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Pulmonary thromboembolic disease – clinical and etiological aspects in internal medicine department

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ABSTRACT

Background: Pulmonary embolism (PE) represents the third most frequent vascular disease following acute myocardial ischemic disease and stroke. It is a common and potentially lethal disease. Aim: We observed etiological spectrum, clinical aspects and diagnostic tests for patients with PE. Material and methods: Retrospective observational study that included 53 patients diagnosed with PE between 01.01.2009-31.12.2013. We followed epidemiological aspects, risk factors, clinical manifestations and methods for positive diagnosis. Results: 53 patients which represents 0.66% from the patients admitted in our department (n=8,011), were diagnosed with PE. The main risk factor for PE was malignancy (n=16). Twenty patients with PE presented deep venous thrombosis (DVT) and 12 patients arterial thrombosis (AT). Main clinical syndromes of patients with PE were pulmonary infarction (n=32), isolated dyspnea (n=11) and circulatory collapse (n=10). A lot of paraclinical investigation sustained positive diagnosis, mainly by high performance techniques. Four cases were diagnosed postmortem.

Conclusions: Clinical diagnosis of PE has a low accuracy. Clinical evaluation, even unspecific has a considerable value in the selection of patients who needed further paraclinical diagnostic procedures.

Keywords: pulmonary thromboembolism, clinical diagnosis, investigation.

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Introduction

Pulmonary embolism (PE) is an extremely common and highly lethal condition that is a leading cause of death in all age groups. PE is the third most common cause of death in the US, with at least 650,000 cases occurring annually. It is the first or second most common cause of unexpected death in most age groups. The highest incidence of recognized PE occurs in hospitalized patients. Unfortunately, the diagnosis is missed more often than it is made, because PE often causes only vague and nonspecific symptoms. Deep vein thrombosis (DVT) and PE are much more common than usually realized. Most

patients with DVT develop PE and the majority of cases are unrecognized clinically. Untreated, approximately one third of patients who survive an initial PE die of a future embolic episode [1]. Most patients succumb to PE within the first few hours of the event. In patients who survive, recurrent embolism and death can be prevented with prompt diagnosis and therapy. The incidence of PE may differ substantially from country to country; observed variation is likely due to differences in the accuracy of diagnosis rather than the disease incidence [1,2].

Material and Methods

It is a retrospective observational study that included 53 patients diagnosed with pulmonary embolism during 5 years (01.01.2009-31.12.2013), which represented 0.66% from the patients admitted in our department (n=8,011). We followed epidemiological aspects, risk factors, clinical manifestations and methods for positive diagnosis.

Results and Discussion

Patient's age was between 30-81 years, majority (n=38) were > 55 years old; 31 patients were females and 22 patients males. In literature, PE is predominantly a disease of older individuals. The incidence of venous thromboembolic events in the elderly is more common among men than women. In patients younger than 55 years, the incidence of PE is higher in females [1].Risk factors are exposed in table 1.

Table I - Risk factor for PE

Risk factors		Number of patients (n)
Malignancies (n=16)	Bowell	5
	breast	3
	Lung	5
	Ovary	3
Congestive heart failure (CHF)		10
Thrombophilia (n=6)	factor V Leiden mutation causing resistance to activated protein C	3
	antiphospholipid syndrome	3
Surgery (n=9)	fracture of the femur	9
Chronic obstructive pulmonary disease (COPD) (n=4)		4
Postpartum (n=4)		4
Idiopathic (n=4)		4

The main risk factor for PE in our study was malignancy (n=16), and the most frequent malignancies associated with PE were bowel (n=5) and lung (n=5).The causes for PE are multifactorial and are not readily apparent in many cases. The main causes are: venous stasis, hypercoagulable states (acquired or congenital thrombophilia: deficiencies in protein C, protein S, and antithrombin III, factor V Leiden mutation), immobilization, surgery and trauma: fractures of the femur and tibia are associated with the highest risk, pregnancy, oral contraceptives and estrogen replacement therapy, malignancy: neoplasms (most commonly associated with PE are pancreatic, pulmonary, genitourinary, colorectal, gastric, and breast carcinoma), other risk factors: stroke, venous catheters, previous history of venous thromboembolism, congestive heart failure, fractures of the long bone, obesity, varicose veins, inflammatory bowel disease [1,2]. A part of these causes were also diagnosed in our patients. Surgical patients have long been recognized to be at special risk for DVT and PE, but the problem is not confined to surgical patients. Prospective studies show that in the absence of prophylaxis acute DVT may be demonstrated in any of the following: general medical patients placed at bed rest for a week (10-13%), patients in medical intensive care units (29-33%), patients with pulmonary disease kept in bed for 3 or more days (20-26%), patients admitted to a coronary care unit after myocardial infarction (27-33%), patients who are asymptomatic after coronary artery bypass graft (48%). These patient groups are at high risk for clinically unrecognized DVT, and half or more of the patients with DVT also can be shown to have suffered

a PE, even though the majority have had none of the classic symptoms of PE. PE is common in all trimesters of pregnancy and the puerperium, and the incidence of PE is increased in women receiving oral contraceptive or hormone replacement therapy [2, 3].
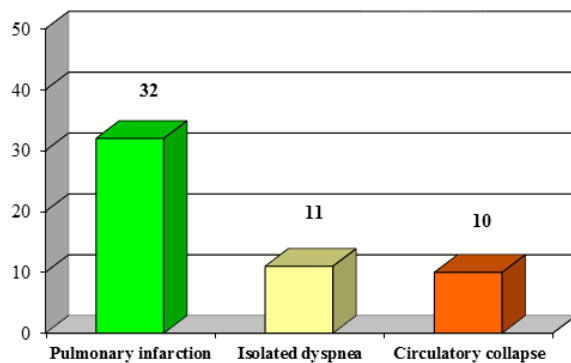

Figure 1 – Clinical syndromes of the patients with PTVD

Patients with PE were classified into three clinical syndromes (Figure 1): pulmonary infarction (n=32);isolated dyspnea (n=11);circulatory collapse (n=10).Our patients with pulmonary thromboembolism presented associated events (Figure 2):20 patients deep venous thrombosis (DVT): lower legs (n=14), upper extremities or neck veins (n=6).
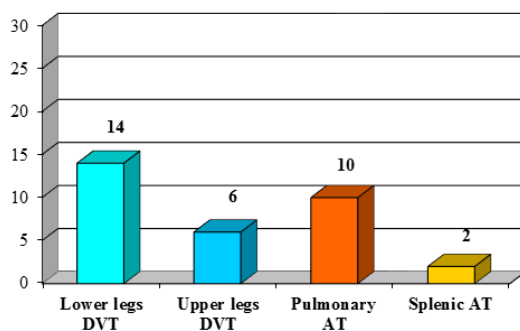

Figure 2 – Associated events for patients with PTVD

12 patients presented associated arterial thrombosis (AT): pulmonary arterial thrombosis (n=10), splenic arterial thrombosis (n=2). In literature, the presentation of patients with PE can be categorized into 4 classes based on the acuity and severity of pulmonary arterial occlusion: massive PE, acute pulmonary infarction, acute embolism without infarction and multiple pulmonary emboli. Most patients with PE have no obvious symptoms at presentation. In contrast, patients with symptomatic deep vein thrombosis (DVT) commonly have PE confirmed on diagnostic studies in the absence of pulmonary symptoms. The most common symptoms of PE in the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study were dyspnea (73%), pleuritic chest pain (66%), cough (37%), and hemoptysis (13%). Clinical signs and symptoms are nonspecific; therefore, patients suspected to have PE must undergo diagnostic tests until the diagnosis is ascertained or eliminated or an alternative diagnosis is confirmed. PE should be suspected in any patient with unexplained dyspnea, tachypnea, or chest pain. All patients suspected of PE must be risk stratified, ideally with a criteria-validated clinical decision rule [2]. Wells criteria, which actually allow clinicians to compartmentalize patients into pulmonary embolism-unlikely and pulmonary embolism-likely groups; this really helps clinicians to make decisions on the next appropriate test and diagnosis (table 2).

Table II - Modified Wells criteria – clinical decision rule for evaluation of patients with suspected PE [4]

Variable	Points
Clinical symptoms and signs of deep venous thrombosis (DVT)	3
Alternative diagnosis less likely than PE	3
Heart rate greater than 100 beats/minute	1.5
Recent immobilization or surgery	1.5
Previous venous thromboembolism	1.5
Hemoptysis	1
Malignancy	1
'PE unlikely ≤ 4 'PE likely > 4	

The positive diagnosis was sustained in our study by a lot of paraclinical investigations, mainly by high performance techniques:

a) partial pressure of oxygen in arterial blood < 80 mmHg was present in 33 patients, but the predictive value of hypoxemia is quite low [4].

b) D-dimer was positive at majority of our patients (n=50). The data from literature show that D-dimer test misses 10% of patients with PE,

while only 30% of patients with positive D-dimer findings have a confirmatory diagnosis of PE. Review of the current evidence for new diagnostic modalities suggests that in patients with low-risk normal D-dimer assays, PE is reliably excluded; no further testing is required. The D-dimer test has an excellent negative predictive value for the exclusion of pulmonary embolism in the low- or moderate-probability patients group [5].

c) electrocardiogram was performed at all patients and show the following chances: tachycardia (n=24); right bundle branch bloc (n=11); non-specific ST-T changes (n=27). Consistent with literature data, the most common ECG abnormalities of PE are tachycardia and nonspecific ST-T wave abnormalities. But these findings are not sensitive or specific enough to aid in the diagnosis of PE. The classic finding of right-heart strain demonstrated by an S1-Q3-T3 pattern is observed in only 20% of patients with proven PE [2].

d) chest X-ray reveals modifications at 45 patients represented by: pulmonary infarction; pleural effusion; atelectasis (Figures 3,4). Initially chest radiography findings are commonly normal. However, in later stages, the X-ray film may show radiographic signs that include a Westermark sign (dilatation of pulmonary vessels and a sharp cutoff), atelectasis, a small pleural effusion, and an elevated diaphragm. Although chest radiograph findings may indicate an alternate diagnosis, this study alone is not sufficient to confirm the diagnosis of PE [2,4].
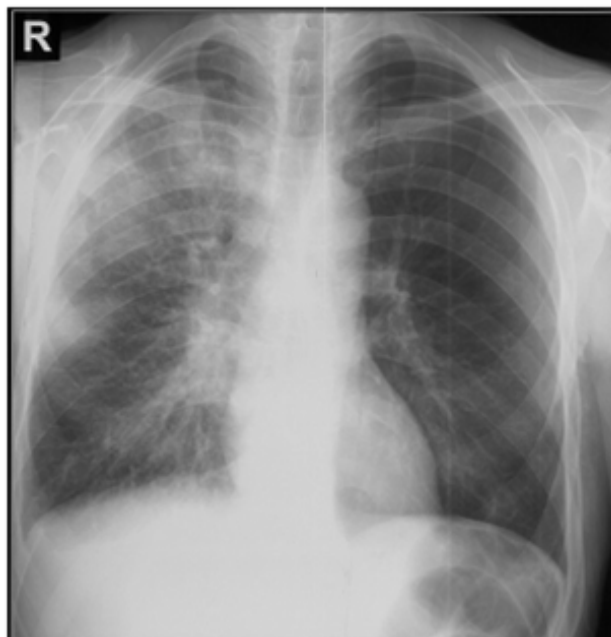

Figure 3 – A postero-anterior chest radiography in a 53 years old male patient with acute pulmonary thromboembolism and right lung cancer reveals multiple heterogeneous opacities, with irregular borders and subcostal intensity in upper 2/3 of the right lung; enlargement of right hilum.

Figure 4 – A postero-anterior chest radiography in a 43 years old female patient with pulmonary infarction shows a homogenous triangular opacity in the left pulmonary base with a convex contour toward the hilum.

e)   spiral CT scanning was done at 49 patients and shows characteristic findings: pulmonary infarction; pleural effusion; arterial thrombosis (Figures 5,6,7).
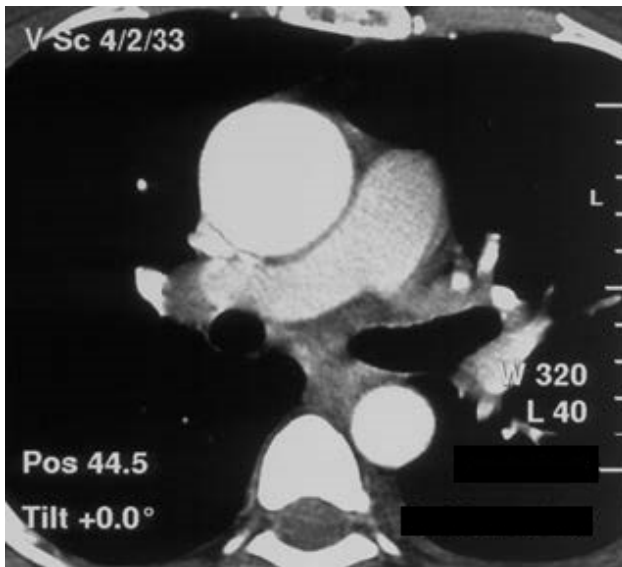

Figure 5 – Contrast enhanced spiral CT scan in a 43 years old female patient with acute pulmonary thromboembolism and thrombophilia reveals a full filling defect in the right pulmonary artery

Figure 6 – Spiral CT scan in a 53 years old male patient with acute pulmonary embolism and right lung cancer reveals a right retrohilar tumor 3,5/3 cm, with spiculated projections in surrounding lung parenchyma; right pleural effusion
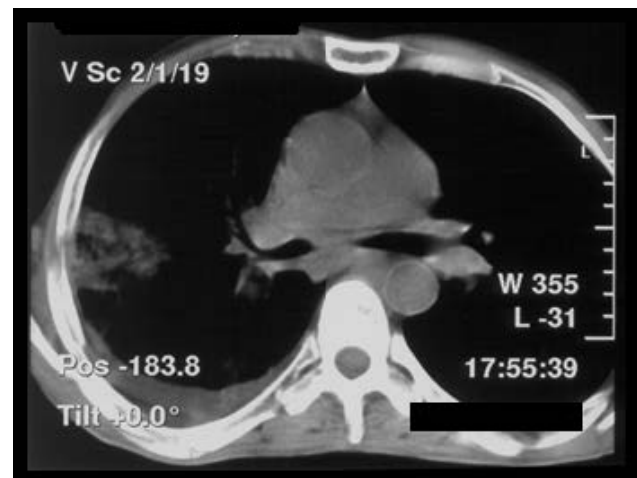

Figure 7 – Spiral CT scan in a 53 years old male patient with acute pulmonary embolism and right lung cancer reveals a right triangular mass, in contact with pleura, nonhomogenous (pulmonary infarction); right pleural effusion

The role of a spiral CT scan for the diagnosis of PE has evolved over the last decade. Spiral CT can visualize main, lobar, and segmental pulmonary emboli with a reported sensitivity of greater than 90%. The spiral CT scan can detect emboli as small as 2 mm that are affecting up to the seventh border division of the pulmonary artery. The only problem with spiral CT is that small subsegmental emboli may not be detected. The CT scan has another benefit, an alternate diagnosis may be suggested in up to 57% of the patients. The spiral CT scan has sensitivities for PE reported to be 53-100%. The specificity has been reported to be 78-96%. The negative predicted value is 81-100%, and the positive predictive value is 60-100% for detecting emboli in segmental or larger arteries. Upon CT scan imaging, positive features include a central intravascular filling defect within the vessel lumen, eccentric tracking of contrast material around a filling defect, and complete vascular occlusion. Smooth filling defects making an obtuse angle with a vessel wall may represent chronic thrombi or recent recanalization. The parenchymal findings of oligemia, pulmonary hemorrhage (ground-glass attenuation), and pulmonary infarction (peripheral wedge-shaped pleural-based opacifiation) may be seen. But pulmonary angiography remains the criterion standard for the diagnosis of PE. Positive

results consist of a filling defect or sharp cutoff of the affected artery. Nonocclusive emboli are described to have a tram-track appearance. Negative pulmonary angiogram findings, even if false-negative, exclude clinically relevant PE [6, 7].

f)isotope lung scanning was done in our study (n=40) and shows also specific aspects: two or more large mismatched segmental perfusion defects (high probability for PTVD); one moderate plus one large mismatched segmental perfusion defect (intermediate probability) (Figures 8, 9). Ventilation-perfusion (V/Q) scanning of the lungs is an important diagnostic modality for establishing the diagnosis of PE.
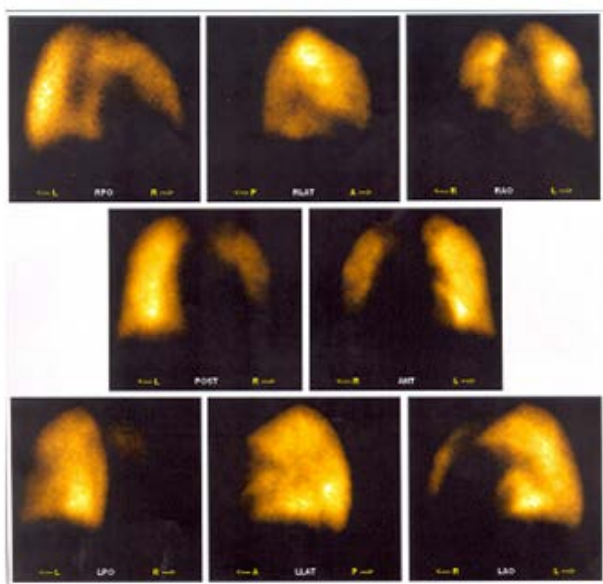

Figure 8 – Isotope lung scanning in a 73 years old male patient with acute pulmonary thromboembolism identifies multiple segmental filling defects throughout right lung

The scans should be interpreted primarily as a diagnostic or nondiagnostic pattern, indicating whether the patient has a high likelihood or does not have a high likelihood of having PE:

a)   normal V/Q scan findings or findings indicating a high probability:

o normal V/Q scan findings indicate an absence of any perfusion defects. Four percent of these patients still may have PE. Unless the patient has features indicating very high clinical suspicion, these findings may be considered negative for PE;

o high-probability scan findings are 2 or more segmental or 1 larger perfusion defect in the presence of normal chest radiography findings and ventilation scan findings. Approximately 87% of these patients were found to have PE. If accompanied by high pretest probability, the likelihood of pulmonary emboli increases to 95%.
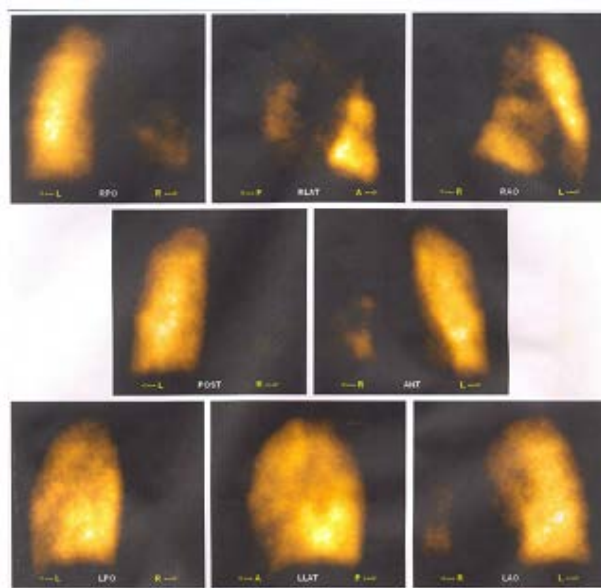

Figure 9 – Isotope lung scanning in a 53 years old male patient with acute pulmonary thromboembolism and lung cancer identifies segmental filling defects at right upper and inferior lobe; marked reduced perfusion in the segments ofthe middle lobe and in the segments of left upper lobe

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b)   nondiagnostic scans interpreted as

low or intermediate probability:

o low-probability scan findings consist of small perfusion defects associated with corresponding abnormalities upon chest radiograph or ventilation scan. A single segmental perfusion defect with normal chest x-ray findings and nonsegmental perfusion defects are common nondiagnostic patterns. Twelve percent of the patients with this pattern have PE, unless the patient has a very low pretest probability or clinical suspicion. Further diagnostic studies must be carried out to confirm or exclude the diagnosis of PE;

o intermediate probability is indicated by those patients with any V/Q abnormality that is not classified as high or low probability. Approximately 30% have PE; therefore, the finding of this scan pattern must be followed by further investigation to definitely exclude the diagnosis of PE [2,8].

g) echocardiography (n=50) reveals following findings:
• right ventricular and atrium dilatation;
• right ventricular hypokinesia;
• systolic flattening of interventricular septum;
• tricuspid regurgitation;
• pulmonary arterial dilatation;
• increased pressure in pulmonary artery;
• disappearance or reduction of inspiratory collapse of the inferior vena cava.

Echocardiography has limited accuracy in the diagnosis of PE. Overall sensitivity and specificity for central and peripheral PE is 59% and 77%. Echocardiography may demonstrate right ventricular dysfunction in acute PE, predicting a higher mortality and possible benefit from thrombolytic therapy [8].

c) compressive ultrasonography for detection of proximal DTV (n=20).

Four patients were diagnosed with PTDV by necropsy. In literature, autopsy results show that as many as 60% of patients dying in the hospital have had a PE, but the diagnosis has been missed in about 70% of the cases [1, 10].

Conclusions

PTVD presented with a low frequency in Internal Medicine Department. The main risk factor for PTVD in our study was malignancy. Pulmonary infarction was the most frequent presentation. Almost 1/3 of patients presented DVP and 12 patients associated arterial thrombosis. Positive diagnosis was confirmed by isotope lung scanning and spiral CT scanning. Four cases were diagnosed postmortem. Clinical diagnosis of PTVD has a low accuracy. Clinical evaluation, even unspecific, has considerable value in the selection of patients in whom there is a need for further diagnostic procedures

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