

IMAGING' S ROLE IN THE MANAGEMENT OF PULMONARY THROMBOEMBOLISM

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Abstract: The progress made in recent years in terms of managing patients with suspicion of pulmonary embolism, improved the accuracy of indentify this pathology and made the diagnosis algorithms be safer and easier to use in the daily practice. In spite of these, pulmonary embolism is maintained among the pathology with increased morbidity and mortality. The difficulty of diagnosis, which derives from unspecific clinical picture, with variations from the lack of symptoms up to sudden death, make necessary a complex approach, based on a combination of clinical, laboratory and imaging examinations. The contribution of imaging is major, starting from basic examinations (x-ray, echo exam), and ending with more complex (like AngioCT), each having their role in diagnosis, risk assessment and therapeutic attitude to follow.

Cuvinte cheie: trombembolism pulmonar, examinări imagistice

Rezumat: Progresele făcute în ultimii ani în ceea ce privește gestionarea pacienților cu suspiciune de TEP au îmbunătățit acuratețea depistării acestei patologii, și au făcut ca algoritmi de diagnostic să fie mai siguri și mai ușor de utilizat în practica de zi cu zi. În ciuda acestora, trombembolismul pulmonar se menține printre afecțiunile cu mortalitate și morbiditate crescută. Dificultatea diagnosticării, ce derivă din tabloul clinic nespecific, cu variații de la lipsa simptomatologiei până la moarte subită, face necesară o abordare complexă, bazată pe îmbinarea elementelor clinice, cu examinările de laborator și cu cele imagistice. Aportul acestora din urmă este major, pornind de la examinările de bază (radiografie CP, examen echo), și finalizând cu examinările mai complexe (Angio CT), fiecare având rolul lor în diagnosticarea, evaluarea riscului și decizia atitudinii terapeutice de urmat.

Pulmonary thromboembolism (PE) is a clinical condition resulting from thrombotic obstruction of the pulmonary artery or their branches. The clots can be migrate from the deep vein, from the cavities of the heart or, more rarely may be formed in situ.

Due to nonspecific symptoms, PE is suspected in most patients who present respiratory symptoms (dyspnoea, tachypnea), and chest pain. In the clinical practice, in order to confirm or to rule out the diagnosis, we use imaging investigations.

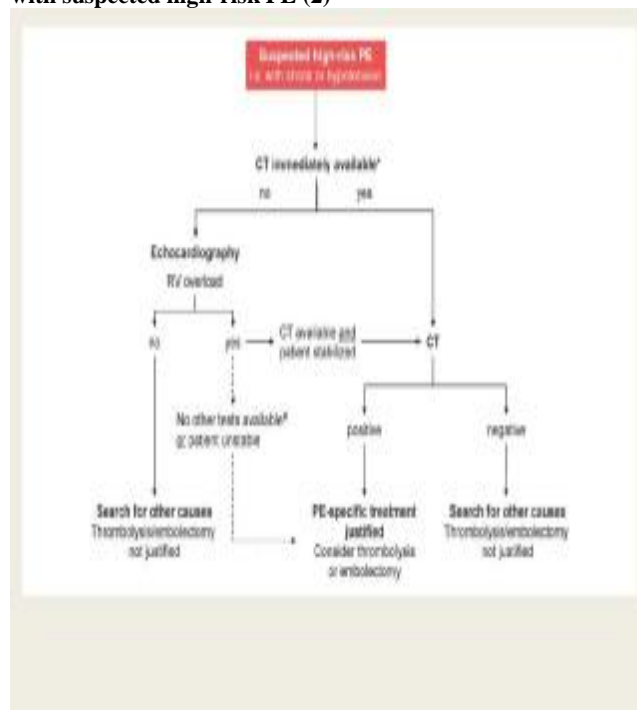
The European Society of Cardiology suggests in the last guideline, an algorithm of diagnosis of patients with clinical suspicion of PE. Thus, patients with high risk, are hemodynamically unstable patients, with severe hypotension (<90mmHg), or cardiogenic shock in the absence of rhythm disorders, hypovolemia or sepsis which could explain the hemodynamic deterioration (figure no. 1).(2)

Patients with moderate/low risk will be evaluated from the perspective of clinical pretest probability of PE and by the values of plasma D-Dimers. For patients with moderate/low probability test and negative D-dimers, we can exclude the diagnosis of PE and they do not necessitate anticoagulant medication.

Elevated D-dimers values in patients with moderate/low or high pretest probability require additional investigations (figure no. 2).(2)

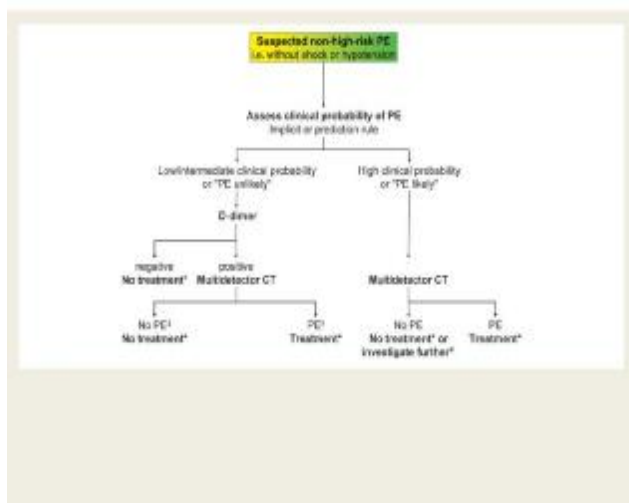
We will elaborate, more broadly, the main imaging investigations and their contribution in the diagnosis of PE.

Figure no. 1. Proposed diagnostic algorithm for patients with suspected high-risk PE (2)



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Figure no. 2. Proposed diagnostic algorithm for patients with suspected non high-risk PE (2)



1. Chest X-ray is usually the first investigation carried out; it has no diagnosis role, being used especially in the detection of other alternative pathologies, like congestive heart failure, acute pneumonia, pneumothorax. Most of the times, it has normal aspect, but it is known that a normal x-ray in the presence of stormy modified gas respiratory values, is highly suggestive for PE.(2)

Signs suggestive for PE, that we can see on a X-ray, are: unilateral pulmonary artery dilatation (Fleishner's mark), superior cave vein and azygos vein dilatation, the sudden interruption of juxtahilar vessels, Hampton's mark, atelectasis, ascending hemidiafragm, focal olighemia(Westenmarkt mark), pleural effusions (20-50% of cases).(2,7)

Two studies, performed on patients diagnosed with PE, X-ray results showed in 75-90% of cases pathological signs. Radiological signs have varied depending on size and number of de emboli, and their hemodynamic determination in the pulmonary circulation. In the case of small emboli pulmonary modification had time to install (for example, in 24 to 72 hours, is time to develop atelectasis and alveolar infiltrates, that are difficult to differentiate from pneumonia).(7) X-ray may also be used in subsequent decisions concerning complementary investigations should be carried out, considering their side effects(radiations, post contrast nephropathy): a normal X-ray indicate that might be useful to perform a V/Q scan, while a modify one suggests that scintigramma could be non diagnostic, and we rather should perform an angio CT.(1)

2. Peripheral venous ultrasound

Because US of lower limb is a relatively simple procedure to perform and interpret, without risk and without being an invasive procedure, many authors have included it in the initial stages of the diagnostic algorithm of the PE. In most cases, the source for PE is a deep vein thrombosis (DVT) of inferior limbs. Studies have shown that in approximately 70% of cases with PE diagnosed, the existence of a DVT. The only criteria for establishing the diagnosis of DVT is full incompressivity of the vein, which equates to the existence of a thrombus.(1)

Identification of a DVT in a patient with suspected PE, is of major importance, since it constitutes sufficient argument for the initiation of anticoagulant therapy, without doing additional tests.(2)

Recently, it is believed that making venous CT, which can be combined with chest angio CT in one procedure, is more precise for the diagnosis. PIOPED II Study demonstrated an

increase of number of deep thrombosis in a rate of 7 to 26% by this method.(2)

3. Transthoracic echocardiography (TTE)

Although it is a simple method of investigation, without risk, its role in the diagnosis of PE is limited, due to its low sensitivity and specificity, and as a result it is not recommended as the investigation of choice in diagnostic strategy of the PE. The guidelines recommended it only at patients with massive PE, for those in whom angio CT is not available or cannot be done. The big advantages are the fact that it is noninvasively and that it is available in majority of health units.(7) Diagnosis criteria of PE varies from one trial to another, but generally are based on identifying signs of overstress of right heart, as right ventricular (RV) dimensions, RV/LV ratio > 1, the degree of tricuspid valve regurgitation; due to the low sensitivity (60-70%), a negative ultrasound examination cannot rule out the existence of the PE. On the other hand, it is known that the signs of overload or dysfunction of the right heart may due to other cardiac or pulmonary pathologies, in the absence of a PE.

Therefore, they sought signs with higher specificity, the results being limited. The ' 60-60' sign ,which signifies the time of ascent of systolic pulmonary flow(<60ms), associated with a systolic gradient between 30-60mmHg, or McConell mark, defined by the decrease of the contractility of RV wall, are signs which appear to have a higher VPP, even there is a concomitant lung disease.(2)

Cassaza et al. analyzed 161 patients diagnosed with PE and RV myocardial infarction (MI); in the case of PE, Mc Conell sign was identified at 70% of them, while at the ones with MI was found in 67%, concluding that Mc Conell is specific for PE only in the absence of RVMI.(7)

An European study analyzed 119 cases were identified thrombi in the right heart; they were analyzed in terms of morphological aspects, concluding that patients with mobile, thin, long thrombi, showed worse prognosis compared to those with amorphous appearance of thrombi, less mobile, with a rate of 89% to 40% for PE; of these, the rate of death in the firs situation was 42%, in the second was no death report.(7)

For patients hemodynamically unstable, in shock or hypotension, the absence of right heart dysfunction signs at the TTE is a sufficient argument to rule out PE as a cause of instability. Moreover, in this case, the echography can establish differential diagnoses: acute cardiac tamponade, MI, acute valvulopathy dysfunction. For the patients with PE which are hemodynamically stable, Echocardiography is a useful instrument for risk stratification.(2)

4. Ventilation/perfusion Scintigraphy (V/Q Scan)

Before the widespread use of CT scans, the V/Q scan was a valuable part of the screening method for patients with suspicion of PE, being knew that a normal scan, practically exclude the possibility of this diagnostic. Today, it remains a valid option for patients who have elevated levels of plasmatic DD, and which cannot perform a CT exam because of intolerance for contrast material nor have chronic kidney failure. The diagnosis is based on highlighting the areas of ventilation / perfusion mismatch, arising when parts of the lung, served by a pulmonary vessel are ventilated but no perfused because of an thrombus at that level; probability is based on the size and number of the mismatch.(3)

PIOPED Nord American study, has compared the usefulness of V/Q scan versus angiography as the gold standard in the diagnosis of PE; they were setting 4 probability categories: low, intermediate, high and non-diagnostic, on the basis of certain criteria which are still widely discussed; the accuracy of this method, in the case of patients with

intermediate or nonconclusive results is much improved by using clinical probability trials, by determine the DD levels, by use of venous US.(2)

5. *Pulmonary Angiography*

Is a technique that dates back to the 1950s, and to the development and refinement of angio-CT, was the gold standard in the diagnosis of the PE. The diagnostic criteria established over 40 years ago, are view the defects of intravascular filling, vascular amputation, regional oligemia and the present of an asymmetric, slow flow; through direct angiography can be located the thrombi of vessels at subsegmentar level, that sizes up to 1-2 mm. The literature data, noticed that the sensitivity of pulmonary angiography is approximately 98%. Although it is an invasive method is a relatively safe method. The complications described: hematoma, renal failure, respiratory dysfunction, death, appearing in less than 1% of cases. However, most practitioners avoid it, especially in cases where it has taken into account or was given thrombolytic therapy. Today, it is a method rarely used, reserved for those with ambiguous CT results, or for those who practice interventional procedures such as catheter thrombolysis or embolectomy.(1,2)

6. *Computed tomography with contrast substance (Angio CT)*

Along with the introduction of the MDCT with high temporal and spatial resolution, angio CT has become in daily practice the method of choice for diagnosis of PE, in patients with clinical suspicion of it. MDCT lets you view the pulmonary arterial bed up to the last segment. Positive diagnosis is based on direct observation of a defective filling, surrounded by a fine blade of contrast substance at the intra-arterial level or of more indirect signs, such as vascular amputation or absence of vascular filling.(1,5)

A negative MDCT exam, rules out the diagnosis of PE the patients with non increased clinic probability. Remains the problem of patients with high pre-test probability and a negative MDCT; PIOPED II multicenter study has illustrated a major discrepancy between the results of CT and pre-test probability score established by Wells. Keep as the subject of debate, the necessity in this case of additional testing, such as vascular US, V/Q scan.(1,2,5,6)

Numerous studies have been done over the past 15-20 years, in idea of studying, the specificity and sensitivity of this exam, analysing the results obtained in daily practice. Most investigators agree that the use of single-slice helical CT is sufficient for the diagnosis of PE at the large vessels level, but may not be used to the exclusion of the emboli find at the segment levels. Obviously, using a four-slice CT scanner has grown much the diagnose value, the PIOPED II study, showing a sensibility of 83% and a specificity of 96%. Quanadly et al. have compared the results obtained by dual-slice CT with pulmonary angiography, and have obtained a 90% sensitivity, and a specificity of 94%. Appearance of multislice CT (16 or 64) improved interobservers compliance, that reaching a rate of 94%.(7)

An important aspect is the imaging of the heart, RV failure being the major cause of death in patients with PE. The CT determinations, correlate fairly well with the severity of the clinic, there is evidence that a report VD diameter /VS diameter ratio > 1.5 is sufficient proof to establish the diagnosis of massive PE. Value >0.9, along with putting the paradoxical motion of the IVS to the left, are signs that show the need for admission of patients in an intensive care unit.(1,6)

The severity of the PE was associated with the degree of obstruction of the pulmonary arterial bed, highlighted by CT. Some scores (e.g. Miller), have been settled and modify just to be able to be used in the framework of this technique; the degree

of obstruction, expressed as a percentage, was correlated with the severity of the clinic. Thus, an index of > 40% of obstruction is associated with severe right ventricular dysfunction, necessitating implementation of aggressive therapies.

Studies have shown that a RV/LV ratio > 1, combined with an index of vascular obstruction > 40%, increase the PPV for mortality at 3 months at 18.8%.(6,7)

7. *Magnetic resonance angiography (MRI Angio)*

MRI is a useful method of investigation in patients with suspicion of PE and with relative or absolute contraindications for performing the CT, as is the case of the patients with chronic kidney failure or that of the pregnant women, patients with isolated thrombosis of cava or iliac vein.(2)

Many aspects related to pulmonary circulation were studied, such as PE, with the possibility of determining the age of thrombus, establishing the degree of pulmonary hypertension, the vessel elasticity at this level, and concomitant identify deep vein thrombosis and of congenital disease. The number of studies that have considered the use of MRPA in detecting PE has grown steadily in recent years. Recent reports focuses on the use of 2D and 3D preview, and more recent studies refers to the improved 3D technique with contrast material, the latter having the advantage of a quick and safe interpretations. Bergin et al. investigated the accuracy of 2D technique in case of 26 patients with confirmed chronic PE by angioCT, and found a sensibility of 36% and a specificity of 65% for central thrombosis, and higher values for the segmental ones, 72% respectively 59%.(7)

8. *Future Perspectives: intravascular ultrasonography (IVUS)*

Although it is widely accepted value of angiography as a diagnostic method in the PE, there are situations, such as those in which vessel occlusion is only partial, and leave room for interpretation; through angiography may not be appropriate viewing thin thrombus, soldering to the walls because making cross sections on the entire length of the vessel is virtually impossible. Hence, the need for the use of a technique that allows you to view the entire lumen (up to small vessel, 1.5-3 mm) and of vascular walls (their movement, changes in the structure in case of pulmonary hypertension), that was found in the case of intravascular ultrasonography (IVUS).(7) Studies done on this technique are small, and are still in the beginning; it was described the use of IVUS in the case of one patient with pulmonary atherosclerosis, which cannot be visualized by angiography.(8) A full description of the anatomy of the lung using IVUS was carried out by Kawano; recorded descriptions of it were confirmed by Stahr et al. In ex vivo studies, was concluded that old clots, organized in the chronic PE can be detected using IVUS, being described as a second layer in the inside of the vas. A research group, described the use of IVUS in one case of acute PE; They described that could bypass the obstruction, and have viewed two thrombi sticky of the vascular wall and others that were fleeting free in the lumen.(9) Studies have shown the superiority of IVUS versus angiography in identifying residual thrombi; Unfortunately, in the case of pulmonary circulation still shows important shortcomings: it is an invasive method, which involves sometimes high-dose of irradiation; steerable catheters are not used, and are difficult to control at the level of the pulmonary circulation, and as a result there are a limited number of vessels which may be investigated as.(7) IVUS has gained ground in several studies, which concerned the implantation of filters to the IVC. Ebaugh et al. reported success in 24 of 26 cases, without the use of fluoroscopy.(10)

The progress over the last decade in terms of management of the PE by the proposed diagnostic algorithms,

have made that addressing to this disease to be safer, and with greater therapeutic opportunities. The practitioner must take into account besides symptomatology, clinical and para clinical investigations that we can apply, their contribution in diagnosis based on clinical trials, and managed them in a diagnostic algorithm, on which all subsequent attitude depends. Still, the trials consider more diagnostic strategies, which want to be easiest and safer, to involve as little invasive investigations and why not, with a low-cost as possible.

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