion is performed by bronchial collateral circulation and thus secondary ventilation and perfusion disturbances do not occur. Mosaic perfusion appearance of the parenchyma is more evident later, in the CTA acquisition and not during the early arterial phase (10).

Indirect CTA signs: pulmonary infarction occurs in 10-15% of cases, especially in peripheral obstruction, a few hours or days after the onset of the PE episode and is transient in nature. It shows a typical appearance initially of "ground-glass" infiltrate evolving towards alveolar consolidation plated on pleura, with the top toward the hilum (with or without the evidence of the obstructed vascular lumen) and undergoes most frequently, full resolution or scarring connected with

the pleura or cavitation when an infectious process is added (*figure 2*).

In the case of a massive or medium PE resistivity increase in pulmonary arterial bed can cause increased retrograde pressure with difficult ejection of blood into the pulmonary artery trunk with final effect of RV (right ventricle) and central pulmonary arteries dilatation. Consequently there is an increase in RV diameter compared to LV (left ventricle), with bulging of inter-ventricular septum towards the left ventricular cavity. In the absence of cardiac gating it is recommended that RV measurement to be taken at the level of the "four chambers" axial plane type, in analogy with echocardiographic window. When RV is dilated the RV/LV ratio is greater than one (11-13).

After days the thrombus tends to attach to the wall when it starts a process of organizing with PE evolution towards chronicity and secondary pulmonary hypertension. It is believed that approximately 60-65 % of patients have an evolution towards full resolution and 35-40 % for thromboembolic organization. Of these approximately 5-10 % develops chronic thromboembolic pulmonary hypertension (CTPH). The period of time until the CTPH occurrence can't be predicted. It may occur after a few months or years from the initial PE episode (8).

CTPH

CTA diagnosis of CTPH is crucial because the chronic thromboembolic type of pulmonary hypertension in selected cases is curable by thromboendarterectomy. The

Figure 1 - 45y, female with acute onset of dyspnea suspected of acute PE confirmed at CTA with newly discovered inherited form of homocystinemia (a) MPR and (b) MIP, coronal, filling defect in the right pulmonary artery extending in the superior lobar artery and its segmentaries, intermediary trunk and medial lobar artery (arrow) and filling defects in the superior lobe and medial lobe segmental arteries (small arrows)

Figure 2 - (a) MPR coronal and (b) axial, HRCT acquisition, with pulmonary infarct in early onset - "ground-glass" infiltrate plated to the pleura in the right superior lobe (arrow)

organized thrombus, adherent to the wall appears as an eccentric, flattened defect at an obtuse angle with the vessel wall sometimes with calcifications included or as irregular or nodular arterial wall or as an abrupt narrowing of the vessel diameter or abrupt cutoff of distal lobar or segmental artery. There may be recanalization of thrombosed vessel. Less frequent and more difficult to delineate are the thrombi with webs or bands appearance in the segmental artery territory (14). Segmental narrowing and irregular of the lumen contour can occur by thrombus recanalization or medium hypertrophy situation encountered also in primary pulmonary hypertension.

CTPH progression in time determines RV wall hypertrophy with dilatation of the central arteries and mosaic perfusion in the periphery (*figure 3*). A main

pulmonary artery greater than 29 mm in diameter associated with segmental artery/bronchus ratio greater than 1, in more than 3 lobes are signs with 100% specificity for pulmonary hypertension (15). Mosaic perfusion is typical for CTPH having a role in etiologic diagnosis even in the absence of evidence of organized thrombosis of the vascular bed. Hypoperfusion areas are patchy, dark areas of lucent lung parenchyma secondary to reduced number and vasoconstriction of the arterial vessels. Free parenchyma compared to the hypoperfused seems more "opaque" and thus can be confused with the appearance of "ground-glass" infiltrates.

Bronchial arteries can suffer a process of hypertrophy and thus become visible in thin sections in the vicinity of pulmonary arteries. If pulmonary infarction

Figure 3 - 45 y, female with increased pressure in pulmonary artery at admission, suspected of CTPH with CT signs of chronic PE (a) eccentric wall adherent filling defects in the main pulmonary trunk, right and left lobar arteries (arrows) and a main pulmonary artery diameter of 39 mm (b) HRCT acquisition, mosaic perfusion pattern especially in the right lung with hypoperfused areas - patchy, dark areas of lucent lung parenchyma secondary to reduced number and vasoconstriction of the arterial vessels (small arrows) and normal parenchyma - more "opaque" with false appearance of "ground-glass" (arrow)

was present in the acute phase, it may appear as a scar or tissue mass or cavity

Differential diagnosis of PE includes other types of emboli like fat, septic, hydatid cyst, air, in situ thrombosis or pulmonary artery sarcoma (9). The mosaic perfusion pattern needs to be differentiated from mosaic pulmonary parenchyma in small air disease in the latter the mosaic pattern is more geographic and the vessels are of normal caliber and number.

Aiming to reduce population medical irradiation there are some attempts in promoting PE evaluation by magnetic resonance angiography (MRA). At present, there are isolated and small-scale studies that do not allow the establishment of clear criteria for MRA indications in PE. One can anticipate a possible role in the evaluation of CTPH or recent episode of PE in hemodynamically stable patient with allergy to iodine contrast (16,17).

Cardio-pulmonary radiography (chest X-ray) has a real role through increased accessibility and the ability to identify other causes that can cause similar symptoms as PE.

Acute PE

Common changes include atelectasis, minimal pleural effusion, usually occupying cardiophrenic angle, pulmonary infiltrates and raised diaphragm. Pulmonary infiltrates classically plate the pleura but may have various forms not always triangular which may create confusion.

The classic signs considered specific for PE like the Hampton hump (diaphragmatic hump) and Westmark sign (olighaemia distal to the obstructed pulmonary artery) occur rarely (18).

Another sign quite hard to outline is the increase in diameter of the right descending trunk of the pulmonary artery with peripheral olighaemia.

In the case of a massive PE right heart or global cardiac dysfunction may occur with cardiomegaly.

Radiographic changes are variable depending on the size and number of thromboemboli and hemodynamic characteristics of each patient. If the PE is small changes occur over time. At about 24 to 27 hours the natural evolution leads to surfactant loss and collapse of the alveoli consequently with the appearance and progression of lamellar atelectasis and to local edema with alveolar infiltrates that look like typical pneumonia. The reperfusion of the affected territory makes both processes to disappear after a few days (19).

CTPH

Often the chest X-ray may be normal but it also can

present changes that might suggest CTPH. Possible signs are: asymmetry of diameter or dilatation of bilateral hilar pulmonary arteries, association of areas of hypoperfusion with hyperperfusion areas, the latter with the appearance of interstitial infiltrates or more advanced as alveolar infiltrates, fibrotic scar lesions in contact with the pleura, as a marker of a history of pulmonary infarction and cardiac silhouette changes like of the right heart dilatation, visible by the disappearance of retrosternal space on the lateral view.

Understanding PE becomes "complete" by searching of the initial factor - deep venous thrombosis (DVT) and by assessing the impact on the right heart. Evaluation in DVT is done by ultrasound of peripheral deep veins. Most studies of deep vein ultrasound give to the method a sensitivity and a specificity of 95 % in symptomatic patients. In patients suspected of PE venous ultrasonography is useful in highlighting deep vein thrombosis as the source of pulmonary thromboembolism even if at least 50 % of patients have no proof of DVT. The absence of deep vein thrombosis in patients suspected of PE is due to complete migration of the thrombus in the pulmonary arterial bed (20).

Currently, there are studies that propose the evaluation of DVT by CT venography (CTV) or MRI venography (MRV) in patients with PE when pelvic vein thrombosis is suspected, ultrasonography having a low sensitivity in this area. The major disadvantage of CTV is pelvic irradiation of reproductive organs. Probably the indication of CTV as a single scanning or as a second acquisition after evaluation of pulmonary circulation should be limited to particular situations such as patients with repetitive PE or those in which the response to anticoagulant treatment is unsatisfactory and the ultrasound is negative. MRV has the advantage of being non-irradiating.

Functional assessment of the heart in patients with right heart dysfunction in acute PE or CTPH is made by echocardiography or transesophageal echocardiography the latter could visualize the thrombus in the pulmonary artery trunk (21,22).

CONCLUSIONS

CTA is actually considered the gold standard of diagnosis in suspected acute PE. Angiography plays a primary adjuvant therapeutic role or a diagnostic role in case of inconclusive CTA examinations. In case of CTPH, CTA serves as a confirmation tool for the thromboembolic etiology and in conjunction with digital subtraction angiography is mapping the emboli vital for curative thromboendarterectomy. CTA increasingly

proves its role in the diagnosis of unsuspected PE in cancer patients, during the routine examinations performed according to the oncology protocol discovery that has a negative impact on patient prognosis. In cases where CTA refute the diagnosis of PE, the examination may reveal other causes that may explain the patient's symptoms and also may outline other unsuspected changes in the scanned field, with medical impact, in patients with confirmed PE.

Digital subtraction angiography maintains especially a therapeutic role.

MRA starts to become of interest in the evaluation and follow-up of subacute or chronic PE.

Chest X-ray has not changed over time its place in PE assessment and continues to be of secondary importance.

REFERENCES

- Laporte S, Mismetti P, Decousus H, et al: Clinical predictors for fatal pulmonary embolism in 15,520 patients with venous thromboembolism: Findings from the Registro Informatizado de la Enfermedad Tromboembolica venosa (RIETE) Registry. *Circulation* 117:1711, 2008
- van Belle A, Buller HR, Huisman MV, et al: Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. *JAMA* 295:172, 2006.
- Paul D. Stein, Pamela K. Woodard, John G. Weg et al. "Diagnostic Pathways in Acute Pulmonary Embolism: Recommendations of The PIOPE II Investigators" *The American Journal of Medicine* (2006) 119, 1048-1055
- Mythreyi Bhargavan, Jonathan H. Sunshine, Rebecca S. Lewis, Saurabh Jha, Jean B. Owen, Joyce Vializ "Frequency of Use of Imaging Tests in the Diagnosis of Pulmonary Embolism: Effects of Physician Specialty, Patient Characteristics, and Region", *AJR* 2010; 194:1018–1026
- Andetta R. Hunsaker, Michael T. Lu, Samuel Z. Goldhaber and Frank J. Rybicki "Imaging in Acute Pulmonary Embolism With Special Clinical Scenarios" *Circ Cardiovasc Imaging*. 2010;3:491-500
- Hagspiel KD, Polak JF, Grassi CJ, Fایتelson BB, Kandarpa K, Meyerovitz MF "Pulmonary embolism: comparison of cut-film and digital pulmonary angiography." *Radiology*. 1998 Apr;207(1):139-45.
- Eyer BA, Goodman LR, Washington L. Clinicians' response to radiologists' reports of isolated subsegmental pulmonary embolism or inconclusive interpretation of pulmonary embolism using MDCT. *Am J Roentgenol* 2005; 184:623–8.
- Stavros V.Konstantinides, AdamTorbicki, GiancarloAgnelli et al. "2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism. The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS)", <http://dx.doi.org/10.1093/eurheartj/ehu283>
- Conrad Wittram, Michael M. Maher, Albert J. Yoo, Mannudeep K. Kalra, Jo-Anne O. Shepard, Theresa C. McLoud, "CT Angiography of Pulmonary Embolism: Diagnostic Criteria and Causes of Misdiagnosis" *RadioGraphics* 2004; 24:1219–1238
- Daehee Han, Kyung Soo Lee, Tomas Franquet, Nestor, L. Muller, Tae Sung Kim, Hojoong Kim, O Jung Kwon, Hong SikByun, "Thrombotic and Nonthrombotic Pulmonary Arterial Embolism: Spectrum of Imaging Findings" *RadioGraphics* 2003; 23:1521–1539
- Matej Podbregar, Bojan Krivec and Gorazd Voga, "Impact of Morphologic Characteristics of Central Pulmonary Thromboemboli in Massive Pulmonary Embolism" <http://journal.publications.chestnet.org/> on 10/25/2014
- Halil Dogan, Lucia J. M. Kroft, Menno V. Huisma, Rob van der Geest, Ying Li O, Hildo J. Lamb, Albert de Roos "Assessment of Right Ventricular Function in Acute Pulmonary Embolism Using ECG-Synchronized MDCT", *AJR* 2010; 195:909–915
- Kumamaru KK, Hunsaker AR, Bedayat A, et al. "Subjective assessment of right ventricle enlargement from computed tomography pulmonary angiography images". *Int J Cardiovasc Imaging* 2011 Jun 14
- Le Gal G1, Righini M, Parent F, van Strijen M, Couturaud F. "Diagnosis and management of subsegmental pulmonary embolism." *J Thromb Haemost*. 2006 Apr;4(4):724-31.
- Elena Pepa, Carole Dennie, John Veinot, Susana Hernandez Mupiz "Pulmonary Hypertension: How the Radiologist Can Help" *RadioGraphics* 2012; 32:9–32
- Hale Ersoy, Samuel Z. Goldhaber, TianxiCai, Tuan Luu, Joshua Rosebrook, Robert Mulkern, Frank Rybicki "Time-Resolved MR Angiography: A Primary Screening Examination of Patients with Suspected Pulmonary Embolism and Contraindications to Administration of Iodinated Contrast Material" *AJR* 2007; 188:1246–1254
- Reiter G, Reiter U, Kovacs G, et al. "Magnetic resonance-derived 3-dimensional blood flow patterns in the main pulmonary artery as a marker of pulmonary hypertension and a measure of elevated mean pulmonary arterial pressure." *Circ Cardiovasc Imaging* 2008; 1:23–30
- L R Goodman, R J Lipchik "Diagnosis of acute pulmonary embolism: time for a new approach." <http://dx.doi.org/10.1148/radiology.199.1.8633154>
- Dalen JE, Haffajee CI, Alpert JS, et al. Pulmonary embolism, pulmonary hemorrhage and pulmonary infarction. *N Engl J Med* 1977;196:1431-1436.
- Douglas S. Katz, Kristen Fruauff, Anca-OanaKranz, and Man Hon" Imaging of deep venous thrombosis: A multimodality overview" www.appliedradiology.com, March 2014
- GelarehSadigh, Aine Marie Kelly, Paul Cronih"Challenges, Controversies, and Hot Topics in Pulmonary Embolism Imaging" *AJR* 2011; 196:497–515
- Philip A. Araoz, Linda B. Haramati, John R. Mayo, Eduardo Jose Mortani Barbosa, Jr., Frank J. Rybicki Patrick M. Colletti "Panel Discussion: Pulmonary Embolism Imaging and Outcomes" *AJR* 2012; 198:1313–1319